Atopic dermatitis and the skin barrier

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What *is* Atopic Dermatitis?

- Allergic (inappropriate) reaction to environmental antigens
- Genetic component

What *causes* Atopic Dermatitis?

- Allergens: respiratory or percutaneous route
- Hypersensitivity mediated by IgE antibodies
- Barrier dysfunction
Signalment (Dogs)

- Age at onset: 1-7 years
- Breeds: Retrievers, Terriers, Dalmatians, Shar-pei, Shiba inus, others
- No sex predilection

Clinical Signs (Dogs)

- Pruritus
- Erythema
- Feet, face, axilla, ears, conjunctivitis
Atopy and Cats

- Etiology: presumed to be similar to dogs
- Signalment (age, breed, sex): not well described
Clinical Signs (Cats)

- Facial / head / neck pruritus
- Miliary dermatitis
- Eosinophilic granuloma complex
- Self-induced alopecia
Secondary infections (Dogs)

- *Staphylococcus pseudintermedius*
  - Epidermal collarettes, papules, pustules
Secondary infections (Dogs)

- *Malassezia pachydermatis*
  - Waxy brown exudate: skin or proximal claws, erythema interdigitally or under tail
  - Interdigital, folds, generalised
**Malassezia in Cats**

- Sometimes associated with atopic dermatitis
- Generalised: also look for systemic disease

*Courtesy Dr. B. Holm*

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**Malassezia pachydermatis**

- Diagnosis by cytology via acetate (‘Scotch™’) tape preparation or skin scrapings
Atopic dermatitis: Diagnosis

- History
  - seasonal, < 7 years old at onset
- Clinical Signs
  - pruritus feet, face, axilla, ears
- Rule outs
  - food allergy, ectoparasites, etc

Atopic Dermatitis: IF owners want hyposensitisation

- Intradermal testing (IDT)
- Serologic testing
  - Allergen specific IgE
  - Use Gribbles
The skin barrier

Layers of the Epidermis
**Extracellular Lipid Matrix**

- Stratum corneum lipids
  - Ceramides
  - Free fatty acids
  - Cholesterol

![Image of extracellular lipid matrix](image-url)


**Barrier function theory**

- Loss of barrier function
  - Abnormality in lipid layer of the stratum corneum
  - Decreased epidermal filaggrin
  - Inherited or results 2° to inflammation?
- Allows:
  - allergen ‘penetration’
  - *Staphylococcus* spp (& *Malassezia*) to ‘stick’ to the stratum corneum
  - Water loss (increased TEWL)
Barrier Function and Atopic Dermatitis

Transpidermal Water Loss (TEWL)

Epidermal Barrier Dysfunction: Atopic Dermatitis

From Hudson TJ. Skin barrier function and allergic risk. Nature genetics 2006; 38:399 - 400.
Epidermal Barrier Dysfunction: Human Atopic Dermatitis

- AD patients have:
  - Increased TEWL
  - Lipid lamellae are decreased in number
  - SC lipid composition is altered:
    - Decreased ceramides
      - Primary defect and a consequence of inflammation

- Striking similarity in human and canine barrier impairment leads to allergen sensitization

Normal Canine Skin
Stratum Corneum Lipid Lamellae

lamellar and continuous intercellular lipids
(Inman, Vet Pathol 2001)
Canine Atopic Dermatitis
Stratum Corneum Lipid Lamellae

abnormal and discontinuous intercellular lamellae
(Inman, Vet Pathol 2001)
Fixing the skin barrier: past, present and future - man and dog compared: Marsella R, Vet Derm 2013

**Dogs:**

- Topical application of ceramides, free fatty acids & cholesterol
  - ↑ lipid lamellae & improved stratum corneum ultrastructure
- 2 clinical studies: significant clinical benefit

Dogs:

- Topical application of essential oils & unsaturated fatty acids (spot on & spray)
  - Open clinical trial: 8 weeks
  - Significant ↓ clinical scores & pruritus
Fixing the skin barrier: past, present and future - man and dog compared: Marsella R, Vet Derm 2013

Dogs:
- Oral administration of essential fatty acids
  - Megaderm/ EFA Z - Virbac
- Improved the ultrastructural appearance of the stratum corneum
- No evaluation of any correlation w/ clinical improvement

Discussion/Clinical Relevance:
- Therapies directed at skin barrier repair used effectively in human medicine for years
- Therapies in dogs have shown efficacy
  - Topical lipid containing products, EFAs
Management of the atopic dog
Multimodal Management of Allergic Skin Disease

To keep below pruritic threshold need to manage all possible pruritic stimuli & flare factors

- Fleas
- Infection
- Food allergy
- Atopic Dermatitis

Pruritus!

Flare factors controlled

Pruritic Threshold

Comfortable

Management of atopic patients

- Topical therapy
- Atopica
- Apoquel
- Systemic glucocorticoids
- Fatty acids
- Antihistamines
- Desensitization
Topical Therapy

- Direct delivery of active agent to the skin
- Can be sole therapy avoiding side effects of systemic medications
  - Example: topical vs systemic corticosteroids
- Decrease need for systemic therapy
  - Example: Topical antimicrobial therapy
Disadvantages of Topical Therapy

- Owner compliance
- Increased expense: choose wisely
- Potential for irritation or contact dermatitis
  - Especially in already inflamed skin
- Can be absorbed percutaneously or ingested via grooming
  - Are the agents or vehicles toxic?
  - Do they contain corticosteroids?

Chronic topical corticosteroids: thin, atrophic skin accompanied by large comedo present on ventral abdomen of a dog
Topical Pharmacological Agents with Anti-Pruritic Activity

- Short term use of medium potency glucocorticoid sprays
- Cortavance (Virbac)
  - 0.0584% hydrocortisone aceponate
  - Mometasone
    - 0.1% cream or ointment

Tacrolimus ointment
- Similar to cyclosporine, better absorbed
- Applied twice daily for a week & then tapered to control clinical signs
- Slow onset of action, so less helpful in acute flares
- Can be irritating
- May be cost prohibitive

Systemic therapy
Cyclosporine

- Atopica®, Novartis
- Dogs: 5 mg/kg q24 h
- Cats: 7 mg/kg q24 h

Day 0

Day 90

Courtesy Dr. Helen Power
Cyclosporine: Side-effects

- Anorexia, vomiting, diarrhea
- Papillomas, pyoderma
- Hypertrichosis
- Renal / hepatic disease (rare)
- Gingival enlargement
Cyclosporine & *T. gondii*

- Cats infected with *T. gondii* prior to CsA administration failed to develop clinical illness after administration of CsA
- Cats that have high CsA concentrations when first exposed to *T. gondii* can develop fatal infection

**When to use Atopica™**

- Owners want a rapid response w/o steroids
- Need to stop steroids and allergy test
- Poor candidates for hyposensitization
  - Older dogs in good health
  - Owner declining injections/oral drops
- Other Rx have failed or side-effects are too severe
Apoquel ® (oclacitinib – Zoetis)

- Janus-kinase - 1 inhibitor
- interferes with interleukin production
- especially IL 31 (mediator of pruritus at the nerve level)

Apoquel ® (oclacitinib – Zoetis)

- 0.4 to 0.6 mg/kg bid x 2 weeks then q24 h
- Contraindications: neoplasia, demodicosis
- Ok to test (skin or serologic) for allergies
**AD: Corticosteroids**

- **Dogs:**
  - Prednisolone
  - 1 mg/kg/d, then taper

- **Cats:**
  - Prednisolone:
    - 1.5 mg/kg q24h, then taper

**Antihistamines**

- **Canine:**
  - Cetirizine 1mg/kg bid
  - Chlorpheniramine
    - 0.2-0.8 mg/kg bid-tid

- **Feline**
  - Chlorpheniramine
    - 2-4 mg/5 kg q 12 hrs
  - Cetirizine
    - 0.5mg/kg PO q 12-24hrs
Essential fatty acids

- Evidence that diets high in essential fatty acids are beneficial
- Multiple anti-inflammatory and immunomodulatory properties.
- Omega 6 and omega 3

Clinical efficacy

- Clinical studies have documented efficacy of omega-3 or omega-6/omega-3 combinations
  - A lower dose of prednisolone after 2 months
  - A lower dose of cyclosporine after 12 weeks
  - Allow at least 4-6 weeks for an initial effect and 8-12 weeks for a full effect
Hyposensitisation

- Intradermal testing (IDT)
- Serologic testing
Hyposensitisation

- 70-80% of dogs improve
- Route of administration
  - SCIT
  - SLIT
  - Intralymphatic
- Life long treatment
Summary

- Atopic dermatitis is a complex disease and management requires a multifaceted approach