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 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”

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

**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

<table>
<thead>
<tr>
<th>Pollen</th>
<th>Food</th>
<th>Allergens</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birch</td>
<td>Apple, carrot, celery, cherry, pear, hazelnut</td>
<td>proteins that are heat labile</td>
<td>cross reactive proteins pollen/food</td>
</tr>
<tr>
<td>Ragweed</td>
<td>Banana, cucumber, melons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grass</td>
<td>Melon, tomato, orange</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mugwort</td>
<td>Melon, apple, peach, cherry</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.

**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"

**What kind of nut is this?**

A. Pecan
B. Almond
C. **Hazelnut**
D. Macademia

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

Recently described cross-reactivities

Cypress pollen and peach
Mesquite and lima bean

Cross-reactivity

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

Case #3

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

Case #4

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

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

IgE-Mediated (most common)
- Systemic (Anaphylaxis)
- Oral Allergy Syndrome
- Immediate gastrointestinal allergy
- Asthma/rhininitis
- Urticaria
- Morbilliform rashes and flushing
- Contact urticaria

Non-IgE Mediated
- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

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

Immuneologic

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>


Gundling
The diagnostic test for non-IgE mediated adverse food reactions depends upon the suspected underlying etiology...

A few commonly asked questions...

What is the role of IgG testing in the diagnosis of food allergy?

Serum IgG testing

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

---

Can patients who have tested negative for celiac disease still have problems with “gluten”?

Recent papers to consider:


---

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.

The reaction to RCM is caused by direct mast cell degranulation.

IgE mediated reaction
“Immediate (Type 1) hypersensitivity”

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

What are some other “non-allergic” causes of food adverse reactions?
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

Immunologic

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

Does the severity of one food allergic reaction predict the severity of the next?

No!

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
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
- Atopy predisposes people to RCM allergic reactions
- When in doubt, prescribe and demonstrate the use of epinephrine!

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

Reasons for Referral to Allergy/Immunology

- **Persons with a diagnosed food allergy**
- **Persons who have experienced allergic symptoms in association with food exposure (convincing history)**.
- **Persons who have limited their diet** based upon perceived adverse reactions to foods or additives.
- **Persons with known eosinophilic esophagitis** *Atopic families* with, or expecting, a newborn who are interested in identifying risks for, and preventing, allergy.

Adapted from AAAAI.org; ed slides