Allergic Skin Conditions of the Dog

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Pruritic Pathway

Neurogenic Skin Disorders

- Acral lick dermatitis
  - Central, spinal, or peripheral origin
- Acral mutilation syndrome
- Lumbosacral stenosis
- Caudal Occipital Malformation (Chari Syndrome)
- Tail dock, declaw, etc neuroma
- Trigeminal neuritis
- Others

Peripheral Neuritis

- Rare
- Impossible to document antimortum
  - Sudden onset
  - Intense UNILATERAL pruritus (pain?)
  - Poor response to steroids
  - Difficult to treat

Spinal Neuritis

- Uncommon
- Variable speed on onset and progression
- Typically symmetrical
- Variable response to steroids

Treatments for Neuropathies

- Amitriptyline: 1-2 mg/kg q12h
- Gabapentin: 5-10 mg/kg q8h
- Pregabalin: 2-4 mg/kg q12h
- Phenobarbital: 1- 3 mg/kg q12-24h
**Behavioral Skin Disorders**

**DOG**
- Acral lick dermatitis
- Flank sucking
- Foot licking
- Self-nursing
- Tail biting

**CAT**
- Traumatic alopecia
- Tail sucking
- Barbering

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**Foot Licking**

**Differential Diagnosis**

- Allergy
  - Atopy
  - Food hypersensitivity
  - Contact
  - Drug (?)
- Malassezia pododermatitis
- Demodicosis
- Helminthosis
- Hookworms
- Pelodera

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**Perineal Licking**

- Psychogenic or pathologic basis
- Pathologic causes most common
  - Anal sac disease
  - Malassezia dermatitis
  - Mucocutaneous pyoderma

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**Urticaria-Angioedema-Anaphylaxis**

- Potentially life threatening condition
- Result of sudden and massive mast cell degranulation
  - Immunologic or non-immunologic causes
  - Superficial, middle, or deep vascular plexuses targeted

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**Common Causes of Urticaria**

- Insect stings/bites
- Foods
- Vaccinations
- Drugs

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**Treatment**

- Identify cause!!
- Medical treatments
  - None
  - Antihistamines
  - Glucocorticoids
  - Epinephrine
  - Shock treatments
- Prevent re-exposure!!
Atopic Dermatitis

**Definitions**

**Atopic Dermatitis**
A genetically predisposed inflammatory and pruritic skin disease with characteristic clinical features associated with IgE antibodies most commonly to environmental allergens.

**Atopic-like Dermatitis**
A genetically predisposed inflammatory skin disease with clinical features identical to atopic dermatitis in which IgE antibodies to environmental allergens are not demonstrable.

**Initial Sensitization Process**

![Initial Sensitization Process](Image)

Courtesy: Zoetis
Mast Cell Activation

- Various triggers
  - Non-immunologic
  - Immunologic: IgE, IgG
- Multiple mediators released
  - Histamine
  - Leukotrienes
  - Prostaglandins
  - Proteases
  - Cytokines
  - Etc.

Histamine Receptor Activities

H1: ↑ vascular permeability, alter pruritus via sensory nerves
H2: ↑ gastric acid secretions, smooth muscle relaxation, inhibit antibody synthesis, T-cell proliferation and cytokine production
H3: Neurotransmitter in CNS
H4: Regulates neutrophil release from bone marrow, mast cell chemotaxis

Atopic Dermatitis- Pathogenesis

- Genetic predisposition
- Altered epidermal barrier
- ↓ Lipids/ceramides in stratum corneum
- Altered epidermal barrier function
- ↑ Percutaneous antigen absorption
- ↑ Antigen presenting cells
Epidermal Lipids

WHAT ARE THEY?

Epidermal Lipids

WHAT ARE THEY?

Epidermal Lipids

WHAT ARE THEY?

Epidermal Lipid defects in skin disease

Healthy dog

Atopic dog

Atopic Dermatitis- Pathogenesis

Mast cell/basophil releasability
Overactive phosphodiesterase isoforms
Keratinocytes (↓ defensins, colonization)
Stem cell factor (↑ in atopic and normal skin)
Fat metabolism (↓ absorption/↑ clearance; Δ 6 ± Δ 5 desaturase deficiency)

Pruritic Threshold

Canine Atopic Dermatitis

- Early age at onset: 6 – 36 months
- Breed predisposition – familial history
- Initially seasonal
- Progressive in clinical severity and duration of disease
Canine Atopic Dermatitis
- Nonlesional pruritus usually
- Pruritus stops with appropriate glucocorticoid administration
- Multiple routes for re-exposure
  - Skin
  - Lungs
  - GI tract

Prednisolone* Responsiveness

<table>
<thead>
<tr>
<th>Excellent</th>
<th>Poor</th>
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<tbody>
<tr>
<td>Uncomplicated Atopy: 99%</td>
<td>Food allergy: 80 - 90%</td>
</tr>
<tr>
<td>Food Allergy: 10 - 20%</td>
<td>Drug allergy: 95%</td>
</tr>
<tr>
<td>Early insect allergy: 99%</td>
<td>Scabies: 99%</td>
</tr>
<tr>
<td>Mild contact dermatitis: 99%</td>
<td>Malassezia derm: 95%</td>
</tr>
<tr>
<td>Etc</td>
<td>Bacterial hypersensitivity: 95%</td>
</tr>
<tr>
<td>Etc</td>
<td>Hormonal hypersensitivity: 95%</td>
</tr>
<tr>
<td>Etc</td>
<td>Behavioral disorders: 95%</td>
</tr>
<tr>
<td>Etc</td>
<td>Chronic insect allergy: 50%</td>
</tr>
</tbody>
</table>

* Dogs: 1 mg/kg q24h  Cats: 2 mg/kg q24h

Clinical Features of Canine Atopy
- Recurrent otitis externa
- Facial pruritus ± ear disease
- Pedal pruritus
- Axillary ± inguinal pruritus
- Generalized pruritus

Clinical Features of Canine Atopy
- Staphylococcal pyoderma
- Malassezia dermatitis
- Pyotraumatic dermatitis
- Acral lick dermatitis
- Anal sacculitis
- Hyperhidrosis

Feline Atopy
- Uncommon
- Uncertain pathogenesis
  - Transdermal exposure?
  - Respiratory exposure?
  - Oral exposure?
- Good response to medical management usually

Feline Atopy
- Recognized age at onset:
  - Purebreds: 12-36 months
  - Mixed-breeds: adulthood
- Lesional or nonlesional pruritus
- Protracted seasonality
- Coincidental asthma?
- Pruritus stops with appropriate glucocorticoid administration
Clinical Features of Feline Atopy or Food Hypersensitivity

- Pruritic otitis externa
- Facial pruritus
- Head and neck pruritus
- Generalized pruritus
- Miliary dermatitis
- Traumatic alopecia
- Eosinophilic granuloma complex

Atopic Dermatitis - Diagnosis

- History
- Physical examination
- Exclusion
  - Clinical testing
  - Skin biopsy
- Allergy testing – For allergens selection and not for diagnosis!!

Methods of Allergy Testing

- None: Use regionalized “off the shelf” extracts
- In vivo methods
  - Dechallenge/challenge
  - Prick testing
  - Intradermal testing
  - Patch testing
- In vitro methods
  - Basophile degranulation test
  - Serologic allergy tests

RESPIT™ Regionally-specific immunotherapy

- Standardized allergen extracts defined by geographic region
- Inclusion based on
  - Aerobiology
  - Allergenicity
  - Cross-reactivity

Customized vs. Standardized Immunotherapy for Canine Atopic Dermatitis

Good-excellent response rate (%)
Intradermal Skin Testing
- “Gold standard” for atopy
- Can be used in all species
- Little or no value in other allergic conditions
- Labor intense
- Expensive

Prerequisites for Intradermal Testing
- Test in correct season: 60 day window?
- Test non-inflamed skin
- Adequate drug withdrawal

IDST Drug Withdrawal Requirements
- Oral steroids: 3 weeks minimum
- Injectable steroids: 6 weeks minimum
- Antihistamines: 2 weeks
- Nutraceuticals: 2 weeks
- Cyclosporine: None?
- Apoquel: None

Serological Allergy Test Methods
- Radioallergosorbent test (RAST)
- Enzyme-linked immunosorbent test (ELISA)
- Liquid-phase enzymoimmunometric assay (VARL)
- High-affinity Fc epsilon receptor α-chain detection system (HESKA)

Serological Allergy Testing
- Rapid and easy
- Minimal drug interference
- Less seasonal influence
- Frequent “false-positives”
- Lab errors?
- Subclinical allergies?
- Parasitism can induce false positives
- Mite cross-reactions

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Allergen</th>
<th>Allergen</th>
<th>Allergen</th>
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<tbody>
<tr>
<td>Feline</td>
<td>Domestic</td>
<td>Mite</td>
<td>Plant</td>
</tr>
<tr>
<td>Canis</td>
<td>Equus</td>
<td>Mite</td>
<td>Plant</td>
</tr>
<tr>
<td>Bovine</td>
<td>Domestic</td>
<td>Mite</td>
<td>Plant</td>
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Serology Testing - Accuracy

<table>
<thead>
<tr>
<th>Lab</th>
<th>FBS</th>
<th>CALb</th>
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<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>33.3</td>
<td>0</td>
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<tr>
<td>B</td>
<td>0</td>
<td>0.7</td>
<td>3.5</td>
</tr>
<tr>
<td>C</td>
<td>30.8</td>
<td>27.7</td>
<td>28.9</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>1.7</td>
<td>3.3</td>
</tr>
</tbody>
</table>


Agreement between allergen-specific IgE assays and ensuing immunotherapy recommendations from four commercial laboratories in the USA

- 10 atopic dogs
- Samples sent to Bio-Medical Services, VARL, Heska, and IDEXX
- Diagnostic agreement across all dogs and all laboratories: 70%
  - Agreement expected by chance: 66%
- ASIT agreement across dogs and laboratories: 72%
  - Agreement expected by chance: 69%
- Highest level of chance-corrected agreement between Heska and IDEXX

Food Hypersensitivity

- Genetic predisposition not required
- Allergens
  - Water-soluble proteins and glycoproteins
  - ≥4,000 Daltons??
- Variable clinical presentations
  - Skin
  - Non-skin
  - Combination

Reported Allergens in the Dog

<table>
<thead>
<tr>
<th>Proteins</th>
<th>Grains</th>
<th>Others</th>
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</thead>
<tbody>
<tr>
<td>Beef</td>
<td>Corn</td>
<td>Potatoes</td>
</tr>
<tr>
<td>Chicken</td>
<td>Oats</td>
<td>Kidney beans</td>
</tr>
<tr>
<td>Pork</td>
<td>Rice</td>
<td>Pasta</td>
</tr>
<tr>
<td>Rabbit</td>
<td>Wheat</td>
<td>Dairy products</td>
</tr>
<tr>
<td>Turkey</td>
<td>Commercial dog food</td>
<td></td>
</tr>
<tr>
<td>Soy</td>
<td>Commercial dog treats</td>
<td></td>
</tr>
<tr>
<td>Horse meat</td>
<td>Chocolate</td>
<td></td>
</tr>
<tr>
<td>Lamb</td>
<td>Food additives</td>
<td></td>
</tr>
<tr>
<td>Fish (various)</td>
<td>Food preservatives</td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>Food preservatives</td>
<td></td>
</tr>
</tbody>
</table>

Reported Allergens in the Cat

<table>
<thead>
<tr>
<th>Protein</th>
<th>Grain</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef</td>
<td>Barley</td>
<td>Commercial food</td>
</tr>
<tr>
<td>Chicken</td>
<td>Corn</td>
<td>Clam juice</td>
</tr>
<tr>
<td>Fish (various)</td>
<td>Cod liver oil</td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>Food additives</td>
<td></td>
</tr>
<tr>
<td>Dairy products</td>
<td>Food preservatives</td>
<td></td>
</tr>
<tr>
<td>Horse meat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pork</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whale meat</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cross-Reacting Foods in Humans

Dairy products: caseins, bovine serum albumins, lactoglobulins  
Fish: parvalbumin  
Crustaceans  
Poultry: chicken serum albumin  
Milk: cow, goat, sheep  
Egg: ovalbumin, ovomucoid  
Wheat, barley, rye

Food Hypersensitivity

Source of exposure:
- Daily ration
- Treats & supplements
- Medications
- Scavenged/hunted foods
- “Digested” allergens
- Matter in drinking water

Clinical Features: Canine Food Hypersensitivity
- Atopic-like pruritus
- Persistent urticaria
- Recurrent or persistent otitis externa
- Recurrent episodes of acute moist dermatitis
- Lumbosacral pruritus
- Scabies-like pruritus
- Generalized pruritus

Clinical Features of Feline Atopy or Food Hypersensitivity
- Pruritic otitis externa
- Facial pruritus
- Head and neck pruritus
- Generalized pruritus
- Miliary dermatitis
- Traumatic alopecia
- Eosinophilic granuloma complex

Food Hypersensitivity - Diagnosis
- History
- Physical
- Diagnostic exclusion
- Serologic testing?
- Food dechallenge/challenge

Serologic Testing for Food Hypersensitivity
- Validity?
- Challenge testing required
NutriScan Test

- Not for testing for food allergies, but rather tests for food sensitivities and intolerance.
- Food allergy is a more immediate reaction mediated by production of IgE and IgG antibodies.
- Food sensitivity and intolerance measures a more delayed body response to offending foods by measuring production of mucosal IgA and IgM antibodies.

Nutriscan - Dog Food Sensitivity Kit

<table>
<thead>
<tr>
<th>Panel 1:</th>
<th>Panel 2:</th>
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<tbody>
<tr>
<td>Beef</td>
<td>Chicken Eggs</td>
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<tr>
<td>Corn</td>
<td>Barley</td>
</tr>
<tr>
<td>Wheat</td>
<td>Millet</td>
</tr>
<tr>
<td>Soy</td>
<td>Oatmeal</td>
</tr>
<tr>
<td>Cow’s Milk</td>
<td>Salmon</td>
</tr>
<tr>
<td>Lamb</td>
<td>Rabbit</td>
</tr>
<tr>
<td>Venison/Deer</td>
<td>Rice</td>
</tr>
<tr>
<td>Chicken</td>
<td>Quinoa</td>
</tr>
<tr>
<td>Turkey</td>
<td>Potato</td>
</tr>
<tr>
<td>White Fish</td>
<td>Peanut/Butter</td>
</tr>
<tr>
<td>Pork</td>
<td>Sweet Potato</td>
</tr>
</tbody>
</table>

Dietary Dechallenge & Challenge

- Modify entire diet
  - Water
  - Food
  - Flavored chew toys
  - Snacks: commercial, accidental, natural
  - Oral medications: Just flavored or all?
- Modify household’s lifestyle

Lifestyle Changes

- Eliminate access to snacks
- Visitors
- Toddlers, senior citizens
- Litter boxes, barns, etc
- Kitchen @ mealtimes
- No hunting
- Leash walking only
- Basket muzzle?

Time Course for Testing

- Initial test period: 4 weeks
- Results:
  - No change in level of pruritus: Not food allergy
  - 50% or greater improvement: probably food allergy
    - Continue diet until pruritus disappears entirely
    - Continue diet until pruritus is reduced to its lowest level
- Prove response by challenge with original diet and snack foods
Dietary Dechallenge & Challenge

- Dietary history required for accurate formulation of test diet
- At onset only?
- Entire course of disease?
- Types of diets available
  - Home cooked
  - Commercial
    - OTC limited ingredient diets
    - Veterinary limited ingredient diets
    - Altered molecular weight foods

Home cooked Diets

<table>
<thead>
<tr>
<th>Proteins</th>
<th>Carbohydrates</th>
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<tbody>
<tr>
<td>Tofu</td>
<td>White potatoes</td>
</tr>
<tr>
<td>Rabbit</td>
<td>Sweet potatoes</td>
</tr>
<tr>
<td>Venison</td>
<td>Brown rice</td>
</tr>
<tr>
<td>Ostrich</td>
<td>White rice</td>
</tr>
<tr>
<td>Exotic fowl</td>
<td>Barley</td>
</tr>
<tr>
<td>Fish</td>
<td>Lentils</td>
</tr>
<tr>
<td>Shell fish</td>
<td>Pinto beans</td>
</tr>
</tbody>
</table>

Commercial Limited Ingredient Foods

Veterinary Prescription Diets

Hydrolyzed “Hypoallergenic” Foods

Starch, Hydrolyzed Chicken Liver, Soybean Oil, Hydrolyzed Chicken
Starch, hydrolyzed soy protein isolate, vegetable oil, partially hydrogenated canola oil, corn oil

Brewers rice, hydrolyzed soy protein, chicken fat, natural flavors, dried beet pulp, vegetable oil

Maize starch, feather hydrolysate, copra oil, soya oil, fructo-oligo-saccharides, fish oil

**Dietary Dechallenge & Challenge**
- Determine significance of any change rechallenge
- Mix original food into special diet
  - Flair: 15 minutes → 7 days
  - No change
    - Incorrect diagnosis
    - Different allergen: treat, etc

**Long-term Management**
- Continue feeding diet used for testing
- Home cooked diet: balance for nutritional completeness
- Commercial diet: read label each time a new supply is purchased
- Do individual ingredient challenges to determine which ingredient(s) is the allergen
- Select new commercial food based on challenge testing

**Allergies Are Forever!!**
**Drug Hypersensitivity**

- Underreported
- Reaction can change nature and severity at each challenge
- No “diagnostic” tests that will
  - Confirm a drug reaction
  - Identify the offending drug

**Cutaneous Drug Reactions**

- Pleomorphic eruptions
- Immunologic or nonimmunologic mechanisms
- Immunologic sensitization: 7-14 days
- 1st reaction usually within 21 days
- Reaction pattern can change at each exposure
- Often last drug added

**Predisposing Factors**

- Nature of drug
- Route of administration
- Prolonged or repeated use of drug
- Simultaneous use of multiple drugs?
- Preexisting medical conditions?
- Simultaneous topical and systemic use of same drug?

**Breed Predispositions**

**Localized:**
- Poodles, Bichon Frise, Yorkshire and Silky terriers, Pekingese, Maltese terriers

**Generalized:**
- Doberman pinscher, miniature Schnauzer, Shetland sheepdog, Dalmatian, Australian shepherd, Old English sheepdog, Scottish terrier, wirehaired Fox terrier, Greyhound

**Common Offending Drugs**

**DOGS**
- Potentiated sulfas
- Penicillins
- Cephalosporins
- Topicals

**CATS**
- Penicillins
- Cephalosporins
- Sulfas
- Topicals

**Reaction Patterns**

- Contact dermatitis
- Exfoliative erythroderma
- Nonlesional pruritus
- Maculopapular
- Erythema multiforme
- Vasculitis
- Fixed reaction
Reaction Patterns Con’t

- Autoimmune-like
- Superficial suppurative necrolytic dermatitis of Schnauzers
- Focal panniculitis
- Toxic epidermal necrolysis
- Urticaria – angioedema
- Miscellaneous

Contact Dermatitis

- Dogs: 26.8 %  Cats: 42.9%
- Ears most commonly affected
- Prompt resolution with dechallenge

Exfoliative Erythroderma

- Dogs: 19.8%  Cats: 0%
- Persistent or paroxysmal
- Prompt resolution with dechallenge

Nonlesional Pruritus

- Dogs: 11.9%  Cats: 21.4%
- Most often due to flavoring agents, dyes, or binders
- Prompt resolution with dechallenge

Maculopapular

- Dogs: 9.9%  Cats: 0%
- Mimics superficial folliculitis
- “Sterile” cytology
- Follicular scarring in chronic cases

Erythema Multiforme

- Dogs: 7.9%  Cats: 7.1%
- Spectrum of severity
- Other causes
- Variable time to resolution with dechallenge
**Toxic Epidermal Necrolysis**

- **Dogs: 1.0%  Cats: 0.0%**
- Life threatening condition
- Usually fatal with >30% of body involved
- Very fragile skin
- Severe scarring possible

**Vasculitis**

- **Dogs: 5.0%  Cats: 7.1%**
- Document by diascopy
- Pressure point predisposition
- Severity varies with vessel size
- Slow healing with dechallenge
- Scarring expected

**Fixed Reaction**

- **Dogs: 2.9%  Cats: 7.1%**
- Reaction recurs at the same site with rechallenge
- Variable time to resolution

**Autoimmune-like**

- **Dogs: 2.9%  Cats: 7.1%**
- Lesions clinically and histologically mimic true autoimmune disorders
- Superficial pemphigus and lupus patterns most common
- Variable response time to dechallenge

**Superficial Suppurative Necrolytic Dermatitis of Schnauzers**

- Miniature Schnauzers only
- Shampoo triggered
- Systemic and cutaneous signs follow bathing by 48-72 hours
- Prompt healing with dechallenge

**Focal Panniculitis**

- **Dogs: 2.0%  Cats: 7.1%**
- Injection reaction
- Pre-neoplastic ??
- Slow healing with scarring
Urticaria - Angioedema

Dogs: 1%  
Cats: 0.0%

- More common in practice situation
- Urticaria most commonly seen with topicals
- Rapid resolution with dechallenge

Miscellaneous

- Any eruption on any body part could be drug induced.

Diagnosis

- Suspicion & exclusion
- Skin biopsy
- Spontaneous resolution with dechallenge
  - Which drug??
  - Rechallenge??

Treatment

- Remove offending drug(s)
- Supportive care
- Corticosteroids?
- AVOID DRUG FOREVER!!