Notes: Dermatology: Dana A. Liska, DVM, DACVD

Refer to a dermatologist (sooner rather than later) for

- allergy testing and allergen specific Immunotherapy (ASIT) after diagnosing atopic dermatitis
- unusual cases
- when a patient is not responding to what seems to be appropriate therapy
- cases of otitis with rod shaped bacteria

Four step approach: Easy to difficult:

1. Address parasites; in general the isoxazoline class is excellent for fleas, ticks and (off label) mites
   a. Market research recently showed that 52% of clients report they purchase flea/tick therapy from the vet\(^1\). That leaves 48% purchasing from outside your pharmacy. Dispense flea and tick therapy from the exam room base on the pet’s medical need. Ex: oral therapy for patient bathed frequently
   b. Simparica for Fleas
   c. Sarolaner starts killing fleas within 3 hours and has >96.2% efficacy at 8 hours until day 35\(^2\)
   d. For Flea allergy dermatitis: Flea counts done 8 hours after application of fleas show that Simparica maintains 99.8-100% reduction at day 35. This is important for the flea allergic dog as the sooner we can kill fleas the sooner they will experience relief and experience prolonged rapid speed of kill.
   e. In a Flea Infested Home: 2 doses of Simparica resulted in extinction of fleas by day 60\(^3\). In the past I told clients to expect 3 months so this a full month sooner. At day 14 there was >95% reduction in adult fleas. This is fabulous for the dog with FAD.
   f. Apoquel is not just a therapy for long term use. It can easily replace a steroid for acute flares associated with flea exposure.

\(^1\) Vet Street through Dec 2015 MAT

\(^2\) R.H. Six, et al; Evaluation of the speed of kill, effects on reproduction, and effectiveness in a simulated infested-home environment of sarolaner (Simparica™) against fleas on dogs; Vet. Parasitol (2016)

\(^3\) R.H. Six et al. Efficacy and safety of sarolaner (Simparica™) against fleas on dogs presented as veterinary patients in the United States; Vet. Parasitol (2016)
2. Manage secondary infections. If you treat for infection and the patient is completely non-itchy then consider endocrine disease as the underlying cause. There is a small subset of patients with relapsing infections as the only sign of an allergic etiology so keep this in mind.

   a. The benefits of performing tape cytology rather than just guessing at which infection is present: Good for the practice, the client, the patient, the staff and for the DVM

   b. Topical therapy: Evidence based medicine to say that if you stock a shampoo that contains\(^4\),\(^5\)

      i. Staph: 2 to 4% chlorhexidine or benzoyl based shampoo

         1. Study design bathed dogs for 5 minutes contact time

            a. Twice weekly for non-resistant strains
            b. Every other day for resistant strains.
            c. I still advocate for 10 minutes contact time and bath as frequently as possible.

      ii. Yeast: 3% Chlorhexidine or Chlorhexidine-azole shampoo

      iii. Study of topical sprays\(^6\): Investigators concluded that any of the 2-4% products: miconahex triz, chlorhex + phytosphingosine or triz chlor 4 spray were effective at inhibiting staph in vitro for at least 10 days. The only product that did not last 10 days was 1% chlorhexidine digluconate. Need more clinical studies so best to use these products often: alone (once or twice daily?) or in between baths

   c. I will share two clinical cases that demonstrate some, but not all, resistant strains of bacteria can lose degrees of resistance if you can avoid systemic antimicrobials and employ topical therapy alone

   d. Oral antimicrobials for yeast\(^7\).

      i. Ketoconazole or fluconazole, either at 5 mg/kg PO once daily. In the study, after 3 weeks of therapy, patients were evaluated and yeast numbers had dropped by 96-98%. Treat for 4 weeks and recheck.

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\(^4\) Mueller et al,. Vet Dermaol Aug 2012

\(^5\) Murayama et al, Vet Dermatol 2010; Dec; 21(6) 586-92


\(^7\) Sickafoose et al, Vet Ther. A non-inferiority clinical trial comparing fluconazole and ketoconazole in combination with cephalexin for the treatment of dogs with *Malassezia* dermatitis. 2010; 11(2)
ii. Terbinafine: Based on the results of a 2015 study\textsuperscript{8} my current recommendation is to aim for 35-40 mg/kg, orally, once daily.

e. Systemic Antimicrobials for Staph\textsuperscript{9}:
   i. Good evidence for high efficacy was noted with 1-3 consecutive subcutaneous injections of cefovacin at 8 mg/kg given 2 weeks apart.
   ii. Fair evidence for moderate to high efficacy: Amoxi-clavulanic acid at 12.5 mg/kg, BID, 21-28 d Cefadroxil, 22-35 mg/kg, BID, 28-42 d. Clindamycin, 5.5 mg/kg, BID, 21 d. \textbf{Attention:} another study indicates that 11 mg/kg by mouth twice daily give better pharmacokinetic profiles. TMPS, 30 mg/kg, QD or BID, 42 d. Sulfadometoprim, 55 mg/kg day 1, 27.5 mg/kg thereafter, 21-42 d.
   iii. ISCAD paper (International Society of Companion Animal Infectious Diseases)\textsuperscript{10}. Includes:
      1. What antibiotics are best for different tiers of treatment.
      2. When is it appropriate to perform culture and sensitivity testing.

f. Remember Client Barriers to Compliance\textsuperscript{11}:
   i. Dosing frequency
   ii. Multiple medications
   iii. Difficulty administering medication
   iv. Long course of therapy
   v. Poor/Low absorption if given with food
   vi. Poor understanding: disease and/or Rx
   vii. Dissatisfaction with time spent with DVM
   viii. Not partnering w client re treatment decisions
   ix. Client unwilling to ask questions
   x. Client's lifestyle
   xi. Client's beliefs: Natural vs. pharmaceutical western vs. eastern medicine


\textsuperscript{11} Maddison et al, Vet Ireland Journal, Jan 2011
g. My recommendation: think about frequency, duration, dose, & client Compliance Factors: choose therapy with the least frequent dosing interval: For the shortest period of time (This doesn't mean treat for 7 days but rather treat for 5-7 days past resolution of infection, At the highest dose

3. Food Allergy: Non-seasonal dermatitis: ONLY way to diagnose is dietary elimination trial
   a. Dogs:
      i. Age \( < 1 \) yr of age in 48% \( < 3 \) yrs of age in 83%
      ii. Older dogs affected also
      iii. Gender predisposition has not been identified
   b. Cats:
      i. 21 % of cats w/ AFR had concurrent GI signs
      ii. Age of onset before 3 yrs. of age: 72% of Atopics 52% of Food allergic
      iii. Age of onset after 6 yrs. of age: 26% of Food allergic 12% of Atopics
   c. Avoid OTC diets for dietary elimination trials:
      i. 2015 Publication:
         1. 52 foods/treats, obtained from online & retail sources, not identified by name
            a. 31 labeled correctly
            b. 20 potentially mislabeled
            c. 1 contained non-specific meat ingredient that could not be verified
            d. 16/52 = 30% (+) for meat ingredient not listed on label
            e. 4/52 = 7.6% claimed to contain beef but actually had none
            f. Pork: most common undeclared meat in 7 / 52 = 13%

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15 Raditic et al, J Anim Physiol Anim Nutr, 2011
16 Okuma et al. Food Control, 2015; 50: 9
### d. Common Food Allergens in dogs

**Common food allergens in dogs and cats (27 papers – 1967-2013)**

<table>
<thead>
<tr>
<th>Food</th>
<th>Number &amp; Percent</th>
<th>297 Dogs</th>
<th></th>
<th>Food</th>
<th>Number &amp; Percent</th>
<th>78 Cats</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef</td>
<td>102 (34%)</td>
<td></td>
<td></td>
<td>Beef</td>
<td>14 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td>51 (17%)</td>
<td></td>
<td></td>
<td>Fish</td>
<td>13 (17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chicken</td>
<td>45 (15%)</td>
<td></td>
<td></td>
<td>Chicken</td>
<td>4 (5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheat</td>
<td>38 (13%)</td>
<td></td>
<td></td>
<td>Wheat</td>
<td>3 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soy</td>
<td>18 (6%)</td>
<td></td>
<td></td>
<td>Corn</td>
<td>3 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamb</td>
<td>14 (6%)</td>
<td></td>
<td></td>
<td>Dairy</td>
<td>3 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corn</td>
<td>13 (4%)</td>
<td></td>
<td></td>
<td>Lamb</td>
<td>2 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg</td>
<td>11 (4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pork, Fish, Rice</td>
<td>Each (2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Pick elimination diet based on diet history of the dog
- Use veterinary prescription or home-cooked diet
- Do food challenges

### e. Number of flares upon individual ingredient food challenge

**Positive Challenges**

<table>
<thead>
<tr>
<th>Food Items</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>One</td>
<td>22</td>
<td>44%</td>
</tr>
<tr>
<td>Two</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>Three</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Four</td>
<td>2</td>
<td>4%</td>
</tr>
</tbody>
</table>


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17. Olivry T, et al. BMC Veterinary Research 2015. 11: 225
f. Dogs: Food trial length to achieve ≥ 50% improvement\textsuperscript{15}

How Long to Do a Food Trial?

- 209 dogs: Clinical remission ≥ 50%

<table>
<thead>
<tr>
<th>Duration (weeks)</th>
<th>Cumulative % improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>~52</td>
</tr>
<tr>
<td>5</td>
<td>~89</td>
</tr>
<tr>
<td>8</td>
<td>~96</td>
</tr>
<tr>
<td>13</td>
<td>~100</td>
</tr>
</tbody>
</table>

\textsuperscript{15}Olivry T, et al. BMC Veterinary Research 2015. 11: 225.

g. Cats: Food trial length to achieve ≥ 50% improvement\textsuperscript{15}

How Long to Do Food Trial?

- 40 cats: Clinical remission ≥ 50%

<table>
<thead>
<tr>
<th>Duration (weeks)</th>
<th>Cumulative % improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>~40</td>
</tr>
<tr>
<td>5</td>
<td>~61</td>
</tr>
<tr>
<td>6</td>
<td>~80</td>
</tr>
<tr>
<td>8</td>
<td>~92</td>
</tr>
<tr>
<td>13</td>
<td>~100</td>
</tr>
</tbody>
</table>

\textsuperscript{15}Olivry T, et al. BMC Veterinary Research 2015. 11: 225.
4. When all these have been addressed, or if the patient has a true seasonal pattern then atopic dermatitis is your diagnosis.
   a. Favrot’s criteria for diagnosing AD\textsuperscript{19}: 5 of the following = 85\% sensitivity and 79\% specificity
      i. Onset of signs < 3 years of age
      ii. Dog living mostly indoor
      iii. Glucocorticoid responsive pruritus
      iv. Alesional pruritus at onset
      v. Affected front feet
      vi. Affected pinnae
      vii. Non-affected pinnal margins
      viii. Non-affected dorsal lumbar area
   b. Pathogenesis: current research supports an outside in model\textsuperscript{20}: starts with a defect in the barrier function of the skin\textsuperscript{21}. Allergens penetrate and patients have more trans-epidermal water loss. Immune system


\textsuperscript{21} Piekutowska A et al. J Campar Pathol 2008; 138: 197-203
demonstrates a shift from Th1 to Th2 profile\textsuperscript{22,23} We know that TH2 cells are a source of IL-31; the cytokine that stimulates neuronal itch. The only way to reverse from Th2 back to Th1 is to allergy test and start allergen specific immunotherapy. Please continue to recommend referral to a board certified veterinary dermatologist for your patients with atopic dermatitis, sooner rather than later. Patients can be receiving Atopica, Apoquel and Cytopoint in advance of allergy testing. Steroids and antihistamines need to be discontinued.

c. Zoetis therapies Apoquel and Cytopoint are therapies for blocking pruritus

d. Apoquel:
   i. Small molecule that works intracellularly to inhibit signaling by allergic cytokines.
   ii. Daily oral medication
   iii. Indication: Control of pruritus associated with allergic dermatitis in dogs. Control of atopic dermatitis in dogs.
   iv. For dogs aged 12 months or older
   v. Rapid relief without the side effects of steroids

e. Cytopoint\textsuperscript{TM}
   i. Caninized anti-IL-31 monoclonal antibody. Biological therapy that works extracellularly to inhibit and neutralize cytokine IL-31.
   ii. Injection given in office every 4-8 weeks as needed for pruritus.
   iii. Indication: Aids in the reduction of clinical signs associated with atopic dermatitis in dogs.
   iv. For dogs of any age\textsuperscript{24}.
   v. Long lasting relief that helps restore the quality of life for dogs and owners.

f. Cytopoint is catabolized by the body, broken into its base amino acids which are reused.

g. How to explain it to your clients and staff: We all have antibodies that help us fight infection. This is simply an antibody that helps neutralize itch.

\textsuperscript{22} Shida et al. Vet Immunol Immunopathol. 2004; 102:19-31

\textsuperscript{23} Nuttall et al. Clin Exp Allergy. 2002; 32: 789-95

h. Visual for mechanisms of action:

i. Your TBM can share this excellent handout about when to reach for apoquel and when to reach for Cytopoint.
j. Apoquel is safe
   i. In safety studies
      1. Patients with atopic dermatitis\textsuperscript{25}: reported side effects were similar in dogs treated with either placebo or APOQUEL. In most cases, diarrhea, vomiting, anorexia, and lethargy spontaneously resolved with continued dosing.
      2. Patients with allergic dermatitis\textsuperscript{26}: What owners reported as adverse events were no different between APOQUEL and placebo in the Allergic Dermatitis study. Vomiting and diarrhea were the most common adverse reactions reported. In the first 7 days of the study, the side effects of APOQUEL are very similar to that of the Placebo group. In most of these cases the signs spontaneously resolved with continued dosing.
   ii. No definitive causal relationship has been established the administration of apoquel between apoquel and the development of cancer in dogs.
   iii. What’s on the label:
      1. Apoquel may exacerbate neoplastic conditions
      2. Dogs receiving apoquel should be monitored for the development of neoplasia
         a. My two cents worth: this is common sense for dogs on absolutely any medication
k. Cytopoint is safe: Overview
   i. All ages
   ii. Any medications\textsuperscript{27}
   iii. Adverse events comparable to placebo
   iv. Any concurrent disease
   v. Catabolized, not metabolized


\textsuperscript{27} Data on file. Study report C961R-US-13-051. Zoetis Inc