In Vitro (Serum Testing) vs. In Vivo (Intradermal Testing) Testing in Canine Atopic Dermatitis (CAD)

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Canine atopic dermatitis (cAD) is a genetically predisposed inflammatory and pruritic skin disease, most commonly associated with IgE antibodies to environmental allergens. The symptoms wax and wane and there is a variety of different triggers that may create an acute flare. Identifying these triggers (environmental allergens, food allergens, irritants, bacterial or Malassezia infection or ectoparasites) is important in the management of this disease. Both in vitro (serum testing) and in vivo (intradermal testing) testings are used to identify environmental triggers. Discussion of the other triggers is beyond the scope of this lecture.

Before a decision is made as to either serum test or intradermal test a pruritic dog, it is essential that the diagnosis of cAD has been established. Whether it is in humans with atopic dermatitis (hAD) or in dogs with atopic dermatitis (cAD), the diagnosis is a clinical diagnosis. Be aware that although frequently diagnosed, cAD may also be difficult to diagnose. This is because there are no pathognomonic signs and dogs have a large variation in their clinical presentation ranging from alesional to widespread erythema, crusting, and alopecia.

To diagnose hAD, three of four main criteria need to be present - pruritus, typical morphology and distribution, chronic relapsing course of the disease, and atopic personal or family history. In addition, there must be three minor criteria met from a list of 21.

In veterinary medicine, the criteria for diagnosing cAD have evolved over time. Historically 1 of 2 sets of criteria has been used for making the diagnosis of cAD. The problem with these criteria is the former was never validated while the latter had a limited sample size. The most current guideline was proposed by Favrot. Before applying these criteria to a pruritic dog, other causes of pruritus, such as ectoparasites or infectious causes, need to be ruled out. This is because using Favrot's best criteria, the sensitivity and specificity are about 80%. This means that using only his criteria, a wrong diagnosis will be made about 20% of the time. By ruling out other pruritic diseases before applying the criteria, the positive predictive value (PPV) of these criteria improves. The PPV is the proportion of patients with positive test results who are correctly diagnosed. The discussion of the other causes of pruritus is beyond the scope of this lecture.

Identifying triggers is the foundation for successful treatment once the diagnosis of cAD has been properly established. Effective management of cAD is improved by identifying and managing these triggers, whether it is a barrier dysfunction, a cutaneous adverse food reaction (CAFR), environmental allergens, parasitic or infectious cause.

Identifying food as one of the triggers can only be established via properly performed food trials. Serum testing and intradermal testing for CAFR in dogs have been universally determined to have poor specificity and sensitivity.

Allergy testing (serological evaluation of allergen-specific IgE and intradermal skin testing) is not a criterion needed to diagnose cAD. These tests are used to identify environmental allergens that may trigger symptoms of cAD once cAD has been diagnosed. It is important to diagnose cAD before performing allergy tests of any sort since healthy dogs can develop antigen-specific IgE and not be symptomatic (failure to exceed pruritus threshold). Accurate selection of dogs tested (e.g., diagnosis of cAD has been established) impacts the PPV. This is because the prevalence of a disease in the population being tested has an important influence on the PPV of a diagnostic test. With increasing disease prevalence, there is an increasing likelihood that a patient with a positive test result has the disease and a decreasing likelihood that a positive result is a false positive. The PPV is not intrinsic to the test - it also depends on the prevalence rate of the disease in the tested population. So, if you allergy test all pruritic dogs, the PPV will be much lower than if you only test dogs with cAD.
With regards to testing for environmental allergens, there are 2 methods - *in vivo* (intradermal testing = IDT) and *in vitro* (serum testing). The former detects the presence of antigen-specific IgE fixed to dermal mast cells as well as the ability of the mast cells to release mediators following exposure to the specific antigen, while the latter detects circulating antigen-specific IgE.

Performing an IDT involves sedating the dog, clipping hair from the lateral thorax, and then injecting small amounts of antigen intradermally. After 15 minutes each injection site is evaluated for wheal formation. With serum testing a blood sample is submitted to a laboratory that measures antigen-specific IgE. Regardless of which method is used, it is critical that the interpretation of the allergy test results correlate to the historical features of the disease, particularly in reference to seasonal episodes of symptoms. If a dog only has symptoms in the fall and house dust mite is the only positive reaction, something doesn't fit and the history and test results have to be reassessed.

Information on pollen seasons in different regions can be obtained at [www.aaaai.org/global/nab-pollen-counts.aspx](http://www.aaaai.org/global/nab-pollen-counts.aspx) (VIN editor: link was updated on 11-20-14). Note that the quantity of nonseasonal allergens may fluctuate depending on the season (e.g., house dust mites in the summer and fall, and indoor molds during more humid times of the year).

The advantages of intradermal testing vs. serum testing are:

1. Testing of individual antigens
2. Testing of more antigens
3. Direct testing of the affected organ
4. Lower incidence of false positive reactions compared to *in vitro* testing.
5. Detects cutaneous IgE reaginic antibody (an antibody that degranulates mast cells) and non-IgE reaginic antibodies (IgGd4)
6. Measures functional IgE antibodies - Note: some atopic dogs have been found to have low-affinity (nonfunctional) IgE antibodies

The disadvantages of IDT vs. serum testing are:

1. Necessity to clip the hair
2. Necessity to sedate
3. Drug withdrawal may be more stringent than with *in vitro* tests
4. Experience needed in performing and interpreting IDT results
5. Costs associated with keeping a "fresh" intradermal test kit
6. Inability to perform an IDT if there is widespread skin disease present
7. Anaphylaxis is a potential risk
8. It is a more time-consuming procedure to perform

Serum testing involves measurement of circulating antigen-specific IgE antibodies. The methodology used for these tests varies by laboratory. Some use enzyme-linked immunosorbent assay (ELISA), others use radioallergosorbent test (RAST) technology. The difference between the 2 techniques is the former detects antigen-specific IgE via the use of an enzyme-linked anti-canine IgE antibody in a colorimetric reaction, while the latter uses radioactively tagged anti-canine IgE antibody.

The method of exposing the patient's IgE to the tested antigen also varies between the different laboratories. The RAST and ELISA have allergens bound to a solid substrate, while the liquid-phase immunoenzymatic assay uses a liquid phase first, followed by a binding of the complex to a plastic well. The liquid-phase (VARL laboratory) is reported to expose epitopes on the antigens that are "hidden" when using the solid-phase techniques. Remember that the IgE molecule may bind to any one of multiple epitopes on antigens. Exposing more epitopes increases the likelihood that the patient's IgE will bind to them.
After formation of the IgE/antigen complex, some companies use monoclonal antibodies to bind to the IgE/antigen complex, while others use polyclonal antibodies or mixtures of monoclonal antibodies. Monoclonal antibodies are completely uniform and always bind to the same site of the IgE molecule. However, if that portion of the IgE is hidden, binding will not occur, which can then lead to false negative results. With polyclonal antibodies binding may occur on any of several different sites on the IgE molecule and therefore there is a greater chance of binding and detecting IgE. However, polyclonal antibodies are more likely to bind to other classes of antibodies (e.g., IgG) that share an epitope with IgE leading to a false positive result.

One company (Heska, Allercept®) uses a recombinant human high-affinity IgE epsilon receptor fragment to detect allergen-specific canine IgE. This, in theory, should provide better specificity for binding to IgE and therefore should avoid false positive due to binding to other classes of antibodies (e.g., IgG).

The advantages of serum testing vs. IDT are:

1. You can do from your practice - there is no need to refer
2. No need for clipping of hair
3. No need for sedation
4. No risk of reactions
5. Less stringent drug withdrawal?

The disadvantages of serum testing vs. IDT are:

1. Since the IDT is considered the "gold standard," false positives and negatives occur more frequently than with IDT
2. The quality of the results depends on the quality of the antigen being used and the specificity of the anti-IgE antibody
3. Some laboratories test allergens in groups rather than singly
4. Typically fewer antigens are tested than with IDT

The question that comes up during discussion of serum testing is which serum test is the best. Unfortunately there is no definitive answer. The first thing to remember is that to increase the PPV of any test you need the right population of animals to test. This is exemplified in a study which compared serum allergen-specific IgE levels of West Highland white terriers. Included in the study were 30 dogs with cAD and 18 that did not have cAD. Nonatopic dogs (NAD) were over 5 years of age and had no clinical signs or history of cAD. In the NAD, high-positive ELISA reactions were reported to 45 of 48 allergens. Seventeen of 18 dogs with positive results had positive ELISA to *Dermatophagoides farinae* (house dust mite) and *Tyrophagus putrescentiae* (storage mite). Positive ELISA results in NAD were statistically significantly higher than those in atopic dogs for 44 of 48 allergens, including two allergens representing house dust mite (*D. farinae* and *D. pteronyssinus*). House dust mite is regarded as a commonly significant antigen in cAD. The study concluded that positive allergen-specific IgE ELISAs were not specific for canine AD, and high allergen-specific IgE levels were seen in NAD. Note that the positive test results in the NAD may not be false positive in that they truly could have antigen-specific IgE but they don't have enough disease to exceed the pruritus threshold. This study shows that the PPV of the test is not very high when a disease is tested for in a population with a low incidence of the disease. But if testing only dogs with cAD, these positive ELISA could be significant. So, the first step is to make sure the dog that is being tested has cAD.

Another study evaluated the incidence of false positive results that occurs when serum testing nonallergic patients for allergen-specific IgE. In this study they took serum from 3 different nonallergic sources. These sources were: 1) heat-inactivated fetal bovine serum (FBS); 2) a solution of purified canine albumin in saline (ALB); 3) pooled serum from young, healthy, specific-pathogen-free dogs (SPFS). Each of the above samples was submitted in triplicate to four commercial US allergen-specific IgE testing laboratories. The results revealed substantial variation from laboratory to laboratory in the
percentage of positive determinations reported, with 11.1%, 1.4%, 29.1%, and 3.3% of the total test results reported as positive from the four laboratories. The magnitude of the positive results varied from weakly to strongly positive. The particular allergen reported as positive varied widely between laboratories, between sample sources, and between replicate tests of the identical sample. The authors concluded that commercial serum allergen-specific IgE testing laboratories may report positive results from non-allergic sample sources, potentially complicating the interpretation of results from diseased patients. The individual laboratory and results from each laboratory were not revealed. In contrast to the previous study, these were truly false positive test results.

Lastly, another study had been performed to evaluate the incidence of false positive allergen-specific IgE test results. In this study, the author submitted serum to the 2 companies that were performing serum testing at the time - AREST (ELISA allergen screen from Bioproducts DVM Inc.) and K-9 RAST screen from A&M Biosciences. Serum samples from horses, 3 cats, 3 humans, 2 goats, and a clinically normal dog were submitted for testing. Both tests reported significant positive scores for the clinically normal dog. The ELISA test reported only low positive scores on 1 goat sample, but the RAST panel reported false positives for all species.

Aside from the false positive issue, is there a difference in test results when using different anti-IgE tagging methods? There was a study comparing a monoclonal antibody ELISA (macELISA) test to a test using high-affinity IgE receptor-based ELISA. The results of that study demonstrated that the macELISA is reproducible and the results are comparable to the high-affinity IgE receptor-based ELISA test. However, neither test was evaluated for (clinically) false positive results.

So where does this leave us? Before answering that question, one other study needs to be discussed. In this study, the author (Rosser EJ) compared the results of intradermal testing (IDT) and aeroallergen-specific IgE serum testing (ASIST). Twenty-nine dogs with atopic dermatitis were selected to be in the study. All dogs had warm-weather pruritus, either exclusively or with warm-weather exacerbations. All dogs had intradermal testing (IDT) and an IgE immunoassay [Allercept™ Northeast Regional Allergy Screen - (ANRAS)] performed. There were 45 antigens used in the IDT and 48 antigens tested with the ANRAS. The author divided the dogs into 3 groups based on their history of pruritus as follows: 1) Fifteen dogs with seasonal onset or exacerbation of pruritus from April or May until killing frost (KF); 2) Nine dogs with pruritus from June or July until KF; 3) Five dogs with pruritus from August until KF in five dogs. The results revealed that IDT correlated well with the history in 17 of 29 dogs (59%) for all groups, ANRAS correlated well in 21 of 29 dogs (72%) for all groups, and combining IDT and ANRAS results correlated well in 27 of 29 dogs (93%) for all groups. The author didn't state if the differences were statistically significant. The author concluded that the study strongly supports the simultaneous use of both IDT and ANRAS for the selection of aeroallergens for ASIT in dogs with atopic dermatitis.

Now, what is the answer to the question - serum testing or intradermal testing? Based on the current scientific information and using the available testing, both are valid tests for environmental allergens - not food. Since these tests evaluate IgE differently - the former is measuring serum IgE while the latter is measuring mast-cell-bound IgE, the test results may not be the same. So, as Rosser demonstrated in his study, in at least some patients, combining both serum testing and intradermal testing results gives the best outcome. This is especially true in patients whose test results don't correlate well to their history of pruritus. The author believes that regardless of the testing method, there are other equally (more?) important factors that determine the success of ASIST. These include: being certain that the diagnosis of cAD is correct before testing; eliminate all other triggers (e.g., fleas, pyoderma, Malassezia dermatitis, food) before testing, and lastly both the owner and clinician need to be dedicated to aggressively monitoring and rechecking the patient. The best way to have a frustrated owner and an unsuccessful outcome is to simply serum test a pruritic dog and begin ASIST based on those test results.

**THE USE OF CORTICOSTEROIDS VS. CYCLOSPORINE IN VETERINARY DERMATOLOGY**
Atopic dermatitis (AD) is a commonly diagnosed disease in small animal practice. A hallmark of AD is pruritus. The ACVD commissioned a task force to study the subject of canine atopic dermatitis (cAD) in 2001. As part of this project they reviewed articles concerning the efficacy of the drugs used for the treatment of pruritus. They, then, categorized the effectiveness of these drugs for the symptomatic treatment of AD based on the quality of the evidence. The categories were as follows: "good or fair evidence for use of the medication, insufficient evidence for/against use of the medication, or fair or good evidence against use of the medication."

They divided effectiveness of symptomatic therapy into 4 broad categories:

1. There is good evidence for recommending the use of oral glucocorticoids (GC) and oral cyclosporine (CSA).
2. There is fair evidence for recommending the use of topical triamcinolone spray, topical tacrolimus, oral pentoxifylline, oral misoprostol, and an oral chlorpheniramine-hydroxyzine combination.
3. There is insufficient evidence for or against recommending the use of other oral first- or second-generation type-1 histamine receptor antagonists, aspirin, Chinese herbal therapy, a homeopathic complex remedy, tricyclic antidepressants, ascorbic acid, AHr-13268, cyproheptadine, papaverine, immune-modulating antibiotics or tranilast, and topical pramoxine or capsaicin.
4. There is fair evidence against recommending the use of oral arofylline, leukotriene synthesis inhibitors, and cysteiny1 leukotriene receptor antagonists.

Because glucocorticoids (GCs) and cyclosporine were the only drugs that showed good evidence of effectiveness, we should discuss the advantages and disadvantages of each drug and when to choose one over the other.

Glucocorticoids are commonly used to treat skin diseases in cats and dogs. Because of their immunosuppressive and anti-inflammatory effects they are very effective in treating a wide range of inflammatory and pruritic skin diseases. However, the low cost of the medication and their effectiveness (at least initially) leads them to be overused in the long-term management of cAD. It is always important, before committing to long-term steroid administration, to establish a diagnosis for the pruritus.

Although benefits can be substantial, adverse effects are numerous, including serious metabolic derangements and suppression of the hypothalamic-pituitary-adrenal (HPA) axis. Side effects also may involve the musculoskeletal system, endocrine system, cardiovascular system, central nervous system, and gastrointestinal tract, including the liver.

Specifically, adverse effects in dogs include PU/PD, polyphagia, alopecia, scaling, weight gain, tachypnea, elevated liver enzymes (SAP > ALT), vacuolar hepatopathy, mature neutrophilia, eosinopenia, lymphopenia, GI ulceration, dysregulation of diabetes mellitus, muscle wasting/pot belly, behavioral changes (agression, lethargy), calcinosis cutis, comedones formation, lower urinary tract infection (LUTI), increased incidence of bacterial pyoderma, euthyroid sick syndrome (low TT4 +/- low fT4ed) and development of generalized demodicosis. In cats, PU/PD, polyphagia, induction of or worsening of diabetes mellitus, mature neutrophilia, eosinopenia, lymphopenia, congestive heart failure, weight gain, floppy ears or fragile skin syndrome may occur.

This emphasizes that the use of GC should not be taken lightly. Even though it is a commonly administered medication in small animal practice, there are numerous side effects, as previously mentioned, ranging from an inconvenience (PU/PD) to life-threatening (GI ulcerations). The proper selection of the type and dosage of the GC requires the clinician to take into account the disease being treated, the patient, and the owner.

Except when treating Addison's disease, GCs are administered at supraphysiologic doses (doses that exceed basal production). Physiologic doses of GCs are those that equal the basal production of cortisone in a normal cat or dog. In dogs, daily cortisol
production has been reported to be 0.2 to 1 mg/kg/day. When using GCs the dosage administered is based on its intended use. There is no optimal dosage established in the veterinary literature and each case should be treated individually.

The following is how the author categorizes the doses in dogs. Note - cats typically will need double the canine dose. These doses are in reference to either oral prednisone or (methyl)prednisolone:

1. Antipruritic doses/anti-inflammatory doses: 0.5 mg/kg/day for 7 to 10 days, then tapered to the lowest effective every-other-day dose

2. Immunosuppressive doses: 2.0–4.4 mg/kg/day until the disease is in remission, and then slowly taper to the lowest effective, every-other-day, dose.

The question, as clinicians, that needs to be answered is: What is considered a "safe" long-term dose of GC? When this dose is exceeded, other treatment options should be further investigated.

The following is taken from a paper written by a dermatologist, Candace Sousa. This is the only guideline that I have seen that tries to give the clinician a basis as to how concerned he/she should be about the dose of GCs being administered. This section is her personal beliefs (which I support) regarding a safe dose of GC used long term. Every animal and every disease condition differs.

"The following is my (Sousa) formula for dogs = what she calls her "safe annual steroid dose" formula:

\[ \text{BW (kg)} \times 30 = \text{mg prednisone/year} \]

If a dog required more than what I believed to be the "safe annual dose" of prednisone or prednisolone to control its dermatologic disease (i.e., pruritus from allergies or atopic dermatitis), then I would (my comment - intradermal test) either add a second medication in an effort to decrease the amount of GC needed or change medications (e.g., to cyclosporine.). Steroid treatment protocols generally begin with higher doses and then are tapered but again looking at these calculations in this way can be helpful guides.

To minimize effect on the adrenal pituitary axis, if used for prolonged periods of time, therapy should be limited to intermediate-acting steroids, prednisone, prednisolone or methylprednisolone administered orally every other day. In some cases, triamcinolone or dexamethasone may be required because of a poor response to the others or as an option to reduce the polyuria and polydipsia seen with the other glucocorticoids. In these cases, administration should be limited to every 72 hours."

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

Next, we need to discuss cyclosporine (CSA). In veterinary dermatology, CSA has been used primarily for the treatment of cAD. Side effects in dogs are very limited and are primarily GI (vomiting or diarrhea). Other side effects reported include cutaneous papillomatosis, hyperplastic gingivitis, hirsutism, and papillomatosis. To minimize vomiting the author will administer ondansetron at 0.25–0.50 mg/kg orally for the first 6–7 days. Also, since it has been reported by Novartis that giving food with modified CSA (mCSA) will not alter the effectiveness, the author will routinely have the owners give the mCSA with food. If diarrhea is an issue, increasing the fiber in the diet, by adding either oat/wheat bran or psyllium to the food, will usually correct it.
Before dispensing mCSA, drug interactions that may occur when administering mCSA need to be considered. Cytochrome P-450 is a family of enzymes responsible for the metabolism of many drugs including mCSA. Because mCSA is metabolized by cytochrome P-450 enzymes (cP450), drugs that induce this enzyme system (e.g., phenobarbital, tetracyclines, fluoroquinolones) may decrease the levels (and effectiveness?) of mCSA. On the other hand, drugs that inhibit cP450 will increase the concentration, and potentially the toxicity, of mCSA. Azoles, especially ketoconazole, have significant effects on mCSA levels due to its strong inhibition of mammalian cP450.

P-glycoproteins are part of a larger superfamily of efflux transporters found in the gut, gonads, kidneys, biliary system, brain, and other organs. Using ATP as an energy source, they transport certain hydrophobic substances into the gut, thereby preventing absorption. It also protects the brain by pumping substances out. mCSA is a P-glycoprotein pump inhibitor, while ivermectin is a P-glycoprotein pump substrate. Combining the 2 drugs will increase ivermectin levels in the brain. Using ivermectin at the high dose needed to treat demodicosis or Sarcoptes infestation (300–600 µg/kg daily), can lead to ivermectin toxicity.

Since mCSA may take 4–6 weeks to reach maximum benefits, the author will dispense a tapering anti-inflammatory dose of prednisone for the first 21 days of mCSA therapy. Prednisone is given orally at 0.25 mg/# SID x 7, ½ that dose SID x 7, then that same dose but given q 48 hours for 7 days (3 doses). This allows time for the mCSA to be effective and yet not have the dog continue to be uncomfortable. The dog is then rechecked in 30 days.

At the 30-day recheck if pruritus is controlled, the mCSA is maintained at that dose and frequency for another 30 days. If the pruritus is controlled at that time, the dose is maintained but the frequency is changed to every 48 hours for 30 days. At the end of this time, if the pruritus is still controlled, change the frequency to twice weekly for 30 days. At the end of the 30 days if the pruritus is still controlled, stop the mCSA. If at any point the pruritus increases/resumes, go to the last effective dose/frequency. Once the pruritus is under control, try decreasing the dosage by 25–50% without changing the frequency. If after 30 days at this dose the pruritus is controlled, decrease the dose again by 25–50%. Continue this pattern every 30 days until either the mCSA has been discontinued or the minimum effective dose has been determined. Continue that minimum effective dose long term if necessary. The goal should be to only use the mCSA as an intermediate stop gap while waiting for either a food trial to be evaluated or while waiting for allergen-specific immunotherapy to become effective.

Even though side effects are more limited with CSA than GC, it still has the potential to cause systemic effects. As with the chronic use of GC, dogs on chronic mCSA should have a CBC, serum chemistry profile, a urinalysis, and urine culture done every 6 months. In a study comparing control dogs, dogs on mCSA for at least 5 months, and mCSA and GC for at least 5 months, both groups of dogs receiving mCSA had an increased risk of developing a LUTI compared to the control group. Fifteen percent of the cyclosporine-treated dogs had at least one positive culture. This was significantly different than the 3% rate of infection in the control group. When comparing the mCSA-treated dogs with the mCSA- and GC-treated dogs, the latter had a statistically higher rate of infection than the former (25% vs. 13%). None of the dogs with a positive culture had clinical signs of a LUTI and 36% of the dogs with a positive culture did not have bacteriuria. Twenty-five percent of the dogs with a positive urine culture didn't have pyuria. This study reinforces why a urine culture should be performed if a dog receives mCSA +/- GC for > 5 months. Because bacteriuria and pyuria have poor sensitivity for the detection of a LUTI as does the presence of clinical signs of a LUTI (none of the dogs were symptomatic for a LUTI in the study), a urine culture needs to be performed when dogs receive long-term mCSA regardless of whether they have clinical signs of a LUTI or an abnormal urinalysis.

In the author's opinion the advantages of mCSA vs. systemic GC are:

1. Side effects are more limited and less severe than dogs receiving GC (dose related)
2. No evidence that long-term mCSA is associated with the development of generalized demodicosis
3. Will not destabilize a dog with CHF
4. Will have less clinical effects on regulating diabetic dogs
5. Lower incidence of UTI
6. Does not appear to increase the incidence of bacterial pyoderma or *Malassezia* dermatitis (may decrease it by controlling the AD?)

The disadvantages of mCSA vs. GC are:

1. Higher cost
2. Less predictable effectiveness in treating cAD
3. Delayed onset of relief
4. More severe GI signs
5. More difficult to administer due to the size of the capsule and the taste
6. Higher incidence of drug interactions than with GC.
7. Not effective for adjunctive therapy when treating otitis externa

So here are the following scenarios in which the author will select GC over CSA for the treatment of pruritus associated with cAD:

1. When the dog needs instant, predictable relief from the pruritus
2. When the period of time that the GC will be needed is less than 2 continuous months (or exceeds the "safe annual steroid dose")
3. When cost is a concern
4. When mCSA causes significant GI side effects

When does the author select mCSA over GC for the treatment of pruritus associated with cAD? (Note the diagnosis of cAD must be established and the dog must be free of infections and ectoparasites)

1. When the period of time that the GC is administered is more than 2 continuous months (or exceeds the "safe annual steroid dose")
2. The dog is intensely pruritic and the owner doesn't want to use GC
3. The dog has unacceptable side effects from steroids
4. The dog has a metabolic disease where GC would be contraindicated (e.g., CHF)
5. When the dog has failed an antihistamine and EFA trial

Most commonly in the author's practice, either during drug withdrawal in preparation for intradermal testing or in patients that have not yet begun to respond to allergen-specific immunotherapy.

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