Food Allergy

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Disclaimers

I have no conflict of interest in any of the information I am providing. The information I am providing is free of bias. I have no financial conflicts of interest. Many of the slides I am presenting were originally published by the AAAAI Adverse Reaction to Foods Committee (2007). I have updated several slides and added my own slides when relevant/necessary.

Disclaimers II

• Most of the relevant information that will be discussed is referenced in Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NAIAD-Sponsored Expert Panel. JACI 2010; 126 s1-57.

Outline

• Definitions
• Clinical Manifestations
• Food Allergy Disorders
• Prevalence and Natural History
• Evaluation
• Management
• Prevention
• Causes
• Future Approaches
• Summary and Conclusions
• QUESTIONS!!!
Adverse Food Reactions

Non-immunologic

- Bacterial food poisoning
- Heavy metal poisoning
- Scombroid fish poisoning
- Caffeine
- Alcohol
- Histamine

Toxic / Pharmacologic / Non-Toxic / Intolerance

- Systemic (Anaphylaxis)
- Oral Allergy Syndrome
- Immediate gastrointestinal anaphylaxis
- Asthma/rhinitis
- Urticaria
- Morbilliform rashes and flushing
- Contact urticaria

Immunologic

IgE-Mediated (most common)

- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

Non-IgE Mediated Cell-Mediated

- Induced Enterocolitis
- Protein-Induced Enteropathy
- Eosinophilic proctitis
- Dermatitis herpetiformis
- Contact dermatitis

Adverse Food Reactions

Signs and Symptoms

<table>
<thead>
<tr>
<th>IgE</th>
<th>Non-IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Urticaria</td>
</tr>
<tr>
<td></td>
<td>Angioedema</td>
</tr>
<tr>
<td></td>
<td>Atopic dermatitis</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Throat tightness</td>
</tr>
<tr>
<td></td>
<td>Rhinitis</td>
</tr>
<tr>
<td></td>
<td>Asthma</td>
</tr>
<tr>
<td>Gut</td>
<td>Vomit</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
</tr>
<tr>
<td></td>
<td>Pain</td>
</tr>
<tr>
<td></td>
<td>Anaphylaxis</td>
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</tbody>
</table>

Allergens

- Proteins or glycoproteins (not fat or carbohydrate)
  - Generally heat resistant, acid stable

- Major allergenic foods (>85% of food allergy)
  - Children: milk, egg, soy, wheat, peanut, tree nuts
  - Adults: peanut, tree nuts, shellfish, fish, fruits and vegetables


Anaphylaxis Syndromes

- Food-induced anaphylaxis
  - Food allergy = #1 cause of anaphylaxis in the ED
  - Rapid-onset, up to 30% biphasic
  - May be localized (single organ) or generalized
  - Potentially fatal
  - Any food, highest risk:
    - peanut, tree nut, seafood
      (cow’s milk and egg in young children)
  - Food-dependent, exercise-induced: 2 forms
    - Specific foods (wheat, celery, shellfish most common)
    - Any food (post-prandial)

Fatal Food Anaphylaxis

- Frequency: ~ 150 deaths / year
- Clinical features:
  - Biphasic reaction can contribute – initially better, then recurs
  - Cutaneous symptoms may not be present
  - Respiratory symptoms prominent
- Risk factors:
  - Underlying asthma
  - Delayed epinephrine
  - Symptom denial
  - Previous severe reaction
  - Adolescents, young adults
- History: known food allergen
- Key foods: peanuts and tree nuts dominate (~90% of fatalities), fish, crustaceans
- Most events occurred away from home

Cutaneous Reactions

- Acute urticaria/angioedema – common
- Contact urticaria - common
- Food allergy rarely causes chronic urticaria/angioedema
- 1/3 of children with moderate to severe atopic dermatitis may have food allergy (especially cow’s milk, egg, soy, wheat). Morbilliform rashes may be seen in these children upon food challenge.
- Contact dermatitis (food handlers)

Respiratory Responses

- Upper and lower respiratory tract symptoms may be seen (rhinconjunctivitis, laryngeal edema, asthma)
- Rarely isolated, usually accompany skin
- Inhalational exposure severe
  - Occupational
  - Restaurants
  - Kitchen/Home
**Pollen-Food Syndrome or Oral Allergy Syndrome**

- Clinical features: rapid onset oral pruritus, rarely progressive
- Epidemiology: prior sensitization to pollens
- Key foods: raw fruits and vegetables
- Cause: cross reactive proteins pollen/food

**Latex-Fruit Syndrome**

- 30-50% of those with latex allergy are sensitive to some fruits due to cross-reactive IgE
- Most common fruits: banana, avocado, kiwi, chestnut but other fruits and nuts have been reported
- Can clinically present as anaphylaxis to fruit
- Warn latex-sensitive patients of potential cross-reactivity
- Some fruit-allergic patients may be at risk for latex allergy

**Pediatric Gastrointestinal Syndromes**

- **Enterocolitis**
  - Age Onset: Infant
  - Duration: 12-24 mo
  - Characteristics: Failure to thrive, Malabsorption, Diarrhea
- **Enteropathy**
  - Age Onset: Infant/Toddler
  - Duration: ? 12-24 mo
  - Characteristics: Failure to thrive, Malabsorption, Diarrhea
- **Proctitis**
  - Age Onset: Newborn
  - Duration: 9 mo-12 mo
  - Characteristics: Failure to thrive, Malabsorption, Diarrhea

**GI Syndromes of Children and Adults**

**Gastrointestinal Anaphylaxis or Immediate Gastrointestinal Allergy**
- IgE-mediated
- Acute emesis/diarrhea/abdominal pain
- Can present without other signs or symptoms of an allergic reaction to food
Non-IgE-Mediated Syndromes of the Skin and Lung

- **Dermatitis Herpetiformis**
  - Associated with Celiac Disease
  - Gluten-sensitive, improves on diet
  - Vesicular, pruritic eruption sacrum, extensor knees and elbows

- **Heiner’s Syndrome**
  - Precipitating antibodies to cow’s milk
  - Infantile pulmonary hemosiderosis
  - Anemia, failure to thrive

Disorders Not Proven to be Related to Food Allergy

- Migraines
- Behavioral / Developmental disorders
- Arthritis
- Seizures
- Inflammatory bowel disease

Prevalence of Food Allergy

- Perception by public: 20-25%
- Confirmed allergy (oral challenge)
  - Adults: 2-3.5%
  - Infants/young children: 6-8%
- **Specific Allergens**
  - Dependent upon societal eating and cooking patterns
- Prevalence higher in those with:
  - Atopic dermatitis
  - Certain pollen allergies
  - Latex allergy
- Prevalence seems to be increasing

Estimated Prevalence of Food Allergy

<table>
<thead>
<tr>
<th>Food</th>
<th>Children (%)</th>
<th>Adults (%)</th>
</tr>
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<tbody>
<tr>
<td>Cow’s milk</td>
<td>2.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Egg</td>
<td>1.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Soy</td>
<td>0.3-0.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Peanut</td>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Tree nut</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Crustaceans</td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td>0.1</td>
</tr>
</tbody>
</table>

Prevalence of Food Allergy in Specific Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Food Allergy Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis</td>
<td>35-55%</td>
</tr>
<tr>
<td>Oral allergy synd</td>
<td>25-75% in those w/pollen allerg</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>37% in children (rare in adults)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>20% in acute (rare in chronic)</td>
</tr>
<tr>
<td>Asthma</td>
<td>5-6%</td>
</tr>
<tr>
<td>Chronic rhinitis</td>
<td>Rare</td>
</tr>
</tbody>
</table>

Prevalence of Clinical Cross Reactivity Among Food “Families”

<table>
<thead>
<tr>
<th>Food Allergy</th>
<th>Prevalence of Allergy to &gt; 1 Food in Family</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish</td>
<td>30% - 100%</td>
</tr>
<tr>
<td>Tree Nut</td>
<td>15% - 40%</td>
</tr>
<tr>
<td>Grain</td>
<td>25%</td>
</tr>
<tr>
<td>Legume</td>
<td>5%</td>
</tr>
<tr>
<td>Any</td>
<td>11%</td>
</tr>
</tbody>
</table>

Natural History

- Dependent on food & immunopathogenesis
- ~85% of cases of cow milk, soy, egg and wheat allergy remit by age 7 yrs
  - Declining/low levels of specific-IgE predictive

- Non-IgE-mediated GI allergy
  - Infant forms resolve in 1-3 years
  - Toddler / adult forms more persistent

Natural History (cont)

- Allergies to peanuts, tree nuts, seafoods, and seeds typically persist
- ~20% of cases of peanut allergy resolve by age 5 years.

Prognostic factors include:
- PST <6mm
- ≥2 years avoidance
- History of mild reaction
- Few other atopic diseases
- Low levels of peanut-specific IgE
- Rarely re-develop allergy: role for regular ingestion?
Evaluation: History & Physical Exam

- History: most important
  - Symptoms, timing, reproducibility, treatment and outcome
  - Concurrent exercise, NSAIDs, EtOH
- Diet details / symptom diary
  - Subject to recall
  - “Hidden” ingredient(s) may be overlooked
- Physical exam: assess for other allergic and alternative disorders
- Identify general mechanism
  - Allergy vs intolerance
  - IgE versus non-IgE mediated

Evaluation of Food Allergy

- Suspect IgE-mediated
  - Panels/broad screening should NOT be done without supporting history because of high rate of false positives.
  - Prick skin tests (prick-prick with fresh food if pollen-food syndrome)
  - In vitro tests for food-specific IgE
- Suspect non-IgE-mediated
  - Consider biopsy of gut, skin
- Suspect non-immune, consider:
  - Breath hydrogen
  - Sweat test
  - Endoscopy

Evaluation: Interpretation of Laboratory Tests

- Positive prick test or specific IgE
  - Indicates presence of IgE antibody
    NOT clinical reactivity
  - ~90% sensitivity
  - ~50% specificity
  - ~50% false positives
  - Larger skin tests/higher IgE correlates with likelihood of reaction but not severity

- Negative prick test or specific IgE
  - Essentially excludes IgE antibody (>95% specific)

Specific IgE Levels Associated with 95% Risk of Reaction

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Food</th>
<th>Serum IgE (kU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child</td>
<td>Egg</td>
<td>≥ 7 &lt;2 years</td>
</tr>
<tr>
<td></td>
<td>Cow Milk</td>
<td>≥ 15 &lt;2 years</td>
</tr>
<tr>
<td>Garcia - Ara C, et al. J Allergy Clin Immunol</td>
<td>2001;107(1);185-90</td>
<td></td>
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</tbody>
</table>
Unproven/Experimental Tests

- Intradermal skin test with food
  - Risk of systemic reactions and death
  - Not predictive (high false positive rate)
- Provocation/neutralization, cytotoxic tests, applied kinesiology (muscle response testing), hair analysis, electrodermal testing, food-specific IgG or IgG4 (IgG “RAST”)

Diagnostic Approach: IgE-Mediated Allergy

- If test for specific-IgE antibody is
  - Negative: reintroduce food*
  - Positive: start elimination diet
- If elimination diet is associated with
  - No resolution: reintroduce food*
  - Resolution
    - Open / single-blind challenges to “screen”
    - DBPCFC for equivocal open challenges

* Unless convincing history warrants supervised challenge

Management of Food Allergy

- Complete avoidance of specific food trigger
- Ensure nutritional needs are being met
- Education
- Anaphylaxis Emergent Action Plan if applicable
  - most accidental exposures occur away from home

Management: Dietary Elimination

- Hidden ingredients in restaurants/homes (peanut in sauces, egg rolls)
- Labeling issues (“spices”, changes, errors)
- Cross contamination (shared equipment)
- Seeking assistance
  - Food allergy specialist
  - Registered dietitian: (www.eatright.org)
  - Food Allergy & Anaphylaxis Network (www.foodallergy.org; 800-929-4040) and local support groups
Label reading used to be very challenging!
Example: Cow’s Milk

- Artificial butter flavor, butter, butter fat, buttermilk, casein, caseinates (sodium, calcium, etc.), cheese, cream, cottage cheese, curds, custard, Half&Half®, hydrolysates (casein, milk, whey), lactalbumin, lactose, milk (derivatives, protein, solids, malted, condensed, evaporated, dry, whole, low-fat, non-fat, skim), nougat, pudding, rennet casein, sour cream, sour cream solids, sour milk solids, whey (delactosed, demineralized, protein concentrate), yogurt.

May contain milk:
- Brown sugar flavoring, natural flavoring, chocolate, caramel flavoring, high protein flour, margarine, Simplesse®.

AS of January 1, 2006, all food containing “Big Eight Allergens” (cow’s milk, peanut, tree nut, hen’s egg, soy, wheat, fish, crustacean) in the U.S. MUST declare the ingredient on the label in COMMON language. Does NOT apply to non-Big 8 allergens (e.g., sesame).

Management: Infant Formulas

- Soy (confirm soy IgE negative)
  - <15% soy allergy among IgE-CMA
  - ~50% soy allergy among non-IgE CMA
- Cow’s milk protein extensive hydrolysates
  - >90% tolerance in IgE-CMA
- Partial hydrolysates
  - Not hypoallergenic!
- Elemental amino acid-based formulas
  - Lack allergenicity

* CMA = cow’s milk allergy

Emergency Department Management of Food Allergy

- Epinephrine: drug of choice
  - Self-administered epinephrine readily available at all times
  - If administered, seek medical care IMMEDIATELY
  - <25kg dose is 0.15cc of 1:1000
  - >25kg dose is 0.3cc of 1:1000
- Antihistamines: secondary therapy only: WILL NOT STOP ANAPHYLAXIS. Diphenhydramine 12.5mg (1tsp) per 25lbs of body weight
- Written Anaphylaxis Emergency Action Plan
  - Schools, spouses, caregivers, mature sibs / friends
- Emergency identification bracelet (selected patients)
### Management: Follow-Up

- Re-evaluate for tolerance periodically
- Interval and decision to re-challenge:
  - Type of food allergy (IgE vs non-IgE)
  - Severity of previous symptoms
  - Allergen/Prognosis (cow’s milk vs peanut)
- Ancillary testing
  - Skin prick test/in vitro specific IgE may remain positive
  - Decline in concentration of food specific-IgE is suggestive of development of tolerance

### Food Allergy Prevention

**Previous AAP Food Recommendations 2000:**
- Solid foods: after age 6 mos
- Cow’s milk/dairy: after age 1 yr
- Egg: after age 2 yrs
- Peanut, tree nut, seafood: after age 3-4 yrs

****NO DATA TO SUPPORT THESE RECS*******

**Current 2010 NIAID Recommendations:**
- Solid foods should not be delayed beyond 4-6 months
  - “Insufficient evidence exists for delaying introduction …of potentially allergenic foods beyond 4 to 6 months of age, even in infants at risk of developing allergic disease.”

### Food Allergy Prevention, Cont.

- Pregnancy/lactation: NO DIETARY RESTRICTIONS
- Breastfeeding: Exclusive breastfeeding recommended until 4-6 months of age.
- Cow’s milk or extensively hydrolyzed formula for at risk infants who are not exclusively breast fed

### Prevention: Test the Sibling?

- 2010 expert panel does not recommend testing even in high risk siblings
- Wiggle room in guidelines, however
Egg Allergy and Vaccines

• MMR: Safe, give in pediatric office
• Rabies: Use Imovax which does not contain egg protein as not cultured in chick embryos
• Yellow Fever: Refer to allergist for testing and administration
• Influenza: Evolving and highly controversial. My practice is to perform PST on patients with h/o egg anaphylaxis. If negative, administer full dose. If no h/o anaphylaxis (ie AD), I give full dose with no skin testing. Best done in allergist office (for now).

What Causes Food Allergy?

Future Immunomodulatory Approaches

Immunotheraphy for Food

• Immunotherapy: The process of decreasing an individual’s response to an allergen by repetitively administering allergen to the body.
• Injection
• Oral (OIT)
• Sublingual (SLIT)
OIT for Peanut

SLIT for Peanut

SLIT Peanut: Safety

SLIT: 4182 doses
- Rxn: 480 (11.5%)
- OP: 391 (9.3%)
- UR: 59 (1.4%)
- Abd: 50 (1.2%)
- H1: 11 (0.3%)
- EPI: 0
- Albuterol: 1 (0.02%)

Placebo: 2875 doses
- Rxn: 248 (8.6%)
- OP: 43 (1.5%)
- Skin: 188 (6.5%)
- Abd: 53 (1.8%)
- None required treatment

Summary and Conclusions

- IgE & non-IgE-mediated conditions exist
- The history and physical are paramount
- Elimination diets, skin testing, in vitro assays, and food challenges also have roles in diagnosis
- Avoidance, education, and preparation for emergencies are the pillars of current management
- Periodic re-challenge to monitor tolerance as indicated
- Exciting new therapies are on the horizon