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INTRODUCTION

Atopic dermatitis (AD) is a complex, lifelong disease with many potential manifestations, and many possible modes of treatment. Treatment approaches must be individualized and flexible, combine several modes of therapy, and be aimed at both the primary disease and at secondary complications, to maximize success and client satisfaction. Within this "integrated approach," we see each of the potential therapy possibilities as "tools." Our goal with each patient is to find just the right combination of tools to provide lifelong therapy that is effective, affordable, convenient, and with as few adverse effects as possible. Important elements of this approach include decreasing allergen load, decreasing pruritic load, use of medical treatments for short-term (and if necessary, longer-term) relief, and use allergen-specific immunotherapy if possible for potential long-term control.

DECREASING ALLERGEN LOAD

Very few studies, even in people, address the success of pollen-avoidance measures. In part, this is because the important allergenic pollens are light and windborne, traveling many miles, and pollen avoidance is nearly impossible. An entire industry is built on mite allergen reduction, from special mattress covers, to chemical house treatments, to cleaning services, to special vacuum cleaners and air filters. Dozens of studies in dust-allergic humans demonstrate that dust mite abatement measures can measurable reduce the amount of mite allergen in the household. However, the evidence for clinical effectiveness of these measures is limited and controversial, and just because the mite allergen doesn't mean the patient gets better! In one canine study, the houses of mite-allergic dogs were treated with an acaricidal agent (Acarosan Spray) every 4-6 weeks, until the results of a dust mite allergen test of the house were negative. During this time, the pets themselves received no treatment. About half of the patients in this study experienced benefit. This study is encouraging, but much work needs to be done before we can make a definitive recommendation to our clients.

According to the literature, up to 13% of dogs with AD may also have concurrent food allergy. Therefore, as part of your exploration of the best management plan for each patient, it is always wise to try a hypoallergenic diet trial for at least 6-8 weeks to see if additional improvement results. No one diet or type of diet has been proven best for this purpose; either a novel protein or hydrolyzed protein diet should suffice. The most important concept here is that the diet trial needs to be strict.

Many humans with AD have decreased cutaneous barrier function. This leaky barrier allows easy passage of allergens and irritants through the epidermis. Strengthening this barrier function may thus help to reduce clinical signs. In humans, the primary method of accomplishing this is through application of emollient topical preparations, which is demonstrably effective. In pets, there are no published studies on topical products aimed at enhancing barrier function, but some companies are beginning to imply in their marketing literature that the product may have such an effect. We await careful studies before making any conclusion or recommendation.

DECREASING PRURITIC LOAD

Decreasing pruritic load begins with insuring that good parasite control measures are in place. Following this, one MUST pay attention to the possible contribution of staphylococcal infection. Recurrent pruritic superficial staphylococcal pyoderma is extremely common in atopic dogs, and must be controlled as part of treatment. It is important, in each patient, to determine what portion of the overall itch is related to staphylococcal infection. This can only be evaluated by treatment with antibiotics alone for a period of time identified with the potential contribution of other possible causes. May cause delay in the resolution of infection and will confound your ability to judge response to antibiotics.

Dermatologists are increasingly recognizing the importance of "yeast overgrowth" (Malassezia dermatitis) as a contributing factor to atopic dermatitis, particularly in dogs. Always check for presence of yeast cytologically, and if present along with typical clinical signs (greasy or moist skin with severe pruritus that often does not respond to glucocorticoids), treat with an oral antifungal agent such as ketoconazole, fluconazole, or itranoconazole (5-10 mg/kg once daily for 5-10 days; complete response may take longer). If the pet responds to an antifungal treatment trial, topical therapy may be used to treat and/or help prevent future recurrence. Maintenance treatment with 1-2% ketoconazole shampoo or cream, or ketoconazole-chlorhexidine/miconazole-chlorhexidine shampoos, rinses, or wipes is sometimes effective for prevention of recurrent episodes.

A new line of topical products (Douxo™) contains the ingredient phytosphingosine. This substance is a component of the epidermal barrier, inhibits bacterial growth, inhibits yeast, and has some interesting in vitro anti-inflammatory action. The author has found these products to be useful for some dogs with AD.

Atopic otitis externa (dogs or cats) is common as part of AD, and for some animals is a major manifestation of the disease, and deserves specific attention if present. Chronic inflammation of the ear canals results in overproduction of cerumen, overgrowth of normal yeast and bacterial flora in the ears, and eventually ear infection. Cytology is mandatory to identify the state of the ears initially, and to plan for treatment of any infection that is present. Following resolution of bacterial infection and/or yeast overgrowth, many atopic pets benefit from periodic use of corticosteroid-only ear drops along with periodic cleaning with an ear product with residual antimicrobial action.

MEDICAL MANAGEMENT

Medical management of the AD should begin with the safest drugs to administer longer-term. Antihistamines may benefit 5-20% of pets, and they are always worth trying, though actually there is very little evidence that they are beneficial. Several should be tried for each patient. Good choices in dogs include diphenhydramine or hydroxyzine (2 mg/kg BID-TID). Combination with anti-inflammatory fatty acid supplements may provide additional benefit. There is no evidence that the newer, nonsedating antihistamine drugs now commonly used in human allergy have any additional benefit for animal use.

The "omega-3 and omega-6" anti-inflammatory fatty acids have been shown beneficial for some patients with AD. Most uncontrolled studies report 20-30% efficacy, and their effects seem to me relatively mild and of most benefit in early disease. The most important factor here is that the pet should receive a minimum of about 30 mg/kg/day of the anti-inflammatory fatty acids.
There is no proven clinical effect of the "ratio" of these fatty acids in AD. Recently, pet food companies have increased the amount of fatty acids that are added to certain pet foods, including those intended for amelioration of skin or joint disease. In some cases, the amount of fatty acid present in these diets far exceeds "oral supplementation" levels. Therefore, if the pet eats one of these diets, supplementation with capsules or liquids is not necessary. Even when fatty acid supplementation does not appear to benefit a patient on its own, it may be beneficial as part of combination therapy. Synergistic effects with both antihistamines and with corticosteroids have been demonstrated.

Atopic dermatitis is generally quite responsive to corticosteroid drugs. They may be preferred for older animals that may not live to benefit from immunotherapy, or pets with highly seasonal disease. The chief disadvantages of longer-term use of corticosteroid drugs include development of steroid resistance or "tachyphylaxis," and adverse effects (of both annoying and medically-serious varieties). Oral prednisone or prednisolone (0.5 – 1 mg/kg/day, decreasing to every other day) are much preferred to other potent drugs, or to injectable drugs, for reasons of longer-term safety. Concurrent use of the fatty acid supplements (as above) may decrease the required steroid dose. Animals receiving longer-term oral corticosteroids should have a urine culture performed twice annually to identify silent urinary tract infections. It is wise to check liver enzymes annually.

Topical low-concentration (0.015%) triamcinolone spray is a relatively new corticosteroid formulation approved for canine use in the USA (Genesis™, Virbac). In Europe, more recently a topical hydrocortisone aceponate spray has been approved (Cortavance™, Virbac). The latter corticosteroid is metabolized entirely in the skin, and is not absorbed into the systemic circulation, thus sparing the pituitary-adrenal axis. These solutions can be used for "trouble areas" of atopic dermatitis, such as the ventrum, feet, anal area, etc., or can be sprayed over broader areas of the body. The major advantage of these product is good efficacy with lack of systemic corticosteroid side effects. They also may work even in patients where other corticosteroid formulations have failed. The triamcinolone product is licensed for use for 1 month at a time; with prolonged continuous use, some animals may develop cutaneous atrophy or calcinosis cutis.

Calcineurin inhibitors such as cyclosporine A work by inhibiting production and action of cytokines, and through other mechanisms as well. More recent clinical trials of cyclosporine in dogs with AD demonstrate that this drug has efficacy equal to that of oral prednisone. Only the "modified" version of this drug (Atopica™, Neoral™, and generic forms available) should be used in dogs, as it is much more reliably absorbed. The starting dose is 5 mg/kg/day, which can be given as a single dose or divided into multiple doses. Ideally, CsAM should be given without food, as this will enhance absorption. Improvement occurs gradually, usually beginning after 1-2 weeks of administration and reaching maximum at 4 weeks. If the drug is effective, gradually reduce the dose over a period of several weeks to the minimum required for relief. Perhaps 25% of patients will have some initial gastrointestinal discomfort from CsAM. In most cases, this will abate within a few weeks. Therapy with CsAM is remarkably free from long-term adverse effects. Protocols for combination of CsAM with ketoconazole for AD have not been developed. A major concern here would be potential for development of hepatotoxicity with long-term ketoconazole treatment. Concurrent administration of systemic corticosteroids should be absolutely avoided for more than a few weeks, as such combinations have been associated with development of fatal opportunistic fungal infections. Therapeutic monitoring (serum chemistries, blood counts, or CsA serum concentrations) is neither recommended nor necessary when using CsAM for AD patients.

**ALLERGEN-SPECIFIC IMMUNOTHERAPY**

Allergen-specific immunotherapy (ASIT) is a treatment for atopic dermatitis in dogs and cats wherein extracts of allergens to which the patient is sensitive are injected, in gradually increasing amounts, to lessen or reverse the hypersensitivity state. ASIT has a strong advantage of being nearly free of adverse effects in the great majority of dogs and cats, even with prolonged use. Disadvantages include the fact that it takes several months or more to begin working, that it does not always work, and that it may be relatively expensive.

Most effects of ASIT are thought to be allergen-specific, rather than nonspecific. Thus, accurate testing to identify the offending allergens in each patient is of paramount importance to successful immunotherapy. In particular, the clinician must strive to avoid 'false positive' allergy test results, which would result in including an allergen in the patient’s mixture that is not relevant to that individual’s disease. The exact protocol and schedule for injections will vary according to the allergen preparation; generally, the extract manufacturer will provide an appropriate schedule. Injections are given year-round, and the minimum initial trial period should be 12 months. As far as is known, concurrent treatments with antihistamines, fatty acid supplements, CsAM, or low-dose glucocorticoids will not interfere with response. Treatment is generally considered to be lifelong, though it is possible to attempt discontinued after 2 to 3 years of injections if the animal has responded very well. Expected response rate to immunotherapy is approximately 60-70% "good-to-excellent" response (defined as at least 50% improvement in clinical signs). Response can be seen as soon as 1 month, but more typically takes 3 to 6 months to occur, and the maximum response may take 1 year or longer. Adverse reactions to allergen immunotherapy include localized itch at the injection site and transient worsening for 12-24 hours after the injection (~10% of patients). Generalized anaphylaxis occurs in less than 1% of dogs and cats; such reactions are generally mild and further reaction can usually be prevented by pretreatment with an oral antihistamine 1-2 hours prior to each injection.