Food Allergies & Anaphylaxis

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Learning Objectives

1. Understand the difference between food allergies versus adverse reactions to foods

2. Review of the most common food allergens and specific food allergens in common foods

3. Learn about the clinical course and natural history of some food allergies

4. Review possible mechanisms of resolution/tolerance

5. Recognize the clinical manifestations of food allergies and anaphylaxis and its treatment

6. Interpretation of tests for diagnosis of food allergies (ie skin prick test vs ImmunoCap sIgE blood test)

7. Review of reasons for Allergy referral
Introduction

- Food allergies or food intolerances affect nearly everyone at some point.
- People often have an unpleasant reaction to something they ate and wonder if they have a food allergy.
- Public perception of the prevalence of clinically proven food allergies is significantly higher than the real prevalence.
- This difference is in part due to reactions called "food intolerances" or adverse reactions to food rather than true food allergies.
Prevalence of Food Allergy

Perception by public: 20-25%

Confirmed allergy:
› Adults: 3-4%
› Infants/young children: 5%

Prevalence higher in those with:
› Atopic dermatitis
› Pollen allergies
› Latex allergy

Prevalence increasing—18% increase between 1997-2007
Definition of Food Allergy

- Abnormal immunologic response following exposure to a food that is mediated by IgE molecules directed against specific food proteins that activate mast cells and basophils, or can arise from other cellular processes involving eosinophils or T cells.

- Consequently, Food allergies are broadly categorized into either IgE-mediated or non IgE-mediated processes.

- Some disorders, such as atopic dermatitis or the eosinophilic gastrointestinal disorders, have characteristics of both mechanisms.
### Adverse Reactions to Food

#### A. Nonimmunologic

<table>
<thead>
<tr>
<th>Toxic / Pharmacologic (no dependence of host factors)</th>
<th>Non-Toxic / Intolerance (dependence of host factors)</th>
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</thead>
<tbody>
<tr>
<td>☐ Bacterial food poisoning</td>
<td>☐ Lactase deficiency</td>
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<tr>
<td>☐ Heavy metal poisoning</td>
<td>☐ Galactosemia</td>
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<td>☐ Scromboid fish poisoning</td>
<td>☐ Pancreatic insufficiency</td>
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<tr>
<td>☐ Caffeine</td>
<td>☐ Gallbladder / liver disease</td>
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<tr>
<td>☐ Alcohol</td>
<td>☐ Hiatal hernia</td>
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<td>☐ Histamine</td>
<td>☐ Gustatory rhinitis</td>
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Food Allergies

B. Immunologic Spectrum

- Anaphylaxis
- Urticaria

- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis
- Protein-Induced Enterocolitis
- Protein-Induced Enteropathy
- Eosinophilic proctitis
Pathophysiology: Allergens

- Proteins (not fat / carbohydrate)
  - 10-70 kD glycoproteins
  - Heat resistant, acid stable

- Single food > many food allergens > Multiple Epitopes (proteins)

- Epitope: Areas of a protein to which the immune system can respond

- Conformational Epitopes vs. Linear Epitopes
**Pathophysiology: Allergens**

1. First-time exposure
2. Body overproduces *Ara h 1* IgE antibody
3. *Ara h 1* IgE attaches to mast cells
4. Second Exposure: IgE primed mast cells release granules and powerful chemical mediators
5. Chemical mediators cause symptoms of allergy
Most Common Food Allergens

Major allergenic foods (account for >85% of allergy)

**Children:** milk, egg, soy, wheat and as in adults

**Adults:** peanut, nuts, shellfish, fish

Mnemonic: **WEMPS**

- **W**heat
- **E**ggs (Most common in atopic dermatitis)
- **M**ilk and Soy
- **P**eanuts and tree nuts
- **S**eafood (Crustacean and shellfish and fish)
Milk Allergy

- Most common food allergy in children, usually developing in the first year
- Prevalence 2-3% of infants
- **Milk proteins:** casein (curds) and whey (soluble): lactalbumin, lactoglobulin
- Many patients can tolerated baked milk, and chronic ingestion may induce tolerance
  - Baked milk challenges → following a protocol and under close observation at the Allergy Office or Hospital-based set up (1\textsuperscript{st} Fatality to food oral challenge reported recently)
- Mostly outgrown by 16 years. Median age: 10 years
Egg Allergy

- Second most common in children (Prevalence 1.3%)
- Egg white proteins: ovomucoid, ovalbumin, ovotransferrin, lysozyme C, conalbumin
- Egg protein in influenza, yellow fever vaccines; (MMR no problem)
- As in milk allergy, many with egg allergy may tolerate extensively heated (baked) foods containing egg
- Mostly outgrown by adulthood. Median age in a retrospective review of 881 patients with egg allergy median age to develop tolerance was reported as 9 y/o
Peanut Allergy

- Prevalence rising. It has more than tripled, from 0.4% in 1997 to 1.4% in 2008.
- Average age of presentation: 18 months.
- Although can present later in childhood or adulthood, either as a primary food allergy or as part of the pollen-food allergy syndrome.
- 75% reactions occur with first ingestion.
  - Environmental exposure important.
- The food allergy most commonly associated with anaphylaxis.
- ~20% peanut allergy resolution.
Some IgE-mediated childhood food allergies, such as milk and egg allergies, are more likely to resolve than others (peanut and tree nuts).

Some studies suggest that resolution rates may have slowed compared with impressions from past decades.

The ability to evaluate and predict the natural course of specific food allergies for individual patients is essential to inform personalized patient care.

There are a number of clinical and laboratory factors associated with the natural history of pediatric IgE-mediated food allergy.
Factors Associated With The Natural History of Food allergy

1. Clinical characteristics

- Symptom severity on ingestion has been associated with the timing of resolution of allergy to foods.
- Allergy persistence has been associated with more severe symptoms or lower threshold dose required to elicit a reaction.
- An earlier age at diagnosis and the presence of other comorbid allergic diseases are also associated with a more persistent food allergy phenotype.

2. Allergic sensitization

- Larger SPT wheal size or higher food-specific IgE levels are associated with persistent food allergy.
- The rate of change of food-specific IgE levels or SPT wheal size scan also help predict the likelihood that a food allergy has resolved.
Mechanism of Resolution

- Not fully understood
- Likely that multiple mechanisms are involved.
- Food-specific **IgE levels** tend to **fall over time** in most patients and this loss of IgE is the best known predictor of the development of clinical tolerance.
- Some patients become tolerant even with persistently elevated food-specific IgE levels.
- Loss of IgE is not a requirement for the resolution of food allergy in these patients.
Desensitization for Food Allergy

- Trials ongoing with peanut, milk, egg
- Oral, sublingual, transdermal forms
- Researchers say it’s not ready for prime time
- A few allergists are doing this
- Consensus is avoidance, and Epi
Manifestations of food allergy

- May develop hives, vomiting, diarrhea, swelling of lips/tongue, wheezing, dizziness, respiratory distress, LOC, hypotension (all systemic reactions)
Manifestations of food allergy

- Any systemic reaction should be considered an emergency.
- Most life-threatening are due to respiratory distress, hypotension, or loss of consciousness.
- Reactions may be limited to scattered hives, and upon the next exposure, difficulty breathing and weakness may develop.
- Reactions can occur within minutes to two hours after consumption.
Anaphylaxis

- Food-induced anaphylaxis
  - IgE mediated reaction
  - Rapid-onset
  - Multi-organ system involvement (2 or more systems)
  - Potentially fatal
  - Any food, but highest risk:
    - peanut, tree nut, seafood
Fatal Food Anaphylaxis

- Frequency: over ~100 deaths / year
- Individuals at higher Risk:
  - Underlying asthma
  - Symptom denial
  - Teenagers
  - Previous severe reaction
- Fatal flaw: failure to promptly administer Epinephrine
- **Fatal reactions** most commonly: **Biphasic reaction**
  - initial mild symptoms within 30 minutes of ingesting the food that resolved → recurrence of severe symptoms 1-2 hours following the ingestion.
  - important to observe patients with an acute anaphylactic reaction for at least 4 hours prior to discharge from the emergency room.
- Lack of cutaneous symptoms does not exclude anaphylaxis
Diagnosis: History / Physical

- **History:** symptoms, timing, reproducibility
  - Acute reactions vs chronic disease

- **Diet details / symptom diary**
  - Specific causal food(s)
  - “Hidden” ingredient(s)

- **Physical examination:** evaluate disease severity
  - Identify general mechanism
    - Allergy vs intolerance
    - IgE versus non-IgE mediated
Diagnosis: Laboratory Evaluation

- Prick skin tests (SPT)
- ImmunoCap sIgE (old term: RAST)

The test available for a routine use in the clinic can vary, with some practices using mainly SPT, others mainly sIgE and others both.

The future: Basophil Activation Test (BAT) → Functional assay that uses live basophils in whole blood to detect the ability of IgE to mediate activation of basophils after stimulation with allergen. (It goes beyond detection of IgE binding to Allergen to detect IgE function)
Devices for SPT
Interpretation of Laboratory Tests

- **Positive prick test or RAST**
  - Indicates presence of IgE antibody NOT clinical reactivity (high false positive rate)

- **Negative prick test or RAST**
  - Essentially excludes IgE mediated reactivity

- **Intradermal skin test with food**
  - Risk of systemic reaction & not predictive
  - Contraindicated
Medications can alter the response to SPT

Prior to SPT it is important to take a detailed medication history
Medications that suppress skin wheal

- **Anti-H₁ histamines** (Benadryl, Zyrtec, Allegra)
- **Anti-H₂ histamines** (Pepcid, Zantac)
- **Tricyclic Antidepressants** (Doxepin)
- **Benzodiazepines** (Clonazepam) **Atypical Antidepressants** (Olanzapine)
Recommendations to food allergic patients

- Avoidance, Avoidance, Avoidance
- Keep food containing product out of the house
- Tell family and friends about the food allergy, tell server at restaurant
- Aggressive food label reading!!
- Refer to the Food Allergy Research and Education (FARE) (800) 929-4040, www.foodallergy.org
- Medic Alert Bracelet if anaphylaxis has occurred
- Carry Epinephrine Autoinjector at all times – Epipen, AviQ, Adrenaclikc, etc.
Treatment: Emergency Medications

- **Epinephrine:** drug of choice for reactions
  - Self-administered epinephrine readily available
  - Train patients: indications/technique

- **Antihistamines:** *secondary therapy*

- Emergency plan in writing
  - Schools, spouses, caregivers, mature sibs / friends

- Emergency identification bracelet
Treatment options

- **Epipen/ Auvi-Q:**
  
  Junior: Weight 15-30 kg 0.15 mg Epi
  Regular: Weight above 30 kg 0.30 mg Epi

  **Rx for Two-Pack**

  Education is of utmost importance:

  Indications for use
  Proper administration
  To ER or call 911 if ever used
  - either accidentally or intentionally

  ***Debunk the myth that Benadryl will prevent progression of the reaction-it will not!! Epi, Epi, Epi...!!***
Role of Allergist in food Allergy

- Identification of causative food
- Institution of elimination diet
- Help in education
  - Appropriate use of epinephrine
  - Avoidance measure
- Development of action plan
- Prevention of other allergies
- Determine when tolerance occurs
  - When specific IgE drops to consider observed oral challenges
  - Introduction of baked egg and milk
- Removing “food allergy” label improves quality of life
References

- Sicherer SH, Sampson HA. JACI 2007;120:491-503.
Thank you!!!!

Questions??