# **Integumentary System**

# The Basics of Dermatitis and Atopic Dermatitis in Westies

Updated by Valerie A. Fadok, DVM, PhD

# The Basics of Allergic Dermatitis in Westies

Dermatitis, or inflammation of the skin, is one of the most common medical problems affecting dogs. It has many causes, can take many forms, and can be difficult to diagnose and treat. Many Westie owners become frustrated searching for the underlying cause of the problem and for an effective means to control and cure it. To provide the basis for a discussion of allergic and atopic dermatitis in Westies, this overview describes the basics of dermatitis, causes of dermatitis, and how veterinarians diagnose and treat dermatitis (Figure 2.1).

Skin is a complex organ, consisting of several types of cells with a variety of functions. Many of these cells are involved in the body's natural, protective inflammatory response to stimuli in the environment. In fact, without this inflammatory response, people and dogs would not survive cuts, bruises and other daily traumas, as well as exposure to infectious organisms like bacteria and fungi (Figure 2.2). Common signs of acute inflammation include redness, swelling, heat and pain at the site of injury. One of the most important parts of the skin is its surface layer, the stratum corneum. This layer consists of cells that have lost their nucleus (so they can't divide) but retain important biologic activities. These cells are bathed in protective lipids that help keep water in and organisms and foreign proteins out. While many environmental factors can initiate the inflammatory response in the skin, hereafter referred to as dermatitis, this overview will focus on allergic dermatitis associated with reactions to

food, inhaled substances, parasites, hormones, bacteria and/ or yeast (see **Figure 2.3**).

## Types of Allergic Dermatitis in Dogs

**Urticaria**: Urticaria, also known as hives, is a type of dermatitis that occurs more often in humans and horses than in dogs. Dogs with urticaria have elevated pink or pale patches of skin (called hives or wheals) that can be itchy. When wheals are grouped together, they form larger flat-topped patches called plaques. In a related condition called "angioedema", these patches join together to become moist and swollen; if they develop around the face, the eyes can swell shut, and the muzzle can become very swollen. Urticaria and angioedema are caused by a Type I hypersensitivity reaction that occurs when allergens bind to IgE (allergic antibody) on mast cells. This binding results in the release of histamines and other inflammatory substances that cause dilation of blood vessels. This release accounts for the redness and accumulation of fluid in the skin lesions.

Urticaria and angioedema in dogs can occur in response to food, medications, insect bites, and plant pollens. Some dogs receiving allergy immunotherapy injections can also develop these reactions. Much less common are urticaria lesions that are not associated with an allergic response. These include exposure to sun or extreme high or low temperatures. Treatment of urticaria and angioedema ideally involves avoiding the offending environmental stimulus and medicating the affected animal with epinephrine (if they have anaphylaxis, which is a life-threatening condition), glucocorticoids, and antihistamines. It is important to keep in mind that short-coated dogs, such as English or French





Figures 2.1 - Side and ventral view of a dog with canine atopic dermatitis

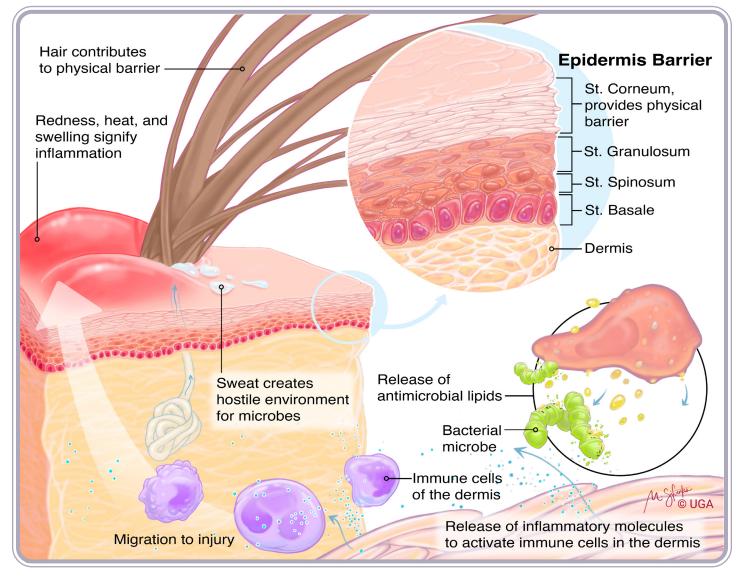


Figure 2.2 -Illustration showing defense mechanisms within the epidermis and dermis

bulldogs, can suddenly develop bacterial skin infections. These infections can resemble urticaria, but require bathing and antibiotics for treatment. Consequently, it is important that owners consult with their veterinarians to ensure that lesions are true hives and not bacterial infections.

Parasitic hypersensitivity: Dogs with this condition develop dermatitis in response to the bites of parasites, such as fleas, ticks and other insects. The most common parasitic allergy is referred to as "flea allergy". Dogs that are sensitive to flea saliva become itchy and can have papules, which are small raised bumps on their backs by their tails, the inner rear thighs, and abdomen. Tick bites can produce dead skin around the bite, ulceration and possibly itching. The scabies mite (Sarcoptes scabiei) can cause intense itching in dogs, as the result of an allergic reaction to the mites and their feces. This mite can be very difficult to find on skin scrapings. Treating for scabies is critical because it can resemble severe

atopic dermatitis. If scabies is not treated, dogs will have a poor response to allergy medications. Dogs also can become allergic to the bites of mosquitoes and Culicoides spp ("nosee-ums"). Dermatitis can also occur in response to intestinal parasites, although this is rare. There does not appear to be any breed predilection for parasitic hypersensitivity.

While the underlying mechanisms responsible for parasitic hypersensitivity dermatitis remain to be identified, the condition is presumed to occur in a manner similar to other allergies, with the body producing allergen-specific IgE and mounting an inflammatory response; there are delayed immunologic reactions as well. Treatment of affected dogs requires parasite control. For dogs with flea allergy, year-round flea control is essential. For acute flare-ups, glucocorticoids or oclacitinib can be given to relieve the itching; antihistamines are rarely effective.

Allergic contact dermatitis: This condition, which also is

# Common Clinical Findings Itching Scratching Hair Loss Thickened and Pigmentation of Skin

called contact allergy or hypersensitivity, differs from atopic dermatitis because the allergen is part of something, such as a plant, medication or fabric that has touched the dog's skin. Fortunately, allergic contact dermatitis is rare in dogs, and unlike humans, they do not seem to be susceptible to poison ivy. When this condition occurs, the skin becomes reddened and develops either small flat lesions that are colored differently from the dog's normal skin, similar larger lesions or, rarely, large fluid filled lesions. Over time, this type of contact dermatitis results in hair loss, greater skin discoloration, and raw or thickened skin. The areas typically affected are the bottoms of paws, the abdomen and the outsides of the ears. In years past, the chemicals and plastics in flea collars were common causes of this type of dermatitis, with lesions appearing around the neck. Fortunately, the newer types of flea collars are far less likely to initiate contact dermatitis. The best documented cause in dogs is a reaction to plants in the Commelinaceae family; these are spiderworts, daylilies, or Tradescantia that grow commonly in the southeastern United States. Dogs that develop contact dermatitis may or may not be itchy, depending on the dog and the allergen.

Allergic contact dermatitis is an example of a Type IV hypersensitivity, which means it is a cell-mediated reaction to an allergen or a delayed type hypersensitivity. Reactions usually occur 48-72 hrs after exposure to the contact allergen, making the offending allergen difficult to identify. The contact allergen interacts with specialized cells in the skin called Langerhan's cells, which then interact with T-lymphocytes. These T-lymphocytes then initiate immune and inflammatory reactions. Because the allergic antibody IgE is not involved, a serum allergy test can't be used to make a diagnosis. Although the precise mechanisms underlying allergic contact dermatitis remain to be determined, this condition is best treated by avoiding the allergen, if it can be identified, and medicating

the dog with drugs that reduce the inflammation, such as glucocorticoids, oclacitinib, or pentoxifylline.

Bacterial hypersensitivity: This type of dermatitis is a condition in which affected dogs are highly sensitive to a species of bacteria known as Staphylococcus (see Figure 2.3). These dogs have very itchy skin. Many dogs develop bacterial infections or pyoderma in the skin when they have allergies, but not all are allergic to the Staphylococcus bacteria. The early lesions of pyoderma are discrete pus-filled lesions that rapidly develop into crusts. They also have epidermal collarettes (circular lesions with a rim of scale). Although mechanisms responsible for bacterial hypersensitivity have yet to be identified, some dogs with recurrent pyodermas make the allergic antibody IgE to Staphylococcus organisms. As a result, anti-Staph IqE can be detected in intradermal skin tests or sometimes in serum allergy tests. Treatment of bacterial hypersensitivity relies on bathing with chlorhexidine shampoos, and the use of antibiotics when necessary. Because of the emergence of antibiotic resistance in canine Staphylococcus pseudintermedius, repetitive antibiotic use is to be avoided. For some dogs, treatment with staphylococcal bacterins can be helpful. Skin barrier repair spot-ons have also been used weekly to help the skin heal itself and to reduce the relapse rate of infections.

Yeast (Malassezia) hypersensitivity: Some dogs will become allergic to yeast organisms on their skin; Westies are particularly prone to this condition and they really suffer. Malassezia hypersensitivity results in intense itchiness in dogs and the infections often recur. Most dogs with recurrent yeast infections in the ears and skin make the allergic antibody IgE to the organism. These dogs require frequent bathing and sometimes treatment with oral antifungal agents. Some dogs will benefit from an allergy vaccine containing Malassezia extract.

Hormonal hypersensitivity: This rare condition is associated with apparent responses to the sex hormones, usually estrogens. Affected animals include intact females and males. With the increased use of topical hormone replacement therapy in humans, this condition can occur in neutered animals as well. Most often, dogs reacting to topical hormone replacement therapy lose hair. Therefore, people using this form of therapy should apply the creams or ointments with gloves and to parts of the body their dog cannot contact. Affected dogs are itchy and may have small red bumps on their rump, inner back of the thighs, and in the genital and anal areas. Enlargement of the vulva and nipples is common. While it currently is not known how the skin becomes inflamed, the condition is successfully treated with neutering.

Canine food hypersensitivity: Food allergies in dogs are also known as adverse food reactions, primarily because some reactions to food are not actually allergic. In fact, pure food allergies, in which the dog's clinical signs are controlled completely with changes in the diet, are relatively rare. It is more common for a dog with atopic dermatitis to have reactions that are triggered by food as well as pollen or other substances. The immunologic basis of food allergy is complex, as some dogs appear to have a Type I hypersensitivity, making IgE antibodies to specific food triggers, while other dogs do not. Therefore, allergy tests can't be used to diagnose a food allergy. Until a test is available for the other immune mechanisms, the best approach is an elimination diet.

Dogs are most commonly allergic to animal proteins in their diets; grain allergies are less common. Affected dogs typically have itchy, flaky skin, though some may develop thickening of the skin, changes in coloring, scales, crusts or redness. The ears, rump, lower legs and groin are the most commonly affected areas. Food allergies can't be differentiated from environmental allergies by looking at the dog. Analysis of

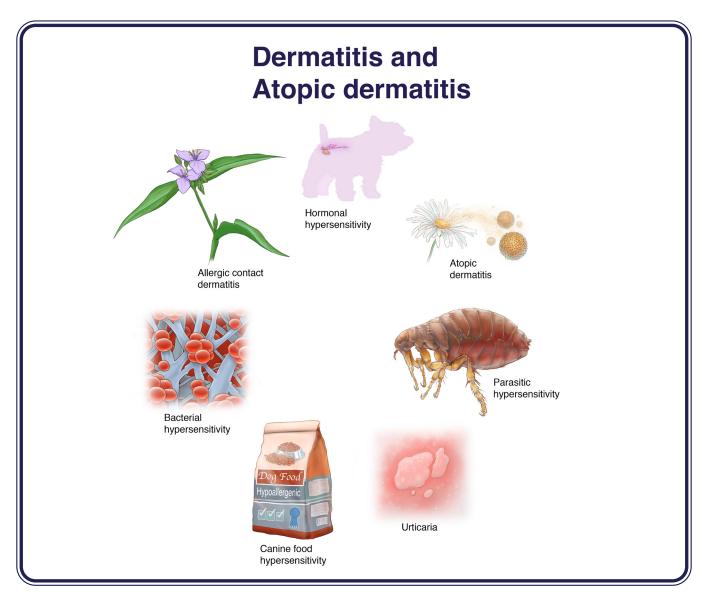


Figure 2.3 - An illustration depicting the most common causes of dermatitis and atopic dermatis

atopic Westies in Switzerland revealed that 50% of them had a combination of food and environmental allergies.

As mentioned above, serum tests cannot be used to predict which foods will be safe to feed. The only reliable way to make a diagnosis is to eliminate specific components of a dog's diet and then add that component back. 'Limited ingredient diets' available over-the-counter are not sufficient as a diagnostic test because they are contaminated with chicken, beef, soy, and other ingredients not listed on the label. Furthermore, these diets are not prepared to the same level of stringency as a veterinary prescription diet. Diet choice should be based on what the dog has eaten before. The best choice is a hydrolyzed diet, preferably one with soy or a protein source that is not made from animal meat. If a veterinary prescription diet is not appropriate, then you can feed a home-cooked diet balanced by a veterinary nutritionist. Presently, 96% food-allergic dogs can be diagnosed with an 8-week food trial; during this trial, no treats, table scraps, rawhides, or flavored medications should be fed without first consulting with the veterinarian. At the end of the 8-week period, if improvement is seen, then diet challenges should be performed to identify the triggers. Once the offending foods are identified, the dog can be transitioned to an overthe counter diet for long term maintenance. The itchiness associated with food allergies can be controlled during the diet trial with oclacintinib or glucocorticoids (steroids).

Atopic dermatitis: This is a lifelong chronic inflammatory disease that tends to progress as dogs get older. A number of factors contribute to the development and the severity of this disease. Although genetics play a role, there are over 40 genes involved. As a result, it is unlikely that this disease could be bred out of dogs. Westies are definitely predisposed to this condition. Several environmental factors also play a role in this disease. Atopic dogs, like people, are susceptible to the effects of air pollution, temperature and humidity changes, and exposure to toxins and irritants such as second-hand smoke. Dogs can become allergic to pollens, molds, dusts, danders, insects, and mites (house dust and storage mites). Some dogs become allergic to Staphylococcus and Malassezia, and some dogs become allergic to proteins in their food, as mentioned above.

Two types of genes are involved in this dermatitis: 1) those associated with the immune system and 2) those involved with the skin barrier. Dogs with atopic dermatitis have a dysregulated immune system, causing immune cells to produce the cytokines (protein messages that cells use to communicate with each other) that cause itchiness and inflammation. As a result, IgE antibodies are generated that are directed against specific allergens. Some cytokines, such

# It is important to control inflammation and itchiness to give other treatments time to work.

as the itch cytokine IL-31, bind directly to nerves to induce itchiness. The other genes of importance cause the top layer of the skin, also known as the skin barrier, to be leaky. As mentioned above, the skin barrier consists of corneocytes (cells) embedded in layers of lipid (fats, particularly ceramides, cholesterol, fatty acids). When functioning normally, this barrier keeps the skin moisturized and prevents penetration by allergens and microbes. Dogs with atopic dermatitis have a disrupted barrier, causing water to leak from the skin and allergens and microbes to be absorbed. Consequently, they have dry and itchy skin. The allergens and microbes activate the defective immune system, resulting in itching and inflammation. Since allergens are absorbed directly through the skin, lesions are most evident on parts of the body that are sparsely haired. Interestingly, there are breed differences in some of the genes affected, with many breeds having a defect in a skin gene called filaggrin; Westies, however, do not!

Another characteristic feature of atopic dermatitis is dysbiosis of the skin and gut. Dysbiosis is an alteration in the microbiome, which is comprised of bacteria, fungi, and viruses. These discoveries have led to research into the use of topical probiotic-like products, as well as probiotics given orally. Fecal microbiota transplants are of great interest, and preliminary findings suggest that this approach could be helpful. For now, it certainly doesn't hurt to give a good probiotic to our dogs orally; however, there is some evidence to show that it is better at preventing or delaying disease rather than treating it. A topical spray containing heat-killed lactobacilli is also showing some promise.

There is no diagnostic test for atopic dermatitis. It is diagnosed based on history and clinical signs, and by ruling out other causes of itch (parasites, infections). Allergy testing is only done if immunotherapy (i.e., allergy vaccine) will be used. It has been demonstrated that response to an allergy vaccine can be just as good with a serum test as with an intradermal test. The key to success with an allergy vaccine is to be patient and give it at least a year to work. In the meantime, other approaches are taken to keep the dog comfortable.

Treatment of Atopic Dermatitis

Treatment of atopic dermatitis requires addressing the disease from multiple perspectives; this is called a multimodal approach (see **Figure 2.4**). Although this disease is lifelong and not curable, it is manageable using a combination of the following five treatments.

First, we avoid what we can avoid. Practically speaking, this means controlling exposure to ectoparasites and known food triggers, Consequently, all dogs with atopic dermatitis should be on good flea control throughout the year, because exposure to fleas makes their disease flare. It is not uncommon for atopic dogs to get other ectoparasites, including scabies mites, so vigilance for ectoparasites is very important. Clearly, there's no way to avoid access to pollens and other allergens.

Second, it is critical to control inflammation and itchiness to

ensure the dog will be comfortable. Medications traditionally used for this include glucocorticoids (steroids), cyclosporine, oclacitinib, and a monoclonal antibody directed against the molecule interleukin 31 (IL-31) causing the itch. When used alone, antihistamines are rarely effective. However, they can help some dogs when used in combination with other medications.

Glucocorticoids (steroids) have been used for many years because they work quickly to reduce itching and inflammation. Nearly every cell in the body has receptors that bind glucocorticoids, hence the wide array of potential side effects. Glucocorticoids affect metabolism, immune function, skin barrier, muscle and ligaments, the gastrointestinal system, and behavior. They are not ideal for long term use. Even in the short term, increased thirst, increased urination with accidents in the house, and behavioral changes (lethargy, aggression) can occur. Dogs requiring glucocorticoids to live comfortably

# Multimodal Approach to Treatment Avoid What We Can Avoid **Optimal Nutrition** Allergy Testing and Immunotherapy Hypoallergenic **Contains** omega 3 **Fatty Acids!** Control Inflammation and Itchiness Bathing and Antibiotics Cyclosporine For treatment of atopic derma

Figure 2.4 - The multimodal approach to treatment of atopic dermatits

should be administered them every other day. The long-acting injectable steroids are not recommended, because the dosage can't be adjusted, if needed. Because glucocorticoids given orally or by injection could have a negative impact on pregnancy, they are not used in pregnant or lactating dogs. Glucocorticoids will interfere with intradermal testing and some serum testing for allergies. As a result, treatment needs to be stopped several weeks before these tests are performed. Glucocorticoids inhibit almost all inflammation, thereby masking the presence of infections.

Cyclosporine (Atopica®, Elanco, CyclavanceTM, Virbac), a drug that reduces inflammation by decreasing the production of many cytokines, has been used for years in atopic dogs. It is given orally daily for 4-6 weeks, then slowly reduced to the frequency that controls the disease. It may need to be administered daily to some affected dogs to achieve best results. The most common side effects of cyclosporine are vomiting and diarrhea (30-40% dogs), but severe infections have occurred in rare instances. To improve the absorption of this drug, it is emulsified in oil; when treated this way, it is called modified cyclosporine. Other formulations of the drug are less effective in dogs, particularly those formulations that are compounded. This medication can be given with a small amount of food if needed; freezing the capsules can help reduce the nausea and vomiting. Cyclosporine has not been studied in breeding, pregnant, or lactating dogs. Cyclosporine does not interfere with intradermal or serum testing for allergies, nor does it inhibit responses to allergy immunotherapy. It is not likely to work well in dogs that have fleas or infections.

Oclacitinib (Apoquel®, Zoetis) is a medication that works by inhibiting an enzyme (Janus kinase 1) that promotes inflammation in atopic dermatitis. In essence, it is a small molecule that enters the dog's cells where it blocks the messages that initiate inflammation and itchiness. It is approved for use in dogs one year of age or older. It is given twice daily for up to 14 days, then once daily. Vomiting and diarrhea are the most common side effects, but these occur in less than 5% of dogs. Very rarely, serious infections have been associated with this medication. Recent research has shown that the chronic use of this medication is not associated with the development of benign tumors or cancers in dogs. Its use has not been studied in breeding, pregnant, or lactating dogs. This medication can work in any type of allergy-induced itching and inflammation. Oclacitinib does not interfere with intradermal or serum testing for allergies, nor does it inhibit responses to allergy immunotherapy. Like cyclosporine, it is not likely to work well in dogs that have fleas or infections.

Cytopoint® (Zoetis) is a biologic injectable treatment for atopic

dermatitis and other allergic skin diseases. It is a monoclonal antibody that binds interleukin 31, and can be used to treat dogs of any age, and dogs taking any other medications. It can also be used in dogs with serious infections (e.g. pneumonia, septicemia), cancer, or other medical conditions for which glucocorticoids, cyclosporine, or oclacitinib would not be used. It is given by injection every 4-8 weeks by a veterinarian. This monoclonal antibody does not interfere with intradermal or serum testing for allergies, and doesn't interfere with responses to allergy immunotherapy. Monoclonal antibodies, while used routinely in human medicine, are relatively new to veterinary medicine. For more information, visit www. cytopoint4dogs.com.

Third, controlling infections is critical to success when caring for atopic dogs. Many affected dogs relapse with infections, which make the disease more severe. The best prevention is regular bathing, particularly given the development of bacterial and yeast resistance to antimicrobial medications. Bathing allergic dogs weekly also helps remove allergens from the skin. A veterinary formulated shampoo containing 2-4% chlorhexidine is best, and shampoos containing lipids (phytosphingosine, ceramides, and/or fatty acids) can prevent the drying effects of baths and help repair the skin barrier. In addition, there are mousses, sprays, and wipes that can be used between baths. If needed, antibiotics or antifungal medications can be administered. If the bacterial infections don't respond, your veterinarian will perform a culture and sensitivity test to determine which antibiotic will actually work. For dogs with yeast infections, oral antifungal agents can be used. Some dogs will get bacterial and yeast infections in their ears. These repeated ear infections can cause permanent changes in the ear canal, setting up a vicious cycle of recurrence. For dogs with recurrent ear infections, prevention with twice weekly ear flushes followed by a topically applied steroid solution can be very helpful.

Fourth, the abnormal skin barrier can be treated with optimal nutrition and by the direct application of lipids to the skin. A high-quality diet having the right balance of omega-6/omega-3 fatty acids is recommended. Over time, these fatty acids can help the skin repair itself. Topical application of lipids (phytosphingosine, ceramides, and/or fatty acids) also is recommended; these can be in the form of shampoos, sprays, foams, and spot-ons. The spot-ons are preferred because they can be applied weekly; Dermoscent<sup>®</sup> makes spot-ons and other products containing essential fatty acids from plant extracts and herbs. Atopivet<sup>®</sup> brand contains important skin lipids that are available in a spot-on, mouse, and a collar.

Last but not least, we recommend allergy testing and allergy

immunotherapy (i.e., allergy vaccine), as this treatment is the only one that can address and abnormal immune response. Any young dog requiring medications year-round is a good candidate for this treatment; older dogs can benefit as well. It is important to recognize that it can take some time for this treatment to be effective; the average response time is about 6-7 months, but in some dogs, a full year is needed. The goal is to reduce the need for medication over the lifetime of the dogs. Following is what to expect:

- 1. Excellent response in 20% of animals. Once immunotherapy is working, these animals do great with flea control and immunotherapy, and they rarely need medication for itching.
- 2. Good response in 40% of animals. If they can be weaned

- off year-round medication, they only might need to be vaccinated in their bad seasons.
- 3. Fair improvement in 20% of animals. These animals do better with immunotherapy but they still need medications to do well. If either modality is stopped, their problems will recur.
- 4. No response in 20% of animals. Unfortunately, we don't why this happens, nor can we predict who will respond before we start. We just have to try it.

Allergy immunotherapy can be done by injection or by a spray or drop under the tongue, making it easier to keep up with it. In general, if this therapy works, it is continued for the life of the animal.

# **Current Research on Atopic/Allergic Dermatitis**

Dreschler Y, Dong C, Clark DE, Kair G. Canine Atopic Dermatitis: Prevalence, Impact, and Management Strategies. Vet Med (Auckl) 2024 Feb 13:15:15-29.

This article reviewed atopic dermatitis, which is a common inflammatory and pruritic allergic skin disease in humans and dogs worldwide. The pathogenesis of atopic dermatitis is multifactorial, immunologically complex, and may involve genetic factors, epidermal barrier dysfunction, microbiome changes, immune dysregulation, and allergic sensitization. Across species, prevalence of atopic dermatitis is on the rise. At present, there is no cure for canine atopic dermatitis. The treatment of this disease is multifaceted and aimed at controlling the pruritus, associated inflammation, and infections, repairing the skin barrier function, and dietary management. This review presents data on prevalence, impact, and complex immunological interactions in atopic dermatitis with a focus on subsequent management of the disease in the canine population. A multimodal approach for management of canine atopic dermatitis to address varying clinical signs and responses to therapies is discussed.

### Marsella R. Advances in our understanding of canine atopic dermatitis. Vet Dermatol 2021 Dec;32(6):547-e151.

Canine atopic dermatitis is a genetically inherited clinical syndrome that encompasses a diversity of mechanisms and can have a variety of triggers. Development of clinical disease is the result of genetic factors and environmental conditions, which shape the resulting immunological response. Clinical disease becomes evident once a threshold of inflammatory response is achieved. Skin barrier impairment plays a role in promoting cutaneous dysbiosis and increased allergen penetration. Keratinocytes shape the response of dendritic cells and subsequent lymphocytic response. It is still unclear whether mutations in skin barrier genes exist in atopic dogs, as they do in humans, or whether the observed alterations are purely secondary to inflammation. A variety of cytokines are proposed as potential biomarkers and treatment targets because they are increased in the serum of atopic dogs when compared to controls, although a correlation between serum levels of these factors and severity of disease is not always present. The main issue with many published studies is that atopic dogs are always only compared to normal controls. Thus, it is unclear whether the changes that we find are truly a signature of canine atopic dermatitis or merely a manifestation of nonspecific broad inflammatory responses. Studies considering comparison with other inflammatory diseases different from canine atopic dermatitis are urgently needed to correctly identify what is specific to this complicated syndrome.

Nuttall TJ, Marsella R, Rosenbaum MR, Gonzales AJ, Fadok VA. Update on pathogenesis, diagnosis, and treatment of atopic dermatitis in dogs. J Am Vet Med Assoc 2019 Jun 1;254(11):1291-1300.

Improved understanding of the pathogenesis of atopic dermatitis in dogs has led to more effective treatment plans, including skin barrier repair and new targeted treatments for management of allergy-associated itch and inflammation. The intent of this review article is to provide an update on the etiologic rationale behind current recommendations that emphasize a multimodal approach for the management of atopic dermatitis in dogs. Increasing knowledge of this complex disease process will help direct future treatment options.

# Acknowledgements

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