Food Allergy Prevention, Detection and Treatment

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I have no relevant financial or commercial interests to disclose.

I do not intend to discuss an unapproved or investigative use of a commercial product or device in my presentation.

After the presentation you should
- Understand new concepts in allergy prevention
- Understand limitations and utility of allergy tests
- Advise families on emergency management
Tests Available

• History
• Prick skin test
• Serum IgE (allergen specific)
  – Extracted whole proteins
  – Components
• Oral Food Challenge
Serum Specific IgE, “RAST”

- Blood test that measures specific IgE
- Not affected by antihistamines
- Slightly less sensitive than prick skin tests
- More costly than skin tests, wait for results
- Negative - virtually eliminates IgE-mediated allergy
- Positive - not proof of symptomatic allergy
- Reported in various ways: “Classes” “Counts” and “kU/L”
Evaluation of Suspected Food Allergy

• To differentiate “allergy” (~3-5% affected by an immune response) from other adverse reactions (~20% avoid food for perceived adverse reactions)
  – e.g., non-allergic adverse reactions include: intolerance (lactase deficiency), toxic effects (food poisoning), pharmacologic effects (caffeine)

• To confirm a food as a cause of a typical allergic reaction when food is a suspected trigger
  – e.g., urticaria, angioedema, wheezing, anaphylaxis, etc., proximate to ingestion

• To evaluate the role of foods in chronic disease
  – e.g., moderate-severe atopic dermatitis in children, allergic gastrointestinal disorders
Food-Specific IgE Antibody Concentrations (or skin test size) Correlate with Risk of Clinical Reactivity

- Food
- Disease
- Age
- Assay (brand)

At certain high IgE values, the chance of a clinical reaction approaches certainty.

Negative test is not zero risk.
Predictive Values Vary By Study (patient selection, criteria of allergic, age, illness, food, history)

<table>
<thead>
<tr>
<th>Food</th>
<th>&gt;50% React</th>
<th>&gt;95% react</th>
<th>&gt;95% (&lt; age 1-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>IgE 2 kU/L</td>
<td>IgE 15 kU/L</td>
<td>IgE 5 kU/L</td>
</tr>
<tr>
<td>Egg</td>
<td>IgE 2 kU/L</td>
<td>IgE 7 kU/L</td>
<td>IgE 2 kU/L</td>
</tr>
<tr>
<td>Peanut</td>
<td>IgE 2 kU/L (history)</td>
<td>IgE 14 kU/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IgE 5 kU/L (no history)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td>IgE 20 kU/L</td>
<td></td>
</tr>
<tr>
<td>Walnut</td>
<td></td>
<td>IgE 18 kU/L</td>
<td></td>
</tr>
</tbody>
</table>

## Cross Reactivity

<table>
<thead>
<tr>
<th>If Allergic to:</th>
<th>Risk of Reaction to at Least One:</th>
<th>Risk:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A legume*</td>
<td>Other legumes</td>
<td>5%</td>
</tr>
<tr>
<td>Peanut</td>
<td>peas, lentils, beans</td>
<td></td>
</tr>
<tr>
<td>A tree nut</td>
<td>Other tree nuts</td>
<td>37%</td>
</tr>
<tr>
<td>Walnut</td>
<td>brazil, cashew, hazelnut</td>
<td></td>
</tr>
<tr>
<td>A fish*</td>
<td>Other fish</td>
<td>50%</td>
</tr>
<tr>
<td>Salmon</td>
<td>swordfish, sole</td>
<td></td>
</tr>
<tr>
<td>A shellfish</td>
<td>Other shellfish</td>
<td>75%</td>
</tr>
<tr>
<td>Shrimp</td>
<td>crab, lobster</td>
<td></td>
</tr>
<tr>
<td>A grain*</td>
<td>Other grains</td>
<td>20%</td>
</tr>
<tr>
<td>Wheat</td>
<td>barley, rye</td>
<td></td>
</tr>
<tr>
<td>Cow's milk*</td>
<td>Beef</td>
<td>10%</td>
</tr>
<tr>
<td>Wheat</td>
<td>hamburger</td>
<td></td>
</tr>
<tr>
<td>Cow's milk*</td>
<td>Goat's milk</td>
<td>92%</td>
</tr>
<tr>
<td>Goat</td>
<td>goat</td>
<td></td>
</tr>
<tr>
<td>Cow's milk*</td>
<td>Mare's milk</td>
<td>4%</td>
</tr>
<tr>
<td>Horse</td>
<td>horse</td>
<td></td>
</tr>
<tr>
<td>Pollen</td>
<td>Other Rosaceae</td>
<td>55%</td>
</tr>
<tr>
<td>Birch</td>
<td>plum, pear, cherry, honeydew</td>
<td></td>
</tr>
<tr>
<td>Peach*</td>
<td>Other fruits</td>
<td>55%</td>
</tr>
<tr>
<td>Peach</td>
<td>apple, pear, cherry</td>
<td></td>
</tr>
<tr>
<td>Melon*</td>
<td>Other fruits</td>
<td>92%</td>
</tr>
<tr>
<td>Cantaloupe</td>
<td>watermelon, banana, avocado</td>
<td></td>
</tr>
<tr>
<td>Latex*</td>
<td>Fruits</td>
<td>35%</td>
</tr>
<tr>
<td>Latex glove</td>
<td>kiwi, avocado</td>
<td></td>
</tr>
<tr>
<td>Fruits</td>
<td>Latex</td>
<td>11%</td>
</tr>
<tr>
<td>Kiwi, avocado</td>
<td>latex glove</td>
<td></td>
</tr>
</tbody>
</table>

Sicherer
JACI
Component Testing: Peanut

These are “stable” proteins associated with true allergy.

Ara h 2 is best associated with reactions

Still, “level” counts

These are pollen-related, unstable proteins

Stable but uncommon in the US
IgE Test Limitations

- Few studies available that correlate clinical reaction to test results
  - Results vary by food, age, and, to some extent, research center
- Reactions could occur despite a “negative” test
  - Several studies show reaction rates over 20% in patients with “undetectable” food specific serum IgE (with suspected allergy by history)
  - Allergist may perform prick skin test with commercial extract and/or fresh food for increased sensitivity. May undertake supervised oral food challenge to confirm allergy or tolerance
- Cross-reactivity
- Results do not predict severity
- THEREFORE:
  - 1) Avoid indiscriminate “panels” of screening tests
  - 2) Apply “prior probability” (reasoning from the history) for test selection/interpretation
1) 4 year old ingested peanut and developed hives. IgE to peanut 4.5 kU/L. Ara h 2 1.5 kU/L. Diagnosis?
History

1) 4 year old ingested peanut and developed hives. IgE to peanut 4.5 kU/L. Ara h 2 1.5 kU/L.

2) Had eaten peanut routinely up to the day of reaction
History

1) 4 year old ingested peanut and developed hives. IgE to peanut 4.5 kU/L. Ara h 2 1.5 kU/L.

2) Had eaten peanut routinely up to the day of reaction.

3) Hives lasted 3 days
Diagnosis

• Based on history, tests
• Suggest consultation with a Board-Certified Allergist-Immunologist
• Guidance in:
Management: Dietary Avoidance

- Hidden ingredients (peanut in sauces or egg rolls)
- Labeling issues (“spices”, changes, errors)
  - Labeling laws cover plain English for milk, egg, wheat, soy, peanut, tree nuts, fish, Crustacean shellfish
  - Advisory labeling is voluntary (“may contain”)
- Cross contamination (shared equipment)
- “Code words” (“Natural flavor”)
CDC’s Voluntary Guidelines

• Result of 2011 FDA Food Safety Modernization Act
• To support implementation of food allergy management and prevention
• Includes instructions for multiple stakeholders: Parental obligations (relates to physician diagnosis and plans), individualized plans, communication strategies, risk reduction, education of stakeholders, response to anaphylaxis, etc.
Autoinjector Dosing

- Manufacturer says 0.15 mg for 33-66 lbs and 0.3 mg for 66 lbs and over
- For infants, ampules/syringe may be too awkward

<table>
<thead>
<tr>
<th>Weight</th>
<th>Options (fixed dose injectors)</th>
<th>Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10 kg</td>
<td>0.15 mg dose</td>
<td>At least 1.5 fold overdose</td>
</tr>
<tr>
<td>15 kg</td>
<td>0.15 mg dose</td>
<td>Perfect</td>
</tr>
<tr>
<td>20 kg</td>
<td>0.15 mg dose, 0.3 mg dose</td>
<td>1.3 fold under-dose, 1.5 fold overdose</td>
</tr>
<tr>
<td>25 kg</td>
<td>0.15 mg dose, 0.3 mg dose</td>
<td>1.7 fold under-dose, 1.2 fold over-dose</td>
</tr>
<tr>
<td>&gt;=30 kg</td>
<td>0.3 mg dose</td>
<td>Perfect, with increasing underdose</td>
</tr>
</tbody>
</table>

Conclusion: Switch from 0.15 mg to 0.3 mg at about 55 lbs (25 kg)

Written Plan and Medical Jewelry

Visit www.foodallergy.org/actionplan.pdf for a comprehensive plan.

Consider cetirizine
Summary About Epinephrine

• Should be available promptly, but within reason (e.g., not in every classroom)
  – Not locked up
• If allowable, child might carry but discuss risk/benefit
• Instructions must address health professional versus delegates
• Antihistamines are comfort care, does not stop anaphylaxis
• Bronchodilators should not be depended upon to treat anaphylaxis
• Argument for having an unassigned dose available (25% of school anaphylaxis without a prior diagnosis*)

My sister treats me like Lucy treats Linus.

Sounds like you’ve got analogy to Peanuts.
Peanut Allergy Appears to Have Increased

Peanut Allergy (Children < 18 yrs) by Year of Telephone Survey

Sicherer et al JACI 2010; 125:1322-6
There are theories about the increase in food allergies.
What are “normal” feeding practices?

- Breast feed
- Weaning
- Solids that are easily managed by an infant
- Progression as teeth erupt
Dietary Prevention Program, US

- Randomized, prospective, 288 subjects, one parent with allergy
- Program:
  - Pregnancy, 3\textsuperscript{rd} trimester-no milk, egg, peanut, reduced soy/wheat
  - Lactation, avoid same, supplement casein hydrolysate
  - Solids at 6 mo, 12 mo-dairy, wheat, soy, 24 mo-egg, 36 mo-peanut, fish
- Followed to age 7 years

Dietary Prevention Program, US Period Prevalence of Disorders


In 2000, American Academy of Pediatrics suggested this feeding approach
Egg Introduction and Egg Allergy

"HealthNuts" study, 2589 infants population-based, cross-sectional study

- Effects seen in high-risk and low-risk infants with cooked egg introduction
- Adjusted for confounding factors
- Confirmed egg allergy

Koplin et al JACI 2010
Risk Factors for Peanut Allergy

YES RISK

Topical Exposure to Creams Containing Peanut


NO RISK
Peanut Allergy Prevalence

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>0.17%</td>
</tr>
<tr>
<td>UK</td>
<td>1.85%</td>
</tr>
</tbody>
</table>

Infant Peanut Consumption

<table>
<thead>
<tr>
<th>Country</th>
<th>Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>7.1 Grams/mo</td>
</tr>
<tr>
<td>UK</td>
<td>0 Grams/mo</td>
</tr>
</tbody>
</table>

Du Toit JACI 2008

The American Academy of Pediatrics rescinded prior avoidance advice...
Exposure Theory
Eczema severity augments impact of household peanut exposure

Brough, Liu, Sicherer J Allergy Clin Immunol 2015;135:164-70
LEAP (Learning Early About Peanut) Study
High risk infants (eczema/egg allergy), 4-11 months age
Negative or small peanut skin tests
Randomized to eat (vs. avoid) peanut to age 5 years

Interim Guidelines

• Infant 4-6 month with allergic problems such as severe eczema, egg allergy
• Evaluate for food allergy (to peanut) with skin test
• Introduce peanut like in LEAP study and maintain in diet (presumed under medical observation)
• Emphasize unknowns (dose, permanency)
• Emphasize 2008 American Academy of Pediatric Report: No reason to avoid allergens in healthy infant

The EAT Study: UK, unselected, randomized to eat allergens early (3 mo)

Evaluated milk, egg, wheat, soy, peanut, sesame, fish. 3 month versus 6 month.

Intention to treat: no difference.

Per protocol, reduced egg, peanut.

Only one-third met per protocol.

What are “normal” feeding practices?

- Breast feed
- Weaning
- Solids that are easily managed by an infant
- Progression as teeth erupt
What are “normal” feeding practices?

- Breast feed
- Weaning
- Solids that are easily managed by an infant via pre-mastication
- Progression as teeth erupt

18% of surveyed Brooklyn mothers (HIV+) premasticated food (Hafeez Arch Pediatr Adolesc Med 2011;165:92-93)
Atopy at 18 months in relation to pacifier use and cleaning practices

Hesselmar B et al. Pediatrics 2013;131:e1829-e1837
“Clueless” actress Alicia Silverstone

“He literally crawls across the room to attack my mouth if I’m eating”

Fox News asked medical and nutritional experts what they thought of the feeding method for humans.

'It doesn't seem like a hygienic practice,' one doctor told the site.
Key References

Thank you