Advances in Allergy/Immunology 2014

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Order of Presentation

Respiratory allergy update
Influenza Vaccination
Anti-IgE for urticaria

Nothing to declare

Manifestations of “Allergy”!

- Itching of the eyes, nose, throat
- Drainage
- Headache
- Cough or throat clearing
- “Bronchitis”
- General misery
- Poor performance in school or at work

Rhinitis
Conjunctivitis
Asthma
Sinusitis

Mesquite, by ZooFari
# Allergic Rhinitis/Asthma/Conjunctivitis

*Inhaled Allergens*

## Categories of Management options:

1. **Maximal preventive measures**
2. **Treatment of symptoms**
3. **Retraining of the immune system**

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## 2. Treatment of Symptoms

### Saline (rarely, budesonide) irrigation

### Oral antihistamines (multiple)

### Nasal sprays

<table>
<thead>
<tr>
<th>Corticosteroids</th>
<th>(multiple)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines</td>
<td>(azelastine)</td>
</tr>
<tr>
<td>Decongestants</td>
<td>(oxymetazoline)</td>
</tr>
<tr>
<td>Mast cell stabilizers</td>
<td>(cromolyn sodium)</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>(ipratropium)</td>
</tr>
</tbody>
</table>

*Clinical pearl: best for treating DRAINAGE*

### Leukotriene inhibitors

- Receptor blockers (montelukast, zafirlukast)
- Production inhibitors (zileuton)

### Inhaled agents

- Corticosteroids (multiple)
- Corticosteroid/LABA (multiple)
- Anticholinergics (ipratropium/tiotropium)
- Mast cell stabilizers (cromolyn sodium)

### Various OTC agents and remedies

### Oral corticosteroids/antibiotics as a last resort
New developments in OTC medication status

The first nasal corticosteroid to go OTC:
Triamcinolone acetonide (Nasacort)

Clinical Pearl: Correct technique for use of nasal spray

Ketotifen eye drops are now OTC (Zaditor, Alaway)
  - antihistamine/mast cell stabilizer

Montelukast (Singulair) is NOT going OTC any time soon.

What to do if your patient’s quality of life is still not satisfactory?

Allergic Rhinitis/Asthma/Conjunctivitis

Inhaled Allergens

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Testing for specific inhalant allergens

Serum specific IgE testing (examples)
  - Dermatophagoides farinae; Dermatophagoides pteronyssinus (dust mites)
  - Cat
  - Cedar/cypress
  - Oak, birch, sycamore, elm
  - Rye grass
  - Ragweed, English plantain
  - Alternaria
  - Aspergillus
Testing for Specific Allergens

Prick skin testing/intradermal testing

Photo by: Gundling

1. Maximal Preventive Measures

Personalized counseling avoidance measures:
- Dust mite cleaning
- Humidity control
- Air filtration improvement (HEPA filters)
- Pollen/mold spore count awareness
- Mold remediation (indoor and out)
- Others

Which allergen is most associated with death due to severe asthma?

A. Alternaria
B. Cat
C. Dust mites
D. Rye grass

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3. **Retraining of the Immune System**

Allergen Immunotherapy- subcutaneous “SCIT”

- Generally works very well
- Very time consuming
- Requires injections every 1-4 weeks
- Associated risks

*New kid on the block!
Oral or “sublingual” allergen immunotherapy*

**Sublingual Immunotherapy**

SLIT-tablets
- Rapidly dissolving tablet held under the tongue until dissolved
- Self-administered, once daily

SLIT-drops
- Extract of allergen held under the tongue, then swallowed
- Self-administered, once daily

2014 – New FDA Approvals

Five grass sublingual tablet
- Oralair by Stallergenes (approved for ages 10-65)

Timothy grass tablet
- Grastek by Merck (approved for ages 5-65)

Short ragweed tablet
- Ragwitek by Merck (approved for ages 18-65)

(Existing off-label use of some drops for the past several years)
Advantages of SLIT

Can be self-administered at home (for the most part)
Probably safer than SCIT

Disadvantages of SLIT

Limited kinds of antigens (allergens)
May not work quite as well as SCIT
Long-term benefit of SCIT is better known

Mechanism of Action

Gut-associated lymphoid tissue (GALT)
- Tonsils/lymphoid tissue of the posterior pharynx
- Peyer’s patches throughout the small intestine
- Lymphoid organs (mesenteric lymph nodes, spleen and liver)

Gut mucosal immune system TRIES to tolerate non-pathogens.

Mechanism of Action

Changes to both humoral and cellular immunity

Antigen uptake by mucosal dendritic cells
Presentation to T cells in the draining lymph nodes
- Activation of T regulatory cells
  - Upregulation of IL-10
  - Increasing levels of specific IgG4
- Downregulation of mucosal mast cells/effecter cells
- Blunting of seasonal increases of specific IgE
- Increased CD8+ T cells
Adverse effects/contraindications of SLIT

- >/= 5% experience itching/pain of the oropharynx
- Cough
- Risk of systemic reactions
- Not for pts with severe, uncontrolled asthma
- Prescribe epinephrine and train in appropriate use

Approved for use in Europe in 2008 and authorized in 31 countries
More than 20 million doses have been given to more than 110,000 pts.

Influenza vaccination

“Doctor, I am allergic to eggs. Can I receive the flu vaccine?”
A. Just give the vaccine
B. Allergy skin test to hen’s egg
C. Allergy skin test to the vaccine
D. Give a test dose
E. Avoid completely

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But wait........
What is the best approach to administration of the influenza vaccine in patients who are allergic to hen’s egg?

Influenza

294,128 hospitalizations
23,609 deaths

Much of this morbidity and mortality can be prevented with vaccination.

Egg Allergy

Prevalence 0.5-2% in small children; lower in adults

5-20% of US citizens receive the influenza vaccination—(about 15-60 million vaccines annually)

Ovalbumin content of vaccines
(Inactivated, trivalent)

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afluria</td>
<td>CSL Limited</td>
<td>&lt;1.0 mcg/0.5mL</td>
</tr>
<tr>
<td>Fluarix</td>
<td>GlaxoSmithKline</td>
<td>0.05</td>
</tr>
<tr>
<td>Flucelvax</td>
<td>Novartis Vaccines</td>
<td>Not in package insert</td>
</tr>
<tr>
<td>FluLaval</td>
<td>ID Biomedical Corp</td>
<td>&lt;0.3</td>
</tr>
<tr>
<td>Fluvin</td>
<td>Novartis Vaccines</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>Not in package insert</td>
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Vaccination reactions in egg allergic patients

- 7 published studies
- 1600 patients with egg allergy
  - 0-6.3% involve reactions confined to the skin
  - 0-4.8% involve mild respiratory or GI symptoms

  *No hypotension*
  *No need for epinephrine*

3,640 patients with reported egg allergy in an adjuvanted H1N1 vaccine:
- 1.2% had skin reactions
- 0.7% had respiratory reactions, including 2 that were given epinephrine (authors concluded these reactions were not anaphylaxis)

Studies with non egg-allergic controls:
*Similar rates of reactions*

185 patients with a history of anaphylaxis or severe reaction to egg ingestion, vaccinated with TIV:
- 119 received a divided dose
- 66 received a single dose

  *No serious reactions*

As of 2 years ago...

*Recommendations for Influenza Vaccination in the Egg Allergic Patient:*

**Type of reaction...**

- **HIVES ONLY:**
  - ok to administer vaccine in a primary care setting
- **POSSIBLE SYSTEMIC REACTION:**
  - refer to A/I office for work-up of the egg allergy administration in a setting prepared for anaphylaxis

Howe LE, et al. Safe administration of seasonal influenza vaccine to children with egg allergy of all severities. Ann Allergy Asthma Immunol 2011; 106:446-7
As of 11 months ago....

Fall armyworm  Public domain- US govt

“Flublok”
Recombinant hemagglutinin proteins produced in an insect cell line.

“Flucelvax”
Prepared from virus propagated in cell culture

These vaccines use no egg protein

The CDC’s revised position:
The trivalent influenza vaccination is contraindicated in patients with, “History of severe allergic reaction to any component of the vaccine, including egg protein, or after a previous dose of any influenza vaccine.”

CDC recommendation this past year: RIV for patients with egg allergy

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6207a1.htm?s_cid=rr6207a1_w#Fig2

The main advantage of the RIV is that it can be PRODUCED QUICKLY
Most recently.....

More data from the AAAAI Practice Parameters: ...supports the safe use of TIV in egg allergic individuals.

“For egg-allergic patients 18 years of age and older, either egg-based or egg-free influenza vaccination can be used.”

“Special precautions beyond those used for any vaccine are not needed.”

Updated Practice Parameters for the
American Academy of Allergy, Asthma and Immunology

- Additional Evidence-Based Guidelines and Resources
- “Update on Egg Allergy and Influenza Vaccine”
- Ann Allergy Asthma Immunol 111 (2013) 301-302

Urticaria

Acute urticaria is frequently due to allergy

Chronic urticaria (>6 weeks) is very seldom due to allergy.

Think “autoimmune” etiology
Mechanism of chronic urticaria:

Not fully elucidated, but IgG antibodies probably trigger degranulation of mast cells and basophils by attaching to:

- IgE
- Fc epsilon RI (cell receptor)
- Fc epsilon RII (cell receptor)


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News Flash!

- Omalizumab (Xolair), previously approved for severe asthma, is now approved for use in chronic urticaria
- Significant improvement after just 1-2 doses in 60-70% of patients.

Summary

- The first nasal corticosteroid spray has gone otc.
- Oral/sublingual allergen IT is now approved for use in the US.
- Two new influenza vaccines are made without eggs.
- Chronic urticaria can be well-treated with omalizumab