Food-Induced Allergic Reactions
Examples

- Eczema
- Urticaria
- Oral allergy syndrome
- Anaphylaxis
- Latex food allergy syndrome
- Exercise food-induced anaphylaxis
- Eosinophilic esophagitis
Others

- Scombroid poisoning
- Food protein-induced enterocolitis syndrome
- Lactose intolerance
- Celiac disease
- Food poisoning
Nomenclature

• Adverse food reaction – any abnormal reaction resulting from ingestion of a food
• Food intolerance – caused by unique physiologic characteristic of host – lactase deficiency
• Food hypersensitivity / allergy – adverse immunologic reaction due to IGE or non-IGE immune reaction
Nomenclature con’t

• Toxic reaction – can affect most healthy individuals if given in appropriate doses – histamine in scombroid poisoning

• Food aversions – not reproducible when given in blinded fashion
Prevalence of Food Hypersensitivity

- Greatest in first few years of life
- Affects 4-6% of children less than 3 years of age
- 35% of children with moderate to severe atopic dermatitis have IGE mediated food allergy
- 6-8% of asthmatic children have food-induced wheezing
Cow’s Milk Allergy

- Onset in first year of life
- 80% outgrow by age 5 years
- 35% develop other food allergies
Peanut Allergy

• Prevalence in young children has doubled during past decade
• 20% of children develop clinical tolerance
## Prevalence of Food Allergies in U.S.

<table>
<thead>
<tr>
<th></th>
<th>Young children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>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>Peanut</td>
<td>0.8%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>0.2%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Fish</td>
<td>0.1%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>0.1%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Overall</td>
<td>6%</td>
<td>3.7%</td>
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Pathogenesis of Food Hypersensitivity Reactions

- Abnormal response of mucosal immune system to antigens delivered by oral route
- Failure of oral tolerance induction
- Gut flora
- Non-oral exposure (dermal) bypasses oral tolerance mechanism
- Antigen properties such as dose or frequency of exposure
- Abnormal GI barrier function (high pH)
- TH2 bias
Food Allergens

• Regional dietary habits and methods of food preparation play a role in prevalence of specific food allergy
• There is virtually no peanut allergy in China, but consumption is the same as in U.S..
• Chinese eat predominantly boiled or fried peanuts and Americans eat almost exclusively dry-roasted peanuts
• Higher heat increases allergenicity of peanut protein
Class I Food Allergy

- Sensitization in GI tract, skin or respiratory route
- Major allergens are water-soluble glycoproteins and relatively heat, acid and protease stable
- Plant allergens: cupin and prolamin superfamilies, proteins of plant pathogen defense system
- Animal allergens – limited number and less cross-reactivity
Class II Food Allergy

- Allergens have cross-reactivity between pollen and food
- Highly heat labile – the food can be eaten cooked, but not raw
- Sensitization by inhaled pollen resulting in cross-reactivity to raw fruit or vegetable
- The mechanism of the Oral Allergy Syndrome
Food Hypersensitivity Disorders
IGE Mediated

- Gastrointestinal: Oral allergy syndrome, anaphylaxis
- Cutaneous: Urticaria, angioedema, morbilliform rashes and flushing
- Respiratory: Acute rhinoconjunctivitis, bronchospasm
- Generalized: Anaphylactic shock
Mixed IGE and Cell Mediated

- Gastrointestinal: Allergic eosinophilic esophagitis and gastroenteritis
- Cutaneous: Atopic dermatitis
- Respiratory: Asthma
Cell Mediated

- Gastrointestinal: Food protein-induced enterocolitis and enteropathy syndromes, celiac disease
- Cutaneous: Contact dermatitis, dermatitis herpetiformis
- Respiratory: Pulmonary hemosiderosis
Gastrointestinal Food Hypersensitivities
Pollen – Food Allergy Syndrome (Oral Allergy Syndrome)

- IGE mediated
- Mild pruritus, tingling, &/or angioedema of lips, palate, tongue or oropharynx; rare systemic symptoms
- DX: +SPT to relevant food, oral challenge + with fresh food and – with cooked food
Gastrointestinal Anaphylaxis

• IGE mediated
• Rapid onset of nausea, abdominal pain, cramps, vomiting, &/or diarrhea; skin and respiratory tract often involved
• DX: +SPT or RAST
Allergic Eosinophilic Esophagitis

- IGE mediated &/or cell mediated
- GE reflux, or emesis, dysphagia, abdominal pain, sleep disturbance, failure to respond to reflux meds
- DX: SPT +/-, endoscopy and bx
Allergic Eosinophilic Gastroenteritis

- IGE mediated &/or cell mediated
- Recurrent abdominal pain, irritability, early satiety, vomiting, FTT, &/or weight loss
- DX: SPT +/-, endoscopy and biopsy
Case Report

• 14 mo. old female presents for evaluation of possible cow’s milk allergy. Breast fed to age 4 weeks when CM based formula added to supplement feedings. Over a 2 week period she developed vomiting, poor weight gain, specks of blood in stools. Soy formula substituted briefly, but discontinued because of vomiting. Then breast fed to age 12 weeks when given 1 feeding with cow’s milk. 90 minutes later had repetitive vomiting, lethargy, blood-tinged diarrhea. DC’d on ex.hyd.casein formula. Avoided cow’s milk & soy to 7 mo. when given cheese in baby food & 90 minutes later developed vomiting, lethargy & need for IV fluid resuscitation. CM and soy avoided until allergy consult.
Food Protein-Induced Enterocolitis

- Cell mediated
- Protracted vomiting and diarrhea ( +/- bloody) not infrequently with dehydration; abdominal distention, FTT; vomiting typically delayed 1-3 hours after feeding
- DX: SPT-, elimination of food protein results in clearing of symptoms in 24-72 hours; re-challenge produces symptoms in 1-2 hours; 15% have hypotension
FPIES con’t

• ½ of patients react to both milk & soy
• Loss of sensitivity to milk in 60% & soy in 25% by age 2 yrs
• Family hx of atopy in 75%
• Also reported with solids: rice, oat, barley, squash, poultry
• Tolerate breast milk & ex.hyd.casein formula
Cutaneous Food Hypersensitivity Reactions

• 2 mo. old exclusively breast-fed female: Mother, a school teacher, wanted to stop nursing as school was starting. She gave baby Enfamil with Lipil which baby spit up, then gave her Similac Advance. 30 minutes later baby noted to have “red skin and pin-head sized bumps all over”, also ears were swollen “like little knobs”, neck looked swollen and voice was hoarse.
Acute Urticaria and Angioedema

- IGE mediated
- Pruritus, hives, and/or swelling
- DX: history, SPT or RAST, +/- challenge
Chronic Urticaria and Angioedema

- IGE mediated infrequent cause
- Symptoms > 6 weeks
- DX: history, SPT or RAST, elimination diet
Atopic Dermatitis

- IGE and cell mediated
- DX: marked pruritus, eczematous rash in classic distribution
- DX: history, SPT, quantitative food-specific IGE (Pharmacia CAP System FEIA), elimination diet, food challenge
Contact Dermatitis

- Cell mediated
- Marked pruritus, eczematous rash
- DX: history in food handlers, especially raw fish, shellfish, meats and eggs; patch test
Dermatitis Herpetiformis

- Cell mediated
- Papulovesicular rash over extensor surfaces and buttocks, pruritus
- DX: skin bx – IGA deposition, IGA anti-gliadin and anti-transglutaminase ab
Respiratory Food Hypersensitivities
Allergic Rhinoconjunctivitis

• IGE mediated
• Symptoms of periocular pruritus, tearing, conjunctival edema/erythema, nasal congestion, rhinorrhea, sneezing
• DX: history, SPT, elimination diet, food challenge
Asthma

• IGE mediated
• Symptoms of cough, dyspnea, wheeze
• DX: history, SPT, elimination diet
• Half of children requiring intubation for severe asthma have food allergy (Roberts, JACI 2003)
Pulmonary Hemosiderosis
Heiner’s Syndrome

- Mechanism unknown
- Recurrent pneumonia, pulmonary infiltrates, hemosiderosis, iron deficiency anemia, FTT
- DX: history, peripheral eosinophilia, cow’s milk precipitins, lung bx, elimination diet
Generalized Anaphylaxis

- 4 mo. old bottle-fed female cared for by grandmother who reported that approximately 2 hours after a “few bites of MaltOMeal” baby developed “bumps and red skin all over and she was breathing like she had asthma”. On the way to the ER she “passed out”. ER notes “marked periorbital edema, erythema of entire body, wheezes bilaterally”. RAST to wheat 17.4, barley 8.3.
Diagnosis

• Quantitative measurements of food-specific IGE antibodies (Pharmacia CAP System FEIA) have been shown to be more predictive of symptomatic IGE- mediated food allergy.

• Prick specific food skin tests – negative test accurately predicts absence of food allergy; positive test less predictive of allergic reaction than specific IGE antibody test.
95% Predictive Level

<table>
<thead>
<tr>
<th>Allergen</th>
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<th>PPV</th>
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<tr>
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<td>Peanut</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Fish</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>15</td>
<td>95</td>
</tr>
</tbody>
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Therapy

- Avoidance
- Clinical tolerance develops over time to most foods except for peanuts, nuts and seafood
- Low levels of peanut-specific IGE in young children is associated with development of clinical tolerance - 20%
- Children with reactions beyond 5 years are unlikely to develop tolerance
Oral Challenge

- May be appropriate when food-specific IGE is below a level which predicts less than 50% reactivity
  - Egg <2kIU/L
  - Milk <2kIU/L
  - Peanut <2 with + history
  - <5 with ? history
Future Therapy

- Anti-IGE antibodies
- TNX-901
- omalizumab
- Chinese herbs
- Cytokine/anticytokines
- Modified/engineered protein immunotherapy
- Sublingual/oral immunotherapy
Prevention

- AAP recommendations: Pediatrics 2008; 121: 183-191
- Exclusive breast feeding for high-risk infants for 4-6 months, if not, use hydrolyzed formula – no evidence for use of soy-based formula for allergy prevention
- Delay introduction of solids for 4 to 6 months
- Delaying introduction of highly allergenic foods i.e. fish, eggs, peanut has no significant protective effect