



Domenico Santoro
Purina Endowed
Associate Professor,
Service Chief,
Dermatology
University of Florida
College of Veterinary
Medicine

Pathogenesis of Canine Atopic Dermatitis in Dogs

Canine atopic dermatitis (cAD) is a hereditary, typically pruritic and predominantly T-cell driven inflammatory skin disease involving interplay between skin barrier abnormalities, allergen sensitization and microbial dysbiosis.¹ Although with some geographic differences, cAD is one of the most common inflammatory and pruritic skin diseases in dogs, affecting between 3% to 15% of the canine population.^{2,3} There is no current definitive test to diagnose cAD, therefore a definitive diagnosis involves matching the patient's symptoms with established clinical criteria while excluding any other chronic, pruritic skin diseases.⁴ Common rule-outs include food allergy, flea allergy, sarcoptic or demodectic mange, and cutaneous infections. Ruling out these potential diseases involves strict elimination diet trials, flea combing, skin scraping and cytology.

Allergy testing is not used to diagnose cAD, as atopic dogs may test negative whereas healthy dogs may test positive. Once other causes of clinical signs are ruled out and a clinical diagnosis of cAD is made, allergy testing can be performed to help identify potential allergens to formulate an allergen-specific immunotherapy.

What Causes cAD?

The pathogenesis of cAD is not fully understood, but we know it involves complex interactions between genetic and environmental factors that lead to immune system dysregulation, epidermal barrier dysfunction, and dysbiosis of the microbiome of the skin.

Certain breeds are more predisposed to cAD, including golden retrievers and Labrador retrievers, terriers and German shepherds.^{3,5,6} While researchers are still working on identifying genetic biomarkers of the disease, it has already been clearly established that the disease is a complex polygenetic disorder with different mutations arising in different breeds.

Environmental factors also can play a significant role. Environmental allergens, such as pollen, yeast and molds, can trigger an immune response and atopic dermatitis in genetically susceptible dogs.

In addition, there have been a few studies looking at the environmental conditions of impacted dogs.⁷⁻⁹ It appears that dogs living in an urban environment are more predisposed to developing cAD than dogs living in a more naturalistic environment. Living in a rural environment, living in outdoor facilities and walking through the woods, fields and/or beaches have been found to reduce the incidence of cAD.

Inflammation and Immune Dysfunction

In dogs with atopic dermatitis, we see both

a localized immune response, in the form of skin lesions, and also a generalized immune response. In these dogs, even normal-looking skin shows an increased expression of mast cells, lymphocytes, eosinophils and other hallmarks of Th2 inflammation. We also see an increase in pro-inflammatory mediators that trigger and create a persistent state of inflammation in the skin of these patients.

In addition, there is a decrease in structural protein of the skin barrier as well as changes in the lipidic components of the skin, specifically a deficiency in ceramides and fatty acids. There are alterations of the local cutaneous structure and immunity that may be associated with an increased penetration of allergens and bacteria, leading to secondary microbial infections. We often see staphylococcal ear and skin infections as well as *Malassezia* overgrowth as a cause of ear and skin infections. These infections can further damage the skin barrier, exacerbating the underlying dermatitis.

The Role of the Microbiome

There is a strong relationship between the microbiome of the skin and the health of the skin. In non-lesioned skin of atopic dogs, we see a relative abundance of pathogenic bacteria, such as *Staphylococcus pseudintermedius*, and fewer beneficial bacteria. We also see a lack of diversity in bacterial and fungal species. Although, when the microbiota balance is restored and we see a reduction in local inflammation and amelioration of the disease, it is not clear yet whether the change in the skin microbiome is causing the lesions (or the disease) or is a result of the underlying atopic disease.

Healing the Damage Done by cAD

Unfortunately, cAD is still an incurable disease and, at times, can be very challenging to manage, increasing owner frustration and fatigue. Topical and systemic medications help to ameliorate the clinical signs and directly or indirectly reestablish the skin barrier. Once the patient is no longer pruritic and the skin lesions are no longer inflamed, there are a number of topical moisturizers containing essential fatty acids, ceramides and cholesterol that can be extremely effective in replenishing the skin lipids and

¹ Eisenschenk, M. C., Hensel, P., Saridomichelakis, M. N., et al. (2024). Introduction to the ICADA 2023 canine atopic dermatitis pathogenesis review articles and updated definition. *Veterinary Dermatology*, 35(1), 3-4.

² Hillier, A., & Griffin, C. E. (2001). The ACVD task force on canine atopic dermatitis (I): Incidence and prevalence. *Veterinary Immunology and Immunopathology*, 81(3-4), 147-151.

³ Picco, F., Zini, E., Nett, C., et al. (2008). A prospective study on canine atopic dermatitis and food-induced allergic dermatitis in Switzerland. *Veterinary Dermatology*, 19(3), 150-155.

⁴ Hensel, P., Santoro, D., Favrot, C., et al. (2015). Canine atopic dermatitis: Detailed guidelines for diagnosis and allergen identification. *BMC Veterinary Research*, 11, 196.

⁵ Jaeger, K., Linek, M., Power, H. T., et al. (2010). Breed and site predispositions of dogs with atopic dermatitis: A comparison of five locations in three continents. *Veterinary Dermatology*, 21, 118-122.

⁶ Imai, A., & Santoro, D. (2015). Canine atopic dermatitis reduces the risk of multicentric B cell lymphoma. *Veterinary Record*, 176, 231.

⁷ Harvey, N. D., Shaw, S. C., Craigon, P. J., et al. (2019). Environmental risk factors for canine atopic dermatitis: A retrospective large-scale study in Labrador and golden retrievers. *Veterinary Dermatology*, 30(5), 396-e119.

⁸ Meury, S., Molitor, V., Doherr, M. G., et al. (2011). Role of the environment in the development of canine atopic dermatitis in Labrador and golden retrievers. *Veterinary Dermatology*, 22(4), 327-334.

⁹ Hakanen, E., Lehtimäki, J., Salmela, E., et al. (2018). Urban environment predisposes dogs and their owners to allergic symptoms. *Scientific Reports*, 8(1), 1585.



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rebuilding the skin barrier. Along with moisturizers, topical acidifiers also can be used to lower the pH of the skin to inhibit the proteases and bacteria that can disrupt the skin barrier.

Nutritional support can help repair the skin barrier by increasing both

the quantity and composition of the lipids in the skin. Diets enriched with functional ingredients such as essential fatty acids, zinc and vitamin A have been shown to play a role in repairing the skin barrier. Polyunsaturated fatty acids, including omega-3 and omega-6, are particularly beneficial

for the skin. Increase in omega-3 helps manage inflammation, including the inflammatory response in the skin, while omega-6 helps restore epidermal turnover and differentiation that's crucial for skin barrier function. Together, these nutrients can be used to help manage canine atopic dermatitis.

Planning for Success: Communicating with Clients About Elimination Diet Trials



McKenna Snidow, DVM
Colorado State
University College of
Veterinary Medicine &
Biomedical Sciences

Q When you are presented with a case that you suspect is either canine atopic dermatitis (cAD) or cutaneous adverse food reaction (cAFR), how do you recommend an elimination diet trial?

A Canine atopic dermatitis and cAFR cannot be diagnosed through visual examination alone and cases can present with similar clinical signs. There may be clues that increase our index of suspicion for a cAFR including lack of seasonality, age, or presence of gastrointestinal signs. For example, dogs < 1 year of age or older dogs with non-seasonal pruritus increase our suspicion of cAFR.¹

Before recommending an elimination diet trial, it's important to perform a complete nutritional assessment that not only assesses the animal and diet history, but also the environment and feeding management. I advocate for using a diet history form to help capture a complete diet history. I also discuss with the owner their own perception and goals for their pet. This helps me determine challenges we may face for a successful elimination diet trial and align our goals before proceeding.

I present an elimination diet trial as a diagnostic test that also provides a therapeutic benefit. I start by determining if an elimination diet trial has been performed previously and if it was done properly. If not, I will emphasize to the client that we should proceed with an elimination diet trial and if we do it correctly, we should only need to do it once.

Q How do you talk to clients about the different types of diets available for elimination diet trials?

A The ideal diet for an elimination diet trial is one with documented efficacy, that the dog will find palatable, and the owner is aligned to feed. Diet selection is always done in collaboration with the owner taking into account the dog's nutritional assessment.

When selecting a commercial diet, I recommend therapeutic diet options with quality controls to ensure the diets are not cross-contaminated with additional protein sources that could compromise the success of an elimination diet trial. I explain to owners that over-the-counter diets, even when indicated as limited ingredient, have a risk for protein cross-contamination through manufacturing that can make an elimination diet trial using these foods difficult to interpret.^{2,3}

When recommending a specific diet, I start by explaining the different types of diets we can use for an elimination diet trial including an amino-acid based, hydrolyzed protein, or novel protein diet. When I have a high index of suspicion for a cAFR, I typically start by recommending an amino acid-based diet as this type of diet is the most hypoallergenic option available. Some dogs with severe food allergies may still react even to hydrolyzed proteins so amino acid-based formulas remove this risk as there are no intact or partially hydrolyzed protein for the immune system to recognize. I will also consider repeating an elimination diet trial with an amino acid-based diet in a dog that has failed a hydrolyzed or novel protein diet trial if we still strongly suspect a cAFR.

Some owners may have a desire

to prepare their dog's food at home for an elimination diet trial using a novel protein source. While feeding an unbalanced home prepared diet temporarily to an adult animal for an 8-week elimination diet trial is generally low risk, a complete and balanced diet should be fed to growing dogs to avoid nutritional deficiencies. If I have owners that would like to home cook for an elimination diet trial, regardless of age, I always offer referral to a Board-Certified Veterinary Nutritionist®.

Q Once you've recommended an elimination diet trial, how do you coach the client for success?

A Understanding the home environment and feeding management is key to understanding the challenges and limitations associated with a successful elimination diet trial. It's rarely an emergency to start an elimination diet trial, and I recommend starting when everyone in the household is fully on board. This includes working around vacations and holidays. When small children are in the home, it's important to be realistic about the opportunities for the dog to consume dropped foods or additional treats. Managing the opportunities the dog has for unintentional food items is essential and requires teamwork from the family. Ensuring the dog is not receiving flavored heartworm or flea/tick preventives is also critical as these medications can cause a dog to fail a food trial.

I acknowledge that many owners give treats as part of the dog's daily routine. If treats cannot be eliminated

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during an elimination diet trial, I work with the owners to find suitable options while also explaining any risk that may be associated with these food items. While vegetables and fruits may seem benign, there may be some risk for cross reactivity.⁴ Ideally, I recommend a commercial treat where the protein source aligns with the protein source of the primary diet recommended.

I provide the owner with a handout that contains all the essential details regarding the diet trial. This handout allows owners to document the

start date of the diet trial, any treats given, and potential adverse clinical signs observed. I request that they bring this handout to their follow-up appointment so we can confirm that the elimination diet trial has been conducted successfully.

The final phase of a dietary elimination trial involves reintroducing the original diet or previously consumed ingredients to the patient. This step is crucial for dogs that showed significant improvement during the trial, as it is the only definitive way to confirm a diagnosis of cAFR. Omitting this step risks

misdiagnosis, unnecessary dietary costs, and delayed identification of other pruritic conditions like canine atopic dermatitis.

- 1 Jackson, H. A. (2023). Food allergy in dogs and cats: Current perspectives on etiology, diagnosis, and management. *Journal of the American Veterinary Medical Association*, 261(S1), S23-S29.
- 2 Raditic, D. M., Remillard, R. L., & Tater, K. C. (2011). ELISA testing for common food antigens in four dry dog foods used in dietary elimination trials. *Journal of Animal Physiology and Animal Nutrition*, 95(1), 90-97.
- 3 Pagani E, Soto del Rio Md, Dalmaso A, et al. Cross-contamination in canine and feline dietetic limited-antigen wet diets. *BMC Vet Res*. 2018;14:283. doi: 10.1186/s12917-018-1571-4.
- 4 Fujimura, M., Ohmori, K., Masuda, K., et al. (2002). Oral allergy syndrome induced by tomato in a dog with Japanese cedar (*Cryptomeria japonica*) pollinosis. *Journal of Veterinary Medical Science*, 64(11), 1069-1070.



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Nutrition's Role in Canine Atopic Dermatitis



Emily Cross, DVM, DABVP
Director of Veterinary Communications

As veterinary health care professionals, we frequently encounter patients with pruritus. One of the main causes of this is canine atopic dermatitis (cAD) due to environmental allergens. Clients often express frustration over this condition and the dog experiences mild to severe discomfort. Therefore, it is essential for general practitioners to be highly skilled in diagnosing and managing pruritic conditions.

Typically there is not a “quick fix” for these patients, so it is important to take a structured approach and have good communication with owners about what to expect in the short and long term. The good news is, we have many options to help pruritic patients, and nutrition is a cornerstone of diagnosis and management plans.

Diagnosing cAD requires ruling out other causes of pruritus, including infections, flea allergy dermatitis and cutaneous adverse food reaction (cAFR). Cytology should be performed to assess for bacterial, fungal or parasitic causes, which can be addressed with topical or oral medications. It is also important to ensure a highly effective flea control medication is being used as directed. If the pruritus is year-round, and infection(s) and flea allergy have been ruled out, an elimination diet trial to rule out cAFR must be completed before a presumptive diagnosis of cAD due to environmental allergens, can be made.

To conduct a well-controlled

elimination diet trial to rule out cAFR, the dog must be exclusively fed a hypoallergenic food. Options include a hydrolyzed, amino acid-based or novel protein diet. Treats, supplements and flavored medications must also be considered. An elimination diet trial is considered successful if the dog experiences at least a 50% decrease in pruritus and flares on a diet challenge.

Purina is at the forefront of nutrition for managing pets with adverse food reactions having launched the first truly hypoallergenic extruded diet for dogs with food allergies (Purina® Pro Plan® Veterinary Diets HA Hydrolyzed®) and more recently an amino acid-based diet (Purina® Pro Plan® Veterinary Diets EL Elemental). PPVD EL is the pinnacle in elimination diets – it is formulated with purified amino acids and low-allergen carbohydrate sources to help minimize the risk of an allergic reaction in a sensitized dog.

For the diagnosis phase of an adverse food reaction, EL is my go-to because it makes the diet history easy (not searching for a novel protein) and is highly effective. After diagnosis of adverse food reaction, transition to another diet, like any of the PPVD hydrolyzed diets, offers more variety for the owner and is tolerated well by the majority of food-allergic patients.

If the elimination diet trial does not lead to a significant improvement in pruritus or they do not relapse on dietary challenge, then we have a presumptive diagnosis

of environmental allergy (cAD). Management of these cases is multimodal and nutrition can still play an important role. There are many functional ingredients that can benefit these patients in both foods and supplements, such as omega-3 fatty acids which can help with inflammation and omega-6 fatty acids to help support a healthy skin barrier.

I often recommend a diet that is specifically formulated with specific vitamins, minerals, and fatty acids which may help manage cAD. Purina® Pro Plan® Veterinary Diets DRM Dermatologic Management® contains omega-3 fatty acids to help nutritionally manage dogs with inflammation associated with pruritus. It also has omega-6 fatty acids, vitamin A and zinc to maintain and protect the skin barrier.

Supplements can also play a role, especially in proactive health. Purina® Pro Plan® Veterinary Supplements Skin Care was recently launched and contains collagen, omega-3 fatty acids (EPA+DHA), omega-6 fatty acids (linoleic acid), vitamin E and zinc, all of which can support skin health in dogs with sensitive skin including those with seasonal allergies.

Critical to success is a careful stepwise approach to the diagnostic workup and a multimodal management plan. Implementing these strategies will lead to a significant improvement in most patients but for tougher cases definitely talk to your pet owners about referral to a dermatologist.

Key Takeaways

- Canine atopic dermatitis (cAD) is defined as a hereditary, typically pruritic and predominantly T-cell driven inflammatory skin disease involving interplay among skin barrier abnormalities, allergen sensitization and microbial dysbiosis. There is no definitive test for cAD and diagnosis relies on clinical criteria and exclusion of other chronic skin diseases.
- While cAD is incurable, management includes topical and systemic medications, along with nutritional support to repair the skin barrier and manage inflammation.
- Conducting a well-controlled elimination diet trial is essential for diagnosing cutaneous adverse food reactions (cAFR) and differentiating it from cAD.
- Diets enriched with essential fatty acids, zinc, and vitamins can significantly aid in managing cAD by improving skin health and barrier function.

