To ensure maximum success and client satisfaction, treatment approaches for atopic dermatitis (AD) must be individualized and flexible, combine several modes of therapy, and be aimed at both the primary disease and at secondary complications. The goal with each patient is to find the right combination of therapies to provide lifelong management that is effective, affordable, convenient, and produces as few adverse effects as possible.

Important elements of every approach to AD include:

- Elimination of allergens where possible - targeting environmental, parasitic, dietary, and microbial allergens
- Augmenting or repairing the epidermal barrier in an attempt to limit percutaneous penetration of allergens and irritants
- Augmenting the epidermal antimicrobial barrier - preventing infections where possible, as opposed to recurring cycles of treatment
- Control of secondary infections when and as they occur
- Modification of the immunologic response through allergen immunotherapy, including new possibilities for an oral "allergy drop" approach
- Controlling the primary factor in patient discomfort; that is, pruritus - and, if possible, modifying the neuroimmunologic "vicious cycles" that contribute to chronicity
- Managing inflammation where possible, targeting the therapy to treat specific signs such as itch

**Practice Guidelines for Canine AD: A Clinical Framework**

AD "Practice Guidelines" form a new concept that applies principles of evidence-based medicine to specific, common case presentations, providing practical recommendations to assist veterinarians in choosing effective treatment protocols. The International Task Force on Canine Atopic Dermatitis, an independent group of clinicians and researchers in veterinary allergy, published a set of Practice Guidelines for canine AD. The guidelines stress that one approach or set of therapies is appropriate for short-term or immediate management of clinical flares, and a second set is used in an attempt to gain longer-term control of the disease.

**Treating Acute Flares**

The most common clinical situation a veterinarian faces in treating canine allergy is the dog with clinical signs that have gone suddenly and completely out of control. Typically, the patient may have erupted with lesions,
may be so pruritic as to be causing extensive self-trauma, and may be dramatically affecting the owner’s quality of life through frustration and lack of sleep!

Treating acute flares should focus on three important elements of the clinical situation:

- **Identification and elimination of "flare factors."** Such factors as varying environmental exposure (pollen counts, etc.) may be responsible for the flare, as might things as simple as development of flea infestation or dietary indiscretion in a dog with a food-hypersensitivity component to its disease. These factors need to be considered and eliminated where possible. Perhaps the most common factor in an acute flare is the development of a staphylococcal or yeast infection. Identification and treatment of such infections are paramount, both as a short-term consideration and in a longer term preventive approach.

- **Improvement of the skin and coat hygiene and care.** Bathing with a nonirritating shampoo may provide temporary relief, remove microbial and environmental allergens, and limit further microbial colonization. There is no good evidence for the superiority of any specific shampoo product and no evidence for increased efficacy of shampoos containing such ingredients as oatmeal, anesthetics, or antihistamines.

- **Reduction in pruritus and lesions with short-term drug therapy.** In acute flares a short course of oral glucocorticoids is a frequent treatment of choice, if the pruritus is widespread. A pet with more regional signs can often be controlled effectively with a topically applied corticosteroid spray.

Interventions that have little or no benefit in treating acute flares of AD include antihistamines, fatty acid supplements, and calcineurin inhibitors. From a strictly evidence-based point of view, no convincing evidence exists to support that conventional antihistamines are beneficial in treating canine AD, especially in an acute flare. Fatty-acid supplements may be beneficial in the long term, but their slow onset of action, over a period of months, makes them inappropriate for acute use. Likewise, though calcineurin inhibitors, such as cyclosporin, can be effective over time, they often take several weeks to have a substantial effect.

**TREATING CHRONIC DISEASE**

After the "forest fire" of a flare is extinguished, the veterinarian and owner must focus on a management plan consisting of therapies that provide safe, effective, long-term relief. The Practice Guidelines stress that, for the patient presented with the goal of developing a long-term management plan, the following elements should be considered:

- **Identification and avoidance of flare factors.** If fleas have been a periodic factor, monthly preventive measures should be instituted. Because infections are so commonly implicated in flares, consideration should be given to reducing skin colonization with frequent use of antiseptic topical products, such as shampoos, sprays, or rinses.
**Improvement of skin and coat hygiene** and possibly epidermal barrier function. In addition to bathing - perhaps with an antiseptic product if infections have been a problem - therapies aimed at repairing the epidermal barrier should be considered. Only limited evidence for effectiveness of such measures is available, but it appears that the evidence may be mounting. Dietary approaches may become useful, for example, supplementation with fatty acids or barrier-enhancing micronutrients. Topical approaches with spray-on or spot-on products are the subject of considerable investigation and may be useful in certain cases.

**Long-term reduction of pruritus and lesions with drugs.** Drugs that have proven effective for long-term control of pruritus and lesions of chronic AD include oral or topical glucocorticoids, topical, oral cyclosporin A (Atopica - Novartis), and in countries where available, injection of various interferon products, such as recombinant canine interferon-gamma (Interdog - Toray) or interferon-omega (Virbagen - Virbac). All of these medications must be individually targeted for patient use, considering not only variation in efficacy but their costs and individual longer-term adverse effect profiles.

**Implementation of strategies to prevent recurrence of signs.** Allergen-specific immunotherapy remains a valuable and proven long-term treatment for canine AD. It is among the very few currently available treatments that is aimed at actually reversing an important part of the underlying pathogenesis of the disease, has an excellent safety profile, and is the only treatment that in some cases can result in a virtual cure of the disease. For needle-shy owners, there is early evidence that a new sublingual "allergy drop" formulation (Allercept Therapy Drops - HESKA) is effective and might even work via different mechanisms that may benefit dogs that have failed conventional "allergy shots."

Interventions that have insufficient evidence for use in controlling chronic AD include antihistamines, pentoxifylline, misoprostol, nonsteroidal antiinflammatory drugs, and leukotriene inhibitors. All of these therapies have received only limited study, and the evidence to date is not convincing that these medications are satisfactory long-term solutions.

**Successful management of AD requires a multimodal approach for success** - be "proactive" (correcting underlying immune dysregulation and improve barrier function, individual maintenance plan of medications for gradual continued improvement and long-term control) rather than "reactive" (short-term "quick fix" steroid therapy with fast relapse and no long-term control). **Client education is key. Set realistic expectations for control not cure! Cases need to be managed aggressively and proactively early in the course of disease to prevent irreversible skin barrier function abnormalities and immune dysregulation. Early referral to a dermatologist before chronic skin changes often leads to better long-term results.**

**Minimum for all AD patients:** • Year-round flea control
- Manage secondary bacterial and yeast infections - major flare factor, can worsen barrier function
- Dust mite control
- Hypoallergenic or high fatty acid/skin barrier support diet
- Barrier repair trial - oral fatty acids, diet, topical
- Frequent bathing, antipruritic topicals
- Regular maintenance therapy and rechecks - control flare factors

**Topical therapy is an extremely valuable addition to the management of pruritic diseases, and in many cases is the most important therapy.** The simple act of bathing itself may relieve pruritus by cooling the skin. Shampoos and rinses can be used to help manage the secondary bacterial and/or yeast infections by reducing the over colonization of staphylococci and yeast especially on carrier sites such as the anal ring, inguinal area, paws and intertriginous (skin fold) areas, and to reduce the absorption of allergens through the skin due to decreased barrier function. Products containing chlorhexidine or chlorhexidine/ketoconazole or miconazole can be used weekly or more often if the owner is able. In theory, this should reduce the frequency and severity of future infections, but studies to confirm this have not been published. Some shampoos and rinses contain ingredients that can help to alleviate pruritus such as hydrocortisone, pramoxine (local anesthetic), oatmeal, and aloe.

**Fatty-acid nutritional supplements** containing omega-3 fatty acids (fish oil, flax seed oil) such as eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA) may help normalize the cutaneous barrier function, have antiinflammatory effects, and may act as a steroid-sparing agent or synergistically with antihistamines. It may take from 6 to 12 weeks before they are effective. The recommended dose for antipruritic effect is 50 mg/kg/day of combined EPA and DHA. Alternatively, a high fatty acid-containing diet may be tried. Fatty acids supplements are reported to reduce pruritus in 20% to 30% of atopic dogs. Recently, several topical lipid/fatty acid preparations have become available that claim to aid in normalizing the skin barrier. Small studies show some effectiveness in restoring the skin barrier and reducing pruritus and inflammation with these products, but larger comparative studies are needed to determine the most effective products, optimal frequency, preferred application technique, and best case selection. A 1- to 2-month trial is needed to judge efficacy. At the very least, these products are very safe and should result in less odor and a shinier hair coat.

**Glucocorticoids** are the mainstay of effective AD therapy. In many cases the side effects outweigh the benefits. Use oral prednisone or prednisolone at the lowest possible dose to control pruritus (“comfortably itchy”) is the goal. A proposed "safe annual steroid dose" has been published: 15 x weight in lb = mg prednisolone/year and can be used as a guide for dogs being managed with long-term glucocorticoid therapy. The minimal use of long-acting injectable glucocorticoids should be avoided in the long-term management of canine AD. Temaril P® is a medication that is a combination of an antihistamine, 5 mg of trimeprazine, and 2 mg of prednisolone. Using Temaril P allows you to provide pruritus relief, often with a lower dose of
corticosteroids than if using plain prednisone. As with other corticosteroids, this product is contraindicated, except when used as emergency therapy, in animals with tuberculosis, hyperadrenocorticism and peptic ulcers. Use may induce parturition when administered during the last trimester of pregnancy, may be associated with other birth-related complications and may result in congenital birth defects.

**Cyclosporine** is a calcineurin inhibitor that is effective as a steroid alternative for treatment of canine AD. It blocks activation of T-cells and the cytokines they produce that are involved in the allergic response reducing inflammation and pruritus. 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. Atopica® is the veterinary form of cyclosporine and is preferred over generics (us.atopica.com). Major advantages include the lack of steroid-related side effects such as polyuria, polydipsia, weight gain, muscle weakness and personality changes. The drug is not fast acting and may take 3–6 weeks for efficacy to be seen, so is often combined with low-dose corticosteroids 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. 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 cases, but are usually self-limiting and can be minimized by slowly building up to the full dose over 10–14 days, pretreating with an antiemetic 2 hours before cyclosporine for the first 10 days, and giving medication with a small amount of food. Other, less common side effects include papillomatosis, hirsutism, gingival hyperplasia, tremors/neuropathies, secondary pyoderma, and lymphoplasmacytic dermatitis. Occasional hypoalbuminemia, urinary tract infections and increased liver enzymes may be seen.

**APOQUEL® (oclacitinib tablet)** 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. It is a novel, targeted, oral Janus kinase-enzyme inhibitor that inhibits the action of many allergic cytokines, including IL-31, which uses the JAK STAT pathway for cell signaling. Studies have shown it is effective and safe in controlling pruritus associated with canine allergic dermatitis and atopic dermatitis. It is more rapid-acting (within 1 hour) than oral prednisolone or dexamethasone injections 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. APOQUEL® should not be used in dogs less than 12 months of age or in dogs with serious infections. APOQUEL may increase the susceptibility to infection and demodicosis and may exacerbate neoplastic conditions. APOQUEL has not been evaluated in combination with systemic immunosuppressive agents such as glucocorticoids or cyclosporine. APOQUEL should not be used in breeding dogs, or pregnant or lactating dogs. The most common side effects seen in dogs administered APOQUEL were vomiting and diarrhea. APOQUEL has been safely used in conjunction with other common medications including antibiotics and parasiticides and with vaccinations. It does not interfere with serum or intradermal allergy testing.35 For full prescribing information go to https://online.zoetis.com/US/EN/Products/Documents/Apoquel_PI.pdf.
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 antiinflammatory cytokines that reduce the Th2 inflammatory cascade. 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 "micromanaged" by a dermatologist. Combining the results of intradermal and serologic testing may result in better treatment outcome. Dogs with ALD have negative test results and show minimal to no response to hyposensitization. Most dermatologists 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. Many atopic dogs still require treatment of acute flares in pruritus with oral and/or topical antipruritic 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.

Recently, sublingual immunotherapy, 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. Several companies, including HESKA, Bio-Medical services, RESPIT and Nelco 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 cases 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. 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.

RESPIT® is a newer form of immunotherapy founded by a veterinary dermatologist offering standardized region-specific allergen immunotherapy (vetrespit.com). No allergy testing is required. This therapy is based on a small unpublished study that showed no statistical difference in results between allergen-specific and nonspecific immunotherapy. This may be an option for owners who decline allergy testing or for dogs that cannot have glucocorticoids withdrawn before testing. A sublingual spray made by Nelco is also offered as a treatment option by RESPIT in addition to the standard subcutaneous injection formulation.

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 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 multimodal preventative treatment plan rather than the "quick fix" of overuse of steroids and antibiotics, we can provide a better quality of life for both the atopic pet and their caregivers. Frequent client communications and followup visits are essential to success.

**Speaker Information**
(click the speaker's name to view other papers and abstracts submitted by this speaker)

Candace A. Sousa, DVM, DABVP (Canine & Feline), DACVD
Zoetis
El Dorado Hills, CA, USA