Management of Canine Atopic Dermatitis

Karen L. Campbell, DVM, MS, DACVIM, DACVD
Professor Emerita, University of Illinois
Clinical Professor of Dermatology, University of Missouri
Avoidance/Elimination of Allergens

• Remove feathers, kapok, wool
• House dust mite control measures
  • Remove carpets, blinds, plants, upholstered furniture, clutter
  • Use plastic or micropore covers for mattresses, box springs, pillows
• Freeze dry food to decrease # of storage mites
Avoidance/Elimination of Allergens

- Use washable curtains
- Wet mop floors
  - 2 times per week
- use a HEPA air cleaners, furnace filters, vacuum cleaners
- Lower the humidity in the house
Products to Kill HDMs
Antihistamines: Mechanisms of Action

- Block H1 and/or H2 receptors
- Stabilize mast cells
- CNS effects
- Sedation
- Response for individual antihistamines is < 25%
- Must be given consistently for effectiveness
- Two week trials for each product if owner interested in trying
- Can be combined with other anti-pruritics to lower doses (steroids, Apoquel, Atopica)
Antihistamines for Dogs

- Diphenhydramine HCl
  - 1-2 mg/kg bid
- Clemastine (Tavist)
  - 0.04-0.5 mg/kg bid
- Hydroxyzine HCl or pamoate
  - 2.2-6.6 mg/kg tid
- Chlorpheniramine
  - 0.5-2 mg/kg bid
- Cetirizine (Zyrtec)
  - 1 mg/kg q 12-24 hr
- Loratadine (Claritin)
  - 0.25-0.5 mg/kg q 24 hr
- Fexofenadine (Allergra)
  - 2-5 mg/kg q 12-24 hr
Amitriptyline HCl

- Tricyclic antidepressant
- Inhibits serotonin reuptake
- Also potent antihistamine
- Do not use in dogs with
  - cardiac disease
  - renal disease
  - hepatic disease
- 1-2 mg/kg BID
- Should wean off when discontinuing
Fatty Acid Supplements

- Gamma-linolenic acid (evening primrose oil): favors production of PGE1 which is anti-inflammatory
- Omega 3 fatty acids: compete with omega 6 fatty acids in metabolism, result in production of less inflammatory cytokines, may also down regulate inflammation
Omega-3 and Omega-6 Eicosanoids

**OMEGA-6 FAMILY**
- Linoleic acid
  - $\Delta-6$-desaturase
    - Gamma-linolenic acid (GLA)
      - Elongase
        - Dihomogamma-linolenic acid (DGLA)
          - $\Delta-5$-desaturase
            - Cyclooxygenase
              - Arachidonic acid
                - Lipoxygenase
                  - Leukotrienes & Lipoxins (series 4)
                - Cyclooxygenase
                  - Prostaglandins & Thromboxanes (series 2)
            - Prostaglandins & Thromboxanes (series 1)
      - Cyclooxygenase

**OMEGA-3 FAMILY**
- Alpha-linolenic acid
  - $\Delta-6$-desaturase
    - Elongase
      - $\Delta-5$-desaturase
        - Cyclooxygenase
          - Eicosapentaenoic acid (EPA)
            - Lipoxygenase
              - Leukotrienes & Lipoxins (series 5)
            - Cyclooxygenase
              - Prostaglandins & Thromboxanes (series 3)
        - Prostaglandins & Thromboxanes (series 2)
      - Elongase
        - $\Delta-4$-desaturase
          - Docosahexaenoic acid (DHA)
Products Available

• Wide variety of combinations of omega 3 and omega 6 fatty acids in various ratios and quantities
• Individual dog responses may vary (varying metabolism)
• Ideally try 3-4 different products, each for 8-12 weeks to see which is most beneficial for a given patient
Redonyl Ultra Soft Chews (ultra-micro Palmitoylethanolamide)

- Hydrolyzed soy protein
- Reported to increase production of the endocannabinoid 2-arachidonoylethanolamide (2-AG)
- Reported to decrease mast cell release of histamine, PGD2 and TNF-alpha
- Reported to support keratinocyte health
Skin barrier repair products

Improve skin barrier function by replacement of missing ceramides and other fats in lipid bilayers of epidermis
Corticosteroids in Treatment of Allergies

- Very effective
- Many side effects: PU/PD/PP, panting, increased risk of infections, weight gain, thinning of skin, hepatomegaly, easy bruising, thromboembolism, adrenal atrophy, diabetes mellitus, pancreatitis, etc. etc.
- Use during flare-ups, if a short allergy season, or if other therapies are not feasible due to owner constraints
Anti-inflammatory Use of Glucocorticoids

• Induction: (5-7 days)
  • Dog: 0.5-1.0 mg/kg
  • Cat: 1-2 mg/kg (prednisolone)

• Maintenance:
  • Dog: 0.2-0.5 mg/kg every other day
  • Cat: 0.5-1.0 mg/kg every other day

• Should NOT use depo products in treatment of allergies in dogs
Cyclosporine

- Targets T-cells
  - inhibit cytokines
- Langerhans cells
  - IgE receptor
  - tissue migration
  - Antigen processing
- Mast Cells
  - histamine release
- Keratinocytes
  - IL-8 receptors
Cyclosporine

• Effective in treatment of ~80% of dogs with atopic dermatitis

• 5 mg/kg/day (attempt to taper to eod after 8 wks; some go into remission)

• Expensive, monitor for side effects
  • GI, renal, hepatic, bone marrow, cutaneous papillomas, other infections (especially fungal), EM, TEN
Cyclosporine

• If vomiting is a problem
  • Give with food and/or freeze the capsules
  • Premedicate with Cerenia or Reglan
    • Cerenia (maropitant citrate) 2 mg/kg PO
    • Reglan (metoclopramide HCl 0.2-0.5 mg/kg PO)
• If expense is prohibitive give with a cytochrome P-450 inhibitor
  • Give with ketoconazole 2.5-5 mg/kg PO
  • Can reduce dose of CsA to 2.5 mg/kg PO
Cyclosporine

• If gingival hyperplasia develops
  • Try reducing dose
  • Azithromycin oral paste
  • Surgical resection if excess tissue

Before and after resection of gingival hyperplasia
Topical Calcineurin Inhibitors

- Tacrolimus
- Pimecrolimus
- Inhibit the activation of T cells and mast cells in the skin
- Useful for treating localized lesions
- Compound as 0.125% tacrolimus
Oclacitinib (Apoquel®)

- JAK 1 (Janus kinase inhibitor)
  - Inhibits production of JAK-1 dependent cytokines involved in allergy
    - At therapeutic dose blocks production of IL-31
    - Also decreases IL-2, IL-4, IL-5, IL-6 and IL-13
    - Rapid (within hours) decrease in itching
    - Reduces cutaneous inflammation
Oclacitinib (Apoquel®)

- Half-life approximately 5 hours
- Recommended dosing
  - 0.4-0.6 mg/kg q 12 hours for 14 days
  - 0.4-0.6 mg/kg q 24 hours for maintenance
- NOT for use in dogs < 1 year
- NOT for use in breeding animals
- NOT for use in dogs with “serious infections”
- Monitor CBC q 3 months and also evaluate dogs for “silent infections”
Oclacitinib (Apoquel®)
Caninized Monoclonal Anti-IL-31 Antibody (CytoPoint)

• For most dogs needed as a once per month subcutaneous injection (lasts longer for some)
• Binds to and neutralizes IL-31 preventing activation of neuronal itch pathways
• Onset of action within 24-48 hrs post-injection
• Dose is 2-4 mg/kg subcutaneous
• Highly specific = minimal side effects
• Dog only (caninized)
• No direct effect on inflammation
Immunotherapy

- Desensitization
- Hyposensitization
- Allergen-specific immunotherapy
- Most specific treatment for atopy
Immunotherapy

• Methods of administering allergen-specific immunotherapy
  • Subcutaneous injections
    • Induction: injections initially given every 2-3 days
    • Maintenance: injections weekly to monthly for maintenance
    • “Rush Immunotherapy” involves giving injections with increased amount of allergens ~ every 30 minutes in hospital and then starting maintenance injections
  • Sublingual (SLIT) – oral allergy drops
    • Given in mouth once or twice daily (on buccal mucosa)
Theories of Hyposensitization

• Increased T-suppressor activity
• Production of IgG blocking antibody
• Decreased number of mast cells
• Decreased histamine release
Selection of Antigens for Immunotherapy

• Correlate history and IDST
• Maximum of 12 antigens per treatment vial
• Can use 2 or 3 treatment sets simultaneously for highly allergic dogs
• Ideal to have separate vials for molds and other allergens
Management of Side Effects During Immunotherapy

- Local Reactions
  - premedicate with antihistamines
- Severe pruritus/exacerbated symptoms
  - reduce dose administered
- Systemic Reactions (Anaphylaxis)
  - epinephrine/supportive therapy
Evaluation of Hyposensitization

- Are additional medications required?
  - antihistamines, corticosteroids, frequency of required use, etc.

- Allow 9 months or longer for maximum benefit
Reported Responses to Hyposensitization

- 25% complete remission
  - 25% low level of pruritus, no additional medications
  - 25% moderate level of pruritus, require other treatment—shorter time than before ASIT
- 25% no apparent improvement
- CAN IMPROVE IF GOOD CE
- (interesting/frustrating that majority of treatments for atopy are each only effective in 75-80% of patients!)
Supportive Treatments

- Flea control is “essential”
- Antibiotics for pyoderma
- Eliminate/minimize exposure
- Frequent bathing decreases antigenic load
- Moisturizers as needed
Supportive Treatments

- Topical agents
  - (oatmeal, local anesthetics (pramoxine), antihistamines, astringents, cooling agents, steroids—hydrocortisone safest)
  - Skin barrier repair products
- Fatty acid supplements
- Redonyl (palmitoyethanolamide)
- Antihistamines
- Occasional need for steroids, oclactinib or IL31-mab
  - especially first 2-4 months of Immunotherapy or in peak season
Pruritic Threshold

- Fleas
- Ragweed allergy
- Beef allergy
- Xerosis
- Staphylococcal pyoderma
Cumulative/Additive Effects

• Allergen load
  • food, fleas, yeast, bacterial products, pollens

• Pruritic factors
  • allergens, dry skin, irritants, toxins (bacterial and yeast products, products from WBCs)
Pruritic Threshold
Affected By:

• Emotional state
• Other diseases
• Weather
• Altered epidermal barrier
  • Irritants, dry skin, trauma
Shampoo Therapy

• Relief from cool water
• Remove surface debris
• Remove bacteria
• Remove irritants
• Remove allergens
Antipruritic Shampoos/Other Topicals

- Oatmeal (binds allergens, anti-inflamm)
- Diphenhydramine (antihistamine)
- Pramoxine (anesthetic)
- Menthol (cools)
- Corticosteroids (hydrocortisone, triamcinolone; anti-inflammatory)
- Ceramides—repair of barrier defect
- Many formulations available: shampoos, rinses, leave-on lotions, creams, sprays
Antipruritic Rinses

- Colloidal oatmeal
  - (1-2 tbsp/gal)
- Aluminum acetate
- Antihistamines
- Anesthetic (pramoxine)
- Lime sulfur (2%)
Adjunctive Therapy for Contributory Factors

- Flea control
- Antibiotics
- Antifungals (anti-yeast)
- Water soaks/humectants
  - if dry skin
- Restricted allergen diet
  - if indicated
- Skin barrier repair products
Additional Therapies being investigated

• Antigen modification
  • drugs that activate Ts cells, CPG, heat-inactivated *Listeria*

• Inhibitors of Th2 cell activation
  • Alafacept
  • Efalizumab

• Probiotics (boost Th1 response)
Future Therapies

- Antibody regulation
  - antiidiotype antibodies
  - Anti-IgE antibodies (omalizumab for humans)
- DNA vaccines
  - Th subset switching
  - Blocking antibodies
  - Immune stimulating sequences
- Antimicrobial peptides
Client Education

- Expect partial responses unless underlying causes identified and treated
- Discuss potential side effects of all medications
- Manage expectations
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Karen L. Campbell, DVM, MS
Diplomate, American College of Veterinary Internal Medicine
Diplomate, American College of Veterinary Dermatology

University of Missouri Veterinary Health Center—Wentzville
1092 Wentzville Parkway
Wentzville, MO 63385

(636) 332-5041
(636) 327-6400 fax

campbellmotsingerk@missouri.edu

klcampbe@Illinois.edu