How (& when, & why) I diagnose atopy - and then what do I do??

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What exactly IS atopy (aka atopic dermatitis, environmental allergy)
Atopic dermatitis (AD) is an allergic reaction against environmental allergens such as pollens and house dust mites. AD is the arguably the second most frequent allergy in dogs (after fleas) and the third most frequent allergy (after fleas and food) in cats. There is a strong genetic tendency in dogs, with golden retrievers, Labrador retrievers, terriers, Dalmatians, and Shar-pies among the predisposed breeds. At the University of California at Davis (UCD), breeds at greatest risk for atopic dermatitis are Golden Retriever West Highland White Terrier, Chinese Shar Pei, Bull Terrier, Bichon Frisé, and the Tibetan Terrier. At Colorado State University (CSU), the three most common groups of breeds examined with atopic dermatitis are retrievers, terriers and spaniels. In the UK, atopic dogs were more likely to have atopic offspring- this was particularly evident for atopic sires. Interestingly, in a large study of West Highland White Terriers, Boxers, and Bullterriers in Sweden, feeding a diet at least partially home-cooked to the dam was associated with a lower incidence of atopic dermatitis in the offspring. A genetic tendency has not been well-documented in cats, but is suspected.

Atopic dermatitis is thought to be mediated by IgE antibodies. The allergens gain entrance to the body by either the respiratory or percutaneous route, binding to antibodies in the skin which are themselves bound to mast cells. This antibody-allergen binding causes the mast cells to release various inflammatory substances (histamine, etc.). Sensitization is probably an interaction of the Langerhans’ cells in the epidermis, which bind the antigen and travel to the regional lymph nodes, and both T and B lymphocytes. It would seem likely that, as in people and mice, the subclass \( T_{H-2} \) is responsible for promoting B lymphocyte overproduction of antibody when the Langerhans’ cell presents the antigen. It has been recently shown that CD4+ T cells (“helper cells”) predominate in the skin of atopic dogs (as they do in people) over CD8+ T cells (“suppressor cells”) although both populations are increased in atopic dogs’ skin compared to that of healthy dogs. In a recent article, atopic dogs were shown to have much higher serum values of IgG1 than other dogs. Recent unpublished work suggests that some atopic dogs may have a defect in filaggrin, an important component of the stratum corneum (the outer most, ‘horny’ layer of the epidermis); this may translate into more susceptibility to both allergen and infective organism access to the skin.

When do I suspect atopy?
Atopic dermatitis may be seasonal or year round. Dogs most commonly start showing signs between one to seven years of age. In a study at UC Davis, the average age of affected dogs was 1.66 years, with 95 % of the dogs first showing clinical signs some time less than 5 years of age. "Exotic breeds”, such as the Akita, Shar-Pei and Chow Chow, may show signs as young as six months. Initially, the season may be quite short,
but as (presumably) the dog becomes allergic to more allergens, year-round pruritus frequently results. Lesions in dogs are generally found on the feet, ears, axilla, and face, with conjunctivitis present more frequently than is commonly reported. Pruritus, typified by erythema, alopecia and hyperpigmentation is the most frequent sign. Clinical signs may become generalized in severe cases.

In cats, lesions are generally found on the face, rarely on the feet, and occasionally generalized. Pruritus, typified by erythema, alopecia and hyperpigmentation is the most frequent sign. Miliary dermatitis and the eosinophilic granuloma complex have also been reported as being secondary to atopic dermatitis in some cases. Age of onset, breed or sex predilections have not been well defined in cats.

**Diagnosis of Atopic Dermatitis**

Atopic dermatitis is diagnosed by history, physical examination, and (except in the "classic" case of recurrent, strictly seasonal "typical" clinical signs, erythema/pruritus of face, etc.) ruling out other causes of pruritus, especially food allergy, ectoparasites, etc. Atopic dermatitis is then definitively diagnosed by intradermal skin testing or serologic tests, looking for allergen-specific IgE. Because of the high incidence of "false positive" (or, at least, clinically nonsignificant) findings, these tests should only be performed if other diagnoses have not been ruled out.

There is a great deal of controversy over which is the more accurate, intradermal skin testing or serologic tests. In three studies, at UC Davis, Colorado State University, and Gifu University (Japan) involving a combination of over 250 dogs, the number of positive responses to hyposensitization were similar regardless of whether the hyposensitization solutions were based on IDST results or ELISA tests.

**What do I do for Treatment of Atopic Dermatitis?**

Owners and veterinarians have several choices for treatments, and sometimes several of these must be used simultaneously (at least at the beginning) in order to bring some relief to the dog. Ideally, the most appropriate treatment is usually hyposensitization injections, which are effective in about which are effective in about 65% of the dogs treated at UC Davis, and 70-80% of the cats in the author’s experience. However, not every owner is willing to do this route. Hyposensitization requires a tremendous amount of clinician-client communication, especially so that the owner knows:

1. Hyposensitization should be continued for at least 1 year before final evaluation of efficacy.
2. If effective, the treatment will almost certainly need to be continued for the animals life (in our study at UCD, only 2 dogs out of over 150 had their hyposensitization discontinued without a recurrence in the following 2 years).
3. If effective, the animal may still need ancillary treatment (antibiotics, antihistamines, fatty acids, etc).
4. Minor side effects (pain at the site of injection) and major side effects (anaphylaxis—very rare).

5. Expense (in the USA): between $500-$1000 per year, depending upon frequency of injections (most dogs receive a maintenance injection q7-10 days) and need for a veterinary examination due to pruritus or minor side effects.

There is some evidence that mold allergens should not be mixed in the same solution as pollens, possibly because the molds have proteases that degrade the antigenicity of the pollen proteins.

If hyposensitization fails or if the owner declines this therapy, antipruritic drugs are then necessary. Prednisolone (1 mg/kg once daily [double for cats], then tapered to the lowest every other day dosage needed) is usually effective. Triamcinolone (3-4 mg/cat) or dexamethasone (0.1 mg/kg daily) then taper; these medicaitons may be used with caution in cats, but are very ‘Cushing-ogenic’ in dogs.

Antihistamines commonly used in dogs are diphenhydramine (2.2 mg/kg t.i.d.), hydroxyzine pamoate (2.2 mg/kg t.i.d.), chlorpheniramine (0.2-0.8 mg/kg b.i.d. to t.i.d.), or clemastine (0.1 mg/kg b.i.d.); in one study diphenhydramine and hydroxyzine were both the most commonly used antihistamines and the most frequently effective. In cats, chlorpheniramine (2-4 mg/5 kg b.i.d.) or clemastine (0.1 mg/kg b.i.d.) may be used.

Tricyclic antidepressants are sometimes helpful in controlling pruritus. In dogs, those used are amitriptyline (2.2 mg/kg b.i.d.), or doxepin (2.2 mg/kg b.i.d.). In cats, the author has used amitriptyline (5-10 mg/cat b.i.d.).

A combination medication of trimiprazine 5 mg and prednisone 2 mg (Temeril-P® [Vanectyl-P® in Canada], Pfizer) has been quite helpful in reducing the amount of prednisone which must be given to atopic dogs. The drug is given at an empiric dose of 1 tablet b.i.d. for dogs less 10 kg, 2 tablets b.i.d. for dogs between 10 and 25 kg, and 3 tablets b.i.d. for dogs over 25 kg.

Products containing essential fatty acids (EFA) have been used as nonsteroidal antipruritics. These drugs apparently interfere with the production and metabolization of arachidonic acid and other "pro-inflammatory" substances. The author has not distinguished a difference in efficacy between EFA supplements of omega 3 fatty acids and those containing a mixture of omega 3 and 6. In dogs, these may have as high as 25% chance of reducing pruritus, particularly when combined with antihistamine treatment. When EFA supplements are included in the dog food, the success rate in one open trial was 42% (good to excellent control of pruritus), in another trial it was 44%.

In this latter trial, dogs responding to the test diet had a different pattern of fatty acid change in the plasma and the skin as compared to the dogs which failed to respond to the diet, suggesting that there are subsets of atopic dogs with different fatty acid metabolism capabilities. Somewhat in contrast, a recent article noted that the improvement seen in atopic dogs with EFA supplementation did not seem to be correlated with total fatty acid intake or with the ratio of omega 6:3 fatty acids. A very well written report documented...
the steroid-sparing effect of EFAs in some atopic dogs.\textsuperscript{13} Another report documented some beneficial effect in the use of dog foods enriched with EFAs,\textsuperscript{14}, while a recent report documented improvement in pruritus when atopic dogs were fed certain diets recommended for atopic dogs.\textsuperscript{15}

Antihistamines in conjunction with essential fatty acids may give relief from clinical signs in as high as 50\% of atopic cats.

Cyclosporine is available as Atopica\textsuperscript{\textregistered} (Novartis) in 10, 25, 50 and 100 mg capsule sizes. Ideally, this should be given on an empty stomach, but if this causes GI upset, administration with food may help. It is well-tolerated in about 80\% dogs. Because low doses are used for treating atopic dermatitis, usually 5-7 mg/kg/day or less, adverse effects are uncommon.\textsuperscript{16} The most common problem is nausea and loss of appetite. Because of expense, particularly in large breed dogs, administration concurrently of ketoconazole will enable a reduction of Atopica\textsuperscript{\textregistered} dosage. (This is due to the body’s metabolism of both drugs).\textsuperscript{17} In general, with a dose of ketoconazole of 5mg/kg, the author has seen good results using only 50\% of the canine dose of cyclosporine (2.5 mg/kg per day instead of 5mg/kg per day). One article suggests that as many as >35\% of atopic dogs treated with cyclosporine for 4 months may not relapse for as long as 40 days after cessation of the cyclosporine.\textsuperscript{18}

Oatmeal-based shampoos, or shampoos containing 0.5-1.0\% hydrocortisone, are also helpful adjunctive therapies in the dog (or rare cat that enjoys a bath). Ideally, they should be used at least two to three times per week. The use of "Resi" products, basically rinses designed to be left on the pet, have given encouraging results. Chief among these is Resi-Cort\textsuperscript{\textregistered} (Virbac) a 1\% hydrocortisone product, which may be used once to twice weekly.

A few relatively new topical products that may be helpful in controlling the pruritus of atopic dogs are:

Genesis\textsuperscript{\textregistered} Spray (VIRBAC). The active ingredient is 0.015 \% triamcinolone acetonide. While not optimal for long term management, this spray has a low risk of corticosteroid side-effects if used on problem areas (especially the feet) to ‘cool down’ the pruritic response.

Allermyl\textsuperscript{\textregistered} Shampoo and Spray (VIRBAC). These contain linoleic acid as a potential anti-pruritic, as well as the anti-infectives piroctone olamine and monosaccharides.

Duoxocalm\textsuperscript{\textregistered} Shampoo and spray (Sogeval). Recently released in the USA, these products contain sphingophytosine, a substance that stabilizes the stratum corneum, as well as hinokitol, a plant derived substance with anti-infective properties. It is now the widest used non-steroid anti-pruritic shampoo in France, according to the company.

Tacrolimus ointment [Protopic: Fujisawa] has been shown to be safe and effective for the treatment of moderate to severe atopic dermatitis in humans. The 0.1\% concentration is recommended for adults and the 0.03 \% for treatment in both children and adults for
long-term intermittent therapy in patients not adequately responsive to, or intolerant of, conventional therapy. The efficacy of the 0.1% product has recently been reported in dogs. This is a semi-expensive product (30 gm tube = $70-120).

References


