Urticaria and Food Allergy

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Edward Brooks, M.D. has disclosed that he is on the Scientific Advisory Board for United Allergy Labs and on the Speaker’s Bureau for Merck Pharmaceuticals.

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Presentation of Urticaria

- Patients typically present with pruritic and elevated papular to plaque-like (plateau) elevations of skin
- The duration of each lesion should help in defining the type of urticaria and therapy
  - Less than 24 hours (each) suggestive of an IgE mediated process and usually respond better with antihistamines
  - Longer than 24 hours (each) implies cell mediated process (contact dermatitis, eczema), IgG/IgM antibody associated (i.e., serum sickness), or vasculitis that usually require steroids or other immuno-suppressants
Urticaria

Perivascular infiltration of lymphocytes with rare eosinophils – may respond to antihistamines

Interstitial edema

Symptomatic Dermatographism

- Simply scratching the skin promotes linear hives within minutes
- Delayed form described
- Typically is short-lived in duration (1/2 to 3 hours) and responds readily to antihistamines

Acute vs Chronic Urticaria

- Acute Urticaria – lasts 6-8 weeks or less
  - Viral syndromes (especially in young children)
  - Insect bites or stings (fire ants, scabies)
  - Food induced reactions (eat this- get that)
  - Medication related (antibiotics, NSAIDs, narcotics)
- Chronic Urticaria – lasting longer than 8 weeks
  - Physical urticarias (dermographism, cholinergic, cold)
  - Urticarial vasculitis
  - Urticaria/angioedema associated with autoimmunity
  - Autoimmune urticaria
  - Idiopathic urticaria
Therapeutic Options

- Therapy with antihistamines work best for most patients with acute types of short-lasting urticaria
- Combination therapy should be attempted if H1 antagonists do not suffice, H2 antagonists, montelukast
- Steroids and other immunosuppressants should be reserved for severe urticaria associated with angioedema of oropharynx or other systemic signs, moderate to severe drug reactions, urticarial vasculitis, and refractory cases of CIU

Anaphylaxis

Defined as symptoms involving >=2 organ systems resulting from food allergy
Food is the most common cause of anaphylaxis treated in ER’s
Peanuts & tree nuts culprit in >90% of fatal cases due to foods

Anaphylaxis

Sx develop in seconds - 4 hours
- Sense of “impending doom”
- Respiratory compromise
- Abdominal symptoms
- Hypotension
- Skin manifestations (in many but not all)
Reaction may be biphasic
- Late sx may be worse than initial sx
- Observe for 4 hours minimum (up to 24 hrs-rebound)
Increased risk for fatal anaphylaxis
- 1) delayed epinephrine administration
- 2) Young adult/teen
- 3) Underlying asthma
- 4) No skin symptoms
### Allergic Food Disorders

**IgE-Mediated**
- Skin: Urticaria, Angioedema, Dermatitis herpetiformis
- Respiratory: Asthma, Rhinitis
- Gastrointestinal: Gluten-associated anaphylaxis, Oral allergy, Celiac Dz.
- Systemic: Anaphylaxis, Food-associated, exercise-induced anaphylaxis

**Non-IgE-Mediated**
- Atopic dermatitis
- Heiner’s Syndrome
- Eosinophilic Esophagitis
- Gastritis/GERD
- Enterocolitis Enteropathy/Proctitis

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### Epidemiology

#### Age groups
- Adults: 2% (additional 3% with mild)
- Infants/Children: 6-8%

#### Foods
- Transient: Cow’s milk, egg, wheat, soy
- Persistent: Peanut, tree nuts, seafood

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### Diagnosis: History/Physical

#### History
- Symptoms, timing, reproducibility, associations (EtOH, exercise)
- Acute reactions or chronic disease?

#### Diet details/Symptom diary
- Specific causal food(s)?
- ‘Hidden’ ingredients?

#### Physical examination
- Exclude non-allergic causes of symptoms – infection, IBD, essential reflux

#### General approach identified
- Allergy versus intolerance
- IgE versus non-IgE mediated
Diagnostic Approach

IgE-mediated acute symptoms
Tests positive - elimination diet
Tests negative - reintroduce (possibly as oral challenge)

IgE-mediated chronic symptoms
Screening tests by history, eliminate positives, if resolved do oral challenges

Non-IgE-eosinophilic disorders
Elimination diet and oral challenges
Therapeutic intervention - steroids
Patch testing (unproven)

Testing - ImmunoCap

Allergen fixed to solid phase matrix – sponge-like with high surface area

Patient serum IgE placed onto Cap, and binds to allergen

Enzyme conjugated anti-IgE placed on Cap binding to patient IgE

Fluorescent substrate bound to enzyme

Fluorescence intensity measured

IgE quantified against standards

Table 98-3: Food-specific IgE concentrations predictive of clinical reactivity

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Decision Point [ULS]</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPF</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg (15-25 y/o)</td>
<td>7</td>
<td>61</td>
<td>95</td>
<td>98</td>
<td>56</td>
</tr>
<tr>
<td>Milk (1-1 y/o)</td>
<td>15</td>
<td>97</td>
<td>94</td>
<td>95</td>
<td>95</td>
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<tr>
<td>Peanuts</td>
<td>15</td>
<td>57</td>
<td>96</td>
<td>100</td>
<td>53</td>
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<tr>
<td>Fish</td>
<td>20</td>
<td>25</td>
<td>98</td>
<td>106</td>
<td>56</td>
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<tr>
<td>Soybeans</td>
<td>30</td>
<td>44</td>
<td>94</td>
<td>93</td>
<td>62</td>
</tr>
<tr>
<td>Wheat</td>
<td>20</td>
<td>61</td>
<td>95</td>
<td>24</td>
<td>87</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>25</td>
<td>61</td>
<td>95</td>
<td>74</td>
<td>87</td>
</tr>
</tbody>
</table>

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Elimination Diets

Types of diets
- Suspected food(s)
- Specific “eat only” diet (rice, water, lamb)
- Elemental diet (hydrolyzed cow’s milk, amino acid)

Timing
- 2 to 6 weeks depending upon disorder (eczema, GI)

Dietary Elimination: Pitfalls

Hidden ingredients
- Peanut butter in sauces or egg rolls

Labeling issues
- “Spices” “Natural flavor” “May contain…”

Cross contamination
- Shared processing equipment

Seeking assistance
- Registered dietitian
- Food Allergy and Anaphylaxis Network
  (www.foodallergy.org, 800-929-4040)

Prevalence of Clinical Cross Reactivity Among Food “Families”

- 5% with legume allergy react to > 1 legume (includes peanut)
- 15% with grain allergy react to > 1 grain
- 30-100% fish allergic react to > 1 fish
- 15-40% tree nut allergic react to > 1 tree nut
- 90% with cow’s milk allergy react to goat milk
- 10% with cow’s milk allergy react to beef
Allergy Testing/challenge

Food

Sensitized

Sensitized

No IgE

No reaction

Clinical reaction

Re-exposure

Tolerance: Resolution of Allergy

Egg, milk, wheat, soy

50% tolerant by age 7

Tree Nut, Seafood

many years to lifetime

Peanut

20% tolerate by adult

Features may require:

Decreased immune response

Waning of IgE response

Modification of T cell responses

Improved gut barrier

Prevention – Old AAP Recommendations

Mother should consider excluding peanuts and nuts from diet while breastfeeding.

Breastfeeding for 6 months: “... exclusively breast-feeding may promote the development of oral tolerance and prevent some food allergy and atopic dermatitis.”

Delayed introduction of solid foods until 6 months of age.

Hypoallergenic formula for supplementation (not soy).

Peanuts, nuts, and seafood should be avoided until 3 years of age, eggs avoided until age 2, and milk avoided until age 1.
Prevention – AAP Recommendations 2008

1. No restrictions on maternal diet.
   At the present time, there is lack of evidence that maternal dietary restrictions during pregnancy play a significant role in the prevention of atopic disease in infants. Similarly, antigen avoidance during lactation does not prevent atopic disease, with the possible exception of atopic eczema, although more data are needed to substantiate this conclusion.

Prevention – AAP Recommendations 2008

2. Breastfeeding for 4 months for high risk infants.
   For infants at high risk of developing atopic disease, there is evidence that exclusive breastfeeding for at least 4 months compared with feeding intact cow milk protein formula decreases the cumulative incidence of atopic dermatitis and cow milk allergy in the first 2 years of life.

3. Breastfeeding for 3 months for all infants.
   There is evidence that exclusive breastfeeding for at least 3 months protects against wheezing in early life. However, in infants at risk of developing atopic disease, the current evidence that exclusive breastfeeding protects against allergic asthma occurring beyond 6 years of age is not convincing.

Prevention – AAP Recommendations 2008

4. Hydrolyzed formula for high risk infants.
   In studies of infants at high risk of developing atopic disease who are not breastfed exclusively for 4 to 6 months or are formula fed, there is modest evidence that hydrolyzed formulas, compared with cow milk formula, in early childhood. Comparative studies of the various hydrolyzed formulas have also indicated that not all formulas have the same protective benefit. Extensively hydrolyzed formulas may be more effective than partially hydrolyzed in the prevention of atopic disease. In addition, more research is needed to determine whether these benefits extend into later childhood and adolescence. The higher cost of the hydrolyzed formulas must be considered in any decision-making process for their use.
   To date, the use of amino acid-based formulas for atopy prevention has not been studied.

5. Soy-based formula is not protective for prevention of allergy.
   There is no convincing evidence for the use of soy-based infant formula for the purpose of allergy prevention.
Prevention – AAP Recommendations 2008

6. No solid food until 4-6 months.
Although solid foods should not be introduced before 4 to 6 months of age, there is no current convincing evidence that delaying their introduction beyond this period has a significant protective effect on the development of atopic disease regardless of whether infants are fed cow milk protein formula or human milk. This includes delaying the introduction of foods that are considered to be highly allergic, such as fish, eggs, and foods containing peanut protein.

7. No dietary restrictions after 4-6 months.
For infants after 4 to 6 months of age, there are insufficient data to support a protective effect of any dietary intervention for the development of atopic disease.

Prevention – AAP Recommendations 2008

8. Long term effects of dietary restrictions unknown.
Additional studies are needed to document the long term effect of dietary interventions in infancy to prevent atopic disease, especially in children older than 4 years and in adults.

9. Eliminate identified food allergens from diet.
This document describes means to prevent or delay atopic diseases through dietary changes. For a child who has developed an atopic disease that may be precipitated or exacerbated by ingested proteins (via human milk, infant formula, or specific complementary foods), treatment may require specific identification and restriction of causal food proteins.

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