
Specific diseases

Topic #1: The Itchy Flaky Dog

Dermatitis Basics and Atopic Dermatitis in Westies

Dermatitis (inflammation of the skin) is one of the most common medical problems in dogs. It has many causes, can take many forms, and is often complicated to diagnose and treat. Many owners experience the frustration of searching for what is causing their Westie to itch and scratch and for effective means to control and cure the problem. This brief overview describes the basics of dermatitis, causes of dermatitis, and how veterinarians diagnose and treat dermatitis. A detailed discussion of atopic (allergic) dermatitis in Westies is emphasized.

Skin is a complex organ, consisting of several types of cells with various jobs and the inflammatory response may involve all or just some of these cells. Inflammation is one of the body's most important protective responses to negative stimuli in its environment. In fact, without the protection offered by inflammation, people and dogs could not survive the constant assault of cuts, bruises and other daily traumas, as well as exposure to infectious organisms like bacteria and fungi. Common signs of acute inflammation are familiar to everyone and include redness, swelling, heat and pain at the site of injury. There are an almost infinite number of things in the environment that the body can perceive as negative stimuli. This paper will discuss the types of dermatitis (inflammation of the skin) associated with reactions to food, inhaled substances, parasites, hormones and bacteria.

One type of dermatitis often seen in humans, but uncommon in dogs is "**urticaria**", also known as hives. Dogs with urticaria have patches of skin (called *wheals*) which are itchy and elevated and may or may not be reddened. These wheals are dry and may group together to form larger flat-topped patches called *plaques*. In a related condition, "**angioedema**", these patches will be moist and appear more swollen. People with severe allergies (like Dr. Robertson!) to some substances like bee venom, will develop urticaria (hives) and angioedema when stung.

Both urticaria and angioedema result from environmental irritants, such as food, medication, insects, and plants, time in the sun or extreme high or low temperatures. The body mounts a defense against the irritant by releasing

histamine from special cells in the skin called *mast cells*. The presence of histamine outside the mast cells triggers a series of events in the body that produce the signs of inflammation.

The treatment of urticaria and angioedema ideally involves avoiding the offending environmental stimulus and medicating with epinephrine or glucocorticoids and possibly anti-histamines.



Canine atopic dermatitis is a more common disorder, affecting at least 10% of dogs, with some breeds more susceptible than others, West Highland White Terriers among them. Canine atopic dermatitis is the dog version of "allergies." Dogs are more likely to experience allergies to things in the environment, such as pollens and dust. When exposed to these allergens, dogs are more

likely to develop itchy red patches on their skin (like hives) than to experience sneezing and stuffy head, like humans. A Westie with severe atopic dermatitis is shown here, in a photograph courtesy of Dr. William Miller, New York State Veterinary College at Cornell University.



Dogs with atopic dermatitis will usually scratch and lick themselves enough to create other skin problems, including hair loss, hair staining from saliva, elevated or puss-filled lesions, dark or particularly rough or thickened patches of skin (*lichenification*). In the photograph at the left (courtesy of Dr. William Miller, New York State Veterinary College at Cornell University) areas of pigmentation and lichenification are seen in the groin and hind legs of this Westie with severe long-standing atopic dermatitis. These problems usually show up on the face, paws, lower legs, elbows and belly. Some dogs may also experience ear infections and have a bad smell to their

skin. Canine atopic dermatitis is considered a Type I hypersensitivity, meaning that the onset of symptoms after exposure to the *allergen* (negative stimulus) is immediate.

The symptoms of atopic dermatitis appear as a result of the inflammatory process. That process is triggered by expression of hypersensitivity (allergies) to particular allergens. Some dogs (like Westies) are genetically programmed to be more sensitive to some things in their environments.

It can be very difficult to understand what is causing atopic dermatitis or even if a dog has it. In the photograph on the left (courtesy of Dr. Tom Manning), a dog with non-specific but atopic/allergic dermatitis is shown, with reddened and itchy lesion under the front legs. The exact mechanism (underlying processes that produce the signs of disease) of atopic dermatitis is not yet known. The current understanding is that when a sensitive dog first inhales, ingests or absorbs the allergen it's sensitive to, its body makes proteins to fight it, called allergen-specific immunoglobulin E (IgE). On subsequent exposures that IgE, mast cells (a specific type of inflammatory cell containing histamine and other pro-inflammatory molecules), along with high numbers of certain white cells called T lymphocytes (T cells), cause the inflammatory response to be produced. Current research is looking into other factors that may play a role in producing the inflammatory response, including other genetically programmed immune problems and skin barrier issues.

We now know that up to 90% of cases of canine atopic dermatitis can be controlled with appropriate and long-term treatment. Treatment includes avoiding contact with the allergen, bathing with medicated shampoo, and giving some combination of fatty acids in the diet, as well as administration of anti-histamines, glucocorticoids and possibly more powerful immunosuppressive drugs like cyclosporin.

Allergic contact dermatitis, or contact hypersensitivity, differs from atopic dermatitis in that the allergen comes from something that has touched the dog's skin, such as a plant, medication or fabric. Allergic contact dermatitis is rare in dogs but when it is present, the skin will be reddened and have small flat lesions that are colored differently from normal skin or similar larger lesions or, rarely, large fluid-filled lesions. Over time, this type of contact dermatitis can produce hair loss, greater discoloration and raw or thickened skin. The areas affected are common contact areas: the bottoms of paws, the belly and the outsides of the ears. The chemical and plastics contained in old style flea collars used to be a common cause of this type of dermatitis, with lesions appearing around the neck, but newer types are less like to produce contact dermatitis around the neck. Patients that develop contact dermatitis may or may not be itchy, and this is very specific both to the contact allergen and to the individual dog.

Allergic contact dermatitis is considered a Type IV hypersensitivity, which means it is a delayed reaction to an allergen and may take a long time to develop (and to eliminate). The contact allergen is thought to be attacked by special skin cells called Langerhan's cells, which then present molecules of the allergen to T cells, which then launch an immune and inflammatory reaction. More research needs to be done to determine the exact mechanism of the disorder. Contact allergic

dermatitis is treated by avoiding the allergen, if it can be identified, and medicating with glucocorticoids.

Dogs can also develop itchy, flaky dermatitis from food allergies; this is known as canine **food hypersensitivity**. This form of dermatitis primarily means itchy skin for dogs, although some may also have many different kinds of lesions or thickening of the skin, changes in coloring, scales, crusts or redness. The ears, rump, lower legs and groin are the most commonly affected areas.

Canine food hypersensitivity is considered a Type I hypersensitivity, producing immediate reactions to ingested allergens. Common foods that produce this type of dermatitis are beef, dairy, chicken, eggs, wheat, corn and soy - all normal ingredients of commercial dog foods, unfortunately. Food additives have not been shown to be a contributor to food allergies. When the offending food ingredient is ingested, abnormalities in the immune system similar to those involved in other hypersensitivities, or in the gastrointestinal tract's barrier allow it to pass into the blood stream rather than be attacked and eliminated. This exposure can lead to mast cells releasing their histamine and causing an inflammatory reaction in the skin. Future research may determine why the skin in particular is so affected.

Like all allergies, determining the allergen and avoiding it is an important aspect of treatment for canine food hypersensitivity. Medications to control itching may also be employed. The other part of treatment is a food change, either to a commercial dog food made with proteins the dog's immune system doesn't have a sensitivity to or to a custom hypoallergenic food, one that doesn't contain the offending allergen, once it is determined. Medication with glucocorticoids has only been completely successful for controlling food hypersensitivity dermatitis in about half of dogs and cats with food allergies.

Parasites, such as fleas, ticks and other insects can also cause dermatitis in sensitive dogs from their bites. This is known as **parasitic hypersensitivity** or more commonly "flea allergy". Dogs with flea saliva sensitivity are itchy and have larger elevated dome-shaped or flat-topped lesions on their backs by their tails, the inner rear thighs and on the belly. Tick bites can produce dead skin around the bite and ulceration and possibly itching as well. 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 complete mechanism of this parasitic hypersensitivity dermatitis is unknown, it is thought to occur in similar fashion to other allergies, with the body producing allergen-specific IgE and mounting an inflammatory response.

Treatment means parasite control. Topical flea and tick preventatives work well. Medication with glucocorticoids may also be administered.

Another rare hypersensitivity is related to levels of sex hormones and is referred to as **hormonal hypersensitivity**. Ninety percent (90%) of cases of this rare type of dermatitis are seen in intact females. Patients are itchy and have small elevated lesions on the rump, inner back of the thighs and in the genital and anal areas. Enlargement of the vulva and nipples is common.

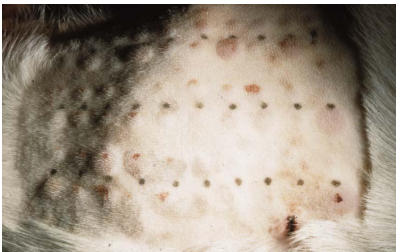
How the skin becomes inflamed is unknown but treatment by neutering is very successful. Administration of testosterone to female patients and estrogen to male patients is another option.

Finally, **bacterial hypersensitivity** is the last type of dermatitis discussed here. Dogs with bacterial hypersensitivity are sensitive to a group of bacteria known as *Staphylococcus*. Their skin is itchy and has discrete pus-filled lesions. Your veterinarian may sometimes refer to this as "pyoderma" – literally translating from medical jargon into "pus-filled skin". Again, the mechanism is not well understood, although it is thought to be Type III hypersensitivity, meaning it is immune system related. These patients can be treated with antibiotics.

Each of the types of dermatitis discussed here involve skin inflammation, often in the form of visible skin disturbances and, especially, itching. Dermatitis is the result of the body's abnormal or overly sensitive defense against irritants or allergens in the environment. Some of these sensitivities are genetically passed on and can be avoided by careful breeding while all can be addressed by avoiding specific allergens.

Treatment

Atopic dermatitis is a difficult condition to treat. The first focus of treatment is usually on alleviating the patient's itching, and then treating secondary infections and inflammation. If your dog is diagnosed with atopic dermatitis, your veterinarian will develop a treatment plan with you that may involve several types of therapy including avoidance of allergens, bathing with medicated shampoo, immunotherapy (allergy shots) and giving some combination of fatty acids, anti-histamines, and glucocorticoids.



Veterinarians can use skin tests to determine which allergens a dog is allergic to. A typical skin test for a dog is shown in the photograph on the left (courtesy of Dr. Tom Manning). The bumps seen here represent positive reactions to small amounts of injected allergens. Fleas, dust mites and pollens

are common allergens. If what's bothering a dog can be determined, avoiding that substance is the best way to treat any allergy. There are many ways to control your dog's exposure to these negative stimuli and they are similar to measures taken for people with allergies, like washing all bedding regularly in hot water, vacuuming all carpets and upholstered furniture, and keeping grass cut short.

Unfortunately, avoiding allergens is not very successful as a sole treatment for dogs with atopic Dermatitis. The allergens can not always be definitively determined and these dogs' systems are so sensitive that other measures are usually needed for relief. However, putting in an effort to avoid known or common allergens does lower the load for the dog and can help in combination with other treatments.

Topical treatments are the next line of defense for the atopic dog. Regular bathing with a shampoo with anti-itch or moisturizing properties may go a long way towards easing your dog's discomfort. Bathing not only removes debris and allergens from contact with the skin, but water itself can be cooling and soothing to inflamed skin.

Other topical treatments include fatty acids and glucocorticoids (discussed below). These substances may also be administered orally. Fatty acids, specifically γ -linolenic acid (found in evening primrose) and eicosapentaenoic acid (fish oil), added to the diet, have been shown to improve the skin condition of atopic canine patients in several studies. It is not known exactly how these fats work and there is debate over the most beneficial dose but it is thought that they are metabolized in the body into substances which have anti-inflammatory properties. Fatty acids are available as diet supplements and can also be included in commercial diets.

Glucocorticoids are drugs which have anti-inflammatory properties. They also act to suppress the immune system (suppress cell activity and antibody production) and in this way go to the source of the problem for atopic patients, rather than just treat the symptoms of inflammation. Prednisone, prednisolone and methylprednisolone are commonly used glucocorticoids. Cyclosporin, another immunosuppressant drug, has also recently been employed for treatment of atopic dogs.

While these drugs can be very effective for treating several disorders, they also carry risks, including pancreatitis, gastrointestinal ulceration and muscle and skin problems. Even dogs on short-term glucocorticoid therapy can experience some side-effects. They will usually drink and urinate and defecate more frequently and may also pant and exhibit behavioral changes. Because these drugs suppress the immune system, dogs being treated with them are more prone to

getting bacterial and other infections. Due to these potential side-effects, glucocorticoids are used when other treatments are not working and then only in the lowest dose necessary.

Another route for treatment of atopic dermatitis is immunotherapy, which uses vaccines made from the offending allergens to desensitize the dog over a period of time. Vaccines are given repeatedly at increasing time intervals, gradually teaching the dog's immune system to tolerate the allergens. Immunotherapy, also known as hyposensitization, has been accepted as a safe and effective treatment for allergies, and has been used for many years on highly allergic people to lower their response to allergens. Hyposensitization therapy ("allergy shots") usually need to be administered regularly (weekly to monthly) for the life of the dog, as the beneficial effects may diminish if injections are stopped.

Finally, it is common to include anti-histamines in a treatment plan for atopic dermatitis. Anti-histamines serve as anti-itch medications. Traditional anti-histamines block skin cells' receptors for histamine, the chemical released by mast cells that can initiate the inflammatory response. Unfortunately, anti-histamines aren't the most effective treatment and may only be effective for 10% of dogs with allergies. Newer versions also block histamine release from mast cells in humans but have not been shown to be particularly effective in dogs and tend to cost more than older anti-histamines. All types of anti-histamines carry the side-effect of mild sedation for the patient.

While properly diagnosing and treating atopic dermatitis is a challenge for veterinarians, the hardest part of treatment is the burden of care it places on the owner. Owner of dogs suffering from allergies need to understand that caring for an atopic dog is a lifelong endeavor which will involve trials of several drugs and doses, bathing, environmental changes and cost. What works for your dog in the winter may not be enough in the spring, when allergens abound. Staying the course on therapies you and your veterinarian agree on will be the biggest determinant in your dog's prognosis for healthy skin.

Current Research on Atopic Dermatitis (Further reading/Scientific background literature and summaries)

Medical research on canine atopic dermatitis over the last few years has focused mainly on a new understanding of the mechanism of the disorder and new treatment options. The theory that atopic dogs have elevated levels of allergen-specific IgE has been challenged continuously and other theories, especially those involving skin cell dynamics, are moving to the forefront. While we still don't have a perfect picture of the mechanism of the disorder, it appears that many more factors are in play than was originally thought. Treatment with fatty

acids has garnered a lot of attention as well. Several studies have also looked into the safety and efficacy of cyclosporine and other drugs.

While many studies have found that hypersensitive dogs have high levels of allergen-specific IgE, other studies have not found a correlation between dogs' general blood level of IgE and skin health (Ledin, et al, 2006). Some researchers started looking into IgG, another immune-related protein. Two recent studies concluded that IgG levels were not a reliable indicator of atopic dermatitis (Hou, et al, 2006; Hou, et al, 2005). While it's still commonly agreed that IgE is playing a role in the skin disorder, it's becoming clear that there may be other factors also involved. As in human AD, it seems that atopic dogs tend to have an imbalance of immune cells and chemicals. Special cell receptors (CCR4), TARC (and immune system chemical), increased leukotriene B4 production, lysosomal enzymes and C3b have each been found in the skin of atopic dogs (Maeda, et, 2004; Maeda, et al, 2005; Breathnach, et, al, 2006; Marsella, et al, 2006). Further research in this area of cell and chemical dynamics continues to be done.

A complete knowledge of the mechanism of atopic dermatitis will lead to the best and most targeted treatments. Current treatments continue to be evaluated for their efficacy and safety while new ones are being developed. Many studies have shown fatty acid supplementation to improve the clinical presentation of the skin of atopic patients (Mueller, et al, 2004; Saevik, et al, 2004; Abba, et al, 2005, Mueller, et al, 2005). Research has focused on trying to understand the mechanism behind the clinical improvement (Gueck, et al, 2004) and determine the best doses and balance of omega-3 and omega-6 fatty acids. One recent study concluded that neither total amount nor ratio was important. For now, fatty acids remain a valuable, but mysterious, aid in the treatment of AD.

Cyclosporine, a systemic immunosuppressive agent, has recently been compared with methylprednisolone (Steffan, et al, 2004). Researchers found that dogs treated with cyclosporine were less likely to relapse or did so after a greater amount of time after stopping treatment. Several other studies have shown cyclosporine to be effective and relatively safe for dogs (Steffan, et al, 2005; Guaguere, et al, 2004; Radowicz, et al, 2005; Burton, et al, 2004, Steffan, et al, 2006). It is thought to have a wider safety margin in dogs than in humans, where regular blood tests are necessary to monitor a patient's health (Steffan, et al, 2004). One study showed 83.9% improvement in dogs' symptoms after about 40 days of treatment (Burton, et al, 2004). The side-effects found have tended to be gastrointestinal in nature. However, all current research recommends the use of cyclosporine for short-term therapy only, up to about six months.

Scientific summaries of a few important references on atopic dermatitis for veterinarians

Pathogenesis:

IgE

Ledin, A., Generation of therapeutic antibody responses against IgE in dogs, an animal species with exceptionally high plasma IgE levels.

- High IgE levels (total serum) did not correlate with health status (atopic, healthy, parasites)
- Immunized 9 high IgE-beagles with new vaccine to reduce level which decreased it by 65% average. May be helpful treatment to look into further.

Marsella, Rosanna, Pilot investigation of a model for canine atopic dermatitis: environmental house dust mite challenge of high-IgE-producing beagles, mite hypersensitive dogs with atopic dermatitis and normal dogs, 2006

This study evaluated the reaction of high-IgE beagles, diagnosed atopic derma dogs and normal dogs to dust mites (sprayed on kennel floor). The dogs were subjected to four exposures of dust mites of increasing concentration and time. Normal and AD dogs were used as controls. The dogs were evaluated for erythema, macules, papules, excoriations, alopecia, lichenification, scaling and pruritis. Biopsies were also taken to evaluate lesions. All high IgE dogs and all AD dogs developed lesions and pruritis after exposure while no normal dogs did. The study only included 6 IgE dogs, 3 AD dogs and 3 normal dogs.

This study was unique in its ability to produce positive APT (atopy patch tests) and dermatitis in all IgE dogs. The experimenters think their results are different from past experiments because of the way the dogs were initially sensitized to dust mites (epicutaneously).

Other important points:

- Humidity level plays a role in the amount of mites in an environment (higher humidity = more mites)
- There may be mutations other than high IgE that facilitate the development of skin lesions
- References Willemse's guidelines for diagnosing atopic dermatitis.

Cell Dynamics

Maeda S., Increase of CC chemokine receptor 4-positive cells in the peripheral CD4 cells in dogs with atopic dermatitis or experimentally sensitized to Japanese cedar pollen.

- "CONCLUSION: The proportion of CCR4+ cells in peripheral blood CD4+ cells was measured in dogs with allergic conditions. The present findings indicate that CCR4+ cells may be involved in the pathogenesis of allergy in dogs as in humans."

Maeda S., Production of a monoclonal antibody to canine thymus and activation-regulated chemokine (TARC) and detection of TARC in lesional skin from dogs with atopic dermatitis.

- "Immunohistochemical analysis using the monoclonal antibody CTA-1 demonstrated that keratinocytes were major TARC producing cells in lesional skin of dogs with AD."

Breathnach, R., Increased leukotriene B4 production, complement C3 conversion and acid hydrolase enzyme concentrations in different leucocyte sub-populations of dogs with atopic dermatitis

This study measured several markers of the inflammatory response in 31 atopic dogs, including 6 Westies. Dogs with AD had all three enzymes measured in increased amounts vs. normal values. C3 to C3b conversion (unlike in humans) and LTB4 concentration were significantly increased in atopic dogs.

- Results indicate a potentially significant role for LTB4 (in early phases), lysosomal enzymes and C3b in the pathogenesis of AD
- Warrents studying using leukotriene antagonists for treatment

Marsella, Rosanna, Cellular and cytokine kinetics after epicutaneous allergen challenge (atopy patch testing) with house dust mites in high-IgE beagles.

This study looked at the cellular and cytokine dynamics of reactions from atopy patch testing with house dust mites in 6 high-IgE beagles. "In human AD, it is currently accepted that imbalances in lymphocyte populations and cytokine production play an important role in the pathogenesis of the disease." Eosinophils should dominate an allergic reaction, not neutrophils.

- Results indicate that there is "an immunological response in which allergens appear to be epicutaneously captured by epidermal Langerhan's cells triggering a progressive infiltration of granulocytes and lymphocytes." (116) Hyperplasia of LC occurred (produce IL12—may be involved in progression to later phases)
- Cytokines present depend on age of lesions: early lesions had proinflammatory cytokines (IL6) and Th2 cytokines (IL13), later lesions

- had an increase in Th1 cytokines (IL18) and increased mRNA expression of TARC
- The authors concluded they had a good model for human and canine AD

Atopic dermatitis references for owners and their veterinarians – For further reading

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