Food Allergy Diagnosis and Management

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Objectives

• Food Allergy Diagnosis and Management
  – Overview of Food Allergy Rates and Symptoms
  – Diagnosis:
    • Importance of the history
    • Diagnostic tools available
    • Interpretation of results and natural history
    • Appropriate referrals
  – Current Food Allergy Guidelines
  – Economic impact of food allergy

• Prevention of Food Allergy (Dr. Sharma)

• Mental Health in Food Allergy (Dr. Herbert)
Food Allergy

• **8% Children** (2.4% multiple, 3% severe reactions)
  – Cow’s milk 2.2%
  – Peanut 1.8%
  – Tree Nuts 1.7%

• **5% Adults**
  – Shellfish 1.9% (3.1% in Blacks)
  – Fruits 1.6%
  – Vegetables 1.3%

• Overall increase in the rates of FA over time
• IgE sensitization to food (milk, egg, peanut) have remained **stable** over the decades (80s/90s vs 2005-06)

-Gupta et al. Pediatrics 2011;128:e9-17
-Sicherer JACI 2014;133:291-307
Risk Factors for FA

• Gender (males in children)
• SES (increased with more affluence)
• Race (Asian and Black children)
• Genetics
• Atopy
• Vitamin D
• Dietary fat – omega-3s
• Obesity (inflammatory state)

• Antacids
• Hygiene/Infections
• Timing and Route of exposure to foods
• Place of birth
  – US born
  – children of immigrants
  – arriving before age 2y
• Microbiome, antibiotic use
• Endocrine disruptors/toxins

-Sicherer JACI 2014;133:291-307
-Keet et al JACI 2012;129:169-175.
## IgE Mediated

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Features</th>
<th>Age</th>
<th>Foods</th>
<th>Natural Hx</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anaphylaxis</strong></td>
<td>Rapid onset, multiorgan</td>
<td>any</td>
<td>PN, TN, F, SF, Milk, Egg</td>
<td>variable</td>
<td>SPT, specific, IgE, Component resolved diagnostics (CRD)</td>
</tr>
<tr>
<td><strong>Angioedema/urticaria</strong></td>
<td>20% acute, 2% chronic</td>
<td>younger</td>
<td>(wheat, soy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td>Immediate vomiting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rhinitis, Asthma</strong></td>
<td>Rarely isolated, inhalation</td>
<td>younger</td>
<td>Wheat, egg, seafood</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral Allergy</strong></td>
<td>Oral itching, 1% anaphylaxis</td>
<td>older</td>
<td>Fruits, vegetables</td>
<td>persists</td>
<td>Prick-prick</td>
</tr>
<tr>
<td><strong>Delayed Meat Induced</strong></td>
<td>6-8 hour delay, rare</td>
<td>α-Gal IgE (CHO moiety)</td>
<td></td>
<td>α-Gal IgE</td>
<td></td>
</tr>
<tr>
<td><strong>Food-exercise induced anaphylaxis</strong></td>
<td>Only within 2 hours of exercise</td>
<td></td>
<td>Wheat, shellfish celery</td>
<td>persists</td>
<td>Exercise test SPT, IgE</td>
</tr>
</tbody>
</table>

-adapted from Sicherer JACI 2014;133:291-307
Persistence vs Resolution of IgE mediated FA

- Higher specific IgE levels
- Larger skin prick test
- Reaction on first exposure
- Atopic Dermatitis Severity
- [www.cofargroup.org](http://www.cofargroup.org)
### Mixed IgE-Cell Mediated Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Features</th>
<th>Age</th>
<th>Foods</th>
<th>Natural Hx</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopic Dermatitis</td>
<td>Food induced in 35% of moderate-severe</td>
<td>Infants &gt; Children &gt; Adults</td>
<td>Egg, milk</td>
<td>resolves</td>
<td>SPT, IgE</td>
</tr>
<tr>
<td>Eosinophilic GI disease</td>
<td>Biopsy proven eosinophils in GI tissue, dysphagia, reflux, weight loss, impaction</td>
<td>any</td>
<td>Many, milk 70%</td>
<td>persistent</td>
<td>Empiric diets, EGD + Bx, SPT, IgE</td>
</tr>
</tbody>
</table>

-adapted from Sicherer JACI 2014;133:291-307
## Non-IgE Mediated

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Features</th>
<th>Age</th>
<th>Foods</th>
<th>Natural Hx</th>
<th>Tests</th>
</tr>
</thead>
</table>
| FPIES                          | **Chronic exposure:** Emesis, diarrhea, poor growth, lethargy  
  **Re-exposure:** 1.5-2 h delay in emesis, hypotension, lethargy | Infancy-toddlerhood | Milk and soy, Solids: rice, oat, banana, other solid foods | resolves   | IgE helps with persistence |
| Food protein induced proctocolitis | Mucousy bloody stools in infants               | infancy           | Milk, soy +/-BF                    | resolves   | Empiric diet               |
| Celiac Disease                 | Autoimmune, enteropathy, malabsorption        | any               | Gliadin (wheat, barley, rye)       | lifelong   | IgA -TTG, HLA and biopsies |
| Heiner Syndrome                | Rare, pulmonary infiltrates, FTT, anemia      | infancy           | milk                               |            | Milk IgG precipitins       |

-adapted from Sicherer JACI 2014;133:291-307
Possible peanut reaction

Panel of food specific IgE levels positive to 10 foods

Patient avoids 10 foods that she was previously tolerating and peanut

Sees Allergy 3 months later

Tolerance now to the 10 foods is unknown

Patients undergoes repeat testing

Multiple OFCs to confirm and go back to original diet

Total costs = $3-4K
Economic Impact of Childhood Food Allergy in the United States

• Purpose:
  – To determine the economic impact of childhood food allergy in the United States and caregivers’ willingness to pay for food allergy treatment

• Population:
  – Cross-sectional survey of 1643 US caregivers of a child with a current food allergy
  – Caregivers were asked to quantify the direct medical, out-of-pocket, lost labor productivity, and related opportunity costs

### Table 2. Direct Medical Costs of Childhood Food Allergy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Children With Visit, % (SE)</th>
<th>Visits per Child, Mean (SE)</th>
<th>Cost, US$</th>
<th>Overall Annual (in Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatrician</td>
<td>42 (2)</td>
<td>.82 (.05)</td>
<td>112&lt;sup&gt;b&lt;/sup&gt;</td>
<td>92</td>
</tr>
<tr>
<td>Allergist</td>
<td>41 (2)</td>
<td>.79 (.05)</td>
<td>175&lt;sup&gt;b&lt;/sup&gt;</td>
<td>138</td>
</tr>
<tr>
<td>Pulmonologist</td>
<td>14 (1)</td>
<td>.07 (.01)</td>
<td>175&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
</tr>
<tr>
<td>Nutritionist</td>
<td>17 (1)</td>
<td>.16 (.04)</td>
<td>100&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16</td>
</tr>
<tr>
<td>Alternative provider</td>
<td>17 (1)</td>
<td>.23 (.05)</td>
<td>100&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23</td>
</tr>
<tr>
<td>Emergency department</td>
<td>13 (1)</td>
<td>.18 (.02)</td>
<td>711&lt;sup&gt;c&lt;/sup&gt;</td>
<td>129</td>
</tr>
<tr>
<td>Inpatient hospitalization stays</td>
<td>4 (1)</td>
<td>.05 (.01)</td>
<td>6269&lt;sup&gt;c&lt;/sup&gt;</td>
<td>314</td>
</tr>
<tr>
<td>Total direct medical costs</td>
<td></td>
<td></td>
<td>724</td>
<td>4292</td>
</tr>
</tbody>
</table>

<sup>a</sup> Direct medical costs are medical costs borne by the health care system associated with the prevention, diagnosis, and treatment of food allergies.

<sup>b</sup> Source: Hospital Outpatient Prospective Payment System.  

<sup>c</sup> Source: Patel et al.  

- Direct medical costs = $4.3 billion
### Table 3. Out-of-Pocket Costs of Childhood Food Allergy

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Reporting Cost (SE)</th>
<th>Mean Direct Out-of-pocket Costs, US$ (SE)</th>
<th>Cost per Child, US$</th>
<th>Overall Annual Cost (in Millions), US$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visits to the physician’s office or health clinic (including copays)</td>
<td>52.5 (2.2)</td>
<td>160 (14)</td>
<td>84</td>
<td>499</td>
</tr>
<tr>
<td>Visits to the emergency room (including copays)</td>
<td>16.1 (1.6)</td>
<td>247 (42)</td>
<td>40</td>
<td>235</td>
</tr>
<tr>
<td>Overnight stays at the hospital</td>
<td>10 (1.4)</td>
<td>411 (182)</td>
<td>41</td>
<td>244</td>
</tr>
<tr>
<td>Travel to and from health care visits (including ambulance use; parking expenses)</td>
<td>27.7 (1.8)</td>
<td>91 (14)</td>
<td>25</td>
<td>149</td>
</tr>
<tr>
<td>Epinephrine injectors (EpiPen, EpiPen Jr)</td>
<td>35.9 (1.9)</td>
<td>87 (4)</td>
<td>31</td>
<td>184</td>
</tr>
<tr>
<td>Antihistamines (Allegra, Benadryl, Claritin, Zyrtec)</td>
<td>50.8 (2.2)</td>
<td>62 (4)</td>
<td>32</td>
<td>188</td>
</tr>
<tr>
<td>Other prescription/nonprescription medication</td>
<td>29.3 (1.9)</td>
<td>122 (13)</td>
<td>36</td>
<td>211</td>
</tr>
<tr>
<td>Non-traditional medicine (such as herbal products)</td>
<td>15 (1.6)</td>
<td>123 (30)</td>
<td>19</td>
<td>110</td>
</tr>
<tr>
<td>Costs associated with special diets and allergen-free foods</td>
<td>37.7 (2.0)</td>
<td>756 (59)</td>
<td>285</td>
<td>1689</td>
</tr>
<tr>
<td>Additional/change in child care</td>
<td>6.7 (0.8)</td>
<td>2158 (323)</td>
<td>145</td>
<td>857</td>
</tr>
<tr>
<td>Legal guidance</td>
<td>2.3 (0.6)</td>
<td>402 (122)</td>
<td>9</td>
<td>55</td>
</tr>
<tr>
<td>Counseling or mental health services</td>
<td>4.5 (0.7)</td>
<td>571 (123)</td>
<td>26</td>
<td>152</td>
</tr>
<tr>
<td>Special summer camp</td>
<td>3 (0.7)</td>
<td>702 (183)</td>
<td>21</td>
<td>125</td>
</tr>
<tr>
<td>A change in schools was needed due to this child’s food allergy</td>
<td>4.2 (0.7)</td>
<td>2611 (497)</td>
<td>110</td>
<td>650</td>
</tr>
<tr>
<td>Other out-of-pocket expenses (eg, cleaning supplies, skin care products, transportation)</td>
<td>9.2 (1.1)</td>
<td>396 (86)</td>
<td>36</td>
<td>216</td>
</tr>
<tr>
<td>Any out-of-pocket costs</td>
<td>74.3 (2.1)</td>
<td>1252 (90)</td>
<td>931</td>
<td>5516</td>
</tr>
</tbody>
</table>

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**Cost of special diets = largest out-of-pocket cost**

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^Out-of-pocket costs: medical costs borne by patient associated with the prevention, diagnosis, and treatment of food allergies. Includes all costs associated with protecting the child from exposure to allergens, including special child care arrangements. The out-of-pocket costs exclude the top 1% of reported costs in each category.
Overall economic cost of food allergy was estimated at $24.8 billion annually ($4184 per year per child)

- Annual opportunity costs totaled $14.2 billion, relating to a caregiver needing to leave or change jobs

- Caregivers were willing to pay $20.8 billion annually for a theoretical effective food allergy treatment
Economic Impact of Childhood Food Allergy in the United States

• Take Away Points:
  – First study to comprehensively quantify the economic impact of childhood food allergy in the United States
  – Childhood food allergy in the United States incurs significant direct medical costs to the US health care system and even larger costs to families with a food-allergic child
History

• Symptoms (ever occur without the food?)
• Dose of the triggering food
• Form of the food
  – Does the patient tolerate the food in a different form (heated, baked, cooked, dried)
• Timing of the reaction (minutes, hours, days)
• Other factors: viral illness, exercise, NSAIDs
• Response to medications (Benadryl, Epi)
• Has the patient tolerated the culprit food (or related food) SINCE the original reaction
Pearls and Pitfalls

• **Pre-test probability is most important**
  – Consider more likely foods for age
  – Consider DDx – lactose intolerance, non-IgE mediated

• **Tolerated foods need not be tested:**
  – milk, egg, soy, wheat, peanut, tree nuts, fish, shellfish, fruits, vegetables, meats

• **Do not discount a negative test with a convincing history**

-Sicherer JACI 2014;133:291-307
Cross-Reactivity and Co-Reactivity

Table 1. Natural History of Food Allergy and Cross-Reactivity between Common Food Allergies.

<table>
<thead>
<tr>
<th>Food</th>
<th>Usual Age at Onset</th>
<th>Cross-Reactivity</th>
<th>Usual Age at Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hen’s egg white</td>
<td>6–24 mo</td>
<td>Other avian eggs</td>
<td>7 yr (75% of cases resolve)*</td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>6–12 mo</td>
<td>Goat’s milk, sheep’s milk, buffalo milk</td>
<td>5 yr (76% of cases resolve)*</td>
</tr>
<tr>
<td>Peanuts</td>
<td>6–24 mo</td>
<td>Other legumes, peas, lentils; coreactivity with tree nuts</td>
<td>Persistent</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>1–7 yr; in adults, onset occurs after cross-reactivity to birch pollen</td>
<td>Other tree nuts; coreactivity with peanuts</td>
<td>Persistent</td>
</tr>
<tr>
<td>Sesame seeds</td>
<td>6–36 mo</td>
<td>None known; coreactivity with peanuts and tree nuts</td>
<td>Persistent</td>
</tr>
<tr>
<td>Fish</td>
<td>Late childhood and adulthood</td>
<td>Other fish (low cross-reactivity with tuna and swordfish)</td>
<td>Persistent†</td>
</tr>
<tr>
<td>Shellfish</td>
<td>Adulthood (in 60% of patients with this allergy)</td>
<td>Other shellfish</td>
<td>Persistent</td>
</tr>
<tr>
<td>Wheat‡</td>
<td>6–24 mo</td>
<td>Other grains containing gluten</td>
<td>5 yr (80% of cases resolve)</td>
</tr>
<tr>
<td>Soybeans‡</td>
<td>6–24 mo</td>
<td>Other legumes</td>
<td>2 yr (67% of cases resolve)</td>
</tr>
<tr>
<td>Kiwi</td>
<td>Any age</td>
<td>Banana, avocado, latex</td>
<td>Unknown</td>
</tr>
<tr>
<td>Apples, carrots, and peaches§</td>
<td>Late childhood and adulthood</td>
<td>Birch pollen, other fruits, nuts</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

It might be prudent to test for foods with **high co-reactivity** if not being consumed but generally avoid testing foods that are **cross-reactive** (exceptions)

Pearls and Pitfalls

• Positive SPT or food specific IgE indicates sensitization not clinical allergy
  – Indiscriminate food testing is poorly informative
  – Leads to unnecessary avoidance
  – Nutritional and growth concerns
  – Cascade of further testing
  – Take care not to “over test”

• Specific IgE levels
  – not correlated to severity
  – trended over time to monitor for persistence/resolution

-Sicherer JACI 2014;133:291-307
Risk Factors for More Severe Reactions

- Concomitant asthma (asthma + PN allergy → most fatal)
- Amount ingested
- Food form (cooked, raw, or processed)
- Co-ingestion of other foods (fats, alcohol)
- Age of the patient
  - Degree of sensitization at the time of ingestion
- Rapidity of absorption, based on whether
  - The food is taken on an empty stomach
  - The ingestion is associated with exercise
- Lack or delayed administration of epinephrine
- Lack of skin symptoms
- Denial of symptoms
- Reliance on oral antihistamines alone to treat symptoms

-J Allergy Clin Immunol 2010;126:S1-S58.
History consistent with food allergy (immune response)?

- Yes
  - History consistent with IgE-mediated allergy (timing, symptoms)?
    - Yes
      - Detailed history to identify possible triggers. Perform serum (consider component tests) and or skin IgE tests to incriminated foods. Consider pre-test probability of a specific allergy (by history, epidemiology) and revise risk assessment according to test results. Positive tests may be confirmatory of an allergy. Negative tests with a compelling history or positive tests with an ambiguous history may warrant an OFC.
    - No
      - Evaluation may include tests for IgE antibodies (APT controversial) but relies most on responses to elimination diets and oral food challenges.

- No
  - Discuss management and any additional tests for adverse reaction caused by toxins (scombroid), metabolic disorders (lactose intolerance), pharmacologic components of foods (caffeine), or undefined mechanisms.

Is the primary illness atopic dermatitis or eosinophilic esophagitis?

- Yes
  - Evaluation of non-IgE mediated illness typically requires elimination diets and oral food challenges. However, history may be compelling for making a presumptive diagnosis.

- No
  - Periodic re-evaluation to assess disease course and or resolution of specific allergies. The timing of retesting varies by specific illness, trigger, history and patient age.

-Sicherer JACI 2014;133:291-307
NIAID FA Guidelines: Management

• Education families on:
  – Carrying medications at all times
    • Twin-pak
    • In purse or bag; not in the car
  – Proper use of medications
  – Preparedness

• Provide a written emergency plan

• Proper dosing of epinephrine:
  – 0.15 mg for ≤ 25 Kg
  – 0.3 mg for > 25 kg
• Benadryl dosing: 1-1.5 mg/kg (max 50 mg)

-J Allergy Clin Immunol 2010;126:S1-S58.
FA Guidelines: Management

• **Avoidance**
  – Label reading, labeling laws, advisory warnings
  – Restaurant precautions – “chef cards”, cross-contact
  – Travel – medication and safe meal preparedness
  – School – written emergency plan, caution with crafts, field trips, mealtimes
  – Home – avoid cross-contact
  – Educate all care givers
  – Vigilance – always have medications ready, medical alert jewelry
  – Avoid home trials
  – Nutritional counseling and growth monitoring
  – Psychological impact – anxiety, bullying, balance in caution

-Sicherer JACI 2014;133:291-307
-J Allergy Clin Immunol 2010;126:S1-S58.
NIAID FA Guidelines: In office Emergency Management

- Elimination of additional allergen exposure
- Immediate IM injection of epinephrine (repeat every 5 min as needed)
- Call 911 or Code team
- Benadryl 1-2 mg/kg
- Albuterol
- Placement patient in a recumbent position with the lower extremities elevated
- Provision of supplemental oxygen
- IV fluids
- Consider H2 Blocker (1-2 mg/kg) and Steroids (1-2 mg/kg)
- EABC OMI
Summary

• You play a key role in patient outcomes for food allergy
• Large Economic impact to food allergy
• The history is the most important part of the evaluation
• Try to decide if it seems to be IgE mediated or not
• Be thoughtful when ordering specific IgE levels or advising avoidance diets
• Provide guidance and education about specific food avoidance, emergency plans and proper medication use when appropriate
• Refer to Allergist for further evaluation and continued management