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SESSION OBJECTIVES

• Discuss common food allergies and their presentation in pediatric patients.
• Discuss management of food allergies in children and common misperceptions.
Food Reactions
A Source of Indigestion

Bonnie Proulx, APRN, PNP
Pediatric Gastroenterology
Children’s Hospital at Dartmouth – Manchester, NH
Quiz

Which patient may have a food allergy?

A. 3 year old with hives and vomiting 15 minutes after eating vanilla ice cream from Baskin Robbins. Child eats ice cream at home with no problems.

B. 46 year old man with episode of syncope 1 hour after eating lobster for dinner. No other symptoms but did complain that he “just didn’t feel right”.

C. 3 month old baby with bloody stools and failure to thrive.

D. 15 year old with chronic, pruritic rash on buttocks and elbows.

E. 25 year old with mouth and lip itching from apples, peaches, and cherries. Cooked fruit causes no symptoms.
Answer

• ALL OF THE ABOVE
Food Reactions

- IgE-mediated Food Allergy Reactions
- Oral Allergy Syndrome
- Non-IgE-mediated Food Hypersensitivity
Food Allergy

- Food allergy is characterized by immunologic responses to specific food proteins.
- Prevalence is greatest in the first few years of life and declines over the first decade.
- Clinical manifestations of food allergy are dependent on the immunologic mechanism:
  - IgE-mediated reactions – rapid onset
  - Non IgE – make take hours or days.
Food Allergy

- Defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food
What It Is Not

- Chemical/pharmaceutical effect
  - **Caffeine**: Tremor, diarrhea, cramps
  - **Tyramine** (cheese): Migraines
  - **Scombroid** fish poisoning (spoiled fish): histadine -> flush, pruritis, bronchospasm, tachycardia
  - **Sulfites** (cheese, wine, beer, dried fruit, lettuce): bronchospasm
  - **MSG**
  - **Aspartame**
- Enzyme deficiency
  - Lactose/fructose
- Malabsorption
- Bacterial toxin
Epidemiology

- As of 2014, 1 in 13 children has a FA
- About 4% of total U.S. population (12 million) has food allergy
  - 6% of children (3 million)
  - 3.5% of adults
- Food allergies in U.S. and other industrialized countries is increasing, along with other atopic diseases
  - Peanut allergy has tripled since 1990
- 8 foods account for 90% of food allergy in U.S.
  - Milk, egg, peanut, tree nuts, wheat, soy, fish, and shellfish
- Each year, 150-200 deaths are attributed to food-related anaphylaxis
## Prevalence

<table>
<thead>
<tr>
<th>Food</th>
<th>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>
</tbody>
</table>
Why Is It Increasing?

• Hygiene Hypothesis

• Food Processing: roasted vs. boiled peanuts

• Topical sensitization

• Your guess is as good as mine
Some food allergies may be “outgrown”

Sometimes “outgrown”
- Eggs
- Milk
- Soy

Usually not “outgrown”
- Peanuts
- Tree nuts
- Fish
- Shellfish
90% of food allergies are caused by a limited number of foods

In Children
- Milk
- Egg
- Peanuts
- Wheat
- Soy
- Tree nuts

In Adults
- Peanuts
- Tree nuts
- Fish
- Shellfish
• The gastrointestinal tract has a barrier system to protect the body from ingested antigens

• Includes immunologic and physiologic barrier
  • Stomach acidity
  • Mucin coat
  • Gastrointestinal enzymes
  • Immunoglobulins
Food Allergy: Natural History

- Most children will outgrow milk, egg, wheat and soy allergy by school age or adolescence
  - Wheat: 29% by 4y, 56% by 8y, 65% by 12y
  - Milk: 80% by 5y

- Nut, fish and peanut allergy tend to be life-long
  - 20% of peanut allergic children outgrow peanut allergy, but 8% of these may re-sensitize
• Children with atopic disease are more likely to have food allergies
• Seen in approximately 35% of children with atopic dermatitis.
• Moderate to Severe atopic dermatitis have 35% increased risk of food allergy
IgE-Mediated Reactions: Pathophysiology

- Bronchoconstriction
- Mucous production
- Cough receptor

- Dyspnea
- Wheeze
- Chest tightness
- Cough

- Increased gastric acid secretion
- Increased intestinal motility
- Increased vascular permeability

- Abdominal pain/cramping
- Vomiting
- Diarrhea
IgE-Mediated Reactions: Pathophysiology

- Itch receptors
- Increased vascular permeability
- Tachycardia
- Increased vascular permeability
- Vasodilation
- Hypotension
- Pruritis
- Flush
- Urticaria
- Angioedema
- Syncope
- Seizures
- Shock
- Death
IgE-mediated Food Allergy Reactions

- Arise when food allergens penetrate the gastrointestinal barrier, initiating the classic immediate hypersensitivity chain of events
- Frequently cause acute urticaria/angioedema
- May cause life-threatening events without cutaneous responses
- Signs/symptoms may occur within minutes to a couple of hours
- The most severe cases involve the cardiovascular and/or respiratory systems, resulting in food induced anaphylaxis
IgE-Mediated Reactions: Clinical Picture

- 80-90% reactions involve the skin
  - Flush
  - Pruritis
  - Urticaria
  - Angioedema

- 70% reactions involve the GI tract
  - Nausea/vomiting
  - Crampy pain
  - Diarrhea

- 30-40% reactions involve the respiratory tract
  - Cough
  - Wheeze
  - SOB
  - Tightness in chest

- <10% reactions involve the cardiovascular system
  - Hypotension
  - Syncope
  - Pre-syncpe
IgE-Mediated Reactions: Clinical Picture

- IgE-mediated food allergy **very rarely** causes chronic symptoms

- Asthma and rhinitis can occur acutely as part of a reaction, but chronic rhinitis and respiratory symptoms in absence of other signs or symptoms of a systemic reaction are not typically due to food

- Chronic abdominal pain or diarrhea may be due to IgE-mediated food allergy but other causes, especially in an otherwise non-atopic patient, are much more common

- Chronic urticaria is rarely found to be caused by food or food additives, in spite of extensive testing
Diagnosing Food Allergy

- **Patient history** is paramount in the selection of foods for testing

- **Consider:**
  - Types of symptom expressed
  - Relationship between symptom onset and ingestion
  - Time since the last reaction
  - Quantity of suspected food ingested when symptoms occurred
  - Activities at the time of (or prior to) symptoms
Diagnosing Food Allergy

- **Patient history** is paramount in the selection of foods for testing
- Skin testing is useful
- In vitro tests (ELISA) are recommended for pts with:
  - Significant dermatographism
  - Severe skin disease and limited surface area for skin testing
  - Suspected marked sensitivities to certain foods
  - Difficulty in discontinuing antihistamines or certain antidepressants
IgE-Mediated Reactions: Testing

**Skin Test**
- Skin pricked through drop of purified protein extract
- Negative predictive value >95%
- Positive predictive value 50%
- Sensitivity >90%
- Specificity 50%
- Results available in 15-20 minutes
- Less expensive than laboratory testing ($16 for SPT vs. $33 for RAST)

**Blood test**
- RAST test: CAP-RAST now able to give quantitative result
- Not as sensitive as SPT for foods for which we do not know cutoff values
- Can do if patient on antihistamines or if skin not clear
- Can be used to follow levels and predict likelihood of patient passing an oral challenge
Skin Testing

- A negative test strongly indicates *against* that food being responsible for the allergic reaction
- A positive test usually requires correlation with a clear positive history or with a food challenge
- A correct result sometimes relies on the use of fresh foods
- Children less than 1 year of age may have IgE mediated food allergy in the absence of positive skin tests, children less than 2 may have smaller wheals
Beware

- Negative ige serum testing does not necessarily rule out allergy

- If highly suspicious, skin or oral food challenge should be considered
Predictive value of IgE testing in positive or negative OFC results

- **Food >95% Positive**
  - sIgE  SPT  sIgE  SPT wheal (mm)
  - Egg white  ≥7
    ≥2 if age <2 y  ≥7  ≤2  ≤3
  - Cow's milk  ≥15
    ≥5 if age <1 y  ≥8  ≤2
  - Peanut  ≥14  ≥8  ≤2 = history of prior reaction
    ≤5 = no history of prior reaction  ≤3
- **Fish ≥20**
Double-Blind, Placebo-Controlled Food Challenge

- Considered the “gold standard” for diagnosing food allergies
- Selection of foods is based on history and/or diagnostic tests
- A positive skin test to a food to which a patient reported an anaphylactic reaction may be considered diagnostic and DBPCFC unnecessary
IgE Mediated Reactions: Oral Challenge Testing

- Oral food challenge is the gold standard for diagnosis
- DBPC is ideal, but not often done outside of academic/research setting
- Open food challenge is most common
- Start with very small dose and slowly increase to normal serving size
- Must have emergency medicine available
- Results can be confounded by subjective reactions
The Oral Allergy Syndrome

- Symptoms are associated with the ingestion of fresh fruits and vegetables.
- Symptoms generally have a rapid onset and resolution.
- Characteristic symptoms include pruritus of the lips, palate, tongue and throat.
- Confined to the oropharynx.
The Oral Allergy Syndrome

• Symptoms of throat closing are a potential systemic and life-threatening reaction and should not be confused with symptoms of oral allergy syndrome, which is a self limiting condition.

• Oral allergy syndrome is frequently seen in patients with seasonal allergic rhinitis due to cross-reactivity between some pollens and foods.
Pollens and cross reactive foods in patients with OAS

- **Pollen/plant**  
  Birch: Apple, cherry, apricot, carrot, potato, kiwi, hazelnut, celery, pear, peanut, soybean
  Ragweed: Melon (eg, cantaloupe or honeydew), banana
  Grass: Kiwi, tomato, watermelon, potato
  Mugwort: Celery, fennel, carrot, parsley
  Latex: Banana, avocado, chestnut, kiwi, fig, apple, cherry
Food is the leading cause of anaphylaxis in children
Anaphylaxis in Food Allergy: Definition

- **Criterion 1** — Acute onset of an illness (over minutes to several hours) involving the skin, mucosal tissue, or both AND AT LEAST ONE OF THE FOLLOWING:
  - Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)
  - Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction (eg, hypotonia, syncope, incontinence).

- **Criterion 2** — TWO OR MORE OF THE FOLLOWING that occur rapidly after exposure TO A LIKELY ALLERGEN FOR THAT PATIENT (minutes to several hours):
  - Involvement of the skin-mucosal tissue
  - Respiratory compromise
  - Reduced BP or associated symptoms
  - Persistent gastrointestinal symptoms

- **Criterion 3** — Reduced BP after exposure TO A KNOWN ALLERGEN FOR THAT PATIENT (minutes to several hours).
Anaphylaxis in Food Allergy: Epidemiology

- Food allergy is estimated to cause 50% of anaphylaxis cases treated in EDs
- One survey estimated 30,000 ED visits per year due to food-induced anaphylaxis
- Peanuts, tree nuts and seafood are responsible for most cases in adults
  - Milk and egg cause most cases in children
- Estimated 150 deaths per year from food allergy in U.S.
Non-IgE-mediated Food Hypersensitivity
• Ige vs. IgG testing

• IgG antibodies are found in both allergic and non-allergic people. Experts believe that the production of IgG antibodies is a normal response to eating food and that this test is not helpful in diagnosing a food allergy.
Food induced enterocolitis

- Generally presents in infants between 1 week and 3 months of age
- Major symptoms are protracted vomiting and/or diarrhea
- Cow milk, soy protein or both are most often responsible
- Symptoms usually resolve after 72 hours of allergen avoidance
Food –induced proctocolitis

- Presents during first few months of life
- Hematochezia is (gross or occult) is a distinguishing feature
- Cow milk or soy protein are usually implicated
- May co-exist with Clostridium Difficile infection
Food-induced Enteropathy

- Malabsorption syndrome
- Presents in first several months of life
- Cow’s milk sensitivity is most frequent cause
- Symptoms:
  - Protracted and/or greasy diarrhea
  - Vomiting
  - Failure to thrive

Intestinal lesions may require 6 to 18 months allergen avoidance for complete resolution
Allergic Eosinophilic Gastroenteritis/Eosophagitis

- Intolerance to multiple foods, IgE or non-IgE mediated mechanisms
- Eosinophils infiltrate esophageal, gastric or intestinal walls
- Symptoms include nausea/vomiting, abdominal pain, diarrhea, GERD, early satiety or food refusal, dysphagia, weight loss, growth failure
- Symptoms subside within 3-6 weeks of allergen elimination
Elimination Diets

• Therapeutic trials
• Used only for a limited period of time (10-14 days)
• Monitor outcomes closely
• Adequate education before starting is key to avoiding failure
Elimination Diets

- Basic Elimination Diet (6 food)
  - Milk, soy, egg, wheat, tree nut, peanut, fish/shellfish
- Targeted Elimination Diet
- Severe Elimination Diet
Celiac Disease

- Gluten-sensitive celiac disease produces a more extensive enteropathy, leading to malabsorption
- Sensitivity is to gliadin, the alcohol-soluble portion of gluten
- Found in wheat, oat, rye and barley
- Treatment requires lifelong elimination of gluten
Food Intolerance

- Accounts for the majority of adverse food reactions
- Not an immunologically mediated response
- May include:
  - Abnormal metabolic responses (ie lactase deficiency)
  - Unusual susceptibility to pharmacologic substances in certain foods (ie caffeine, tyramine)
Fig E1

Adverse Food Reaction

Immune Mediated (Food Allergy and Celiac Disease)
- IgE Mediated (e.g. acute urticaria, anaphylaxis, oral allergy syndrome)
- Non-IgE Mediated (e.g. food protein-induced enterocolitis syndrome)
- Mixed IgE and non-IgE Mediated (e.g. atopic dermatitis, eosinophilic gastroenteritis)
- Cell Mediated (e.g. Allergic Contact Dermatitis)

Non-Immune Mediated (Primarily Food Intolerances)
- Metabolic (e.g. lactose intolerance)
- Pharmacologic (e.g. caffeine)
- Toxic (e.g. scromboid fish toxin)
- Other / Idiopathic / Undefined (e.g. sulfites)
Managing the Patient with Food Allergy

- Nonpharmacologic Management:
  - Strict avoidance of the offending food allergens is the only proven therapy
  - Symptomatic reactivity to food allergens is often lost over time except for:
    - Peanuts
    - Fish
    - Tree nuts
    - Shellfish
Managing the Patient with Food Allergy

• Pharmacologic Management
  • Epinephrine is the treatment of choice for severe reactions to food
  • Doses may be repeated every 15 minutes for up to 3 doses
  • Delayed, biphasic or prolonged anaphylaxis occurs in more than 20% of cases and so extended observation is required in all cases
  • Prophylactic management has not been proven safe or effective
Patient Education

- Allergen identification (ie how to read food labels)
- Avoidance strategies and counseling
- Symptom recognition
- Cautions regarding the possibility of a life-threatening reaction
- What to do in case of accidental ingestion
  - Development of a treatment plan
  - How to self-administer epinephrine
Other concerns

- Nutrition
- Bullying
- Social stigma
- Siblings
- Food introductions in infants
Food Allergy: Prevention

- We do not know how to prevent food allergies

- Diet restriction in pregnancy not recommended

- Exclusive BF for 6 months is best
  - Diet restriction while BF: in high risk patients, avoid high risk foods (peanuts, tree nuts, milk, egg)

- If supplementing, extensively or partially hydrolyzed formula is best

- No evidence that delaying introduction of solid foods has any effect
Food Allergy: Resources for Patients

- Food Allergy and Anaphylaxis Network
  - [www.foodallergy.org](http://www.foodallergy.org)

- American Academy of Allergy, Asthma, and Immunology
  - [www.aaaai.org](http://www.aaaai.org)

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  - [www.acaai.org](http://www.acaai.org)