Canine atopic dermatitis (CAD) is a common skin disorder defined as a hereditary predisposition to develop pruritic inflammatory skin disease associated with IgE antibodies, which typically target environmental allergens.\(^1\) The disease typically affects dogs age 6 months to 3 years and is characterized by pruritus and secondary skin lesions of a characteristic distribution around the face (mouth, eyes), concave aspect of the ear pinnae, ventral abdomen, flexor aspects of elbow, carpal, and tarsal joints, interdigital skin, and perineal area (FIGURES 1 AND 2).\(^1\)

The initial clinical signs of CAD are those associated with pruritus (eg, scratching, rubbing, chewing, excessive grooming or licking); erythema and papules may also be present. Depending on the allergens involved, clinical signs are seasonal or, most commonly, nonseasonal.\(^1\)

**CLEAN SLATE**

Topical once- to twice-weekly therapy using antimicrobial shampoos (eg, chlorhexidine, benzoyl peroxide, miconazole, ketoconazole) and ear cleansers are recommended as an essential component in the long-term management of secondary infected CAD.

**FIGURE 1.** A French bulldog with an acute flare of atopic dermatitis and secondary superficial staphylococcal folliculitis on abdomen. This dog exhibits patches of erythema and edema with excorations on both axillae.

**FIGURE 2.** A chronic atopic dermatitis case with secondary Malassezia dermatitis. Skin lesions feature severe erythema; alopecia; excoriations; and lichenification of axillae, ventral abdomen, perineal area, and caudomedial thighs.
PATHOGENESIS

The pathogenesis of CAD is complex. Percutaneous sensitization to environmental allergens (e.g., dust mites, pollen, mold) and/or allergens from food induces skin infiltration by various inflammatory cells, activation of resident cells, and local production of inflammatory/itch mediators.\textsuperscript{1,2}

Several factors can exacerbate CAD (FIGURE 3),\textsuperscript{1-3} such as:

- Ectoparasites, particularly fleas
- Environmental factors (e.g., increase in seasonal allergen)
- Cutaneous colonization/infection by bacteria (Staphylococcus pseudintermedius) and yeast (Malassezia pachydermatis)
- Epidermal barrier dysfunction

UPDATE ON DIAGNOSIS

Despite significant efforts to identify a “diagnostic test” for CAD, the diagnosis remains clinical. It is based on the following:

- History (BOX 1)\textsuperscript{4,5}
- Characteristic clinical criteria (BOX 2)
- Exclusion of other diseases with a similar clinical presentation\textsuperscript{1,3,6}

Clinical Criteria

Recently, a new set of criteria for CAD diagnosis, known as Favrot’s criteria (BOX 2), has been implemented to help veterinarians interpret clinical findings when confronted with an itchy dog.\textsuperscript{7} These criteria were developed from a large case series of confirmed cases of CAD. Complex statistical analysis was used to identify a set of clinical features that had maximum association with CAD.

However, these criteria have a sensitivity and specificity of about 80% when 5 of 8 are fulfilled. This means that using them as the sole “diagnostic test” would lead to a wrong diagnosis in every fifth dog.\textsuperscript{1,7} Therefore, they should be applied concurrently with a careful workup for exclusion of diagnostic differentials, such as ectoparasitic diseases and skin infections. When they are used in this way, the specificity of diagnosis can be expected to increase markedly.

**BOX 1 Important Details in History of Dogs Suspected of Having CAD**

- Age at onset
- Seasonality of clinical signs
- Pruritus with no skin changes (pruritus sine materia) at onset
- Familial or breed predisposition (e.g., West Highland white terrier, Golden or Labrador retriever, German shepherd, Boxer, French bulldog, bull terrier, shar-pei)\textsuperscript{3,4}
- Previous response to glucocorticoids

**BOX 2 Favrot’s Criteria**

1. Onset of signs under 3 years of age
2. Dog living mostly indoors
3. Glucocorticoid-responsive pruritus
4. Pruritus sine materia at onset (i.e., alesional pruritus)
5. Affected front feet
6. Affected ear pinnae
7. Nonaffected ear margins
8. Nonaffected dorsolumbar area
Exclusion of Other Diseases

Regardless of the history and criteria, CAD should never be diagnosed until diseases that resemble it, such as flea allergy dermatitis, ectoparasitic disease (eg, sarcoptic mange, cheyletiellosis, pediculosis, trombiculiasis, and otoacariasis), and primary skin infections have been ruled out.

The initial steps of a basic workup to rule out ectoparasites are flea combing, skin scraping, hair plucking, and cytologic examination of skin and ear samples. Skin lesions and pruritus associated with flea allergy dermatitis are most common at the lumbosacral area, tail base, and caudomedial thighs, which are not commonly affected areas in CAD. Patients with CAD exhibit frequent, sometimes recurrent, staphylococcal and yeast skin infections, which can exacerbate pruritus and dermatitis; therefore, patients predisposed to secondary skin infection should be considered and screened for CAD.

Skin biopsy results are usually nonspecific and inadequate for diagnosing CAD. However, in some cases, skin biopsy may be indicated to rule out a diagnostic differential, such as cutaneous lymphoma. Cutaneous epitheliotrophic T-cell lymphoma may present with pruritus, excessive scales, and generalized erythema in dogs and may mimic atopic dermatitis lesions.

Intradermal and IgE Testing

Allergy testing, which includes serologic evaluation of allergen-specific IgE and intradermal skin testing, should not be used for the diagnosis of CAD. Many healthy dogs are sensitized to environmental allergens and consequently have positive test results. Furthermore, many dogs with clinical signs of CAD have negative results on these tests; the term atopic-like dermatitis describes this group of dogs. Allergy testing should be carried out only to identify allergens to be used for allergen-specific immunotherapy and desensitization (see Allergen Immunotherapy).

UPDATES ON TREATMENT

CAD is a multifactorial chronic disease that requires a multimodal treatment approach to decrease pruritus and inflammation below the threshold of clinical signs. Guidelines from the International Task Force on Canine Atopic Dermatitis recommend therapeutic interventions based on identifying and managing the flare factors (FIGURE 3), as well as whether the patient is experiencing an acute flare or has chronic skin lesions.

A rational approach to treatment is required; the keys to success are client education and a combination of interventional measures specific for flare factors and symptomatic treatment.

The management of each patient starts with:
1. Identifying and addressing (or, if possible, avoiding) the associated flare factors (FIGURE 4)
2. Using a topical and/or systemic treatment to decrease inflammation and pruritus

Management of Flare Factors

Specific avoidance interventions depend on identification of all the factors associated with a flare for clinical signs in an individual dog. Common flare factors include fleas and fleabite hypersensitivity, bacterial or yeast overgrowth, and food and environmental allergens. CAD due to food and environmental allergens can present with identical clinical signs and may, in fact, be a concurrent problem.

Fleas and Fleabite Hypersensitivity

Dogs with CAD are predisposed to fleabite hypersensitivity if exposed repeatedly to flea salivary antigens. As a result, all dogs with CAD should be protected with year-round flea adulticides combined with relevant environmental measures. Some dogs may present with concurrent clinical signs of CAD (eg, licking feet, ear infections) and fleabite hypersensitivity (eg, pruritus and hot spots in tail base area); these patients need aggressive flea treatment as well as environmental measures.

Bacterial or Yeast Overgrowth

Specific antibacterial/antifungal interventions should be based on regular cytologic evaluation (impression smears, tape) of atopic skin lesions and documented presence of bacteria/yeast at these sites.

Because atopic patients frequently develop recurrent ear and skin infections with Staphylococcus and Malassezia species (FIGURE 5), topical once- to twice-weekly therapy using antimicrobial shampoos (eg, chlorhexidine, benzoyl peroxide, miconazole, ketoconazole) and ear cleansers are recommended as an essential component in the long-term management of secondary infected CAD. The widespread emergence of multidrug-resistant
S. pseudintermedius-associated pyoderma in dogs has increased interest in targeted topical antimicrobial therapy with chlorhexidine shampoos and sprays. More severe or generalized cases of pyoderma may require first-line systemic antimicrobials (BOX 3); bacterial culture and susceptibility testing may be needed in cases of recurrent pyoderma. For Malassezia dermatitis, there is evidence for use of topical miconazole/chlorhexidine shampoo treatment (Malaseb, bayerdvm.com; twice a week for 3 weeks) and, in severe cases, systemic treatments with azole derivatives (BOX 3). Many drug interactions exist with use of azole drugs, especially with ketoconazole. Frequent use of systemic antimicrobials (antibiotics and antifungals) is not recommended because it is likely associated with increased prevalence of drug resistance.

**BOX 3 Systemic Antimicrobial Options for Severe Skin Infection**

**Pyoderma**
- Cephalexin, cefadroxil 15-30 mg/kg PO q12h
- Cefpodoxime 5-10 mg/kg PO q24h
- Clindamycin 5.5-11 mg/kg PO q12h
- Lincomycin 15-25 mg/kg PO q12h

**Malassezia dermatitis**
- Ketoconazole 5-10 mg/kg q24h
- Itraconazole 5 mg/kg q24h for 3 weeks
- Terbinafine 30 mg/kg q24h for 3 weeks

**FIGURE 4.** A 6-year-old mixed-breed dog with CAD and flea allergy dermatitis with severe pruritus and secondary bacterial infection at initial presentation (A, C). After failed allergen-specific immunotherapy, treating fleas and resolving secondary infection, the dog’s allergies became well controlled with frequent medicated baths and lokivetmab, anti–canine IL-31 monoclonal antibody (B, D).
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Food-induced CAD

The Task Force on Canine Atopic Dermatitis recognizes some controversy regarding the association between food and CAD—some dogs with CAD exhibit flares when exposed to food allergens. Such patients likely have recurrent, year-round clinical signs and sometimes have additional gastrointestinal signs (soft stools, vomiting, diarrhea, increased fecal frequency). All dogs with nonseasonal CAD should undergo 1 or more dietary restriction-provocation trials to determine whether food allergens contribute to clinical signs.\textsuperscript{1,3}

The current “gold standard” method for identifying food allergy in animals is to observe improvement of CAD clinical signs when the animal is fed a novel protein diet followed by recurrence of clinical signs when rechallenged with a previously fed food.\textsuperscript{14,15} The novel protein is usually combined with a carbohydrate and is fed as a home-cooked or commercial diet (\textbf{BOX 4}).\textsuperscript{16-18} Commercial novel protein source diets typically include proteins from venison, rabbit, duck, kangaroo, ostrich, or emu and are combined with a carbohydrate source, such as potatoes, sweet potatoes, rutabagas, oats, or barley.

The novel diet is required for a minimum of 6 weeks, although some cases may continue to improve for up to 8 to 10 weeks.\textsuperscript{1,3,19} Additional clinical signs, such as severe skin inflammation, pruritus, ear infections, and superficial pyodermas, influence the length of time required to feed the diet. Furthermore, most dogs with food allergies have additional hypersensitivities, such as

\*Figure 5. (A, C) Skin lesions of superficial canine pyoderma on thorax of atopic dog and skin cytology revealing neutrophils and extracellular and intracellular cocci. (B, D; x100 magnification for C) Malassezia dermatitis affecting ventral abdomen of a dog with CAD and associated tape skin cytology revealing peanut-shaped yeast (x100 magnification for D).
environmental or flea allergies, that could fluctuate daily or seasonally and complicate the length of a food trial.

To avoid gastrointestinal upset in the first few days of introduction and rechallenge, my clinical experience suggests initially mixing the old and new food (50%/50%) before complete transition to new or old food.

Adjunctive treatments for severe skin inflammation, pruritus, ear infections, and superficial pyoderma should be initiated immediately at the start of a diet trial. The treatment should resolve all concurrent clinical signs of pruritus and infection (ears, skin) within 6 to 10 weeks of the diet trial, at which time the symptomatic medications are discontinued, and the patient can be maintained only on the novel food for the following 2 to 3 weeks. The patients are carefully observed during these 2 to 3 weeks; if the clinical signs or pruritus and skin/ear infections do not recur, the patient should be rechallenged with the old diet. A relapse of clinical signs within 14 days of rechallenge is expected in dogs with food allergy, although in most cases, untrained client/owner observation is used to determine relapse.1,3

**Environment-Induced CAD**

**Allergen Control**
The most common causes of CAD in my practice are environmental allergens from dust mites and pollens. House dust mite glycoproteins are likely the most common allergens in atopic dogs; therefore, reducing the numbers of mites and their allergens in the household may help alleviate CAD signs.1,3 Several products are marketed for dust mite allergen reduction; however, only a single uncontrolled study showed the benefit of house dust mite control with an acaricide benzyl benzoate spray (Acarosan Spray, bissell.com) for reduction of clinical signs of CAD in mite-hypersensitive atopic dogs.20 Additional controlled studies correlating dust mite allergen reduction and clinical improvement in atopic dogs are needed; these studies should span several months because of the long persistence of mite allergens in the environment. Another measure to theoretically reduce mite allergens involves frequent and thorough pet mattress and environment washing and vacuuming.

**Allergen immunotherapy**
The sole causal treatment for environment-induced CAD is allergen immunotherapy (AIT), also known as desensitization or hyposensitization.1,3 AIT consists of administering gradually escalating quantities of relevant allergens subcutaneously or sublingually (BOX 5)21-27 until immunologic tolerance to the allergens is established and relapses of CAD clinical signs are prevented.

Molecular and cellular mechanisms of AIT include early mast cell and basophil desensitization effects; an induction of interleukin-10-secreting inducible regulatory T and B cells; regulation of IgE and IgG4 production; and inhibition of responses from
Eosinophils, mast cells, and basophils in the affected tissues.\textsuperscript{21} Rationally, allergens likely to contribute to CAD can be identified by using an intradermal test or serum IgE serology. In vivo challenge by intradermal allergen injection is considered the gold standard; this assay provides functional evidence of hyperreactivity within atopic skin. Results of in vitro assessments of allergen-specific IgE (serum allergy testing) vary between laboratories, and no standardization exists for this test.\textsuperscript{28}

Management of Inflammation and Pruritus

Many cell types contribute to the complex immune network underlying cutaneous inflammation in CAD.\textsuperscript{1,2} After activation, these cells up- or downregulate various modulators, cytokines, and chemokines that promote pathology in food- and environment-induced CAD skin lesions. Several drugs are effective in modulating these cells and mediators in food- and environment-induced CAD (\textit{TABLE 1}). Symptomatic intervention in dogs with food-induced atopic disease should resolve clinical signs within 6 to 10 weeks of a diet trial, whereas patients with environment-induced CAD may experience recurrent flares throughout the year, requiring long-term control.

The guidelines from the International Task Force on Canine Atopic Dermatitis\textsuperscript{1,3} base therapeutic recommendations for pruritus and skin inflammation interventions on whether the patient is experiencing an acute flare or has chronic skin lesions. This distinction can be confusing because most atopic dogs present with a wide spectrum of clinical phenotypes involving chronic pruritus and/or skin lesions ranging from acute erythematous papules to chronic lichenified plaques. As a simple rule of thumb, the management of CAD should focus on:

1. Inducing remission (“get control”) and
2. Initiating long-term management for prevention of flares (“keep control”)

An example of this approach is daily, intensive systemic and topical glucocorticoid administration for a few weeks until clinical signs are resolved (“get control”), followed by only intermittent topical glucocorticoids twice weekly to previously affected areas, with a goal of suppressing subclinical inflammation (“keep control”). Topical therapy aimed at improving epithelial barrier dysfunction may also be appropriate (\textit{BOX 6}).

\textbf{BOX 5 Subcutaneous versus Sublingual Allergen Immunotherapy}

Subcutaneous immunotherapy has been a mainstay of AIT in dogs with CAD for decades, mainly because systemic adverse effects (eg, life-threatening anaphylaxis) are very rare compared with occurrence in human patients.\textsuperscript{1,2} However, subcutaneous AIT in dogs lacks protocol standardization (eg, amount of allergen extract, frequency of administration, administration of purified or recombinant allergen). Two recent trials using a high-dose recombinant house dust mite allergen prevented allergen-induced skin lesions in experimentally sensitized atopic dogs\textsuperscript{22} and reduced clinical scores in dust mite–sensitized naturally atopic dogs.\textsuperscript{23} These observations warrant further larger randomized controlled trials using highly purified or recombinant major allergens for AIT in atopic dogs.

Recently, sublingual AIT, in which allergen extracts are administered in the oral cavity instead of by injection, has emerged as another immunotherapy treatment for allergic diseases in humans.\textsuperscript{24} Sublingual AIT reduces the risk for severe systemic reactions observed in humans receiving subcutaneous AIT; in dogs, however, it requires long-term, q12h administration by the owners, which may influence client compliance.

Despite the demand for high-quality research, no consistent evidence supports the effectiveness of subcutaneous or sublingual AIT for the treatment of human atopic dermatitis.\textsuperscript{21} Only a few studies demonstrate the efficacy of sublingual AIT in experimentally dust mite–sensitized atopic dogs.\textsuperscript{21,22} An uncontrolled open-label study using sublingual AIT treatment (q12h spray application) produced mild clinical improvement in 10 dogs with dust mite–associated natural CAD; a formulation and dosing schedule equivalent to a commercial product (Heska Allercept Therapy Drops, heska.com) were applied.\textsuperscript{27}
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Oral and Topical Glucocorticoids

Glucocorticoids are fast-acting medications that deactivate many inflammatory cells and reduce inflammatory/itch mediators. They are used for both inducing remission and maintaining long-term control in CAD. Unfortunately, prolonged systemic use is associated with polyuria, polydipsia, polyphagia, muscle and skin atrophy, bacterial and fungal infections, demodicosis, and iatrogenic hyperadrenocorticism.1-31

Topical steroids are the mainstay of therapy for bringing localized CAD skin lesions under remission; medium-potency glucocorticoid sprays, such as triamcinolone acetonide (Genesis, us.virbac.com) and a diester hydrocortisone aceponate (Cortavance, us.virbac.com), show high efficacy in CAD.3 The triamcinolone acetonide and hydrocortisone aceponate sprays are currently unavailable in the United States; however, another highly potent diester steroid, mometasone furoate, is available as a cream through pharmacies and is widely used in my practice.

As suggested for human atopic dermatitis, daily application of steroids for 2 to 4 weeks to clear localized skin lesions should be followed with the intermittent use of the same product (eg, 2 to 3 times per week) on the previously affected skin even if visible lesions have disappeared. This “proactive treatment” approach reduces the risk for flares and extends the time of remission in humans32 and dogs33,34 compared with reactive therapy (ie, therapy only when clinical signs are visible). Even though mometasone furoate and hydrocortisone aceponate induce mild dermal degradation through inhibition of collagen I and III propeptides, no visible skin atrophy has been observed in CAD skin lesions during long-term intermittent topical application.33-35

If CAD signs are too extensive to be controlled with only topical formulations, then short-acting oral glucocorticoids are recommended in conjunction with topical steroids.3 Prednisone/prednisolone (0.5 to- 1 mg/kg PO) or methylprednisolone (0.4 to- 0.8 mg/kg PO) should be administered q24h or divided into 2 doses for 5 to 15 days, then reduced or discontinued as signs decrease based on patient response. To reduce the adverse effects and dose of oral glucocorticoids in some allergic dogs, the glucocorticoid-antihistamine combination Temaril-P (trimeprazine 5 mg/prednisolone 2 mg, zoetis.com) can be effectively used; the antihistamine trimeprazine seems to potentiate the low dose of prednisolone, achieving a steroid-sparing effect.36

### TABLE 1 Highly Effective Drugs for Remission and Management of Canine Atopic Dermatitis

<table>
<thead>
<tr>
<th>INDUCING REMISSION: “GET CONTROL”</th>
<th>LONG-TERM MANAGEMENT: “KEEP CONTROL”</th>
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<tbody>
<tr>
<td>Oral and/or topical glucocorticoids</td>
<td>Oral and/or topical glucocorticoids</td>
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<tr>
<td>Oclacitinib</td>
<td>Cyclosporine</td>
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<tr>
<td>Lokivetmab</td>
<td>Lokivetmab</td>
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<tr>
<td>Surgery</td>
<td>Oclacitinib</td>
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</tbody>
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### BOX 6 Improving Epidermal Barrier Dysfunction

The complex process of epidermal differentiation is disturbed in CAD lesions, and the impaired skin barrier offers potential targets for therapeutic intervention, such as fatty acids (oral supplements or topical solutions) and various topical treatments. Weekly bathing with a mild nonirritating shampoo and postbathing topical moisturizers are recommended for each patient; this therapy provides a direct soothing effect to the skin, physically removes surface allergens, and increases skin hydration.15

According to the systematic review of clinical trials, essential fatty acid supplementation is indicated only for long-term management of CAD as an adjunctive treatment; the clinical benefit of essential fatty acid supplements on the skin may take up to 2 months to be seen.15 In recent years, some topical (spot-on, spray, shampoo, emulsion) formulations containing fatty acids and ceramides have been introduced for dogs with CAD; however, their efficacy is inconsistent, and veterinarians should weigh their benefit and cost before deciding to use them.5
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Steroid-Sparing Agents

Medications that may help avoid adverse effects associated with long-term systemic glucocorticoids are also available for dogs with CAD.

Oclacitinib

Oclacitinib (Apoquel, zoetis.com) is the first Janus kinase (JAK) inhibitor approved in the United States and Canada for the treatment of atopic dermatitis in dogs. JAKs are nonreceptor tyrosine kinases activated by various cytokine receptors and regulate the expression of multiple inflammatory genes. JAK inhibition may modulate the immune response to varying degrees, ranging from selective inhibition of cytokine production with anti-inflammatory effects to broader inhibition of cytokine production resulting in immunosuppression. Four JAK families of enzymes (JAK1, JAK2, JAK3, and tyrosine kinase 2) exist in mammals, and different inhibitors target different families.

At this time, oclacitinib is considered to be a selective JAK1 inhibitor, and as such it is proposed to be an anti-itch agent without being immunosuppressive. However, safety studies performed in 6- and 12-month-old dogs with high oclacitinib dosages resulted in adverse effects, suggesting that this drug has potential immunosuppressive properties in dogs (US Food and Drug Administration [FDA] data). A recent study used an integrated modeling approach using isolated canine T cells; the results revealed that oclacitinib appears to have immunosuppressive properties, but only at dosages above those used to treat allergic pruritus in dogs.

Oclacitinib (0.4 to 0.6 mg/kg q12h for 14 days, then q24h as needed) is considered a safe, fast-acting, well-tolerated oral drug with good efficacy for inducing remission and long-term control of CAD in dogs at least 12 months old. It has a very rapid onset of action for itch and a slower one for skin inflammation. Its immunosuppressive properties during in vivo administration are unknown, and opportunistic infections (eg, viral papillomas) or infestations (eg, demodicosis) might develop in susceptible individuals. In these cases, oclacitinib should be discontinued until the infection/infestation clears or is treated adequately; other anti-itch/inflammation drugs may be used for control of CAD in these patients.

Two recent studies indicated that routine hematologic evaluation, serum chemistry, and urine culture are not indicated for dogs receiving oclacitinib up to 630 days; however, clinicians should decide on monitoring in each case on the basis of clinical signs.

Cyclosporine

Oral cyclosporine is a calcineurin inhibitor that, at low doses, exerts an anti-inflammatory and immunomodulatory effect through inhibition of T-cell activation. Cyclosporine is approved for the long-term control of CAD at the starting oral dose of 5 mg/kg q24h for at least 6 to 8 weeks because clinical benefit has slow onset; the full benefit of this drug is usually observed after 8 weeks of administration. Oral steroids or oclacitinib can be administered concurrently in the first 3 to 4 weeks to overcome the slow onset of clinical effect; a recent study showed that the administration of oral prednisolone (1 mg/kg q24h for 7 days then q48h for 14 days) with cyclosporine at 5 mg/kg led to a rapid reduction in pruritus and skin lesions. In patients with good response to cyclosporine, the long-term dose and/or frequency are adjusted as needed for therapeutic effect.

Vomiting and diarrhea are seen in 30% of patients but are usually self-limiting within the first 7 to 10 days; administration with food or freezing the cyclosporine capsules may help decrease gastrointestinal upset. As with many immunosuppressive drugs, opportunistic infections (eg, fungal infections) may develop in susceptible individuals receiving cyclosporine. A retrospective study evaluated the frequency of urinary tract infection and recommended routine urine cultures for dogs receiving long-term cyclosporine; however, some dogs in this study may have had subclinical infections before cyclosporine administration.

Less commonly reported dermatologic adverse effects include gingival hyperplasia, psoriasiform-lichenoid-like dermatitis, and hyperplastic verrucous lesions. These effects usually regress with dose tapering and/or discontinuation of the cyclosporine.

Monitoring of cyclosporine levels during treatment of CAD is difficult because no significant correlation has been found between positive clinical improvement and cyclosporine blood concentration in atopic dogs; clinical response to cyclosporine remains the most reliable method of assessing efficacy in CAD.

Microemulsified cyclosporine (Atopica, elanco.com) is approved for use in dogs with CAD in the United States; the formulation of Atopica is identical to the human formulation, Neoral (pharma.us.novartis.com). A human generic ultramicronized emulsified cyclosporine (Equoral, tevatxteam.com) was shown to be as effective as prednisone in reducing skin lesions and pruritus in atopic dogs, whereas a new
100-mg/mL oral solution of cyclosporine (Cyclavance, Virbac, uk.virbac.com) has recently been approved in Europe for chronic clinical manifestations of atopic dermatitis. A human vegetable oil-based formulation of cyclosporine (Sandimmune, pharma.us.novartis.com) shows marked intraindividual and interindivdual variation in oral bioavailability in dogs and is not recommended for CAD.60

Several human generic formulations of cyclosporine are listed by the FDA as being therapeutically equivalent to Neoral; these formulations have not been tested in atopic dogs for bioequivalence or therapeutic efficacy. Extreme caution is recommended with compounding preparations of cyclosporine because product quality and concentration vary markedly among cyclosporine preparations compounded for animals; as a result, a recent state-of-the-art review on cyclosporine use in companion animals discourages use of compounded cyclosporine.60

Monoclonal antibodies
Biological medicine, an intervention pioneered in the last 30 years in humans, involves the use of monoclonal antibodies to target proteins, such as cellular receptors or soluble molecules, involved in disease pathogenesis.

Monoclonal antibodies are monospecific antibodies made by identical immune cells with a monovalent affinity: They bind to the same epitope (the part of an antigen that is recognized by the antibody). During the past decade, the molecular signature of human atopic dermatitis has been increasingly understood, particularly with a focus on barrier dysfunction and cutaneous/systemic immune activation, allowing development of more targeted therapies.

Recently, a monoclonal antibody capable of neutralizing canine interleukin-31 (IL-31), a cytokine involved in itch in dogs, was developed. Lokivetmab (Cytopoint, zoetisus.com) is approved for use in dogs in the United States.61 Injection of lokivetmab reduced the pruritic response for 3 to 4 weeks after injection without adverse effects; itch decreases within 24 to 72 hours (FIGURE 4). The effect on skin lesions was somewhat lower, with roughly half of the dogs achieving 50% reduction in skin lesions.61

The mechanism of action of lokivetmab is different from that of oclacitinib; lokivetmab binds to IL-31 before it binds to its receptor, thereby preventing the main pruritogenic effect of IL-31. Lokivetmab has the advantage of being extremely targeted. It has a very long half-life and can be safely administered with other drugs for symptomatic CAD therapy. The label allows for repeated SC administration at a minimum of 2 mg/kg, monthly, as needed.61 Initial experience in my practice suggests lokivetmab may be best used in atopic dogs with itch but not severe skin inflammation. Furthermore, lokivetmab therapy was successful in some patients that had an insufficient response to oclacitinib.

Antihistamines
H1-antihistamines (hydroxyzine, cetirizine) inhibit the action of histamine by combining with and stabilizing the inactive conformation of the H1 receptor.1,3 The current conclusion of the International Task Force on Canine Atopic Dermatitis is that there is no conclusive evidence of the efficacy of oral type-1 antihistamines for treatment of active and chronic CAD skin lesions.1,3 Veterinarians who wish to use type 1 antihistamines should limit their prescription to drugs with a demonstrable antihistamine effect in dogs (eg, hydroxyzine 2 mg/kg q12h or cetirizine 0.5 to 1.0 mg/kg q24h).1,3 TVP

REFERENCES


3. Reactive treatment in atopic dermatitis means:
   a. Treatment is applied continuously with daily frequency
   b. Treatment is applied intermittently
   c. Treatment is applied twice weekly only on weekends (Saturday, Sunday)
   d. Treatment is applied only when clinical signs develop.

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**CONTINUING EDUCATION**

**Canine Atopic Dermatitis: Updates on Diagnosis and Treatment**

**LEARNING OBJECTIVES**

After reading this article, practitioners should be able to determine which flare factors (or environmental conditions) are responsible for canine atopic dermatitis (CAD), a common chronic relapsing pruritic skin disease of dogs. The readers will recognize the importance of a rational diagnostic and multimodal therapeutic plan that provides the best management of this disease. Atopic dogs need to be evaluated regularly, and treatment plans should be modified for each patient, particularly with every flare of clinical signs.

**TOPIC OVERVIEW**

CAD is a chronic, incurable, but manageable inflammatory and pruritic disease of the skin. Medications used to treat allergic skin disease mask clinical signs but do not change the disease process unless allergen-specific immunotherapy is implemented.

1. Oclacitinib is a novel
   a. Monoclonal antibody
   b. JAK inhibitor
   c. Glucocorticoid
   d. Calcineurin inhibitor

2. Which of the following lesions and sites would be likely to be present in dog affected by flea allergy dermatitis?
   a. Lichenification and scaling in the ventral neck
   b. Recurrent otitis externa
   c. Self-induced alopecia lumbosacral area, tail base, and caudomedial thighs
   d. Erythematous papules in the interdigital areas

3. Reactive treatment in atopic dermatitis means:
   a. Treatment is applied continuously with daily frequency
   b. Treatment is applied intermittently
   c. Treatment is applied twice weekly only on weekends (Saturday, Sunday)
   d. Treatment is applied only when clinical signs develop

**NOTE** Questions online may differ from those here; answers are available once CE test is taken at vetfolio.com/journal-ce. Tests are valid for 2 years from date of approval.
4. A 2-year-old castrated male dog, Leo, presents with nonseasonal signs of erythema, lichenification, and self-induced alopecia around the eyes, lips, concave pinnae, ventral neck, axillae, groin, and elbow folds. You suspect the patient may have CAD. For immediate treatment of acute flare of CAD, you would recommend:
   a. Oclacitinib
   b. Cyclosporine
   c. Cetirizine
   d. Essential fatty acids

5. Which one of the following interventions (treatment or test) should be your next step for Leo?
   a. Skin scrapes for *Sarcoptes* or *Demodex* species
   b. Dietary restriction-provocation test (food trial)
   c. Allergy serum test
   d. Treatment with essential fatty acids

6. Which diet would be the most suitable for a diet trial in a dog with a beef allergy?
   a. Hydrolyzed beef diet
   b. Store-brand chicken-based diet
   c. Kangaroo-based novel protein diet
   d. None of the above

7. Which one of the following lesions and sites would be least likely to be present in a dog affected by classical CAD?
   a. Lichenification in the groin
   b. Self-induced alopecia on the dorsal thorax
   c. Recurrent otitis externa
   d. Erythematous macules, patches, and papules in the axillae

8. Which of the following medications is the most appropriate for a 2-week treatment of acute CAD flare?
   a. Diphenhydramine
   b. Prednisolone
   c. Cyclosporine
   d. Essential fatty acids

9. Lokivetmab is a caninized monoclonal antibody against which cytokine?
   a. Interleukin-2
   b. Interleukin-31
   c. Interleukin-33
   d. Interleukin-5

10. Proactive therapy is treatment that involves:
    a. Low-dose, q12h continuous application of anti-inflammatory therapy to previously affected skin
    b. Application of anti-inflammatory therapy applied only when skin lesions develop
    c. Low-dose, intermittent application of anti-inflammatory therapy to previously affected skin
    d. Low-dose application of anti-inflammatory therapy applied only when skin lesions develop

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