The Spectrum of Food Adverse Reactions

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Why are you here?

A. LOVE Allergy and Immunology
B. Superior gluteus maximus endurance
C. Exceptionally eager learner
D. Like the speaker I am of Scottish heritage and will stay to the bitter end to make certain that I obtain as much knowledge as possible for my tuition
E. Some combination of the above
No conflicts of interest

Order of Presentation

Cases - to Illustrate
Problem Solving in Food Adverse Reactions
Case #1

A 26 year old woman presents with a question of possible food allergy. She thinks she is allergic to *mango* because the last *three* times she has eaten it she has developed immediate *hives*, worsening sensation of *asthma*, and *abdominal pain*. The most recent event was accompanied by *dizziness*. She is otherwise healthy.

What is the most likely mechanism of this patient’s reaction to mango?

A. Eosinophilic infiltration  
B. Idiosyncratic toxic  
C. Type 1 IgE mediated (immediate) hypersensitivity  
D. Immediate gastrointestinal allergy
What is the most likely mechanism of this patient’s reaction to mango?

A. Eosinophilic infiltration
B. Idiosyncratic toxic
C. Type 1 IgE mediated (immediate) hypersensitivity
D. Immediate gastrointestinal allergy

Case #2

A 32 year old man presents with concern about food allergy. For the past three years he has noted increasing symptoms of itching, possible swelling and irritation in the mouth and throat upon eating certain foods, including apples, nectarines and plums. He asks whether food allergy testing is needed.
The remainder of the H&P is notable for:

- General good health
- Childhood history of eczema
- Springtime hay fever symptoms
- Use of ibuprofen for periodic headaches
- A brother with asthma
- Nasal turbinate edema and rhinorrhea

What is the cause of his problems with food?

A. Food allergy to stable proteins
B. Pollen-Food syndrome
C. Ibuprofen sensitivity
D. Irritation from chemical constituents of the food
What is the cause of his problems with food?

A. Food allergy

B. *Pollen-Food syndrome*

C. Ibuprofen sensitivity

D. Irritation from chemical constituents of the food

Case #3

A 29 year old man has come to the Emergency Room for dysphagia. For years he has felt as if food gets “stuck,” and he has adapted by eating smaller and smaller pieces of food. The ER visit was precipitated by a pediatric size allergy pill becoming “stuck,” upon swallowing, leading to increased difficulty swallowing, frothing at the mouth and pain.

Esophageal biopsy demonstrated:

*Eosinophilic Esophagitis*
What is the normal number of eosinophils per HPF found in the esophagus?

A. 0  
B. 25  
C. 50  
D. 100
Case #4

A 34 year old woman comes to the clinic for evaluation of bad allergic reactions to bee stings. In the course of taking a complete history you learn that she is also worried about food allergy. She develops flushing and bloating SOMETIMES when she walks up the 105 stairs between her parking space and her house. It has worsened with her recent pregnancy and delivery.

What is the cause of her symptoms?

Mast cell activation syndrome (MCAS)
IgE mediated food anaphylaxis
Exercise induced anaphylaxis
Food associated, exercise induced anaphylaxis
What is the cause of her symptoms?

- Mast cell activation syndrome (MCAS)
- IgE mediated food anaphylaxis
- Exercise induced anaphylaxis
- Food associated, exercise induced anaphylaxis

What are typical features of IgE mediated food systemic allergic reactions?

- Occurs within seconds to minutes (rarely hours)
- Occurs with every exposure (rare exceptions)
- Any combination of:
  - Itching/hives/angioedema
  - Wheezing/bronchospasm
  - Abdominal pain/diarrhea/vomiting
  - Dizziness/drop in blood pressure
  - Mucosal edema
- *Clinical pearl = menstrual cramps*
IgE mediated reaction
“Immediate (Type 1) hypersensitivity”

Antigen (allergen) specific cross-linking of IgE receptors on mast cells

Major Food Allergens

<table>
<thead>
<tr>
<th>Kids</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanuts</td>
<td>Peanuts</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>Tree nuts</td>
</tr>
<tr>
<td>Milk</td>
<td>Shellfish</td>
</tr>
<tr>
<td>Egg</td>
<td>Fish</td>
</tr>
<tr>
<td>Wheat</td>
<td>(fruits and vegetables)</td>
</tr>
<tr>
<td>Soy</td>
<td></td>
</tr>
</tbody>
</table>

90% of deaths are caused by anaphylaxis to tree nuts and peanuts!
What are food allergens?

Almost all allergens are:
- Proteins or glycoproteins
- Heat resistant, acid stable

Examples:
- "Lipid transfer proteins"
- "Profilins"
- "PR 10"

Cross-reactivity

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
-Some fruit-allergic patients may be at risk for latex allergy
-Warn latex-sensitive patients of potential cross-reactivity

Refer these patients to an A/I specialist

Adapted from AAAAI.org
Cross-reactivity

“Pancake anaphylaxis”

-food associated anaphylaxis in dust mite (aeroallergen) allergic people who eat pancakes that are contaminated with storage mites!

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
- Allergens: proteins that are heat labile
- Cause: cross reactive proteins pollen/food

Adapted from AAAAI Food Allergy Teaching Slide
Clinical Tip

The diagnosis of Pollen-Food Syndrome can be made easily by asking the right question:

*Can you eat these fruits if they are baked into a pie?*

“*Yes*” Pollen-Food Syndrome

“*No*” Higher risk of major food allergic reactions

Why is this important?

Pollen-Food Syndrome is *generally just annoying*

*True food allergy can kill!*

Clinical Pearl:

The HISTORY (yea!) can play a key role in helping to distinguish the DANGER level of any given food adverse reaction.
Recently described cross-reactivities

Cypress pollen and peach
Mesquite and lima bean

Diagnosis of IgE mediated food allergy

Beyond the history and physical:
Serum specific IgE (to a particular food)
- best for primary care and non-A/I docs
- refer to A/I if high clinical suspicion and the test is negative

In the A/I office:
Prick skin testing
- (NO intradermal testing for food allergy)

Oral challenge
- Do not do this at home!
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</td>
</tr>
<tr>
<td>&lt;2 years</td>
<td>Egg</td>
<td>≥ 2</td>
</tr>
<tr>
<td>Child</td>
<td>Cow Milk</td>
<td>≥ 15</td>
</tr>
<tr>
<td>&lt;2 years</td>
<td>Cow Milk</td>
<td>≥ 5</td>
</tr>
<tr>
<td>Child</td>
<td>Peanut</td>
<td>≥ 14</td>
</tr>
<tr>
<td>Child</td>
<td>Fish</td>
<td>≥ 20</td>
</tr>
</tbody>
</table>

Garcia-Ara C, et al. J Allergy Clin Immunol 2001;107(1);185-90
AAAAI.org

Prick Skin Testing

Gundling
Serum IgG testing for food allergy is

A. essentially irrelevant
B. specific but not sensitive
C. equivalent to prick skin testing
D. useful for eczema but not asthma
Key Point

IgG food testing is not helpful to define meaningful food allergies
Eosinophilic Gastrointestinal Disorders

Symptoms:
In teens/adults: dysphagia, food impaction, GER

Biopsy:
Inappropriate infiltration and degranulation of eosinophils in the GI tract.

Prevalence increasing:
Eosinophilic esophagitis is the most common syndrome, more common in children than adults

Sometimes related to food allergy, but mechanism/s are unclear

Modified from AAAAI.org

Spectrum of Adverse Food Reactions

**Immunologic**

IgE-Mediated
(most common)

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

Non-IgE Mediated
Cell-Mediated

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

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

Celiac tested “negative” patients who still have problems with “gluten”

Recent papers to consider:

Remember...

The severity of prior reactions do not necessarily predict the severity of future reactions!
Epinephrine Prescription

Dr. Gundling’s demonstration of how to use injectable epinephrine:
http://www.youtube.com/watch?v=i6K2_kVmr3E&feature=g-hist

Example: Rx
Epinephrine auto injector (adult) or (child) #2
Use as directed
2 refills

Image: AAAAI Food Allergy Teachings Slides

How to Save a Life!
Must shellfish allergic patients avoid exposure to radiocontrast media?

No! Shellfish allergy is NOT a contraindication to receiving RCM.

Shellfish allergy is due to an *IgE mediated response to tropomyosin*, a muscle protein.

Reactions to RCM are normally caused by **DIRECT mast cell degranulation**, a different mechanism

*Clinical Pearl:*
Atopic disease predisposes people to RCM reactions
IgE mediated reaction  
“Immediate (Type 1) hypersensitivity”

The reaction to RCM is caused by direct mast cell degranulation.
Spectrum of Adverse Food Reactions

Non-Immunologic

Immunologic

Spectrum of Adverse Food Reactions

Non-immunologic

Toxic/Pharmacologic
Bacterial food poisoning
Heavy metal poisoning
Scombroid fish poisoning
Caffeine
Alcohol
Histamine

Non-Toxic/Intolerance
Lactase deficiency
Galactosemia
Pancreatic insufficiency
Gallbladder / liver disease
Hiatal hernia
Gustatory rhinitis
Anorexia nervosa
Idiosyncratic
Carbohydrate malabsorption

Adapted from Sicherer/Sampson
JACI 2006; 117:S470-475
Summary of Clinical Pearls

- Food anaphylaxis can present with menstrual cramps
- The HISTORY is key to distinguishing pollen-food syndrome from severe food allergy
- Allergen cross-reactivity is responsible for odd or seemingly “first exposure” allergic reactions
- When in doubt, prescribe and demonstrate the use of epinephrine!
- Atopy predisposes people to RCM allergic reactions
- Consider MCAS in your ddx of flushing, abd pain and idiopathic anaphylaxis
### Reasons for Referral to Allergy/Immunology

<table>
<thead>
<tr>
<th>Reason</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons with a <strong>diagnosed food allergy</strong></td>
<td></td>
</tr>
<tr>
<td>Persons who have experienced allergic symptoms in association with food exposure (<strong>convincing history</strong>).</td>
<td></td>
</tr>
<tr>
<td>Persons who have <strong>limited their diet</strong> based upon perceived adverse reactions to foods or additives.</td>
<td></td>
</tr>
<tr>
<td>Persons with known eosinophilic esophagitis</td>
<td></td>
</tr>
<tr>
<td><strong>Atopic families</strong> with, or expecting, a newborn who are interested in identifying risks for, and preventing, allergy.</td>
<td></td>
</tr>
</tbody>
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*Adapted from AAAAI.org; ed slides*

### Goals

Improve your **mental schematic** for diagnosis and treatment
Distinguish the **dangerous** from the **annoying**
Recognize **indications for referral** to an A/I specialist
Supplemental Slides

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>Food Pollenosis</td>
<td>25-75% in pollen allergic</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>Chronic rhinitis</td>
<td>Rare</td>
</tr>
</tbody>
</table>

Adapted from AAAAI.org ed. slides
Disorders Not Proven to be Related to Food Allergy

Migraines
Behavioral / Developmental disorders
Arthritis
Seizures
Inflammatory bowel disease

Adapted from: Food Allergy Practice Parameters: AAAAI.org; ed slides

Updated Gell and Coombs Classification of Hypersensitivity Disorders

Type I: Immediate or IgE mediated
Type IIa: Cytotoxic or IgG/IgM mediated
  IIb: Antibody mediated cell stimulating
Type III: Immune complex mediated
Type IVa: CD4+ lymphocyte
  IVb: CD4+ Th2 lymphocyte
  IVc: Cytotoxic CD8+ T lymphocyte (perforin-granzyme B)
  IVd: T-lymphocyte driven neutrophilic inflammation
## Summary of One Algorithm for Food Adverse Reactions

<table>
<thead>
<tr>
<th>Non-immunologic</th>
<th>Immunologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-toxic/Intolerance</td>
<td>IgE mediated</td>
</tr>
<tr>
<td>Pharm/Toxic</td>
<td>Cell-mediated/other</td>
</tr>
<tr>
<td></td>
<td>immunologic</td>
</tr>
<tr>
<td></td>
<td>• IL-5</td>
</tr>
<tr>
<td></td>
<td>• TNF-alpha</td>
</tr>
<tr>
<td></td>
<td>• Activation of dendritic cells, mast cells, B cell AF</td>
</tr>
<tr>
<td></td>
<td>• Others</td>
</tr>
</tbody>
</table>