Treatment of canine atopic dermatitis

Multiple strategies can help control the clinical signs.

By Todd Nash, DVM
Contributing Author

Canine atopic dermatitis is a common diagnosis in veterinary practice, yet treating this chronic skin disorder can be a challenge. Unfortunately, once a confirmed diagnosis of atopic dermatitis is made, a realistic therapeutic expectation is control rather than cure.

This is the most crucial concept to communicate to our clients, but it certainly does not mean we cannot help affected Pets and their families. We can help Pets lead happier lives and sometimes tremendously improve their quality of life. Clients must be fully educated about their Pet's prognosis, treatment options, potential side effects of therapy and the chronic nature of any therapy. Educated clients and dedicated veterinarians can make the difference between Pets with controlled atopic dermatitis and Pets that spend the rest of their lives uncomfortable and unhealthy.

Recent research suggests allergen exposure not only occurs via inhalation, but also via percutaneous absorption and ingestion in dogs.[1,2] Bearing this in mind, the therapeutic approach to atopic dermatitis must include multiple strategies and be tailored to the individual Pet. Multimodal treatment strategies may include a combination of allergen avoidance, dietary management, topical treatments, nonsteroidal antipruritics, corticosteroids, antibiotics, antifungals, hyposensitization and/or immune modulators.

Allergen avoidance

Atopic dermatitis is typically triggered by exposure to allergens, such as pollen or dust mites. Avoidance of allergens is a key component in controlling atopic dermatitis. Consider the following:

Suggest allergy testing to identify possible offending allergens and try to correlate the findings with the Pet's clinical history and likely exposures. If the patient is found to be allergic to cat dander, feathers or tobacco, for example, the client will want to limit the Pet's exposure to those allergens, when possible. Many allergens, particularly airborne pollens, may be difficult to avoid.[3]

Commercially available products containing borate, benzyl benzoate or tannins are purported to reduce house dust mite allergen load in homes. In a European study

of 60 house dust-mite sensitive dogs, 48 percent achieved remission with benzyl benzoate environmental treatment of the home alone. In North America, where dogs are more often simultaneously allergic to multiple classes of allergens, the benefit may not be as pronounced.[4]

A proper diet should not be ignored for Pets with atopic dermatitis. Many Pets may have a concurrent food allergy requiring specific diets devoid of certain ingredients, while others may benefit from a diet designed to help overall skin function.

Anecdotal evidence suggests that the use of air ionizers and allergen-impermeable covers for mattresses, dog beds and pillows may help.

Dogs known to be allergic to grasses can be walked on hard surfaces and have areas for elimination made of sand, gravel or concrete. Some Pets benefit greatly from regularly cleaning their paws, legs and ventrum after each trip outdoors.

Dietary management

A proper diet should not be ignored for Pets with atopic dermatitis. Many Pets may have a concurrent food allergy requiring specific diets devoid of certain ingredients, while others may benefit from a diet designed to help overall skin function. ROYAL CANIN Veterinary Diet™ canine SKIN SUPPORT SS 21™ diet for dogs is well tolerated and readily available as a general diet. ROYAL CANIN Veterinary Diet canine HYPOALLERGENIC HP 19™ may be a good option for specific food-allergic canines.

Topical therapy

Topical therapies help remove allergens, bacteria, yeast and excessive oils, as well as hydrate the epidermis. In addition, antipruritic agents such as colloidal oatmeal can be used topically, although they are most appropriate for localized areas, mild cases or as adjunctive treatments.[5] A wide range of active ingredients are available for shampooing and bathing, and selection should be guided by each Pet's current skin condition (*Table 1,* page 42).

Factors to consider include the types of lesions present (*e.g.*, scale, crust, pustule), dryness, oiliness, presence of *Malassezia*, concurrent pyoderma and the degree of pruritus. Tepid water should be used when bathing, as warm or hot water may aggravate existing inflammation and pruritus.

Weekly bathing with a hypoallergenic shampoo is recommended for mildly affected Pets, when the primary goal is to remove allergens or hydrate the skin. Sufficient contact time (five to 10 minutes) to allow for water's hydrating effect and benefit of the shampoo's active ingredient(s) is essential to the effectiveness of any topical therapy. Humectants and emollients aid in hydration of the skin. When anti-pruritic activity is desired, colloidal oatmeal-containing shampoos and cream rinses may reduce pruritus for 24 to 48 hours. Between baths, an antipruritic spray may be of value to some Pets. Look for those containing pramoxine (a topical anesthetic), diphenhydramine, triamcinolone or hydrocortisone. These can be applied to localized regions or diluted in water and used as a pour-on, allowing the Pet to drip dry afterward.

Superficial staphylococcal pyoderma commonly affects Pets with canine atopic dermatitis. Both Pets with active infections

Table 1: Topical Products Widely Used in the Management of Canine Atopic Dermatitis

Manufacturer	Moisturizing	Antipruritic	Antimicrobial
GlenHaven™	Coconut oil, safflower oil (H/Shampoo™)	Solubilized oatmeal (A1/Shampoo & Conditioner™) Pramoxine, diphenhydramine (A2/Shampoo & Conditioner™) Hydrocortisone (A3/Conditioner™)	Acetic acid/boric acid (F1 & P1/ Shampoo, Conditioner & Wipes™) Miconazole (F2/Shampoo™) Ketoconazole, chlorhexidine (F3/Shampoo™) Chlorhexidine (Y/Shampoo™) Benzoyl peroxide, sulfur, salicylic acid (P2/Shampoo™)
DermaPet®	Coconut oil, safflower oil (DermaLyte™ Shampoo)	Solubilized oatmeal (DermAllay™ Shampoo & Conditioner)	Acetic acid/boric acid (MalAcetic® Shampoo & Conditioner & Wipes) Benzoyl peroxide, sulfur, salicylic acid (DermaBenSs™) Ketoconazole, chlorhexidine, acetic acid) (Mal-A-Ket™)
DVM Pharmaceuticals	Emollients, EFA (HyLyt® efa Shampoo & Creme Rinse)	Pramoxine, oatmeal, EFA (Relief® Shampoo, Creme Rinse & Spray)	Chlorhexidine (ChlorhexiDerm® Shampoo) Benzoyl peroxide (OxyDex® Shampoo) Benzoyl peroxide, sulfur (SulfOxyDex® Shampoo)
Virbac	Glycerin (Allergroom® Shampoo) Glycerin (Humilac® Spray)	Oatmeal (Epi-Soothe® Shampoo & Cream Rinse) Diphenhydramine (Histacalm®) Triamcinolone (Genesis®) Topical Spray)	Chlorhexidine (Hexadene®) Benzoyl peroxide (Pyoben®) Miconazole (Dermazole®) Ketoconazole, chlorhexidine (KetoChlor®)

and those at risk of developing infections may benefit from regular bathing with antimicrobial shampoos. Active ingredients commonly incorporated into shampoos for this purpose include acetic acid, boric acid, chlorhexidine and benzoyl peroxide. Shampoos containing chlorhexidine have good antibacterial activity, provide residual activity, are non-irritating and are effective in the presence of organic debris. Shampoos with benzoyl peroxide have good antimicrobial, degreasing and follicular flushing properties but can be drying and are most often followed with a conditioner.

Many Pets with canine atopic dermatitis develop *Malassezia* dermatitis at some point in the course of their disease. This can severely worsen the pruritus. Topical therapy is an important component of their management. Medicated shampoos, rinses, sprays and wipes can be selected to address the issues of coverage, contact time and owner compliance. Many Pets are best served by prescribing a combination of topical products (*e.g.,* shampoo and wipes)

Table 2: Suggested Antihistamines for Canine Atopic Dermatitis*

- Hydroxyzine 2.2 mg/kg PO t.i.d.
- Diphenhydramine 2.0 mg/kg PO t.i.d.
- Clemastine 0.05-0.1 mg/kg PO b.i.d.
- Chlorpheniramine 0.4-0.8 mg/kg PO b.i.d. (max dose 8 mg)

Source: Plumb's *Veterinary Drug Handbook*, 5th ed. Blackwell Publishing.
* Response to each antihistamine is variable in individual Pets. Trying several successively may be warranted.

Table 3: Potential Side Effects of Corticosteroid Use

- polyuria/polydipsia
- polyphagia
- hepatomegaly
- obesity
- immunosuppression
- behavior changes
- hypertension
- peripheral edema
- sodium/water retention
- alopecia
- infertility
- iatrogenic hyperadrenocorticism
- hypoadrenocorticism
- abortion
- gastric ulceration
- pancreatitis

Source: Kirk's *Current Veterinary Therapy* XII. Philadelphia, Pa.: W.B. Saunders

along with systemic antifungal therapy. The antifungal ingredients available in veterinary formulations suitable for treating *Malassezia* dermatitis include acetic acid, miconazole and ketoconazole.

As with all aspects of managing canine atopic dermatitis, thorough client communication is an essential component of prescribing topical products. Be sure to advise your clients regarding the proper contact time and frequency of application of all shampoos and rinses. At follow-up examinations, check in with clients to address any concerns they have and make sure that they are committed to following your recommendations.

Systemic therapy

Nonsteroidal oral antipruritics. Essential fatty acid (EFA) supplementation is reported to be effective for the management of pruritus in dogs and is most efficacious when both omega-3 EFA and omega-6 EFA are utilized.[6] Cold water fish and marine oils are high in omega-3 EFA, and evening primrose is high in omega-6 EFA. Allow adequate time with EFA therapy to assess efficacy. Although research is conflicting, it has been suggested that a lag phase of three weeks may occur, with maximal effect thought to take as long as three months.[7]

Often EFA use alone will not control pruritus in dogs with atopic dermatitis. Oral antihistamines may act synergistically with EFAs and are often prescribed together for cases with relatively mild pruritus.[8] Tremendous variability in response to oral antihistamine therapy is seen. With these limitations, it is important to give the owner realistic expectations. I typically allow at least two weeks of therapy to proceed before deeming a product unsuccessful in a patient. (Suggested antihistamines are displayed in *Table 2.*)

Anecdotally, amitriptyline, a tricyclic antidepressant, can help relax Pets plagued with chronic pruritus (dose of 1 to 2 mg/kg PO b.i.d.). Potential side effects of antihistamines and amitriptyline include variable sedation and alterations in blood pressure, which may preclude their use in some Pets.

Corticosteroids

Corticosteroids have been a mainstay of antipruritic therapy in dogs, with oral administration preferred. Oral administration allows greater therapeutic flexibility with the lowest effective dose and interval–a goal in therapy to avoid or minimize side effects.[9] However, short-acting

injectable corticosteroids (*e.g.*, dexamethasone) may be appropriate for Pets that require a quicker onset of activity in order to break a pruritic cycle. Oral prednisone, starting with an induction dosage of 1 mg/kg/day will usually result in the effective control of pruritus and accompanying inflammation.[10] After the initial response is achieved, the dose can be tapered to the lowest effective dose. Typically, an oral dose of 0.22 to 0.55 mg/kg /day to every other day will be effective.[10]

Temaril-P® (Pfizer Animal Health) contains 2 mg prednisolone and 5 mg trimeprazine. Anecdotally, it can be used at a low-end dose of half a tablet orally every other day for smaller Pets, one pill orally every other day for medium-sized Pets and one to two pills orally every other day for larger Pets.

Clients should be fully informed of potential problems and side effects of corticosteroids (*Table 3,* page 44), as they are frequently very effective for pruritus control and requested for their Pets with good intentions. Initial blood testing including a complete blood cell count (CBC) with manual differential, chemistry and electrolyte panel, and a complete urinalysis should always be performed to evaluate for potential abnormalities prior to corticosteroid therapy and periodically every three to six months during chronic administration to evaluate for emerging abnormalities.

Cyclosporine therapy

Within the last decade, much attention has been paid to oral cyclosporine for treating canine atopic dermatitis. Cyclosporine works by targeting the immune system, more specifically inhibiting the production and release of interleukin-2 in the skin.

Cyclosporine has been extensively investigated for the treatment of canine atopic dermatitis. A dose of 5.0 mg/kg orally once daily was shown to be effective for reducing pruritus and skin lesions in dogs with atopic dermatitis.[11] Additional research confirmed cyclosporine efficacy for the treatment of canine atopic dermatitis and found the frequency of administration could often be reduced following an initial 30-day induction period.[12] Cyclosporine was also found to be as effective as glucocorticoids for the treatment of canine atopic dermatitis. Adverse effects were minimal.[13]

Clients should be fully informed of potential problems and side effects of corticosteroids, as they are frequently very effective for pruritus control and requested for their Pets with good intentions.

Atopica® (Novartis Animal Health, Inc.) is a veterinary-labeled formulation of cyclosporine approved for treatment of canine atopic dermatitis. Atopica is available in 10-, 25-, 50- or 100-mg capsules and is suitable for dogs weighing at least 4 pounds. Recommended dosage and administration is 5 mg/kg/day orally as a single daily dose for 30 days, after which the product can often be tapered to every other day and then twice weekly until a minimum effective dose is achieved.[14] The dosage should not be decreased; only the dosing interval. Otherwise, efficacy will be adversely affected. Atopica is recommended to be given at least one hour prior or two hours after a meal to maximize drug absorption. Some Pets will experience vomiting during the first week or 10 days of therapy. Giving the drug with food for the first week may decrease the incidence of vomiting. Alternatively, Pets

may be given oral antiemetic therapy prior to administration (*e.g.,* metoclopramide 0.2- 0.5 mg/kg orally). Dogs will typically stop vomiting once their body has adjusted to the medication. Other side effects to monitor include gingival hyperplasia, cutaneous papillomatosis and hirsutism.[14]

For Pets with atopic dermatitis, cyclosporine provides an effective treatment alternative with a relatively rapid onset of activity.

Cyclosporine is metabolized in the liver by cytochrome P450 enzymes. For this reason, other drugs acting on this system may alter cyclosporine levels. Notably, ketoconazole slows the clearance of cyclosporine by 60 percent.[15] This necessitates the administration of a lower dose of Atopica while patients receive ketoconazole. Generally, the dose is reduced 50 percent in this situation.[14] Drugs that induce cytochrome P450 enzymes (*e.g.,* phenobarbital) have the potential to decrease cyclosporine levels.

For Pets with atopic dermatitis, cyclosporine provides an effective treatment alternative with a relatively rapid onset of activity. One factor limiting the client acceptance of Atopica is the cost of therapy. The actual cost will depend on the size of the dog and the most effective, long-term maintenance dosing interval. Because the benefit to the Pet's quality of life is usually appreciated within 30 days, clients often embrace this course of therapy despite the expense. The cost must also be weighed against the cost of chronic antibiotic, antihistamine and topical therapies that are often required when atopy is not adequately controlled.

Systemic antimicrobials

As previously discussed, secondary staphylococcal infections are common in atopic dogs. These may develop on their own or in conjunction with *Malassezia* dermatitis. Oral cephalexin, cefpodoxime, amoxicillin and clavulanate, or sulfadimethoxine and ormetoprim are often effective as initial empirical therapies. Because methicillin resistance is of increasing concern, culture and sensitivity testing should be suggested to the client. Fluoroquinolones are best reserved for the treatment of susceptible infections, when the necessity is confirmed by culture and sensitivity. These bacteria are more often isolated from Pets with deep pyoderma.

Oral antifungal agents are indicated for the treatment of widespread or unresponsive *Malassezia* dermatitis. Fluconazole (2.5 mg/kg/day/orally) and ketoconazole (5 to 10 mg/kg/day orally) are clinically effective against *Malassezia* spp. Pretreatment blood testing, including CBC with manual differential and internal organ function screen, is strongly advised to identify potential hepatic disorders prior to use of azole antifungal agents.

Immunotherapy

Allergen-specific immunotherapy (ASIT), or hyposensitization, is the only therapy for canine atopic dermatitis that may actually alter the natural course of the disease. After allergy testing, a series of diluted allergen injections is formulated for the patient. The concentration and volume are slowly increased until a maintenance dose is achieved. Success rates of 50-80 percent are reported,[16] although almost always in uncontrolled, retrospective studies. A realistic expectation of success in the treatment of an atopic Pet is decrease in

severity and frequency of pruritus and "flare-ups." Complete elimination of signs does not often occur, so clients must be educated on this fact.

The immunological mechanisms by which ASIT decreases clinical signs remain largely speculative, in both dogs and humans. Some of the possible mechanisms that are reported in humans include: modulation of antigen-presenting cell function (induction of tolerance), modulation of T-cell responses (shift from Th2 to Th1 cytokines in tissue), and modulation of antibody response (induction of allergen-specific "blocking" IgG antibodies). A Th2 to Th1 shift has been demonstrated in dogs undergoing ASIT.

With clear client communication and good follow-up therapy, we can help our patients tremendously and make a positive impact on their lives and the lives of their families.

Immunotherapy is generally very well tolerated. Most clients learn to administer the subcutaneous injections to their Pets. Minor adverse reactions, including increased pruritus, urticaria and vomiting, occur uncommonly.[5] Therapy should be initiated in the hospital with the Pet monitored for 20 to 30 minutes after the first several injections (typically administered every two to four days during an induction period). I have had good personal success in my patients with immunotherapy and teach my clients how to properly administer these injections to their Pet. There are only rare exceptions when I have to administer the injections (which the client stores refrigerated at home) in my hospital.

Most of my patients are able to receive injections every two to three weeks after they show positive response to therapy, however, that response may take up to four or five months to achieve. I am careful to explain to my clients the time frames potentially involved and that allergies can change in Pets over time, requiring possible additional testing and changes in the allergen injection content. Pets may also have seasonal flare-ups of pruritus requiring brief periods of oral corticosteroid and antihistaminic therapy (this should be kept at low doses for brief periods to avoid altering the efficacy of the immunotherapy).

Conclusion

Research into canine atopic dermatitis and its management continues. As discussed, many therapeutic options take aim at control rather than cure, which can make this disease a very frustrating one for client and clinician alike, not to mention our patients. With clear client communication and good follow-up therapy, we can help our patients tremendously and make a positive impact on their lives and the lives of their families.

References

1. Olivry T, Buckler KE, Dunston SM, et al. Positive "atopy patch tests" reactions in IgE-hyper-responsive beagle dogs are dependent upon elevated allergen-specific IgE serum levels and are associated with IgE-expressing dendritic cells. *Vet Dermatol* 2002;13:211-229.

2. Marsella R, Nicklin C, Lopez J. Studies on the role of routes of allergen exposure in high IgE-producing beagle dogs sensitized to house dust mites. *Vet Dermatol* 2006;17:306-312.

3. Bevier DE. Long-term management of atopic disease in the dog. *Vet Clin North Am Small Anim Pract* 1990;20:1487-1507.

4. Swinnen C, Vroom M. The clinical effect of environmental control of house dust mites in 60 house dust mite-sensitive dogs. *Vet Dermatol* 2004;15:31-36.

5. Muller GH, Kirk RW, Scott DW, et al. Skin immune system and allergic skin diseases. *Muller & Kirk's Small Animal*

Dermatology, 6th ed. Philadelphia, Pa.: W.B. Saunders, 2001;599-601.

6. Watson T. Diet and skin disease in dogs and cats. *J Nutrition* 1998;128:2783S-2789S.

7. Logas D, Kunkle G. Double-blinded crossover study with marine oil supplementation containing high-dose eicosapentaenoic acid for the treatment of canine pruritic skin disease. *Vet Dermatol* 1994;5:99-104.

8. Paradis M, et al. The efficacy of clemastine (Tavist), a fatty acid-containing product (Derm Caps), and the combination of both products in the management of canine pruritus. *Vet Dermatol* 1991;2:17-20.

9. Scott DW. Rational use of glucocorticoids in dermatology. In: *Kirk's Current Veterinary Therapy XII*. Philadelphia, Pa.: W.B. Saunders, 1995:573-581.

10. Plumb. *Plumb's Veterinary Drug Handbook*, 5th ed. Blackwell Publishing, 2005.

11. Olivry T, Steffan J, Fisch RD, et al. Randomized controlled trial of the efficacy of cyclosporine in the treatment of atopic dermatitis in dogs. *J Am Vet Med Assoc* 2002;221:370-377.

12. Steffan J, Parks C, Seewald W, et al. Clinical trial evaluating the efficacy and safety of cyclosporine in dogs with atopic dermatitis. *J Am Vet Med Assoc* 2005;226:1855-1863.

13. Steffan J, Favrot C, Mueller R. A systematic review and meta-analysis of the efficacy and safety of cyclosporin for the treatment of atopic dermatitis in dogs. *Vet Dermatol* 2006;17(1)3–16.

14. Atopica Technical Monograph.

15. D'mello A et al. Pharmacokinetics of the cyclosporine-ketoconazole interaction in dogs. Res Commun Chem Pathol Pharmacol 1989 Jun;64(3):441-54.Links.

16. Mueller RS, Bettenay SV. Long-term immunotherapy of 146 dogs with atopic dermatitis - a retrospective study. Aust Vet Pract 1996;26:128-132..

Todd A. Nash, DVM, received his veterinary degree from The Ohio State University College of Veterinary Medicine in 1990. He has practiced general and emergency medicine throughout the United States. He joined Banfield in 2001. He currently works at a Banfield hospital in Columbus, OH, where he lives with his wife, Lisa, his daughter Marley, a dog, Shelby, and a cat, Bob.