Atopy represents the inherited tendency to mount a skewed and flamboyant immunological reaction to environmental antigens such as pollens, molds, danders, mites, and food. One of the key features is the development of reaginic antibody, which in mammals is represented by the immunoglobulin IgE. The simple model based on Th1 versus Th2 reactions, so elegantly described in the allergic mouse, is probably too simple for dogs and humans! The pathogenesis of the IgE-mediated immunologic response involves both early and late phase reactions. The allergen binds to IgE on the surface of mast cells to trigger degranulation of preformed mediators, as well as the activation of inflammatory pathways. It is the later phases that contribute to the sustained inflammatory response we see in our patients, and pruritus is the major complaint!

While IgE plays a role, it is only the tip of the iceberg. Much more is going on with cellular infiltrates and the cytokines known to accompany atopic states. Furthermore, the interaction of cytokines with the nervous system promotes the intractable itch that patients with atopic dermatitis often experience. Repressing these cytokines is the goal of therapy and this is done using allergen specific immunotherapy, along with medications such as steroids, cyclosporine, or oclacitinib (Apoquel) to reduce itch and inflammation. Oclacitinib is a Janus kinase inhibitor that blocks the ability of allergic cytokines to stimulate a response. It is more focused than cyclosporine, and appears to have fewer side effects.

There has also been great interest in the contribution of the skin barrier to atopic dermatitis. The skin barrier consists of the corneocytes in the stratum corneum and the lipid in which they are embedded. It has become clear that an abnormal skin barrier is present in the skin of atopic dogs. The defects include abnormal expression of a multifunctional protein called filaggrin as well as reduced levels of ceramides. The dysfunctional barrier in the stratum corneum allows for penetration of allergens, as well as toxins from microbes such as Staphylococcus spp. and Malassezia. Certainly these infections exacerbate the impaired barrier.

Clinical Presentation
Classical clinical signs of atopic dermatitis in the dog include face rubbing, foot chewing, and axilla and belly scratching, lending support to the idea that most atopic dogs experience their allergenic exposure through their skin, rather than through the mucus membranes of the nasal passages. The disease begins early in life and tends to run in certain breeds (e.g., terriers, bully breeds, retrievers, setters). Atopic patients often are afflicted with secondary infections. These infections increase their discomfort and contribute significantly to the difficulties in managing their disease. Over time, the disease increases in severity.

Diagnosis
The diagnosis of atopy and/or atopic dermatitis is based on appropriate history, clinical signs, and ruling out other causes of itch, including occult scabies, flea allergy dermatitis, and, in some cases, food allergy. Intradermal skin testing and/or blood allergy testing are used to select allergens for immunotherapy. Conceptually, skin testing is appealing as we examine the organ directly affected in most of our veterinary patients. However, blood testing remains a valid choice for those animals who cannot be skin tested or whose skin test cannot be interpreted. The choice of the diagnostic lab should be based on the judicious balancing of sensitivity with specificity. Several companies offer serum allergy testing including Veterinary Allergy Reference Laboratory (VARL), Heska, Greer (now via IDEXX), Biomedical Services, Spectrum, and Nelco. It is important to keep in mind that neither skin testing nor serum testing are perfect tests. Clinical knowledge must always be correlated to the results in order to make an effective allergy vaccine.

Treatment
Treatment of atopic dermatitis can be a complicated affair! One must take into account not only the animal’s threshold of tolerance for itch, but the owner’s as well! One must also take into account how much work the owner is willing to do to get the disease process under control and their acceptance of the notions that the disease is not curable and that there is no quick fix! It is my belief that success increases exponentially if we combine multiple therapeutic approaches, including topical. This is the multimodal approach to which we all allude when talking about allergy management. This multimodal approach requires a dedicated owner, and I am always impressed with the devotion of most of our clients toward their animal companions. Basically, we avoid allergens if we can (usually
foods, fleas), use immunotherapy to modify the immune response, control infections and ectoparasites, repair the skin barrier, and control itch.

**Avoidance**

Whenever possible, we want to avoid the allergens or infections that are typical flare factors for pets with atopic dermatitis. Practically speaking, foods and ectoparasites such as fleas are the only allergens we can practically avoid in allergy management. Food allergy or adverse reactions to foods can be part of the atopic problem, so it is always worth considering what role diet plays in an atopic patient. We can help reduce exposure to environmental allergens as well. For dogs with pollen allergies, reducing their time outside during the high pollen counts, along with wiping their faces and feet when they come inside, reduces the ability of the pollen proteins to absorb through the skin. For dogs allergic to house dust mites, frequent vacuuming of the carpets (or even removal of the carpets) will help. For dogs that sleep in the bed with their owners, we can recommend the hypoallergenic bedding that is recommended for people with similar allergies. Bathing weekly with a moisturizing shampoo helps to remove allergens from the skin.

**Immunotherapy**

Specific immunotherapy remains the treatment of choice for the atopic patient. It is a biologic long-term plan for management. The notion that we can retrain the immune system to perceive the environment differently is a powerful one. The observation that this is a difficult process speaks to the fact that injection therapy has to be given frequently and for long periods of time. The success of this therapy will depend on the accuracy of the diagnostic testing, the formulation of the vaccine, and the realization that “one size fits all” will not work. Each program will need to be tailored to the specific needs of the patient with regard to frequency of injections and number of allergens used. In the old days, we generally used one vaccine containing 10–12 antigens and encouraged the owners to believe that eventually one injection every three to four weeks would be sufficient to control their allergens. Now we are finding that many patients can benefit from two vaccines. This enables us to hypoallergenize against 20 or more allergens without diluting the vaccine. These can be given at the same time, although some dermatologists prefer to separate them. Some dogs seem to do better if they continue to take injections weekly; others can decrease to an injection every two to four weeks. Those dogs who have specific seasons in which their signs exacerbate might do well with weekly injections during their bad times and less frequent injections during the off seasons. This individualized approach requires a lot of communication back and forth between clinician and client. We are the cheerleaders for the client-pet team. Using the basic principles of behavioral analysis, we must come up with the positive reinforcement each client needs to continue what can be a difficult regimen. It is important that clients understand that immunotherapy can take several months to be fully effective. Sublingual immunotherapy offers an alternative to injection therapy. Sublingual immunotherapy has been shown to be as effective in dogs as injection therapy. In some dogs, it seems to work faster, and it has been successful in a subset of dogs who have failed injection immunotherapy. The advantages are that no injections have to be given; a potential disadvantage is that the drops have to be given once to twice daily. In humans, the goal is to use the allergy drops (or injections) for three to five years with a goal toward permanent tolerance and stopping the vaccine. We don’t know how many dogs will be able to stop allergy drops, but some have been able to do so. Some dogs who have been started on injections early in life have been able to stop immunotherapy after several years as well.

If **immunotherapy** is the **long-term plan**, it is clear that we need a short-term plan to control the pruritus and clinical signs while we get immunotherapy underway. The **short-term plan** will involve a detailed analysis of the individual’s skin condition. These are the questions I like to ask myself.

**Controlling Ectoparasites and Infections**

*What role do insect hypersensitivities play in this patient’s skin disorder?*

In most of the United States, insects, particularly fleas, really complicate the response to immunotherapy. Fortunately, flea control is much more pleasant than it ever used to be! Whether we can successfully use immunotherapy in the management of insect hypersensitivities, particularly those to fleas, remains controversial. In general, our approach has been to put most of our atopic dogs with flea allergy on vigorous flea control throughout the year. The choice of the product will be determined by the pet’s medical needs, how frequently he/she is bathed, and client preferences. Either oral or topical flea control is effective. We tend to recommend oral flea control products for dogs bathed more than once weekly.

*What role do infections play in this patient’s skin disorder?*
Bacterial and yeast infections of the skin contribute significantly to the allergic animal’s discomfort. Even if these organisms merely sit on the surface of the skin, they produce toxins and metabolites that are significantly irritating or, in some cases, allergenic. Nuttall and Halliwell have shown that atopic dogs have significant levels of anti-Malassezia IgE and IgG in their blood. Although not well documented in our canine patients, superantigen reactions contribute greatly to atopic dermatitis in humans, and I believe they do in dogs as well. Creative approaches to infection control really help our atopic patients. Look carefully for the presence of superficial and deep pyodermas, but also be aware that the mix of bacteria and yeast on the skin surfaces of the muzzle, feet, perianal and perioral areas, and ventrum may manifest as erythematous greasy patches. Cytologies are indicated in almost all atopic patients. A subset of dogs with recurrent pyodermas associated with their allergies will benefit from the use of Staphage Lysate (SPL) in addition to their allergy vaccine. SPL can be put into sublingual allergy vaccines as well. There is evidence to suggest that atopic dogs with recurrent bacterial infections make IgE against staphylococcal proteins. Bacterial skin infections should be managed with topical therapy and, when indicated, systemic antibiotics. Yeast infections can also be managed with topical therapy, but in many cases systemic antifungal agents may be needed as well. Because recurrent Malassezia infections can also be a sign of Malassezia hypersensitivity, the inclusion of Malassezia extracts in injection or sublingual immunotherapy can be helpful.

Repairing the Skin Barrier
There are two ways in which we can help repair the skin barrier. The first is by using oral fatty acid therapy. The recommended dose has been 180 mg eicosapentaenoic acid per 4.5 kg. There is good evidence, though, that diets such as Iam’s Response FP and other fatty acid enriched diets improve the skin and coat quality of atopic dogs. The second way to improve the skin barrier is by using topical therapy. The choice of shampoos and rinses will be determined by the individual. For dogs with itch but no infection, we can use shampoos containing fatty acids, phytosphingosine, or ceramides. It is critical to remember that with shampoo therapy, formulation is a critical part of its efficacy. All of the above can be followed with a soothing crème rinse or leave-ons such as Rescor. Some newer approaches in addition to bathing include the use of topical lipids to stimulate repair of the skin barrier. There is some evidence to show that the topical application of ceramide and phytosphingosine stimulates the keratinocytes to repair the barrier and to resume production of their own lipids. Ceramide and fatty acids are contained in the new product by Virbac, Allerderm Spot-on. Phytosphingosine is contained in the DOUXO line of products by Sogeval. Their DOUXO Spot-on contains highly purified phytosphingosine. Dermoscent makes a line of products containing essential oils of herbs and grains which supply fatty acids to the skin and take advantage of the natural anti-inflammatory and antimicrobial activities present in essential oils. Time will tell how useful these products will be, but we have seen very encouraging results so far. Coat quality and skin quality are enhanced, with perhaps a reduction in the frequency of pyoderma recurrences. In mild atopics, we have noted that these products may even reduce itch. Dechra has begun to add ceramides to their shampoo products, so these products would be expected to help with barrier repair as well. For each of the spot-on lipid products, it is best to apply them on multiple parts of the body and then gently massage them into the skin. The ideal frequency of application is not known. Initially they can be used two to three times weekly then reduced to every two to three weeks for maintenance.

Control of Itch
Itch is the most common sign that drives the owners of atopic dogs into our clinic. We must control itch to buy us the time we need to utilize immunotherapy effectively. Up until recently, the only good evidence we have is for steroids and cyclosporine; however, recently oclacitinib (Apoquel, Zoetis) has been approved, and it can provide excellent and rapid itch control without the side effects associated with glucocorticoids.

Steroids
Glucocorticoids have profound effects on inflammatory pathways and they are very effective in reducing itch. The potential side effects can be divided into two groups: short-term and long-term. The short-term side effects include polyuria, polydipsia, polyphagia, and behavioral changes, which are off-putting to many clients. The long-term side effects include liver enzyme elevations, muscle loss, weakening of the ligaments, thinning of the skin, reduced coat quality, and increased susceptibility to infections. While these side effects do not occur in all dogs, they occur with enough frequency to make the routine use of glucocorticoids less desirable. For some dogs, however (at least prior to Apoquel), glucocorticoids were the only medication that was effective. We try to avoid using glucocorticoids for long-term management of atopy if we can, but using prednisone or prednisolone in short bursts and getting dogs to low-dose alternate day therapy is necessary for some dogs during the induction phase of immunotherapy. Recent
evidence suggest that steroids may actually enhance the induction of T regulatory cells, one of the mechanisms by which immunotherapy is supposed to work. Therefore steroids are NOT contraindicated in dogs on immunotherapy.

Some dogs may require low-dose maintenance steroids with their immunotherapy to remain comfortable. I like to start with the veterinary drug Temaril-P (Zoetis), a tablet containing 5 mg of the antihistamine trimeprazine and 2 mg prednisolone. I find this drug to be very effective in most patients, allowing us to keep the total steroid dose low. I think it is important to try to use this drug and steroids in general in bursts and to stop often to see how the animal will do without it. Candace Sousa has published an easy calculation for long-term steroid use that I have found very helpful. The body weight in lbs is multiplied by 15 (if kg, by 30); the resulting number is the mg of prednisone or prednisolone that the dog can take annually. A 20 lb dog would take 300 mg prednisolone per year, or 1 tablet of Temaril-P every other day. This dose, based on our experiences, has been least likely to cause problems. If this dose is exceeded, the likelihood of problems may be increased and another approach should be considered.

**Cyclosporine**

Initially released as Atopica (Novartis), cyclosporine revolutionized the treatment of atopic dogs and cats, particularly those who had become refractory to steroids or could not tolerate them. Cyclosporine can also be used concurrently with immunotherapy and many dermatologists have said they believe this makes the immunotherapy work better. We use 5–7 mg/kg daily for four to six weeks, then we try to lower the frequency. When used concurrently with immunotherapy, the hope is that we will phase out the cyclosporine after several months. Many dogs can live on Atopica with good control of their allergies, but we still find they need bursts of steroid during bad times. It is not always possible to reduce the frequency, though, and some dogs and cats require daily therapy to remain comfortable. Side effects in the short-term include nausea, vomiting, and diarrhea; these can often be ameliorated by using maropitant (Cerenia, Zoetis) for the first four days of cyclosporine therapy. Long-term side effects include chronic soft stool, gingival hyperplasia, lichenoid psoriasiform dermatitis, and unusual bacterial and fungal infections. In cats, fatal toxoplasmosis has been observed.

**Oclacitinib (Apoquel, Zoetis)**

Oclacitinib is a new medication to control allergic itch. It can be used for short-term control of itch associated with several allergic skin diseases and for long-term use in chronic atopic dermatitis. It is a focused inhibitor of allergy cytokines that works by inhibiting Janus kinases (selectively JAK1); these kinases help transmit the signal of the cytokine to the inside of the cell, resulting in activation. The most common side effects include vomiting, diarrhea, and anorexia (in less than 5% patients). The medication will be available in three tablet sizes (3.6, 5.4, and 16 mg). Dosing is 0.4 to 0.6 mg/kg b.i.d. for 14 days, then once daily for chronic use. It is very important that dogs have good infection control in place (bathing) and good ectoparasite control. Infections and parasites can reduce efficacy of this medication. Visit ExcellenceInDermatology.com and ItchCycle.com for access to more information about canine atopic dermatitis and downloadable resources for your information. You can refer your clients to MyPetItches.com.

**Suggested Reading**


