Clinical Features of “Classical” Atopic Dermatitis

History is an extremely important issue in all skin disease, but especially in diagnosing allergy, where there are some important historical clues that you may be dealing with an allergic pet. A prominent feature of atopic dermatitis (AD) is pruritus, which may be initially unassociated with lesions. The pruritus almost always starts before 3 years of age, may be seasonal at first, and may worsen over time. It is most typically evident on the feet, face, and ventral body surfaces. Breed predispositions must be considered. If corticosteroids have been used for treatment, there is often a good response. It is exceptionally helpful and saves much time to design and utilize a client history form for the purpose of collecting a complete and uniform history on every patient.

There may be no primary rash in atopic dermatitis. Early skin changes may be limited to just erythema or what is termed “pruritus sine materia” (pruritus without lesions). Most visible lesions are secondary to the pet’s scratching, or to complicating diseases such as pyoderma, yeast dermatitis, or seborrhea. Excoriations from scratching may be seen. Also very common is bilateral, chronic, recurrent otitis externa; in fact, bilateral itchy ears and intermittent ear infections is the major or only manifestation of AD in some dogs, and pinnal dermatitis is a hallmark of AD in many patients. Recurrent “hot spots” can be a manifestation of atopic dermatitis. Some dogs and cats have ocular signs (conjunctivitis, lacrimation, rubbing at eyes), and a few have anal pruritus. Severely affected, chronic cases may have dramatic alopecia, hyperpigmentation, and lichenification. Respiratory signs appear uncommonly in dogs.

Diagnostic Criteria for Atopic Dermatitis

Based upon evaluation of groups of patients with atopic dermatitis and comparison with other inflammatory skin diseases, lists of diagnostic criteria have been developed to aid in diagnosis and to select uniform populations of patients for inclusion in clinical trials. Early efforts in human AD by Hanifin and Rajka and by the UK Working Party were adapted for canine AD, first by Willemse and then by Prélaud. Most recently, Favrot et al. conducted an extensive study involving detailed statistical analysis of a very large group of geographically diverse atopic dogs. This study has yielded the most useful, validated set of criteria to date. Using these criteria, one can propose a clinical diagnosis of canine AD with 85% sensitivity and 79% specificity, if any five of the eight criteria are met. Further refinement of the accuracy of the diagnosis can then be achieved by ruling out other common skin conditions that mimic AD. The eight criteria are:

1. Age of onset < 3 years
2. Dog lives mostly indoors
3. Corticosteroid-responsive pruritus
4. Chronic or recurrent yeast infections
5. Affected front feet
6. Affected ear pinnae
7. Non-affected ear margins
8. Non-affected dorsal lumbosacral area

One must remember that these criteria are useful for the diagnosis of typical or “classical” atopic dermatitis, and that atypical presentations may occur that will not satisfy the criteria. In addition, the approximately 80% specificity means that if they are strictly applied, one will make an incorrect diagnosis in 1 out of 5 dogs!

Favrot’s group went further in an attempt to differentiate pruritic disease that is food-induced vs. not food induced. In fact, there is current discussion over whether we should consider “food allergy” as a completely separate disease, or consider it as “food-induced atopic dermatitis,” though this is largely a matter of terminology. Patients with food-induced disease were more likely to have nonseasonal disease and gastrointestinal disturbances, but less likely to have blepharitis, pruritus sine materia, or corticosteroid-responsive pruritus.

Initial Steps in Diagnosis of Atopic Diagnosis

Initially, AD is a diagnosis made clinically using the following three elements; all are required for a proper clinical diagnosis of AD:
1. Compatible history
2. Compatible clinical signs
3. Rule out all other causes of pruritic dermatitis that can appear similar to AD

Items (1) and (2) can be conveniently achieved by careful history and examination, and consideration of the Diagnostic Criteria described above. Next, the following diseases can especially mimic AD, and must be ruled out before you can make a clinical diagnosis: food allergy, flea allergy, mites (especially Sarcoptes and Cheyletiella), pruritic staphylococcal pyoderma due to some other cause, and primary yeast dermatitis. A typical diagnostic evaluation would thus include skin scrapings to help rule out mites; skin cytology to find bacteria and yeast; flea control if fleas are seen or suspected; a hypoallergenic diet trial; treatment for pyoderma with antibiotics if it is suspected or present; treatment empirically for scabies; and treatment for yeast dermatitis if suspected or present.

Considerations in “Allergy Testing”
To reiterate, atopic dermatitis is a clinical diagnosis—it is made using clinical observational skills and elimination of alternative differential diagnoses. AD is not diagnosed by use of an “allergy test”—allergy tests are useful only to plan immunotherapy once you have achieved the diagnosis of AD. To complicate matters, an appreciable number of dogs (perhaps as many as 20% to 30%) with classical clinical features of AD will be negative on all types of “allergy tests.” These patients have been termed “atopic-like dermatitis”; why they exist and whether there is any difference in therapeutic response in this subpopulation remains to be elucidated.

Timing
There has been demonstration in humans that the results of allergy testing can vary throughout the seasons. This is not true with every dog, in every situation; however, if you have to choose a time to allergy-test, the best time would be just after the pet has been exposed to every pollen and dust allergen for that season. In cold-weather areas, this means that allergy testing is best done in the late summer to fall, just after everything is done pollinating. In this case, the allergic response may be maximally active.

Intradermal Testing
Intradermal testing (IDT) is the method of choice for many specialists. IDT has the advantage that it is a biological method that in some ways mimics the pathogenetic mechanism of the actual disease. A positive intradermal test requires not only presence of specific IgE antibody, but functional mast cells and microvascular response. With the notable exception of house dust mite allergen, intradermal testing appears to be relatively free from positive reactions in nonallergic dogs. It is also considered by some authorities to be more sensitive than serum-based methods. There are important drawbacks to IDT, the most obvious of which are its requirement for referral, and for discontinuation of treatment (corticosteroids, antihistamines) for weeks to months prior to the test.

Serology
Allergen-specific IgE serology is increasingly used both by specialists and by general practitioners. When done reliably and used properly, these tests are very valuable tools to use in formulating an immunotherapy prescription. These are “IgE Tests”—they measure only the amount of allergen-specific IgE present in the serum, and not whether this IgE is functioning to cause an allergic reaction in a pet. As is now hopefully clear, it is certain that “there’s more to allergy than just IgE.” Serology is convenient and accessible, but in some cases seems to lack specificity: with this test, the big problem may be “false-positive” reactions. Some people call these “clinically insignificant true positives” because the animal may actually have serum IgE against one or more allergens, but without clinical significance. One strong advantage of the serum allergy tests are that they are unaffected, or at least less affected, by therapy. Though these serum-based methods have much to offer—especially when referral to a specialist is not possible—they must be used and interpreted cautiously.

Which Test Is Best?
It is useful to examine some of the components of different serum-based tests so that we might understand some of their advantages and disadvantages. For example:

- Allergenic extracts can vary in their content substantially from manufacturer to manufacturer, and to a lesser degree from lot to lot. This could have profound implications on the results of a serum test, and perhaps even more impact on immunotherapy results.
- All serum-based assays depend critically on a detection reagent to specifically bind to and detect IgE, without detecting any other antibody class such as IgG or IgM. Monoclonal antibodies, polyclonal
antibodies, “multiclonal” or “oligoclonal” antibodies, and recombinant IgE-receptor fragments are the
detection systems in use currently.

- Allergen-specific IgE tests are not standardized and regulated in veterinary medicine, as they are in human
  medicine. Every laboratory has its own reporting system, quality control and standardization procedures,
  and criteria for positive.

Based on what we know, which serum-based test method is best? In large part, that depends on what is meant by
“best”? To elaborate:

- If we use “response to immunotherapy” as our criterion for evaluating success, among commercial serum
  testing companies, no method has been conclusively shown to be better than any other. The studies have
  simply not been done.
- If we use “correlation with IDT” as our criterion, no method has been shown superior; moreover, use of
  IDT as a “gold standard” can be questioned on theoretical grounds.
- If we use “technical performance” (issues such as repeatability, occurrence of false positive reactions, etc.),
  the picture is slightly clearer. Both Greer Laboratories and Heska have published extensive data on the
  performance criteria of their test systems, and in fact their test results seem to correlate with each other
  fairly well. Most other laboratories have not reported such information.

Overall, if both are available, should one ideally use an IDT or a serum-based test? Again, neither test is perfect.
With either IDT or serum-based testing, it is clear that non-allergic animals sometimes have positive test results, and
that some animals with clinically diagnosed AD have negative tests. Performing both tests probably gives the most
information on a patient’s relevant sensitivities.

Hints for Interpreting Allergen-Specific IgE Tests
The following list is based on the author’s clinical observations, impressions, and experience rather than
scientifically proven fact.

- An IgE test is not a serum chemistry. There are no carefully established uniform standards and controls,
  normal ranges, etc. Don’t take any value to be an undeniable truth. You must always ask yourself, “Does
  this result make sense with the patient’s clinical picture?”
- Monosensitization exists commonly with house dust mites—some pets are dust-mite sensitive only. It does
  not exist commonly with pollens. If you have only one or two pollens very positive, caution—these may
  not be significant, or at least they don’t tell the whole story.
- Mold spore allergy is common in some areas, uncommon in others. Many dogs positive on serum-based
  tests to molds are negative on a confirmatory IDT. This author believes that many mold-positive serology
  results are not clinically significant.
- If you do have a dog with positive mold scores, make sure you’ve tried antifungal therapy. I believe that in
  some cases, mold-positives are correlated with Malassezia hypersensitivity.
- If you receive a test result that doesn’t seem to make sense with the patient’s clinical picture, don’t
  immediately proceed with immunotherapy. If something doesn’t seem to tell the whole story, make sure
  you’ve done a diet trial—could there be concurrent food allergy? It is very common that we will do an IDT
  to confirm suspicious or “borderline” enzyme-linked immunosorbent assay (ELISA) test results—consider
  referral for an IDT.
- Use the expertise of your lab! They are generally very good at keeping all these things in mind and
  providing appropriate immunotherapy recommendations, but if you question something, call their technical
  service advisers and ask.
- If you are an expert at clinical diagnosis of AD, you should find around 75% of samples positive and 25%
  negative. If 100% are positive, your lab may have problems with false positives.

References available upon request.