

What's New in Canine Atopic Dermatitis- Part 2

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Treatment of AD: An evidence-based systematic review of therapies recommended for atopic dermatitis has been published and recently updated in 2015.^{1,2}

Recommendations for **acute flares** include: identification and avoidance of flare factors (flea control, diet trial; dust mite, mold, pollen control in the environment); antimicrobial therapy for skin and ear infections; improvement in skin and coat hygiene and care (frequent bathing with hypoallergenic shampoo), and reduction of pruritus and skin lesions with short term potent topical corticosteroids such as 0.015 % triamcinolone and oral oclacitinib 0.4-0.6 mg/kg bid x 14 days then SID **or** prednisolone or methylprednisolone at 0.5 mg/kg q 24-48 h until clinical remission, then discontinued or tapered to the lowest possible alternate day dose. Recommendations for **chronic AD and strategies to prevent relapse** include: the above, plus allergen-specific immunotherapy, oral/ topical fatty acid supplementation, topical corticosteroids, and once daily oclacitinib, low dose alternate day glucocorticoid therapy or cyclosporine therapy. Oclacitinib is approved for the control of pruritus associated with allergic dermatitis and atopic dermatitis in dogs 1 year or older and may be used in acute and chronic cases. Canine Atopic Dermatitis Immunotherapeutic* is a new monoclonal antibody treatment for dogs with atopic dermatitis that offers sustained relief of itch and inflammation. *This product license is conditional. Efficacy and potency test studies are in progress.

Minimum for all AD patients:^{1,2}

- Control itch and inflammation (oclacitinib, cyclosporine, corticosteroids at lowest effective dose, frequency)
- Year round flea control- prefer oral systemic product due to frequent bathing
- Manage secondary bacterial and yeast infection- major flare factor, can worsen barrier function
- Hypoallergenic or high fatty acid/ skin barrier support diet (Hills Derm Defense, RC Skin Support)
- Barrier repair trial- oral fatty acids, diet, topical
- Frequent bathing, anti-pruritic topicals
- Immunotherapy- either subcutaneous injections or oral allergy drops

Anti-pruritic therapies

Glucocorticoids are very effective but in many cases the side effects outweigh the benefits. Use oral prednisone or prednisolone at the lowest possible dose to control (not eliminate) pruritus- “comfortably itchy” is the goal. A safe steroid dose has been

published: 15 x weight in lbs= mg prednisolone/ year and can be used as a guide in dogs on long-term glucocorticoid therapy.³ Long-acting injectable glucocorticoids should be avoided as much as possible in the long-term management of canine atopic dermatitis. A combination of an antihistamine, 5 mg of trimeprazine, and 2 mg of prednisolone effectively provides pruritus relief, often with a lower dose of corticosteroids than if using plain prednisolone.⁴

Oclacitinib was recently approved for the control of pruritus associated with allergic dermatitis and for the control of atopic dermatitis in dogs 12 months of age or older. Is a novel, targeted, oral Janus kinase-enzyme inhibitor that inhibits the action of many pro-allergic and pro-inflammatory cytokines, including IL-31, which use the JAK STAT pathway for cell signaling. Studies have shown it is effective and safe in controlling pruritus associated with canine allergic dermatitis⁵ and atopic dermatitis⁶ It is more rapid-acting (within 1 hour) than oral prednisolone or dexamethasone IM injections in laboratory models⁷ without steroid-related side-effects. The approved dose is 0.4-0.6 mg/kg PO bid x 14 days, then once daily for maintenance therapy. It is available in 3.6, 5.4, and 16 mg scored unflavored tablets. The most common side-effects are vomiting, diarrhea and anorexia, which are mild and self-limiting in most cases.^{5,6} In a longer compassionate use study⁸ of 247 dogs with a mean duration of therapy 401 days (up to 630 days), the percentage of dogs with ≥50% reduction from baseline by day 90 was 63.9% for pruritus, and 66.4% for dermatitis. 91% of owners saw significant improvement in their dog's quality of life. The most frequently reported adverse events were vomiting and diarrhea, urinary tract infection/cystitis, pyoderma and otitis. Overall hematology and serum chemistry mean laboratory values remained within the normal reference range. Oclacitinib has been used safely with many common medications including parasiticides, antibiotics and vaccines. It does not interfere with serum or intradermal allergy testing.⁹ For full prescribing information go to www.Apoquel.com.

Canine Atopic Dermatitis Immunotherapeutic*- details in separate set of notes

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This product is a caninized anti-canine interleukin-31 (IL-31) monoclonal antibody. Canine Atopic Dermatitis Immunotherapeutic* aids in the reduction of clinical signs associated with atopic dermatitis in dogs. It further offers sustained reduction of the clinical signs for 1 month. Canine Atopic Dermatitis Immunotherapeutic* is a ready-to-use, sterile liquid that specifically targets and neutralizes canine IL-31, which is involved in sending the itch signal to the brain.¹⁰ By targeting the IL-31 pathway, Canine Atopic Dermatitis Immunotherapeutic* interrupts the cycle of itch and inflammation in dogs with atopic dermatitis.

Cyclosporine: is a calcineurin inhibitor that blocks the activation of T-cells and the cytokines they produce that are involved in the allergic response to reduce pruritus and inflammation. Studies have shown that the symptoms of canine AD can be well controlled with the use of cyclosporine, 5 mg/kg q 24 hours in approximately 50-70 % of cases with increasing percentages with longer term use.^{11,12} The branded form is preferred over generics due to more predictable bioavailability. Major advantages include the lack of steroid-related side-effects. The drug is not fast acting and may take 3-6 weeks for efficacy to be seen, so is often combined with low dose glucocorticoids for the first 2-3 weeks. The major disadvantage to the use of this drug is the cost but this can be lessened with every other day or half dose daily therapy, which can be attained in 40-50 % of cases.¹¹ All infection and parasites should be resolved/ ruled-out before starting cyclosporine therapy to maximize efficacy. Gastrointestinal side effects occur in approximately 15-25 % of cases¹¹, but are usually self-limiting and can be minimized by slowly building up to the full dose over 10-14 days, pre-treating with an anti-emetic 2 hours before cyclosporine for the first 10 days, and giving medication with a small amount of food.¹³ Freezing the capsules also helps prevent vomiting in many cases and does not reduce efficacy.¹⁴ Other less common side-effects include papillomatosis, hirsutism, gingival hyperplasia, tremors/ neuropathies, secondary pyoderma, and lymphoplasmacytic dermatitis.^{11,12} Occasional hypoalbuminemia, urinary tract infections and increased liver enzymes may be seen.^{11,12} Cyclosporine does not interfere with serum or intradermal allergy testing.¹⁵

Antihistamines are beneficial in only about 10- 15% of canine AD cases¹⁶ and recently an examination of evidence-based treatments for canine AD shows that there is little evidence that antihistamines are of use in treating moderate-severe pruritus in the dog with AD.¹ However, antihistamines may provide a small and limited benefit in some dogs with very mild AD.² A recent retrospective study showed that 26 % of pet owners reported that antihistamines were very or extremely effective in treating their atopic dogs.¹⁷ It is worth trying several different classes of antihistamines with proven activity in dogs, one at a time for 14 days each, as they have few side-effects and may act as steroid-sparing agents along with essential fatty acids in very mild cases of AD. The author has had the best success with hydroxyzine, cetirizine and trimeprazine with prednisolone. The recently discovered H4 receptor antagonists currently under study may be more effective in the future.

Allergen-specific immunotherapy is the only treatment that can prevent the progression of AD and may result in a cure in some cases. Immunotherapy is thought to normalize the immune response by increased production of T regulatory cells and anti-inflammatory cytokines that reduce the Th2 inflammatory cascade.¹⁸ Once a clinical diagnosis of atopic dermatitis is made, the dog can be tested for the presence of allergen-specific IgE antibodies in an attempt to select allergens to include in the

allergen-specific immunotherapy (ASIT) vaccine. The currently available tests include the intradermal test (IDT) and allergen-specific IgE serology (ASIgES) for measurement of allergen-specific IgE. It seems that no matter which test is performed to select allergens (serologic or intradermal), published reports show that about 60-70 % of dogs with AD show at least a 50 % improvement of their AD when treated with ASIT when “micro-managed” by a dermatologist, and about 20 % will not require other medications for itch control.¹⁹ Combining intradermal and serologic test results can result in better treatment outcomes.^{20,21} Dogs with ALD have negative test results and show minimal to no response to hyposensitization. Most dermatologists, including the author, recommend that injections be given once weekly, after the initial induction schedule is followed, for 1 year before a final assessment of response is made in order to maximize the chance of success. Most atopic dogs still require treatment of acute flares in pruritus with oral and/or topical anti-pruritic medications, but the frequency of medications, especially systemic glucocorticoids, often can be reduced. The dose and frequency of ASIT injections often needs to be adjusted during the induction period and this is where the “art of therapy” rather than using a “cookbook formula” comes in. The author believes that in most cases, dermatologists are best able to perform and interpret skin and serologic testing results and make the needed initial injection dosage and frequency adjustments. Once the atopic patient is stabilized on a vaccine and maintenance medication schedule, the general practitioner often can manage the case very successfully.

Recently, **sublingual immunotherapy (“oral allergy drops”)**, used for years in people for the treatment of allergic rhinitis, has been tried in small groups of dogs in pilot studies with success similar to standard subcutaneous immunotherapy.²²⁻²⁴ Most allergy companies are offering sublingual formulations of their immunotherapy vaccines. Vaccines are glycerin-based and administered by the owner twice daily using a special oral applicator. Dogs may respond in 1-3 months in some cases²³ and seem to have fewer side-effects than with subcutaneous vaccines. In one study, 50 % of dogs who failed the standard subcutaneous vaccine improved with the sublingual formulation.²³ In people, the vaccine often can be discontinued after 3-5 years with long-lasting remission of clinical signs. It remains to be seen if this is the case in dogs. More studies are needed to determine the optimal dosing frequency and protocol, and how long-term efficacy compares with subcutaneous immunotherapy. This is an option for owners who cannot give injections to their pets, but requires continuous twice daily dosing, which may decrease compliance.

Topical therapy: Shampoos and rinses should be used to help treat the secondary bacterial and/or yeast infections by reducing the over colonization of staphylococci and yeast; and to reduce the absorption of allergens through the skin due to decreased

barrier function. **Using a water softener** can help make shampoos more effective and bathing less irritating and drying.²⁶ The new Douxo mousse formulations make application much easier for pet owners and can be used in between baths. Dogs should be bathed with a hypoallergenic, moisturizing shampoo containing barrier repair ingredients.^{1,2} Products containing chlorhexidine or chlorhexidine/ ketoconazole or miconazole can be used in dogs prone to recurrent pyoderma and yeast infections, and may be alternated with the hypoallergenic shampoo to avoid drying of the skin. In theory, this should reduce the frequency and severity of future infections. Most AD dogs benefit significantly from bathing at least 1-2 times weekly.

Fatty acid nutritional supplements containing omega-3 and omega-6 fatty acids may help normalize the cutaneous barrier function and have mild anti-inflammatory effects. It may take from 6 to 12 weeks before they are effective. The recommended dose for anti-pruritic effect is 65-75 mg/kg/day of combined EPA and DHA.²⁷ Alternatively, a high fatty acid-containing, barrier repair diet such as Science Diet Derm Defense, Royal Canine Skin Support, Hills J/D, Purina DRM or Eukanuba FP can be tried. Fatty acid supplements are reported to reduce pruritus in 20% to 30% of atopic dogs.²⁸

Recently, several **topical lipid/ fatty acid preparations** have become available to help normalize the skin barrier. These include: Bayer's Dermoscent Essential-6[®] spot-on, and Ceva's Duoxo[®] shampoos, sprays, mousse and micropipettes. Several small studies²⁹⁻³³ show some effectiveness in restoring the skin barrier and reducing pruritus and inflammation with these products. The author recommends applying these products once daily directly over dry, itchy areas until the condition resolves, then using once-twice weekly for maintenance. A 1-2 month trial is needed to judge efficacy, and they are best used as part of a multimodal treatment. These products are very safe and should result in less odor and a shinier hair coat. It is unknown if dogs already on oral fatty acid supplements or high fatty acid diets will benefit further with topical lipid therapy.

Finally, in refractory cases consider repeating basic dermatologic diagnostics such as skin scrapings and skin cytology first, followed by culture for resistant bacteria such as MRSP, biopsy for autoimmune disease or cutaneous neoplasia, laboratory/ endocrine evaluation, and referral to a boarded dermatologist. This is especially important for cases where standard AD therapy is ineffective or no longer works, if lesions appear unique or more severe than normal, or when new clinical signs develop in a previously well-controlled case. Avoid repeated polypharmacy without a diagnosis- this often leads to owner frustration and financial exhaustion.

By incorporating an upbeat supportive attitude, involving your hospital team and following a proactive diagnostic approach and multi-modal preventative treatment plan rather than the “quick fix” of overuse of corticosteroids and antibiotics, we can provide a better quality of life for both the atopic pet and their caregivers. New medications such as oclacitinib and the Canine Atopic Dermatitis Immunotherapeutic are promising alternatives to corticosteroids for the treatment of acute and chronic atopic dermatitis. Frequent client communications and follow-up visits are essential to success.

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