

## Nonpharmacologic Approaches to Canine Atopy

Canine atopic dermatitis (AD) is challenging to treat. Next to flea-bite hypersensitivity, AD ranks as one of the top two hypersensitive skin conditions of dogs throughout the world. Estimates suggest that up to fifteen percent of the canine population may suffer from AD, though true prevalence and incidence is unknown.<sup>1</sup> AD is a “genetically programmed disease of dogs in which the patient becomes sensitized to environmental antigens that in nonatopic animals create no disease.”<sup>2</sup> The clinical signs are variable, and there are no pathognomonic features.<sup>3</sup> Rather, one diagnoses it by identifying strongly associated atopy criteria and eliminating other differential diagnoses. Allergy testing takes place thereafter in order to either implement allergen avoidance strategies, or to select specific allergens for hyposensitization formulations.<sup>4</sup>

The cause of atopy involves a complex interaction between genetic susceptibility, environmental factors, and abnormal immune responses, although the pathophysiology is incompletely understood.<sup>5</sup> What is clear is that conventional treatment approaches do not fully succeed in controlling the pruritus or resolving the skin damage associated with AD. Allergen avoidance is often impossible. Hyposensitization, even when ultimately effective, may require interim treatment until the hyposensitization takes hold. Pharmacologic approaches can be costly, occasionally harmful, and incompletely effective. As clients increasingly request “natural” treatments for their animals, it behooves veterinarians to understand what non-pharmacologic options are available and which have proven efficacy. Even if drug dosages can only be reduced with concurrent natural product administration, clients are often grateful. For example, essential fatty acids (EFAs) added to the antihistamine regimen may provide synergistic relief.<sup>6</sup> In addition to EFA research, information has become available on the use of botanical (Chinese herbal and capsaicin) and homeopathic treatments for canine AD.

### Essential Fatty Acids (EFAs)

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<sup>1</sup> Hillier A and Griffin CE. The ACVD task force on canine atopic dermatitis (I): incidence and prevalence. *Veterinary Immunology and Immunopathology*. 2001;81:147-151.

<sup>2</sup> Scott DW et al. *Muller & Kirk's Small Animal Dermatology, 5<sup>th</sup> Edition*. Philadelphia: WB Saunders Company, 1995; p. 500.

<sup>3</sup> DeBoer DJ and Hillier A. The ACVD task force on canine atopic dermatitis (XV): fundamental concepts in clinical diagnosis. *Veterinary Immunology and Immunopathology*. 2001;81:271-276.

<sup>4</sup> Ibid.

<sup>5</sup> Marsella R et al. The effects of capsaicin topical therapy in dogs with atopic dermatitis: a randomized, double-blinded, placebo-controlled, cross-over clinical trial. *Veterinary Dermatology*. 2002;13:131-139.

<sup>6</sup> Paterson S. Additive benefits of EFAs in dogs with atopic dermatitis after partial response to antihistamine therapy. *J Small Animal Practice*. 1995;36:389-394.

Over twenty trials on oral EFA supplements or EFA-rich diets in dogs have taken place since 1987.<sup>7</sup> Results indicate that EFAs may be beneficial, though large scale, long duration, randomized, controlled, and blinded remain to be done.<sup>8</sup> The mechanisms of action of EFAs involve anti-inflammatory and immunomodulatory properties. These include: modulation of cutaneous eicosanoid (prostaglandin and leukotriene) production, inhibition of cellular activation and cytokine secretion, modulation of cytotoxic activity, decremental production of serum IgE, and correction of epidermal lipid defects.<sup>9</sup> Interestingly, a recent placebo-controlled, double-blind, cross-over pilot study in atopic horses showed that administration of flaxseed (*Linum usitatissimum*) was able to reduce lesional area of the skin test response of atopic horses, alter hair fatty acid profile results, and counter inflammation with no adverse side effects.<sup>10</sup>

### Chinese Herbs

Researchers at the University of Minnesota College of Veterinary Medicine recently evaluated a Chinese herbal mixture ("P07P") containing licorice (*Glycyrrhiza uralensis*), white peony (*Paeonia lactiflora*), and rehmannia (*Rehmannia glutinosa*). In this randomized, double-blind, placebo-controlled study of fifty dogs with AD, packets of powder with P07P or placebo added to food once daily for 8 weeks.<sup>11</sup> Dogs were assessed for erythema, surface damage, overall coat condition, seborrhea, pruritus, and general demeanor; owners recorded daily itch scores. The predefined primary outcome measure was the owners' assessment of response at end of treatment. Results showed improvements in 37.5% of dogs receiving P07P, while only 13% of dogs in placebo group improved. This difference was not, however, statistically significant ( $p=0.09$ ). Nevertheless, the withdrawal rates were significantly higher for the placebo group due to worsening of the condition ( $p=0.04$ ), and the mean daily itch score in the latter half of the study was significantly higher than baseline in the placebo group, but not in the treatment group. Pruritus scores showed a significant deterioration from baseline at the final visit in the placebo group, but not for those receiving P07P. The erythema score showed a significant difference between groups in change from baseline, though surface damage, seborrhea, overall coat condition, general demeanor scores did not. No serious adverse effects were noted. Thus, P07P may be beneficial as a novel non-steroidal therapy for management of dogs with AD.

### Capsaicin

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<sup>7</sup> Olivry T et al. The ACVD task force on canine atopic dermatitis (XXIII): are essential fatty acids effective? *Veterinary Immunology and Immunopathology*. 2001;81:347-362.

<sup>8</sup> Ibid.

<sup>9</sup> Ibid.

<sup>10</sup> O'Neill W et al. Flaxseed (*Linum usitatissimum*) supplementation associated with reduced skin test lesional area in horses with *Culicoides* hypersensitivity. *Can J Vet Res*. 2002; 66:272-277.

<sup>11</sup> Nagle TM et al. A randomized, double-blind, placebo-controlled trial to investigate the efficacy and safety of a Chinese herbal product (P07P) for the treatment of canine atopic dermatitis. *Veterinary Dermatology*. 2001; 12:265-274.

Another natural remedy for AD involves topical application of capsaicin, an alkaloid found in chili peppers. Capsaicin successfully treats humans with several forms of pruritic and painful dermatologic conditions, possibly by affecting the levels of substance P on type C sensory neurons. A recent double-blind, placebo-controlled, crossover clinical trial evaluated the twice-daily topical application of 0.025% capsaicin applied in atopic, pruritic dogs with AD.<sup>12</sup> While owners noted temporary worsening of pruritus after the first week of capsaicin therapy, they ultimately reported significant improvement, although investigators did not. The therapy was well tolerated, and the study suggests that capsaicin warrants further evaluation as an adjunctive antipruritic agent in dogs with AD.

### **Homeopathy**

Homeopathic remedies are some of the most controversial among complementary and alternative medical approaches. Proposed as working through a “principle of similars”, exceedingly small doses are administered to individuals who are experiencing similar symptoms or syndromes as those which would be caused by a substance given in pharmacologic or toxic doses. The small doses, specially prepared in successive dilutions with interposed vigorous shaking, supposedly invoke resolution of symptoms. A commercial preparation specifically designed to treat animals with dermatologic conditions (“Skin and Seborrhea Remedy” by Homeopet, West Hampton Beach, New York) was studied according to a protocol recommended by the manufacturer.<sup>13</sup> This remedy contained homeopathic sulfur, staphysagria, psorinum, graphites, and arsenicum album in an ethanol-containing vehicle. Potencies of each remedy were not listed in the study. The exact mechanisms of action of homeopathy are unknown. Results showed that the homeopathic solution was no better than placebo. Only one out of eighteen dogs in the treatment group, and one out of eighteen in the placebo group responded. All other dogs received no benefit.

### **Research Design**

Studying AD in dogs presents many difficulties.<sup>14</sup> Comparison between studies using different products can be tricky, as study populations may vary, and heterogeneity of diagnoses are often used as inclusion criteria. Definitions of what constitutes improvement may vary. When evaluating similarities and differences in owners’ and investigators’ assessments of response to treatment, are they analyzing the same thing, or different ones such as pruritus vs. erythema or surface damage? One must look at long-term effects, in order to avoid confounding variables such as a change in the guardian’s initial enthusiasm for the study and a change in the owners’ recollection of the baseline severity; a study of at least three months’ duration is recommended. Are there decreasing levels of glucocorticoid in the system from prior administration? If so, researchers must allow several months for “wash out” from the system. Are the

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<sup>12</sup> Marsella, R et al. Op.cit.

<sup>13</sup> Scott DW et al. Treatment of canine atopic dermatitis with a commercial homeopathic remedy: A single-blinded placebo-controlled study. *Can Vet J.* 2002; 43:601-603.

<sup>14</sup> Olivry T. Op. cit.

benefits from short-term trials maintained with time? Is there a placebo control? What is the withdrawal rate, and how does that affect the results? For AD studies, is there a concurrent food hypersensitivity that may complicate the outcome? If an elimination diet takes place, researchers need to verify that owners complied.

### **Conclusion**

Much remains to be learned about the pathophysiology and treatment of AD. In the meantime, safe and often effective measures do exist that may help provide relief for veterinary patients.