Integumentary System

The Basics of Dermatitis and Atopic Dermatitis in Westies

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Westie Health E-Book

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 atopic (allergic) dermatitis in Westies, this overview describes the basics of dermatitis, causes of dermatitis, and how veterinarians diagnose and treat dermatitis *(Figure 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. Common signs of acute inflammation include redness, swelling, heat and pain at the site of injury. While many things in the environment can initiate the inflammatory response in the skin, hereafter referred to as dermatitis, this overview will focus on dermatitis associated with reactions to food, inhaled substances, parasites, hormones and bacteria.

Types of Allergic Dermatitis in Dogs

Urticaria: Urticaria, also known as hives, is a type of dermatitis that occurs more often in humans than in dogs. Dogs with urticaria have dry, elevated patches of skin (called wheals) that are itchy and that may or may not be reddened. When wheals are group together they form larger flattopped patches called plaques. In a related condition, "angioedema", these patches become moist and swollen. People with severe allergies to substances like bee venom develop urticaria and angioedema when stung. It is a Type I hypersensitivity reaction that occurs when allergies bind to IgE (allergic antibody) on mast cells. This binding results in the release of histamines which cause vasodilation. This accounts for the redness and accumulation of fluid in the skin lesions.

Urticaria and angioedema occur in response to environmental irritants, such as food, medication, insects, and plants, time in the sun or extreme high or low temperatures. Treatment of urticaria and angioedema ideally involves avoiding the

Figures 1 and 2 - Canine atopic dermatitis in Westies *(Photographs courtesy of Dr. William Miller, Cornell University)*

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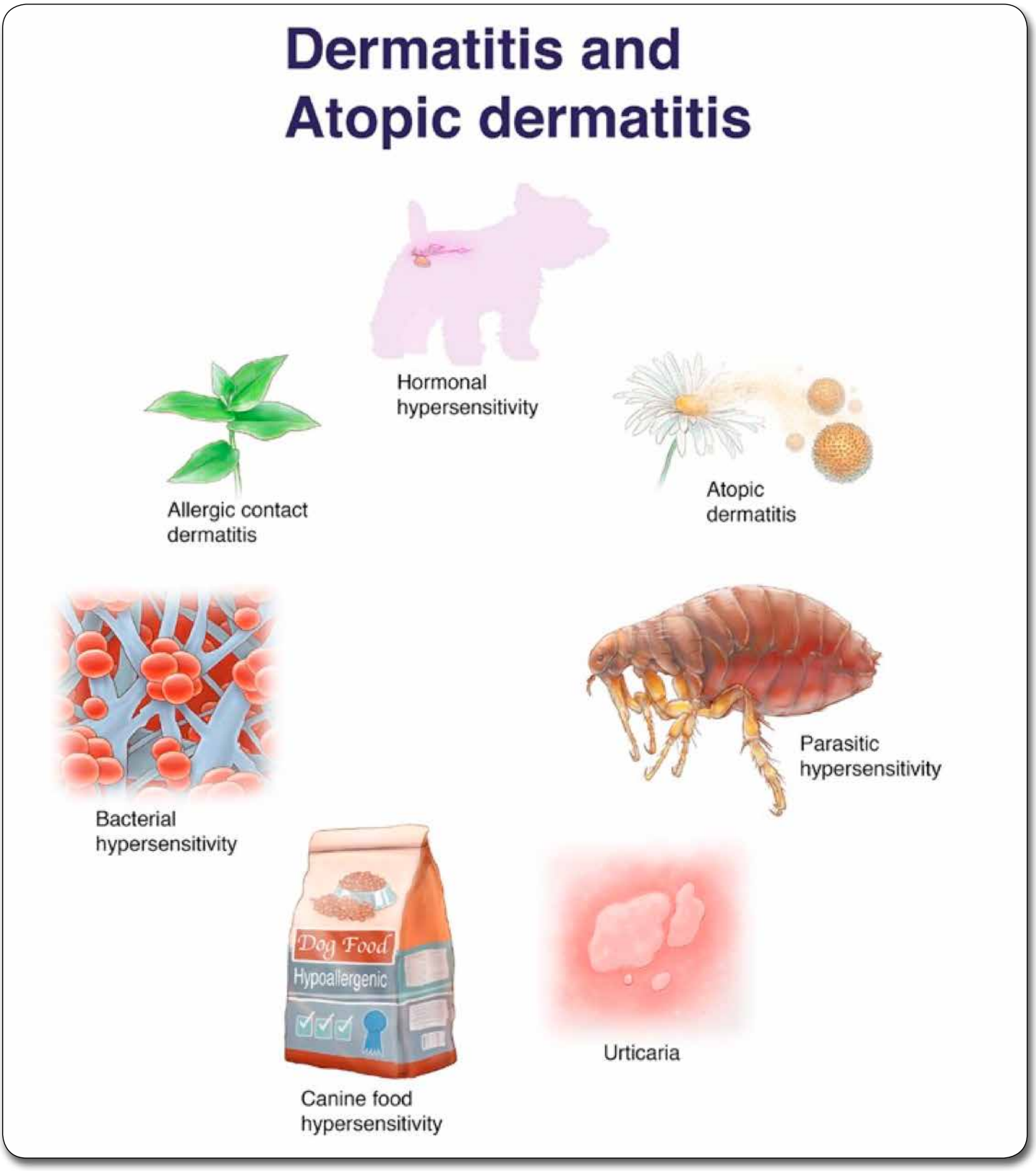

Figure 3 - An illustration depicting the most common causes of dermatitis and atopic dermatitis

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Common Clinical Findings

- Itching
- Scratching
- Hair Loss
- Thickened and Pigmentation of Skin

offending environmental stimulus and medicating the affected animal with epinephrine (anaphylaxis) and glucocorticoids and anti¬histamines. It is important to keep in mind that short coated dogs, such as English or French bulldogs, can suddenly develop bacterial infections in the skin. These infections can resemble urticaria, but require bathing and antibiotics for treatment. Occasionally, Westies can develop inflammatory skin infections than resemble urticaria. 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 have large elevated domeshaped or flattopped lesions on their backs by their tails, the inner rear thighs and abdomen. Tick bites can produce dead skin around the bite and ulceration and possibly itching as well. Dogs also can become allergic to the bites of mosquitoes and Culicoides spp ("no-see-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 allergenspecific 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 itch.

Allergic contact dermatitis: This condition, which also is 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. However, when it 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 fluidfilled 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. 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 occur usually 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 the immune and inflammatory reaction. 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 glucocorticoids, oclacitinib, or pentoxyfylline, drugs that reduce the inflammation.

Bacterial hypersensitivity: This type of dermatitis is a condition in which affected dogs are highly sensitive to a group of bacteria known as Staphylococcus. These dogs have itchy skin, with discrete pusfilled lesions. Based on these lesions, this condition also may be referred to as "pyoderma," which means "pusfilled skin". They also have crusts, and epidermal collarettes

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(circular lesions with a rim of scale). Although mechanisms responsible for bacterial hypersensitivity have yet to be identified, some dogs with recurrent pyodermas make IgE and IgG antibodies to Staphylococcus organisms. Treatment of bacterial hypersensitivity relies on bathing with chlorhexidine shampoos, and the use of antibiotics when necessary. Because of the emergence of methicillin resistance in canine Staphylococcus pseudintermedius, repetitive antibiotic use is to be avoided. For some dogs, treatment with staphylococcal bacterins can be helpful.

Yeast (Malassezia) hypersensitivity: Some dogs will become allergic to the yeast on their skin. 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 IgE (allergic) antibodies to the organism. These dogs require frequent bathing and 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 animal's sex hormones. 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. 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 have small elevated lesions 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 allergy in dogs is also known as adverse food reactions, primarily because some reactions to food are not actually allergic. In fact, pure food allergies, where the dogs' 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 food triggers, while other dogs do not. Some of the same immunologic abnormalities seen with atopic dermatitis are associated with food hypersensitivity in dogs.

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.

There is no diagnostic test for food allergy. There are serum tests that can be done, but they are not accurate enough 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 and then challenge with that component. '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. 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. If a veterinary prescription diet is not appropriate, then a home-cooked diet balanced by a veterinary nutritionist can be fed. Presently, 96% 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 consulting with the veterinarian first. At the end of the 8-week period, if improvement is seen, then diet challenges should be done to identify the triggers. At that point, the dog can be transitioned to an over-the counter diet for long term maintenance. The itchiness associated with food allergies can be controlled during the trial with oclacintinib or glucocorticoids (steroids).

Atopic dermatitis: This is a genetically predisposed hypersensitivity to environmental allergens to which normal dogs do not respond. These allergens include 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. Genomic diagnostic tools are being used to identify the genes associated with the development of atopic dermatitis in dogs.

Two types of genes are involved: 1) those associated with the immune system and 2) those involved with the skin barrier. Dogs with atopic dermatitis have a dysregulated immune system,

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causing immune cells to produce the cytokines (protein messages that cells use to communicate with each other) that underlie the dog's clinical signs. These clinical signs include itchiness and inflammation. As a result, IgE antibodies are developed that are directed against specific allergens. Some of these cytokines, such as IL-31, bind directly to nerves to cause itch.

The other genes of importance cause the top surface of the skin, also known as the skin barrier, to be defective. This 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 the penetration of 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. The allergens and microbes activate the defective immune system, resulting in the itch 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!

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. 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.

> *"It is important to control inflammation and itchiness to give other treatments time to work."*

Second, we recommend allergy testing and immunotherapy (i.e., allergy vaccine), particularly for dogs with clinical signs that occur regardless of the season. Immunotherapy is the only treatment available that changes the abnormal immune response in this lifelong disease. Fortunately, this can be achieved using sublingual immunotherapy (allergy drops) which can be just as effective as injections. However, it is unrealistic to expect that an allergy vaccine will control all clinical signs in all dogs. Use of an allergy vaccine should be considered successful if it reduces the dog's need for daily medication. In many cases, the allergy vaccine will help the medications work better. If an allergy vaccine can be used in young dogs when the immune system is most malleable, it may be needed for only 3-5 years. It is important to recognize, however, that some dogs may require their allergy vaccine for life.

Third, infections can be controlled with bathing and the use of antibiotics and antifungal agents when needed. Bathing is the primary approach to infection control because of the emergence of methicillin resistance (antibiotic resistance) in canine Staphylococcus pseudintermedius. Bathing allergic dogs every week helps remove allergens from the skin. A veterinary formulated shampoo containing 2-4% chlorhexidine is best, and shampoos containing lipids (phytosphingosine, ceramides, fatty acids) can prevent the drying effects of baths and help repair the skin barrier. If needed, antibiotics can be given. For dogs with yeast infections, oral antifungal agents can also be used.

Fourth, the abnormal skin barrier can be repaired by optimal nutrition and by the application of lipids directly to the skin. A high quality diet with 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. Many dogs may require twice weekly baths initially, but the frequency can be reduced to a manageable level (e.g., twice monthly).

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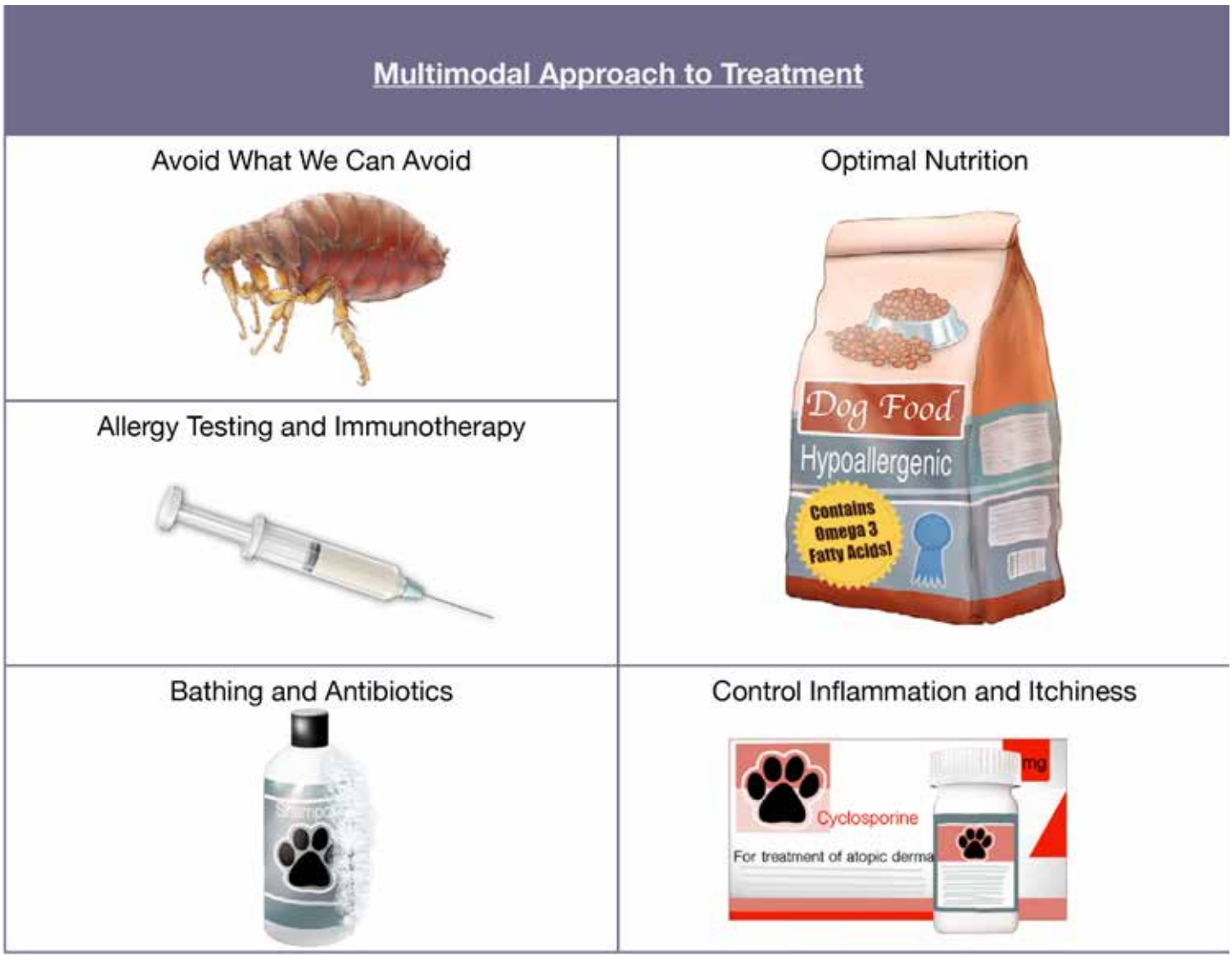
Fifth, it is important to control inflammation and itchiness to give other treatments time to work. Medications traditionally used for this include glucocorticoids (steroids), cyclosporine, oclacitinib, and a monoclonal antibody directed against the molecule (IL-31) underlying the itch. When used alone, antihistamines are rarely effective. However, they can help some dogs when used in combination with other medications.

Glucocorticoids (steroids) have been used traditionally because they work quickly to reduce itch 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 Gastro-Intestinal (GI) 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 be seen. Dogs needing glucocorticoids to live should be administered them every other day. Glucocorticoids given orally or by injection could have a negative impact on pregnancy, so they are not used in pregnant or lactating dogs. Glucocorticoids will interfere with intradermal testing and some serum testing for allergies, so treatment needs to be stopped several weeks before these tests are performed. Glucocorticoids inhibit almost all inflammation, so the presence of infections can be masked.

Cyclosporine (Atopica®, Elanco), a drug that decreases the production of cytokines and that is used in human transplant patients, has been used over the last decade in atopic dogs. It is given orally daily for 4-6 weeks, then slowly reduced to the frequency that controls the disease.



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Some affected dogs may need to take it daily for best effects. The most common side effects are vomiting and diarrhea (30-40% dogs), but severe infections have occurred in rare instances. The efficacy of cyclosporine is dependent on a microemulsion process that makes it more absorbable. Other formulations of the drug may be less effective for dogs, particularly those that are compounded. While this drug should not be given with a full meal, a small amount of food will not inhibit its efficacy. Cyclosporine has not been studied in breeding, pregnant, or lactating dogs. Cyclosporine does not interfere with intradermal or serum testing for allergies. 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 blocks the intracellular signal that occurs after the cytokine binds to its receptor. 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, and can be 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. Its use has not been studied in breeding, pregnant, or lactating dogs. This medication can work in any type of allergic itch and inflammation. Oclacitinib does not does not interfere with intradermal or serum testing for allergies. Like cyclosporine, it is not likely to work well in dogs that have fleas or infections.

Caninized monoclonal antibody directed against canine IL-31 (Cytopoint®, Zoetis), the molecule that initiates itchiness in atopic dermatitis, is a biologic agent rather than a drug. It is approved for use in dogs that have a diagnosis of atopic dermatitis to help reduce itch and inflammation. Because it is a monoclonal antibody and not a drug, it can be used to treat dogs of any age, and dogs being treated with other drugs. 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. Monoclonal antibodies, while used routinely in human medicine, are new to veterinary medicine. For more information, visit www.cytopoint4dogs.com

Current Research on Atopic/Allergic Dermatitis

Due to the clinical impact of atopic/allergic dermatitis in dogs, it is important that both basic and clinical research be performed on these diseases. In this section, three recent articles that provide clinically relevant information about these conditions will be reviewed.

Gonzales AJ, Fleck TJ, Humphrey WR, Galvan BA, Aleo MM, Mahabir SP, Tena JK, Greenwood KG, McCall RB. IL-31- induced pruritus in dogs: a novel experimental model to evaluate anti-pruritic effects of canine therapeutics. Vet Dermatol. 2016 Feb;27(1):34-e10.

Dogs with atopic/allergic dermatitis develop itchy skin that then requires treatment, typically with medications that alter the inflammatory/immune responses to allergens. The purpose of this study was to determine if an experimental model of allergic skin conditions could be developed by administering a specific inflammatory mediator called interleukin-31, that often is present in dogs with naturally-occurring skin diseases. After successfully inducing the itching behaviors that occur in dogs with these diseases using this approach, the investigators then were able to compare changes in the dogs' behaviors after administration of different anti-

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inflammatory compounds (prednisolone, dexamethasone and oclacitinib). As a result of this study, it now is possible to test the efficacy of new compounds in a reproducible way.

Hensel P, Santoro D, Favrot C, Hill P, Griffin C. Canine atopic dermatitis: detailed guidelines for diagnosis and allergen identification. BMC Vet Res. 2015 Aug; 11:196.

This paper is open access and can be freely downloaded. The International Committee for Allergic Diseases in Animals has reviewed the veterinary literature and developed guidelines for the diagnosis of canine atopic dermatitis. The diagnostic approach is to rule out other skin conditions with clinical signs that resemble or overlap with atopic dermatitis, to carefully interpret the history and clinical signs of each dog affected with atopic dermatitis, and to utilize allergy testing with the primary purpose of pursing allergen-specific immunotherapy.

Olivry T, DeBoer D, Favrot C, Jackson HA, Mueller RS, Nuttal T, Prelaud P. Treatment of canine atopic dermatitis: 2015 updated guidelines from the International Committee on Allergic Diseases of Animals (ICADA). BMC Vet Res. 2015 Aug; 11:210.

This paper is open access. It reviews the literature published since the publication of the 2010 guidelines. It summarizes those guidelines and updates them where necessary. Emphasis is on individualizing the program for each dog and using multimodal therapy.

Michels GM, Ramsey DS, Walsh KF, Martinon OM, Mahabir SP, Hoevers JD, Walters RR, Dunham SA. A blinded, randomized, placebo-controlled, dose determination trial of lokivetmab (ZTS-00103289), a caninized, anti-canine IL-31 monoclonal antibody in client owned dogs with atopic dermatitis. Vet Dermatol. 2016 Dec;27(6):478-e129.

This paper describes the first use of a caninzed monoclonal antibody in the treatment of atopic dermatitis. The monoclonal antibody is directed against canine IL-31, a major cytokine that mediates the itch and inflammation seen with AD. When given subcutaneously, dogs experienced significant relief compared to those dogs treated with placebo, and this relief persisted for at least one month.

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