What's New in Atopic Dermatitis?

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As you know, some of our Westies really suffer from atopic dermatitis, a chronic inflammatory disease. We are beginning to understand how complicated this disease can be. As we all know, there are genetic components, but there are major environmental influences as well. These include allergens (pollens, molds, mites, insects, danders), but also air pollutants and changes in temperature and humidity. And the more we learn about the bacteria, yeast, and viruses that live on our skin, the more we understand the role of dysbiosis (the dysregulation of the microbiome in the skin and the gut). So what new information do we have about atopic dermatitis? We can divide it into new ideas about pathogenesis, diagnosis, and treatment options.

Pathogenesis

Microbiome studies. Pathogenesis is a term we use to talk about how a disease develops and progresses, and the factors that influence it. We have learned that dogs with atopic dermatitis have an altered distribution of bacteria, fungi, and viruses on their skin. We call these organisms the skin microbiome, and the changes in it dysbiosis. This shift is what can lead to recurrent infections with staphylococci, as the proportion of pathogenic staphylocci increase. But what about the gut microbiome? An interesting paper published by Dr. Ana Rostaher and colleagues compared the gut microbiome between atopic and healthy dogs *(Rostaher A et al. Animals 2022; 12:2377)*. The bacterial microbes in the gut are significantly less diverse in atopic dogs compared to healthy dogs and the composition has changed. Basically there are fewer and different types of bacteria present compared to healthy dogs. We know from work done in humans that a diverse population of bacteria in the gastrointestinal tract early in life can be protective against food allergy and atopic dermatitis in children.

While this study was done in Beagle dogs, it is possible that many atopic dogs will have these changes in their gut microbiome, although there may be breed-specific differences. That these changes are important is supported by the observation that atopic dogs in Turkey given fecal microbial transplants (FMT) showed significant decreases in itch and skin inflammation, increased skin hydration, and a shift in the gut microbiome toward normal within 28 days of treatment *(Ural K. Ankara Univ Vet Fak Derg 2022; 69:211*). The FMT capsules used are commercially available through Animal Biome in Oakland, California.

It is important to note that both of these studies used very small numbers of dogs (< 10) so more studies will be needed to see if these observations are true of large numbers of atopic dogs.

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Association of behavior changes with atopic dermatitis in dogs. It has been known for some time that human patients with atopic dermatitis have increased tendencies to anxiety, depression, sleep disorders, and in children, attention-deficit disorders. Is there an association between behavior and atopic dermatitis in animals? Dr. Lindsay McAuliffe and colleagues recently studied this question *(McAuliffe LR et al. J Amer Anim Hosp Assoc 2022; 58:4.)*. Eighty-six surveys were completed in the clinic by owners of atopic dogs; in addition, 145 surveys were completed online. After analysis, 141/231 surveys were assessed as valid, and used for statistical analysis. The control population of heatlhy dogs (over 40,000) were from the C-BARQ, the canine behavioral assessment and research questionnaire data base. Atopic dogs compared to healthy dogs were found to be less trainable, showed more stranger- and owner-aggression, more aggression toward familiar dogs, and more fear of other dogs. In addition, they were more sensitive to touch, were more excitable, and more attention-seeking.

These results are important, because they suggest that atopic dogs may have anxiety as do atopic humans. When we as veterinarians are treating them, we want to consider their quality of life, as well as that of their owners. We hope to get good control of atopic dermatitis early in the lives of these dogs, so that we can prevent some undesirable behaviors from becoming hard-wired.

Diagnosis

It is always important to remember that we have no specific test to tell us if a dog has atopic dermatitis or food allergy. We have to make a clinical diagnosis. The purpose of our allergy testing, whether intradermal testing or serum testing, is to pick allergens for immunotherapy. Interpreting tests for food can be very tricky. Having a positive reaction to a food doesn't tell us a dog or cat has an allergy to that food, it tells us the dog makes allergic antibody (IgE) to that food, which may or may not be relevant to the skin or gut disease the pet has. And what makes it more tricky is the fact that not all dogs with food allergy make these allergic antibodies; they have a cell-mediated immune response, especially if they have gastrointestinal signs. What we must keep in mind is that a positive test can be helpful, but a negative test does not rule a food allergy out.

So what is new with allergy testing? Molecular allergology. As of early this year, a new serum allergy test The Pet Allergy Xplorer or PAX (https://nextmune.com/product/pax-serum-test/) is available that tests for IgE to the specific allergenic molecules within the pollens, molds, dusts, danders, mites, insects, and foods. Dr. Thierry Olivry, who many of us know as a talented researcher, is the medical director, and has worked for over a year to develop this test for the veterinary profession. The test is currently available for dogs,but will be available for horses and cats later this year.

It is important to understand the differences between the old way of testing and this new molecular way. In the past, allergy testing, whether by intradermal or by serum, was done with crude allergenic extracts. Let's take house dust mites as an example. To make an allergenic extract, house dust mites are grown in the laboratory, then harvested, ground up, and

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put into a solution. You can understand why we call this a crude preparation. There is a lot of variation from preparation to preparation, and the actual allergen content is 2% or less. For skin testing, that means there are 98% proteins that are extraneous, and that means they might be irritating and cause false positive reactions. With serum testing, using the crude extract could result in false negatives.

As veterinarians and pet owners, we will need to learn that the results from the Nextmune PAX serum test will be quite different from what we have seen in the past. Because we have used crude extracts, we have become accustomed to large numbers of positive results from intradermal testing and serum testing. The PAX test will give us fewer positive results than we are used to. We have learned recently that one reason for false positives in serum testing is the presence of cross-reactive carbohydrate determinants. These are IgE antibodies that bind not to allergenic proteins, but to carbohydrates (sugar groups) that are shared among many pollens and insect allergens. We see results in which our dogs or cats have positive reactions to almost all pollens and insects, which makes it difficult to generate immunotherapy. If we put too many allergens in the immunotherapy we risk increased side effects and less efficacy. With the PAX test, we will have fewer positive reactions, but they will be relevant, allowing us to generate immunotherapy that hopefully will be more successful.

We are learning that the timing of this test may be very important. Positive reactions tend to peak in the late summer or early fall, after a dog or cat has been exposed to multiple pollens. Some of these dogs or cats will have negative tests in the winter.

Treatment

Most of us are aware of medications such as Apoquel®, Cytopoint™, Atopica™, glucocorticoids, and allergy immunotherapy. Some of the new ideas about treatment include diets specifically formulated for atopic dogs, new oral supplements, and topical treatments that repair the skin barrier and help improve the quality of the skin and coat. They often help our medications and allergy immunotherapy work better.

Diet. Nutrition is not new in the treatment of skin disease. What is new is the reformulation of diets specifically to support the atopic dog. These are not meant as diets for food trials; they are meant to support the skin barrier and immune system of atopic dogs. These include Hill's Complete®, Royal Canin Skin Support®, and Purina DRM®. While Hill's will promote Complete® as a diet appropriate for a diet trial, I do not recommend it. Dogs who are allergic to chicken and/or egg may not tolerate this diet.

Nutritional supplements. Two nutritional supplements have shown some promise with atopic dogs. The goal is to use these medications to help our other therapies work better; they may not be sufficient for sole control. One product is called Redonyl® Ultra from Dechra and is available without a prescription. The active ingredients are palmitoylethanolamide (PEA), as well as omega-3 and omega-6 fatty acids. This supplement has been shown to provide some control of itch and inflammation in dogs with mild to moderate atopic dermatitis; however, it is best used with other medications. Published papers are limited in number, but there is some evidence. Another oral product is Dermaquin® from Nutramax. This product contains hardy kiwi and beta-glucan to provide anti-inflammatory activity and omega-3 and omega-6 fatty acids for skin barrier repair. This product has also been shown to improve atopic dermatitis in dogs with mild to moderate atopic dermatitis. The ideal use of these nutritional supplements in dogs with moderate to severe atopic dermatitis is as support for the primary therapy to get the maximal control of the disease. We promote multimodal therapy for our atopic dogs: control itch and inflammation, use ectoparasite control to avoid fleas and other parasites, control infections with bathing and skin barrier repair, and allergy immunotherapy. Using supplements like Redonyl® or Dermaquin® to support the skin barrier can help our anti-inflammatory therapies work better.

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Topical lipids for skin barrier repair can be incredibly helpful. They improve the quality of the coat and skin and help reduce the number of relapses of bacterial skin infections. The use of these products can assist in the reduction of itch and recent evidence suggests they can help our anti-inflammatory medications work better. Dermoscent® laboratories have studied the topical use of essential oils for 2 decades. They have developed a line of products whose efficacy is supported by publications and presentations at major dermatology meetings throughout the world. There are 3 major lines, the Dermoscent® line, the PYOclean® and PYOspot® line, and the ATOP-7® line. These products contain essential oils from herbs and grains, as well as plant extracts chosen for their anti-inflammatory and antimicrobial activity. There are shampoos, sprays, mousses, wipes, and otic products. I am particularly fond of the spot-ons, as they are easy for us as pet owners to use. The products are applied once weekly for 4-8 weeks, then as needed. Dermoscent Essential 6 spot-on is especially helpful for dogs with dry flaky itchy skin; it can help reduce the recurrence of skin infections. PYOclean® shampoo and spray have been shown to be as effective as chlorhexidine in the treatment of bacterial and yeast infections; PYOspot® spot-on when used weekly can reduce the number of relapses of skin infections an allergic dog gets in a year. This reduction allows us to use fewer antibiotics, and avoid resistant infections. The use of ATOP-7 spot-on can help extend the duration of Cytopoint efficacy in atopic dogs. These studies are small and need repeating, but they are very encouraging.

Atopivet® is a line of products containing sphingolipids and hyaluronic acid (https://www.dechra-us.com/Files/Files/SupportMaterialDownloads/US/02SD-ATO22025-0822-Atopivet-Detailer-final-2.pdf). These are available from Dechra as a spot-on, a mouse, and a collar. The collar is designed to allow the dispersal of the lipid and the hyaluronic acid over the body. Both of my atopic Westies have started wearing these collars, and I am seeing some improvement in skin quality. One publication supports their use as well; Dr Rosanna Marsella showed that twice weekly application of the spot-on resulted in reduced itch and inflammation in atopic beagles with allergy to house dust mite *(Marsella R et al. BMC Vet Res 2020; 16:92)*.

Topical heat-treated probiotic. The last novel treatment idea is the use of heat-killed lactobacilli to help correct the dysbiosis associated with atopic dermatitis. Most of us are familiar with lactobacilli as components of some of the probiotics we take. Two species of Lactobacillus, L. rhamnosus and L. reuteri are heat-killed in a process called tyndallization. This process kills the bacteria, but allows the cells to remain intact. These bacteria have the ability to stimulate the growth of beneficial bacteria and inhibit the growth of pathogens. The other ingredients have some anti-inflammatory activity as well as moisturizing activity. The product is called LinkSkin, and is available through Nextmune. Dr. Domenico Santoro has published one paper showing its ability to reduce itch and inflammation in atopic dogs. Clearly more evidence is needed, but the approach is biologic rather than pharmacologic, and offers some promise.