**Another Itchy Dog**

New Understanding of the Pathophysiology of Canine Allergic Disease

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**Skin Diseases are Common**

2011: VPI Pet Insurance¹

1. Ear Infections
2. Skin Allergies
3. Skin Infections

8.2 million dogs with allergic disease ²

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**Rule Out Infectious Causes of Itching Prior to Diagnosing Allergy**

Infectious Diseases
- Ectoparasites
  - Fleas
  - Sarcoptes
  - Demodex
- Bacterial
  - Staphylococcal pyoderma
- Fungal
  - Malassezia Dermatitis
  - Dermatophytosis

Allergic Diseases
- Flea Allergy Dermatitis
- Food Allergy Dermatitis
- Atopic Dermatitis
Severe itching for 3 months, lives in rural wooded area, no prior history of skin disease, owner found dead fox on property

Homer: 9 yo MN Mixed Breed

- **Scabies**

Gertrude: 2 yo FS English Bulldog

- **Generalized Demodicosis w/ Secondary Pyoderma**

Louise: 5 yo FS Pit Bull X

- **Superficial pyoderma**
Corky: 3 yo MN W Highland White Terrier

- 7 year history of increasingly severe non-seasonal itching
- Malassezia dermatitis

We are Focusing on Allergic Disease

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Allergic Diseases
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Buttons: 8 yo FS Poodle Mix

- Severe itching over back end since camping trip in late fall,
  stopped flea preventative 2 months ago
- Flea Allergy Dermatitis
  (with secondary pyoderma)
Misty: 6 yo FS Cocker Spaniel mix

Food Allergy
(with secondary Malassezia dermatitis, otitis)

Reuben: 2 yo MN Shepherd-Collie mix

Atopic Dermatitis
(with secondary Malassezia pododermatitis)

Chronic Itch Takes a Toll On:

1. Pet’s quality of life
2. Human-animal bond
3. Pet owner’s trust of veterinarian
The Emotional Rollercoaster of Atopic Dermatitis is as Big a Problem as the Dermatitis Itself

Owner Notices Itching

Initial Concern & Sympathy

Frustration

Guilt

Optimism and Frustration with Info Search

No Effective Solution

If Find Effective Solution

Alternating Hope and Disappointment While Trying Solutions

Why should we care about the new pathophysiology of allergic disease?

1. Understanding how disease works provides basis for optimal therapy
2. Hope for a targeted therapy: more effective, less side-effects

What We Were Taught:

Cross linking of Allergen-specific IgE bound to the surface of Mast cell: degranulates, releases inflammatory mediators.

And that Itch came from Mast cells, IgE and Histamine.

Recent Research: Atopic Dermatitis

Allergen exposure through skin, may be epidermal barrier defect

Dust mite releasing allergens

Allergen is absorbed through epidermis with decreased barrier function

Langerhans Cell

Allergen is Engulfed By Langerhans Cell
Langerhans cell enters into the lymph node

Langerhans cell within the lymph node makes contact with the naïve T-cell

Naïve T-cell changes to T helper 2 cell

T helper 2 cell releases cytokines IL-4 and IL-13

Cytokines are key to allergic itch cycle

What are Cytokines?

1. Protein messages sent from one cell to another, stimulating receiving cell to action
2. Think of them like "text messages" between neighbors
3. Many types of cytokines
4. Interleukins (IL) are important type of cytokine in allergic disease


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Interleukins (IL) are important type of cytokine in allergic disease
Janus Kinase Enzymes (JAKs)

1. Family of intracellular cell signaling enzymes
2. Named after Janus, two-faced Roman god of doorways, due to enzyme containing 2 nearly identical binding sites
3. Important for cell communication, regulation of activity
4. JAK enzyme signaling pathway used by many allergic cytokines to trigger itch, inflammation in skin

Allergic cytokines use JAK enzyme signaling pathway to initiate itch cycle, regardless of cause of itch

How Do Cytokines and JAKs Signal the Cell to Respond?

1. Cytokines bind to receptors on cell membrane
2. Activation of JAK enzyme on intracellular portion of cytokine receptor
3. Proteins (STATs) sent to cell nucleus to convey signal, cause the cell to respond
4. Triggers itch, inflammation in skin
Neuronal stimulation through JAK: Key component in itch cycle in allergic dogs

IL-31 binds to cutaneous neurons → Activating JAK → Sends neuronal signal to brain

Current Therapies Have Limitations

Could a More Targeted Approach For Treatment of Atopic Dermatitis Work?

Atopica® binds cyclophilin and inhibits calcineurin function
Effects on: NFAT signaling and antigen presentation

Atopica® is a registered trademark of Eli Lilly and Company. Its subsidiaries and affiliates.

Corticosteroids bind corticosteroid receptors present in all cells
Effects on: immune system, CNS, metabolism, homeostasis

APOQUEL® inhibits JAK1 and JAK3 enzyme function
Effects on: JAK1 and JAK3 dependent cytokines driving clinical signs

Anti-IL-31 monoclonal antibody
Effects on: IL-31, a key JAK1-dependent cytokine driving clinical signs

Management of Atopic Dermatitis

Acute Flares
- Mild shampoos
- Topical/oral GCs
- Oclacitinib

Chronic Atopic Dermatitis
- Improve skin and coat hygiene
- Topical/oral GCs
- Oclacitinib
- Cyclosporine
- Allergen-specific immunotherapy (prevent flares/recurrence)


Summary

1. Cytokines orchestrate the cycle of itch and inflammation in allergic skin disease
2. Allergic cytokine signaling requires Janus Kinase (JAK) enzyme system
3. The JAK system could be targeted for itch control
References


Allergen-specific Immunotherapy