

DVM^{TO}DVM BULLETIN

SPOTLIGHT ON CANINE ATOPIC DERMATITIS

SPRING 2016

Atopic Beagle colony helps researchers

University of Florida research offers insights into canine and human allergic disease

Differential diagnosis: Atopic dermatitis vs allergic pruritus

Michele R. Rosenbaum, VMD, DACVD, shares what she's learned in her practice

Upcoming meetings

Don't miss these opportunities to meet fellow veterinarians, earn CE credit, and learn about recent breakthroughs

Recent breakthroughs in understanding atopic dermatitis may revolutionize treatment

Dogs with atopic dermatitis are seen all too commonly in every veterinary practice. Among dogs seen by veterinarians, 17%, or 8.5 million, suffer from pruritus. Of these, 1.3 million suffer from either seasonal or chronic atopic dermatitis.¹

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Current and emerging treatments for atopic dermatitis

Traditionally, glucocorticoids, cyclosporine and immunotherapy have been the mainstay treatments for atopic dermatitis.² Though effective, these treatments have serious limitations. Glucocorticoids carry safety and side effect baggage, as does cyclosporine—which has the additional limitation of relatively slow efficacy.^{2,3} Immunotherapy is effective in only about 60% of dogs and may take up to a year to show results.² The recent introduction of **APOQUEL**[®] (oclocitinib tablet), a JAK-1

and JAK-3 inhibitor indicated for both atopic dermatitis and allergic itch caused by fleas, food and contact allergy, has expanded the armamentarium for veterinarians treating these difficult conditions.⁴ Because of its highly targeted mechanism of action, APOQUEL provides fast pruritus relief with a smaller side-effect burden and fewer long-term safety concerns compared with corticosteroids and cyclosporines.⁴

As our understanding of this challenging and complex disorder evolves, **fresh insights into the pathobiology of canine atopic dermatitis** continue to spur the creation of novel treatments with the potential to **interrupt the itch cycle** and improve the lives of atopic dogs and their owners.⁵

Atopic dermatitis is more complex than once thought

Historically, canine atopy was characterized as a type I hypersensitivity reaction to inhaled allergens, mediated by the binding of allergen-specific IgE antibodies to cutaneous mast cells.⁵

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IMPORTANT SAFETY INFORMATION:

Do not use APOQUEL in dogs less than 12 months of age or those with serious infections. APOQUEL may increase the chances of developing serious infections, and may cause existing parasitic skin infestations or pre-existing cancers to get worse. APOQUEL has not been tested in dogs receiving some

medications including some commonly used to treat skin conditions such as corticosteroids and cyclosporines. Do not use in breeding, pregnant, or lactating dogs. Most common side effects are vomiting and diarrhea. APOQUEL has been used safely with many common medications including parasiticides, antibiotics and vaccines.



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However, recent findings suggest that the **pathophysiology of atopic dermatitis is complex** and goes beyond IgE activation.⁵

Atopic dogs appear to have **dysfunctional skin barriers that allow excess permeability**. The cycle of itch begins when allergens cross this permeable epidermal barrier and are presented to immune mediators. Once exposed, immune cells in the skin are sensitized, primed to rapidly respond to the allergen again.⁵ Future exposures trigger rapid T-cell activation and release of **pruritogenic and pro-inflammatory cytokines such as interleukin (IL)-31**. These cytokines bind to receptors on the surface of neurons, starting the itch cycle.^{5,6}

The itch cycle—the self-perpetuating culprit behind refractory itch

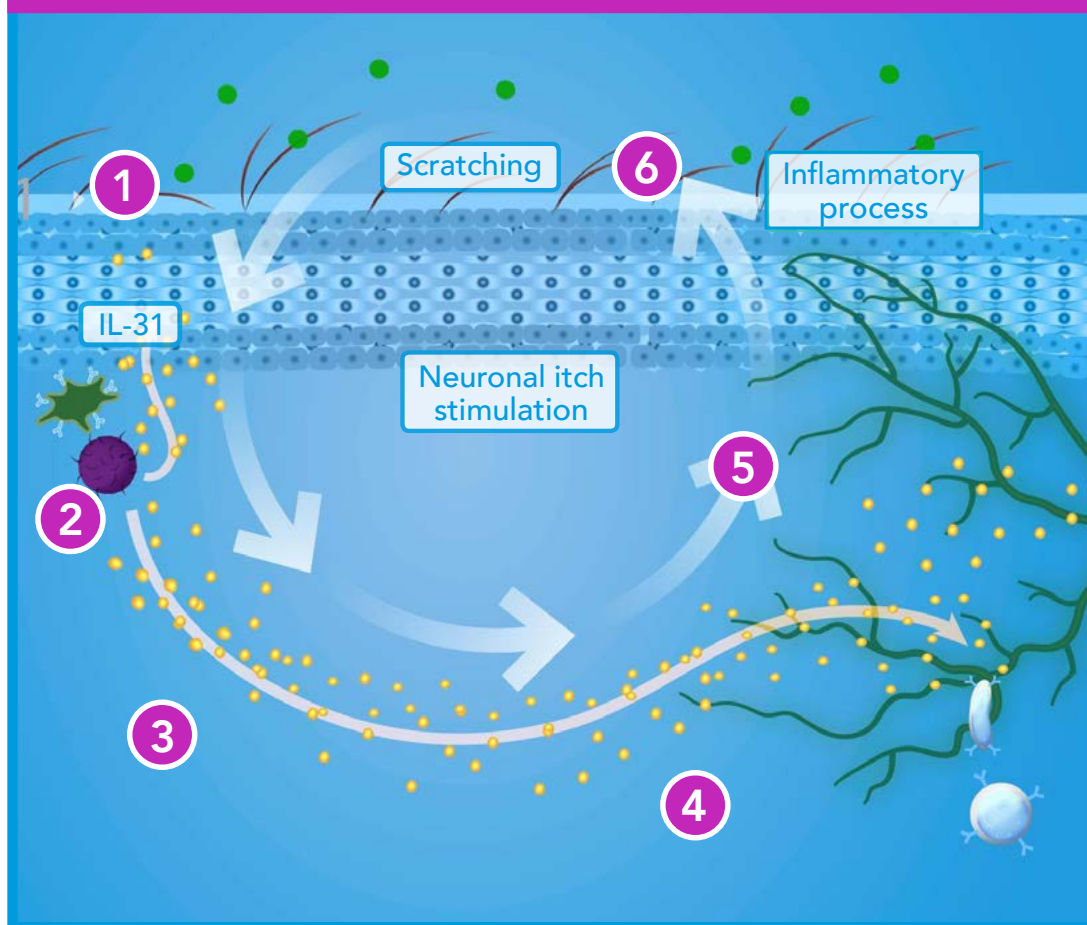
The “itch cycle” is a self-reinforcing cascade of events that begins with initial neuronal itch stimulation, immune-mediated inflammation and resultant itch/scratching.⁵

Highly targeted treatments may halt the itch cycle while minimizing collateral immunosuppression

Recently, **targeted treatments have shown great promise** in inhibiting specific cellular processes, thereby halting the itch cycle without causing excessive side effects or immunosuppression. For example, targeting the JAK enzymes released by activation of pruritogenic cytokines can **block itch with far less interference in immune processes**.⁷

Current research focuses on even more specific upstream targets: cytokines themselves.^{5,6} **Monoclonal antibodies (mAbs) show great promise in neutralizing pruritogenic and pro-inflammatory cytokines such as IL-31**, preventing their activity and release of JAKs. This precisely targeted antibody therapy can help to greatly attenuate the neuronal itch sensation. Reducing itch decreases scratching and the resultant skin damage, ultimately helping to **halt the cycle of itch so healing can take place**.^{6,8}

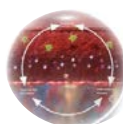
THE ITCH CYCLE



- 1 EXPOSURE** Allergens enter via the skin, often due to a disturbed or dysfunctional epidermal barrier⁵
- 2 SENSITIZATION** Allergens are detected by the immune system and presented to immune cells, priming the immune system to respond to the allergens in the future⁵
- 3 CYTOKINE RELEASE** Further exposures to the allergen trigger T-cell activation and the release of itch- and inflammation-causing cytokines, such as IL-31^{5,6}
- 4 JAK ENZYME RELEASE** These cytokines, such as IL-31, send an itch-promoting signal from the nerve to the brain via signal transduction pathways such as JAK-STAT⁶
- 5 ITCH/SCRATCH STIMULATION** Itch stimulation in the nerves of the skin triggers scratching, which, combined with cytokine-induced inflammation, further weakens the epidermal barrier⁵
- 6 EPIDERMAL DAMAGE** The weakened barrier makes the dog more vulnerable to transdermal allergens, thus restarting and perpetuating the cycle of itch⁵



To learn more about the causes of canine dermatitis, [click here](#).



To learn more about the neuronal pathways that stimulate pruritus in dogs, [click here](#).

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its role in canine pruritus and naturally occurring canine atopic dermatitis. *Vet Dermatol*. 2013;24:48-53.e11-2. doi:10.1111/j.1365-3164.2012.01098.x. 7. Gonzales A, Bowman J, Fici G, Zhang M, Mann D, Mitton-Fry IM. Oclacitinib (Apoquel®) is a novel Janus kinase inhibitor with activity against cytokines involved in allergy. *J Vet Pharmacol Therap*. 2014;37:317-324. doi:10.1111/jvp.12101. 8. Olivry T, Bainbridge G. Clinician's Brief. Advances in veterinary medicine: therapeutic monoclonal antibodies for companion animals. March 2015. Available at: http://www.cliniciansbrief.com/sites/default/files/attachments/ZoetisCN_Mar_FNL.pdf. Accessed January 6, 2016.



CANINE  CURIOSITIES

Colony of dogs with atopic dermatitis facilitates clinical research into canine and pediatric atopy



A colony of atopic Beagles has allowed Dr Marsella's team to test promising drugs for use in both pets and children afflicted by atopic dermatitis

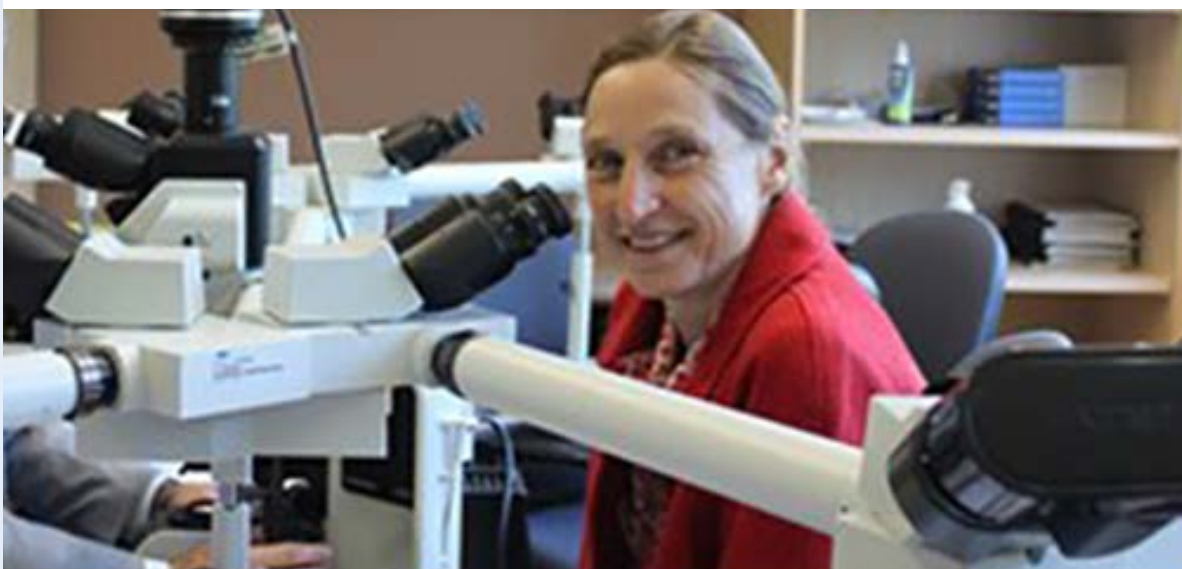
Rosanna Marsella, DVM, DACVD, has a special interest in the causes of and treatments for atopic dermatitis, which affects both dogs and children. To help with her research into this topic, she has developed an innovative way to study the immunology of allergic skin diseases.

dogs are naturally susceptible to atopic dermatitis and are genetically more similar to humans than mice are. Dr Marsella's atopic Beagles have allowed her team to test promising drugs for use in both pets and children afflicted by atopic dermatitis. In addition, the dogs have helped

researchers investigate the use of beneficial bacteria to minimize the development of allergies, and have also served as a model for the study of peanut allergy. One of Dr Marsella's ultimate goals is to use her findings to help create a vaccine for children suffering from food allergies.

Dr Marsella plans to expand her research efforts into allergic skin

Dr Rosanna Marsella in the newly renovated dermatology laboratory at the University of Florida College of Veterinary Medicine



Dr Marsella hopes her research will help lead to a vaccine for children with food allergies.

Dr Marsella, a Professor in the Department of Dermatology at the University of Florida College of Medicine, notes, "Dogs naturally develop atopic dermatitis that is clinically and immunologically identical to the human condition, thus constituting the ideal species for an animal model that can help identify ways to prevent or halt the progression of the disease."

Using a colony of Beagles with naturally occurring atopic dermatitis, Dr Marsella was able to develop and validate just such an animal model. This is the only model of its kind currently being used in research. The Beagle model is a major improvement over the mouse model, because

disease in both dogs and children through a collaborative long-term effort with the University of Florida College of Medicine. This collaboration will increase overall understanding of mechanisms of atopy and identify safe new treatments for atopic disease, improving the quality of life for affected patients.

To learn more about Dr Marsella's experimental models and how her research may apply to treatment of dogs with atopic dermatitis, read [this article in the Journal of Investigative Dermatology](#).

Differential diagnosis: Atopic dermatitis vs allergic pruritus

What key indicators should make a veterinarian suspect atopic dermatitis (AD) in a pruritic dog?

Diagnosis should start with signalment and history. AD usually begins between 6 months and 3 years of age, may be seasonal (pollens) or non-seasonal (dust mites and molds), and often worsens over time. AD is usually very steroid-responsive, absent significant skin infection, so it's a good idea to ask about response to previous steroid treatment. Examine for erythema, alopecia and excoriations, especially on the face, medial pinna, medial elbows and forelimbs, paws, caudal metacarpal/tarsal regions, axilla and groin.

In severe or chronic cases, look for hyperpigmentation and lichenification.

What steps should be taken to confirm the diagnosis?

Always start with a basic derm database, with skin scrapings and skin and ear cytology, as appropriate. Start an anti-parasitic trial and, if infection is present, use systemic and topical antibiotics and/or antifungals (Steps 1 and 2). If pruritus persists after elimination of parasites or infection, institute a strict food trial for up to 8 weeks (Step 3). If the itch continues, especially if it is steroid-responsive, diagnosis of AD can be made (Step 4).

How can a veterinarian address a dog's clinical signs while confirming the AD diagnosis?

Many veterinarians have traditionally prescribed corticosteroids in a tapering dose, but this can cause side effects such as excessive urination, drinking, panting, weight gain and lethargy. In dogs over 12 months of age, I now

recommend APOQUEL[®], (oclacitinib tablet) which is highly effective at controlling allergic itch and works within 24 hours, to keep the dog comfortable during the 4 steps of diagnosis.

Towards the end of each diagnostic trial, APOQUEL can be discontinued and remaining itch can be assessed in 24-48 hours. Using APOQUEL this way gives relief to both the patient and the owner while the veterinarian searches for the underlying cause of the itch.



Michele R. Rosenbaum, VMD, DACVD, Senior Veterinary Dermatologist, East Region, Zoetis
Rochester, NY

FOUR STEPS TO DIAGNOSING ATOPIC DERMATITIS

Treat/rule out underlying causes first, in this order:



Once other causes have been treated/ruled out, diagnose:



4 **Atopic dermatitis**

Do you have any tips on how to talk to owners about the prognosis for atopic dermatitis?

Owners should know that the "C" word we use with AD is "Control," not "Cure." It's about working with owners to find an appropriate, individualized maintenance regimen to maximize control of itch and infection while minimizing side effects.

FOR FURTHER EXPLORATION

Interested in learning more about the pathophysiologic mechanisms of the itch cycle in canine atopic dermatitis? [Click here for an informative article that clarifies our current understanding of the underlying disease processes](#) (JAVMA subscription required):

Marsella R, Sousa CA, Gonzales AJ, Fadok VA. Current understanding of the pathophysiologic mechanisms of canine atopic dermatitis. *JAVMA*. 2012;241(2):194-207. doi:10.2460/javma.241.2.194.

UPCOMING  EVENTS

Don't miss these important veterinary meetings

THE 8TH WORLD CONGRESS OF VETERINARY DERMATOLOGY (WCVD)

May 31-June 4, 2016 in Bordeaux, France

The first WCVD in 4 years, the conference will feature representation from many of the major veterinary organizations from around the world. The congress will be organized around six main themes:

- + Genetics and genomics of the skin and skin diseases
- + The living skin—skin biology and ecosystem
- + Infectious diseases
- + Skin as an immune organ—allergy
- + New trends in therapy
- + New diagnostic approaches



Don't miss these Zoetis-sponsored events:

Three important oral presentations and 3 posters, including results of laboratory and clinical trials on a new caninized anti-IL-31 monoclonal antibody that helps reduce the signs of atopic dermatitis in dogs.

A 2-hour symposium, The Next Horizon: Targeted Antibody Therapy for Canine Allergic Skin Disease, featuring speakers Dr Thierry Olivry, Dr Andrea Gonzales, and Dr Doug DeBoer (June 1).

To learn more or register, visit the WCVD website at www.vetdermbordeaux.com.

THE AMERICAN COLLEGE OF VETERINARY INTERNAL MEDICINE (ACVIM) 2016 FORUM

June 8-11, 2016 at the Colorado Convention Center in Denver, Colorado

The ACVIM Forum is a continuing education meeting, offering current information and research on five ACVIM specialties:

- + Cardiology
- + Small animal internal medicine
- + Oncology
- + Large animal internal medicine
- + Neurology



The 2016 ACVIM Forum is expected to have more than 3,000 attendees and offer over 460 hours of CE credit.

Don't miss this Zoetis-sponsored event:

Antibody Therapy: The Next Horizon in Canine Atopic Dermatitis, presented by Dr Philip Bergman and Dr Laura Stokking (Thursday June 9, 7:30 – 9:30 PM)

To learn more about the ACVIM forum or register, visit www.acvim.org.

