Treating Atopic Dermatitis: New Strategies for Practice Implementation of Allergen-Specific Immunotherapy

November 5 – 18, 2012

By Douglas DeBoer, D.V.M., DACVD

AAHA gratefully acknowledges Heska Corporation for their sponsorship of this web conference.

Douglas J. DeBoer, D.V.M., Diplomate A.C.V.D.
School of Veterinary Medicine
University of Wisconsin-Madison

Allergen-Specific Immunotherapy (ASIT)

- What is it?
- Why implement it in your practice?
- Barriers to implementation
- The role of appropriate diagnosis
- ASIT as a component of a multimodal treatment plan
- Sublingual immunotherapy (SLIT)
1. **What is ASIT?**

**Allergen-Specific Immunotherapy for AD**

- Allergen extracts mixed together according to each patient’s sensitivities
- Administered in gradually-increasing doses

**What is ASIT?**

- The *only* form of therapy for AD that is aimed at, and can potentially reverse, the underlying pathogenesis of the disease
- The *only* form of therapy for AD that can potentially produce great benefit to the patient without the use of drugs
- The *only* form of therapy for AD that can potentially produce permanent benefit, i.e. “cure” of the disease
**Mechanisms of ASIT**

- Modulation of Th1 vs. Th2 lymphocyte response

**Mechanisms Allergen-Specific Immunotherapy**

**Helper T-Lymphocyte Subsets**

- Th1 → IFN-γ → IgG
- Th2 → IL-4, IL-5, IL-13 → IgE
- Treg → IL-10
“BLOCKING ANTIBODY”

ALLERGEN

IgG

Mast Cell

Mechanisms
Allergen-Specific Immunotherapy

- Downregulation of effector cell activity (mast cells, eosinophils)
- Induction of immunologic ‘tolerance’
- Many effects may occur through effects on dendritic cells

2. Why Implement ASIT in Your Practice?
**Benefits of ASIT**

- **Very safe**, especially considering the alternative of long-term corticosteroid treatment
- Can be used long-term, with continued effect (does not 'stop working' after a time)
- **Cost-effective** – much less expensive than some drugs and frequent veterinary visits
- **Client-friendly** – especially new sublingual formulation
- **Profitable** – recurring revenue stream without any upfront investment

**Disadvantages of ASIT**

- Takes time to start working
- Does not work for every animal
- Slight risk of adverse reaction (shots)

**3. Barriers to Implementation**
ASIT Why is it not used more often?

- “I don’t really know how to use it”
- “It doesn’t work”
- “Owner afraid of needles”
  - New sublingual method is needle-free

ASIT Why is it not used more often?

- “Treatment sets are expensive”
  - $35-40/month is affordable to many clients
- “Testing is expensive”
  - Don’t create your own barrier to testing!

4. The Role of Appropriate Diagnosis

- __________
- __________
- __________
- __________
- __________
- __________
- __________
- __________
AD is a Clinical Diagnosis
Required Steps

1. History consistent with AD
2. Clinical signs consistent with AD
3. Rule out all other causes of pruritic dermatitis that appear similar to AD

Atopic Dermatitis
History

- Pruritus (with few/no lesions?)
- Onset at young age (<3 yr)
- May be seasonal at first
- May worsen over time
- Feet, face, ventrum
- Typically good response to corticosteroids

Atopic Dermatitis
Clinical Signs

- May be no primary rash...just erythema
- Most visible signs are secondary lesions
- Excoriations from scratching
- Secondary infections
- Seborrhea
- Bilateral chronic recurrent otitis externa
- Conjunctivitis or anal pruritus
- Respiratory signs are rare
AAHA Web Conference: Treating Atopic Dermatitis: New Strategies for Practice Implementation of Allergen-Specific Immunotherapy

Atopic Dermatitis
Rule out all other similar diseases

- Parasites: fleas or mites
  - Sarcoptes, Cheyletiella
- Pruritic pyoderma of nonallergic cause
- Primary yeast dermatitis without AD
- Food allergy

\[ \text{AD} \]

The Role of “Allergy Testing”

The Truth About “Allergy Tests”

- No allergy test is perfect
  - All will generate some false positive reactions
  - Some atopic animals will be negative
- Allergy tests do not answer the question: “Does this itchy dog have allergies?”

Parasites: fleas or mites

- Sarcoptes, Cheyletiella

Pruritic pyoderma of nonallergic cause

Primary yeast dermatitis without AD

Food allergy

No allergy test is perfect

- All will generate some false positive reactions
- Some atopic animals will be negative

Allergy tests do not answer the question: “Does this itchy dog have allergies?”
Why Allergy Test?

- Allows clinician to offer immunotherapy instead of symptomatic treatment
  - “I've made a clinical diagnosis of AD. Which allergens should I select for immunotherapy?”
- May permit avoidance measures

5. ASIT in a Multimodal Treatment Plan
A New and Integrated Approach

- **Old approach:** managing inflammation, reacting to the end process of the disease

- **New approach:** much broader, multifaceted approach; proactive to correct actual disease pathogenesis where possible

---

A New and Integrated Approach

- Elimination of allergens
- Skin hygiene, augmenting epidermal barrier
- Control and prevention of secondary infections
- Managing inflammation
- Modifying immune response

---

Selection and Formulation of Allergen-Specific Immunotherapy
Effects of immunotherapy are mostly (but not entirely) allergen-specific
- Identify all substances to which patient is hypersensitive
- Avoid ‘false positive’ test results

**Allergen Selection**

- Often, no need to treat with every positive allergen
  - Select 10-12 allergens based on:
    - Strongest test reactivity
    - Greatest exposure
    - Base on patient’s history
    - Base on botanical group of pollen
    - Base on known cross-reactivities of allergens
    - Importance of mold sensitivity in your area
- Follow company recommendations

**Setting Client Expectations**

- AD is a lifelong disease that is usually very controllable, but often not curable.
- ASIT takes some time to work, and does not work in all animals.
- ASIT is only part of an overall management plan that will also include:
  - Temporary control of pruritus while waiting for ASIT to work
  - Infection control and prevention; parasite control
  - Periodic use of additional anti-inflammatory medications to control flares
No problem:
- Antihistamines, fatty acid capsules
- Antibiotics, antifungals
- Topical products
- Low-dose oral corticosteroids
- Cyclosporine A

How do you know what's working?
- Every 3 months, try to taper the concurrent meds

In some animals, the benefit of ASIT is partial control
- Concurrent meds may be tapered down to very low levels
- Owner may be convinced that the combination of ASIT plus concurrent meds provides best control

Important to recheck (3, 6, 12 months)
- Infection control
- Avoiding other flare factors (fleas...)
- Make sure no reactions
- Schedule adjustments
  - Reactions - reduce dose
  - Adjustment of any concurrent medications

Schedule adjustments

Infection control

Avoiding other flare factors (fleas...)

Make sure no reactions

Schedule adjustments
  - Reactions - reduce dose
  - Adjustment of any concurrent medications

Reactions

Schedule adjustments

Reactions - reduce dose
About 60%-70% of dogs have “acceptable improvement” (>50% reduction in signs)
Response starts after several months
Best response after 1 year or more

Localized itch in area of dosing, or transient worsening after dose (~10%)
Generalized anaphylaxis (<1%) is a risk with shots
  - Pretreat with antihistamine and do next few injections in hospital
  - Switch to sublingual formulation

Use medical consultation services from ASIT supplier
Allergen-specific immunotherapy (ASIT) via administration of allergen extracts into the oral cavity, instead of by injection

Widely used in Europe for treatment of human allergies

"Allergy Drops" instead of "Allergy Shots"

Absorption through oral mucosa
Captured by unique oromucosal dendritic cells
Induction of immunologic tolerance

<table>
<thead>
<tr>
<th>How Supplied</th>
<th>Shots</th>
<th>Drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approx $35-40/month</td>
<td>2-3 vials of increasing strength</td>
<td>3 bottles of increasing strength</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concurrent Medication OK?</th>
<th>Shots</th>
<th>Drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes; takes some time to work!</td>
<td>Yes; takes some time to work!</td>
<td></td>
</tr>
</tbody>
</table>

Workup
Clinical diagnosis of AD, followed by allergy test
Clinical diagnosis of AD, followed by allergy test

Cost to client
Approx $35-40/month
Approx $35-40/month
**How Does it Differ from Allergy Shots?**

<table>
<thead>
<tr>
<th>Shots</th>
<th>Drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>How Supplied</td>
<td>2-3 vials of increasing strength</td>
</tr>
<tr>
<td>Cost to client</td>
<td>Approx $35-40/month</td>
</tr>
<tr>
<td>Concurrent Medication OK?</td>
<td>Yes; takes some time to work!</td>
</tr>
<tr>
<td>Workup</td>
<td>Clinical diagnosis of AD, followed by allergy test</td>
</tr>
<tr>
<td>Ingredients</td>
<td>Saline-based allergen extracts in a saline diluent</td>
</tr>
<tr>
<td>Schedule</td>
<td>Frequent injections at first, gradually taper to q 2-4 weeks</td>
</tr>
</tbody>
</table>

**How Does it Differ from Allergy Drops?**

<table>
<thead>
<tr>
<th>Shots</th>
<th>Drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>How Supplied</td>
<td>2-3 vials of increasing strength</td>
</tr>
<tr>
<td>Cost to client</td>
<td>Approx $35-40/month</td>
</tr>
<tr>
<td>Concurrent Medication OK?</td>
<td>Yes; takes some time to work!</td>
</tr>
<tr>
<td>Workup</td>
<td>Clinical diagnosis of AD, followed by allergy test</td>
</tr>
<tr>
<td>Ingredients</td>
<td>Saline-based allergen extracts in a saline diluent</td>
</tr>
<tr>
<td>Schedule</td>
<td>Frequent injections at first, gradually taper to q 2-4 weeks</td>
</tr>
</tbody>
</table>
How Does it Differ from Allergy Shots?

<table>
<thead>
<tr>
<th>Shots</th>
<th>Drops</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How Supplied?</strong></td>
<td>2-3 vials of increasing strength</td>
</tr>
<tr>
<td><strong>Cost to client</strong></td>
<td>Approx $35-40/month</td>
</tr>
<tr>
<td><strong>Concurrent Medication OK?</strong></td>
<td>Yes; takes some time to work!</td>
</tr>
<tr>
<td><strong>Workup</strong></td>
<td>Clinical diagnosis of AD, followed by allergy test</td>
</tr>
<tr>
<td><strong>Ingredients</strong></td>
<td>Saline-based allergen extracts in a saline diluent</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
<td>Frequent injections at first, gradually move to q 2-4 weeks</td>
</tr>
</tbody>
</table>

Administration is Easy!

What Response Rate Can I Expect?

- Newly-diagnosed cases: ~60% good-excellent
  - About equivalent to shots
  - Multicenter field trial; hundreds of dogs over several years

Using Heska ALLERCEPT® Therapy Drop product, as reported in *Veterinary Dermatology* 23(Suppl 1): 65, 2012
What Response Rate Can I Expect?

- Patients who have failed allergy shots: ~50%

<table>
<thead>
<tr>
<th>Response</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>28%</td>
</tr>
<tr>
<td>Good</td>
<td>15%</td>
</tr>
<tr>
<td>Fair</td>
<td>23%</td>
</tr>
<tr>
<td>Poor</td>
<td>34%</td>
</tr>
</tbody>
</table>

Using Heska ALLERCEPT® Therapy Drops product, as reported in Veterinary Dermatology 23(Suppl 1): 65, 2012.

Is it Safe?

**YES, very!**

- Can be used safely even if there is a history of anaphylaxis from allergy testing or shots
- Adverse effects are uncommon, mild
  - Transient worsening
  - Itchy mouth
  - Upset stomach

Current Products

- **ACTT™ Allergy Drops (Bio-Medical)**
  - No patient efficacy data reported
- **ALLERCEPT® Therapy Drops (Heska)**
  - Multicenter patient efficacy study – 60% response
- **Allerpaws (Nelco)**
  - Studied in experimental model, no patient efficacy data reported
- **Oromucosal Spray (Respit™)**
  - No patient efficacy data reported
Client Compliance

- Owner fear of needles
  - Limits compliance with injection schedule, which may limit efficacy
  - Prevents them from testing pet, because they would never consider giving injections

Questions?
Instructions for CE Certificate

1. To complete the evaluation, please go to the following website: http://www.keysurvey.com/1463234/1241/
2. After completing the evaluation, you will automatically be linked to the Continuing Education Certificate. The CE certificate can only be accessed after the evaluation is completed.
3. Download the CE Certificate (in PDF format) to your computer and print enough copies for those persons viewing the web conference with you.

Questions to the Speaker

Please email your questions to webconference@aaahenet.org by Sunday, November 25, 2012.

Dr. DeBoer will provide written responses to all of the questions and they will be posted on AAHA’s website by Friday, December 7, 2012.

Thank you for your participation!

AAHA gratefully acknowledges Heska Corporation for their sponsorship of this web conference.