Medical Management of Allergic Skin Conditions

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Commonly Used Treatments

- Avoidance
- Topicals
- Medical treatments
  - Glucocorticoids
  - Antihistamines
  - Psychotropic agents
  - Nutraceuticals
  - Immunomodulatory agents
- Immunotherapy

Topical Antipruritic Therapy

- Usually an adjunctive treatment
- Useful in
  - Removing surface allergens
  - Removing surface bacteria or yeast
  - Hydrating the skin
  - Providing some antipruritic activity

Medical Therapeutic Options

Dog

<table>
<thead>
<tr>
<th>Duration (months)</th>
<th>Oral Steroids</th>
<th>Antihistamines</th>
<th>Immunotherapy</th>
<th>Cyclosporine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young</td>
<td>Old</td>
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</tr>
<tr>
<td>0-2</td>
<td>1st</td>
<td>OK</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>2-4</td>
<td>OK</td>
<td>---</td>
<td>1st</td>
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<tr>
<td>4-6</td>
<td>---</td>
<td>---</td>
<td>1st</td>
<td>1st</td>
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<tr>
<td>&gt; 6</td>
<td>---</td>
<td>---</td>
<td>OK</td>
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Cat

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Useful Otic Steroids

- Hydro B – 1020 – Hydrocortisone acetate
- easOtic® - Hydrocortisone aceponate
- Tresaderm®- dexamethasone
- Otomax™ - betamethasone
- Anamax®- triamcinolone
- Surolan®- prednisolone
- Mometamax™, Posatex™ - mometasone
- Zelotril Oto – Hydrocortisone acetate and succinate
Relative Steroid Potency

<table>
<thead>
<tr>
<th>Drug</th>
<th>Potency</th>
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<tbody>
<tr>
<td>Hydrocortisone acetaate</td>
<td>1</td>
</tr>
<tr>
<td>Hydrocortisone acetonate</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>5</td>
</tr>
<tr>
<td>Isoflupredone</td>
<td>14</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>25</td>
</tr>
<tr>
<td>Betamethasone valerate</td>
<td>30</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>231</td>
</tr>
</tbody>
</table>

Tresaderm®: 5 drops/ear q12h
PosateX™: 4 drops/ear q24h

20 drops = 1.0 mg of dexamethasone = 6.25 mg prednisolone
8 drops = 0.2 mg of mometasone = 11.6 mg prednisolone

Allerderm spot-on

EM observation on treated sites in atopic dogs

Lower part of stratum corneum

Allerderm spot-on

Oral Treatments

- Glucocorticoids
- Antihistamines
- Psychotropic agents
- Nutraceuticals
- Immunosuppressive agents

Glucocorticoid Therapy

Anti-inflammatory prednisolone doses
- Dog: 1.0 mg/kg q24h
- Cat: 2.0 mg/kg q24h
- Horse: 2.0 mg/kg q24h

Alternate drug conversion factors
- Methylprednisolone: 0.8
- Dexamethasone: 0.1
- Triamcinolone: 0.4

Termaril-P

- Trimeprazine tartrate: 5 mg
- Prednisolone: 2 mg

<table>
<thead>
<tr>
<th>Weight of Dog</th>
<th>Initial Dosage</th>
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<tbody>
<tr>
<td>Up to 10 lb</td>
<td>1/2 tablet, twice daily</td>
</tr>
<tr>
<td>11-20 lb</td>
<td>1 tablet, twice daily</td>
</tr>
<tr>
<td>21-40 lb</td>
<td>2 tablets, twice daily</td>
</tr>
<tr>
<td>Over 40 lb</td>
<td>3 tablets, twice daily</td>
</tr>
</tbody>
</table>

After 4 days, reduce dosage to 1/2 of the initial dose or to an amount just sufficient to maintain remission
### Rational Steroid Therapy
- Use carefully
- Use short-acting oral drugs only
- Administer daily beyond clinical remission
- Maintain remission with EOD administration
- Reduce dosage to lowest acceptable level – LEAVE SOME ITCH!!

### Antihistamine Therapy
- Hundreds available
- Unpredictable efficacy
  - Response determined by rotating 14 day drug trials
  - May lessen or eliminate pruritus
- Safe long term

### Contraindications for Antihistamine Therapy
- Glaucoma
- Retentive disorders
- Seizure disorders
- Hepatic dysfunction
- Cardiac arrhythmias
- Pregnancy
- Drug interactions
- Competitive sports, etc

### Psychotropic agents
- Central modification of pruritic stimulus
- Separate peripheral actions
- Same contraindications as antihistamines
- Potentially useful agents
  - Amitriptyline
  - Phenobarbital

### Neural Focused
- Amitriptyline: 1-2 mg/kg q12h
- Gabapentin: 5-10 mg/kg q8h
- Pregabalin: 2-4 mg/kg q12h

### Potentially Effective Drugs - Dog
- Cetirizine: 1 mg/kg q24h
- Chlorpheniramine: 0.4 mg/kg q8h
- Clemastine: 0.05-0.1 mg/kg q12h
- Diphenhydramine: 2.2 mg/kg q8h
- Hydroxyzine: 2.2 mg/kg q12h
- Loratadine: 1-2 mg/kg q24h
- Amitriptyline: 1-2 mg/kg q12h
- Pentoxifylline: 25 mg/kg q12h
### Potentially Effective Drugs - Cat

- Chlorpheniramine: 2-4 mg/cat q12h
- Cetirizine: 5 mg/cat q24h
- Clemastine: 0.68 mg/cat q12h
- Diphenhydramine: 2.2 mg/kg q12h
- Loratadine: 5 mg/cat q24h
- Amitriptyline: 0.5-1.0 mg/kg q12h
- Cyproheptadine: 2 mg/cat q12h

### Fatty Acid Supplements

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Dog Dosage</th>
<th>Cat Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derm Caps</td>
<td>Per label</td>
<td>Per label</td>
</tr>
<tr>
<td>EPA</td>
<td>40 mg/kg</td>
<td>???????</td>
</tr>
<tr>
<td>GLA</td>
<td>&gt;40 mg/kg</td>
<td>&gt;8 mg/kg</td>
</tr>
<tr>
<td>IAMS Foods</td>
<td>Per label</td>
<td>Per label</td>
</tr>
</tbody>
</table>

### Drug Combinations

- Simultaneous administration of different modes of action can:
  - Make ineffective drugs effective
  - Increase efficacy beyond each individual drug
  - Allow significant reduction in steroid dosage

### Apoquel® (Oclacitinib)

- A targeted Janus kinase (JAK1 and JAK3) inhibitor
- Inhibits pro-inflammatory and pruritogenic cytokines
- Immunomodulatory vs immunosuppressive
- Dose: 0.4-0.6 mg/kg q12h x14 days then q24h

### JAK Signaling Summary

JAKs activate the intracellular proteins called Signal Transducer and Activator of Transcription (STAT) to induce gene transcription and biological responses.
A blinded, randomized, placebo-controlled trial of the efficacy and safety of the Janus kinase inhibitor oclacitinib (Apoquel®) in client-owned dogs with atopic dermatitis


Table 5. Adverse reactions, day 0–16

<table>
<thead>
<tr>
<th></th>
<th>Oclacitinib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse reactions</td>
<td>(n = 152)</td>
<td>(n = 147)</td>
</tr>
<tr>
<td>observed during days 0–16*</td>
<td>(n=1%)</td>
<td>(n=1%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7 (4.6)</td>
<td>5 (3.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (3.9)</td>
<td>6 (4.1)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>4 (2.6)</td>
<td>0</td>
</tr>
<tr>
<td>New dermal, epidermal or subcutaneous mass†</td>
<td>4 (2.6)</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>3 (2.0)</td>
<td>2 (1.4)</td>
</tr>
</tbody>
</table>

*Adverse reactions were tabulated per animal; animals with pre-existing conditions are not listed.
†Masses included papillomas in two placebo-treated dogs and a histiocytoma in one oclacitinib-treated dog. The other masses did not have specific diagnoses.

Long-term compassionate use of oclacitinib in dogs with atopic and allergic skin disease: safety, efficacy and quality of life.
Cosgrove, SR, Cleaver, DM, King, VL, et al.
Vet Dermatol 2015; 26: 373–385

- Dogs received 0.4–0.6 mg/kg oclacitinib twice a day for 14 days, then once a day for up to 630 days
- Results:
  - Percentage of dogs showing ≥50% reduction from baseline on day 90 was 63.9% for pruritus and 66.4% for dermatitis.
  - Adverse reactions uncommon: Urinary tract cystitis, vomiting, otitis, pyoderma, and diarrhea (>5% of dogs)
  - Haematology and serum chemistry remained normal
A blinded, randomized clinical trial comparing the efficacy and safety of oclacinib and ciclosporin for the control of atopic dermatitis in client-owned dogs
Little, PR, Xing, VL, Davis, KR, et al
Vet Dermatol 2015; 26: 23–48

- Assessed on days 1, 2, 7, 14, 28, 56 and 84.
- Percentage reduction from baseline for owner-assessed pruritus
  - changed from 25.6 to 61.0% in the oclacinib group compared with 6.5 to 61.5% in the ciclosporin group
- Differences were significant at all time points up to day 28.
- On day 56, ciclosporin-treated dogs showed a similar decrease in pruritus to oclacinib-treated dogs.
- Three times as many adverse events attributed to gastrointestinal signs were reported in the ciclosporin group

Immunosuppressive Agents

- Azathioprine: 2.2 mg/kg q24h
- Chlorambucil: 0.1-0.2 mg/kg q24h
- Cyclosporine:
  - Dogs: 5 mg/kg q24h
  - Cats: 7 mg/kg q24h

Cyclosporine
Sanimmune® - Novartis (capsules, suspension)
Neoral® - Novartis (capsules, suspension)
Generic (capsules, suspension)
Atopica® - Novartis (capsules, suspension)

Levels in skin higher and persist longer than in blood

Food or no food?

Cyclosporine Interactions

- Increased blood levels – azoles, macrolides, doxycycline, high-dose glucocorticoids, cimetidine, grapefruit juice
- Decreased blood levels – anticonvulsants, trimethoprim-sulfa, ciprofloxacin, terbinafine
- Avermectins?

Cyclosporine Effects

- Inhibit T lymphocyte
- Decreased IL-2, IL-3, IL-4, IL-5, TNF-α, INF-γ
- Inhibit mast cell/eosinophil production
- Inhibit histamine release
- Inhibit neutrophil chemotaxis
- Inhibit NK cell activity
- Inhibit B lymphocytes

Cyclosporine Efficacy

- Dogs: 15 – 75%
- Cats: Better
Immunotherapy

- True immunologic modulation
- Antigen specific response
- Lifelong treatment required
- Sublingual or subcutaneous administration
- 50-75% response rate
- Response rate influenced by
  - Owner expectations
  - Degree of allergy of patient

“Off the Shelf” Immunotherapy

- Allergy testing not required
  - Center Labs: 1980s
  - RESPIT: 2010s
- Most common regional allergens included?
- Injectable or oral immunotherapy options
- Safety?
- Efficacy?

Customized vs. Standardized Immunotherapy for Canine Atopic Dermatitis

<table>
<thead>
<tr>
<th></th>
<th>Good-excellent response rate (%)</th>
</tr>
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<tbody>
<tr>
<td>High dose customized</td>
<td>[Bar graph showing response rates]</td>
</tr>
<tr>
<td>Low dose customized</td>
<td></td>
</tr>
<tr>
<td>Standardized</td>
<td></td>
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</table>


ASIT Administration Schedule

<table>
<thead>
<tr>
<th>Day</th>
<th>Vial #1</th>
<th>Vial #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1.0</td>
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<tr>
<td>15</td>
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<td>17</td>
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<td>19</td>
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<td>22</td>
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<td>26</td>
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<td>30</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>56</td>
<td>1.0</td>
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</tr>
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After Day 65 injections are given every 3 weeks