Disclosures

• Mylan Pharmaceuticals – in past have been on speaker’s bureau
Objective

• Participants will be able to discuss the mechanisms of food allergies.

• Participants will be able to plan appropriate evaluation and treatment of food.
Definition of Food Allergy

- **Food allergy**: the manifestation of an abnormal immune response to antigen delivered by the oral route.

- Not all “food allergies” are actual immune mediated reactions but are “food intolerances”
Adverse Food Reactions

- Food Allergy
  - IgE-mediated only
  - No proven immunologic mechanism
- Food Anaphylaxis
- Food Intolerance
  - idiosyncratic
  - metabolic
  - pharmacologic
  - toxic
Some Conditions Related to Food Intolerance*

- Gastrointestinal disorders
- Structural abnormalities: hiatal hernia, pyloric stenosis, Hirschsprung's disease, tracheoesophageal fistula
- Disaccharidase deficiencies: lactase, sucrase-isomaltase complex, glucose-galactose complex
- Pancreatic insufficiency: cystic fibrosis
- Gallbladder disease
- Peptic ulcer disease
- Malignancy
- Metabolic disorders

*--Non-immunologic adverse reactions to food.

- Galactosemia
- Phenylketonuria
- Pharmacologic-related conditions
- Jitteriness (caffeine)
- Pruritus (histamine)
- Headache (tyramine)
- Disorientation (alcohol)
- Psychological disorders
- Neurologic disorders
- Gustatory rhinitis
- Auriculotemporal syndrome (facial flush from tart food)
Food Hypersensitivity Syndromes:

IgE

- Anaphylaxis
- Urticaria/Angioedema
- Erythematous Morbilliform Rash
- Oral Allergy Syndrome
- Rhino-conjunctivitis
- Laryngeal edema

Non-IgE

- Atopic Dermatitis
- Allergic Eosinophilic Gastroenteritis
- Allergic Eosinophilic Esophagitis (EoE)

- Contact Dermatitis
- Dermatitis Herpetiformis
- Dietary Protein Enterocolitis
- Food-induced pulmonary hemosiderosis (Henier’s Syndrome)

Adapted from Spergel, J.
**Immune Mechanisms**

- Protein digestion
- Antigen processing
- Some Ag enters blood

**IgE-Mediated**
- IgE-receptor
- Mast cell
- Histamine
- Histamine Release

**Non-IgE Mediated**
- TNF-α
- IL-5

**Adapted from AAAAI slide set**
Eight most common food allergies

1. Milk
2. Egg
3. Peanuts
4. Soy
5. Wheat
6. Tree nuts
7. Shellfish
8. Fish
## US prevalence of food allergies

<table>
<thead>
<tr>
<th>Food</th>
<th>Age 1-5 (%)</th>
<th>Adults (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Egg</td>
<td>1.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Peanut</td>
<td>1.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Tree Nuts</td>
<td>1.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Fish</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Shellfish</td>
<td>0.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Overall</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

Sampson, H.A. *Food Allergy*. Allergy 2005:60 (Suppl. 79) 19-24
Sicherer, S. *Epidemiology of food allergy* – JACI (2012)
Manifestations of Allergic Reactions

- **Skin**
  - Characterized by pruritic, transient, erythematous raised lesions, sometimes accompanied by localized swelling (angioedema).

- **Gastrointestinal**
  - Vomiting, Diarrhea, Abdominal pain

- **Pulmonary**
  - Cough, wheeze, stridor, throat tightening, change in voice

- **Multi-Systems**
  - Anaphylaxis = life threatening

Manifestations of Allergic Reactions

http://dermnetnz.org/reactions/urticaria.html
Manifestations of Allergic Reactions – Multi-system

- **Anaphylaxis**: Multi-organ reaction associated with IgE-mediated hypersensitivity.
  - Fatal food-related anaphylaxis
    - Often unaware that they had ingested the incriminated food
    - Often delay in receiving adrenaline therapy.
  - Peanuts, tree nuts, shellfish
  - Other common causes
    - Medications, venoms (bee sting), immunotherapy
Diagnosis Of Allergic Diseases

- Thorough medical history
- **In-Vivo** testing
  - Percutaneous (skin prick testing)
- **In-Vitro** IgE testing (serum immunoassays)
  - RAST test (semi-quantitative)
  - Fluorescent studies (quantitative)
    - ImmunoCAP®
    - Food Component testing
- For Food Allergies:
  - Elimination diets
  - Oral food challenges (open or DBPCFC)
Skin Prick Testing

• **Advantages:**
  – Minimally invasive, good reproducibility, results fast (15 minutes)
  – Quantifiable and can allow the evaluation of multiple allergens at once
  – Good correlation with the results of in vivo challenges
  – Can be used in the evaluation of:
    • Food allergy
    • Allergic rhinitis, Asthma, Insect sting allergy IgE mediated anaphylaxis, Drug reactions (b-lactams)
Skin Prick Testing

- **Disadvantages:**
  - Risk of anaphylaxis
  - Avoid anti-histamines for 5 – 10 days
  - Depends on allergen extract and limited by skin reactivity and skin area
  - Impracticable in severe eczema or in patients who cannot discontinue the use of certain medications that have antihistaminic effects (tricyclic antidepressants)

Pearls and pitfalls of allergy diagnostic testing: report from the American College of Allergy, Asthma and Immunology/American Academy of Allergy, Asthma and Immunology Specific IgE Test Task Force Linda Cox, MD, et al.
Skin Prick Testing:

- Positive prick test
  - Indicates presence of IgE antibody NOT clinical reactivity

- Aeroallergens:
  - ~98% sensitivity
  - ~82% specificity

- Foods:
  - ~90% sensitivity
  - ~50% specificity
  - ~50% false positives
  - Larger skin tests/higher IgE correlates with likelihood of reaction but not severity

- Negative prick test
  - Essentially excludes IgE antibody


www.flickr.com/photos/artgeek/2088243047/
In Vitro Testing

- Measure serum levels of antigen-specific IgE

**Advantages:**
- Use in patients with severe cutaneous disease (atopic dermatitis)
- In patients who cannot discontinue medications (antihistamines)
- In patients with a history of severe anaphylaxis

**Disadvantages**
- Increased cost
- Delays in providing results (2-3 weeks)
- Laboratory reliability
- Not as sensitive as skin testing
- Sensitivity (70% - 90%) and specificity (50% - 80%)
In Vitro Test Info

• Direct correlation between the food-specific IgE level and the probability that an individual will react to an ingested food.

• These blood levels are similar to skin prick test with wheal ~10 mm or greater

• In general, specific IgE <2 ku/L – then 50% chance of tolerating food (depends on food)

<table>
<thead>
<tr>
<th>Allergen</th>
<th>kUₐ/L</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV[+]</th>
<th>NPV[++]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg</td>
<td>7</td>
<td>61</td>
<td>95</td>
<td>98</td>
<td>38</td>
</tr>
<tr>
<td>Infants ≤2 yr</td>
<td>2</td>
<td></td>
<td></td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td>15</td>
<td>57</td>
<td>94</td>
<td>95</td>
<td>53</td>
</tr>
<tr>
<td>Infants ≤1</td>
<td>5</td>
<td></td>
<td></td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Peanut</td>
<td>14</td>
<td>57</td>
<td>100</td>
<td>99</td>
<td>36</td>
</tr>
<tr>
<td>Fish</td>
<td>20</td>
<td>25</td>
<td>100</td>
<td>99</td>
<td>89</td>
</tr>
<tr>
<td>Soybean</td>
<td>30</td>
<td>44</td>
<td>94</td>
<td>73</td>
<td>82</td>
</tr>
<tr>
<td>Wheat</td>
<td>26</td>
<td>61</td>
<td>92</td>
<td>74</td>
<td>87</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>≈15</td>
<td></td>
<td></td>
<td>≈95</td>
<td></td>
</tr>
</tbody>
</table>

Sampson, Allergy 2005: 60 (Suppl. 79): 19–24
In Vitro Food specific IgE Predictive Values Vary by Age

- Results from 861 milk and 764 egg oral food challenges (Japanese children)

50% and 95% Predictive Value for Food Specific-IgE and SPT

<table>
<thead>
<tr>
<th>Food</th>
<th>~95% Positive</th>
<th>~50% Negative†</th>
<th>~95% Positive</th>
<th>~50% Negative†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow’s milk</td>
<td>≥15&lt;sup&gt;16&lt;/sup&gt;</td>
<td>≤2&lt;sup&gt;23&lt;/sup&gt;</td>
<td>≥8&lt;sup&gt;21&lt;/sup&gt;</td>
<td>≥7&lt;sup&gt;21&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>≥5 if younger than 1 year&lt;sup&gt;132&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg white</td>
<td>≥7&lt;sup&gt;16&lt;/sup&gt;</td>
<td>≤2&lt;sup&gt;23&lt;/sup&gt;</td>
<td>≥7&lt;sup&gt;21&lt;/sup&gt;</td>
<td>≤3&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>≥2 if younger than 2 years&lt;sup&gt;133&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peanut</td>
<td>≥14&lt;sup&gt;16&lt;/sup&gt;</td>
<td>≤2 with and ≤5 without history of peanut reaction&lt;sup&gt;24&lt;/sup&gt;</td>
<td>≥8&lt;sup&gt;17,21&lt;/sup&gt;</td>
<td>≤3&lt;sup&gt;17&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fish</td>
<td>≥20&lt;sup&gt;16&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Food specific-IgE measured with ImmunoCap™ and SPT with lancet (ref 17 & 21,) and bifurcated needle

Food Hypersensitivity Treatment

- **Basis of Therapy:**
  - Dietary elimination of the offending food
- **Patient Dietary Education:**
  - Patients and parents must also be made aware that the food protein, as opposed to sugar or fat
- **Patient Emergency Treatment:**
  - Develop *Emergency Action Plan* for the treatment of reactions caused by accidental ingestion
  - Injectable epinephrine and an oral antihistamine should always be readily available
  - Caregivers must be taught the indications for the use and administration of emergency medications

Sicherer. S. *American Family Physician*. Vol. 59/No. 2
Jan 15, 1999; 415-429
Safety Tatoos, Epinephrine Versions
EMERGENCY ACTION PLAN

PATIENT: ________________________________ DATE: __________________

DIAGNOSIS: _______ FOOD ALLERGY TO: ____________________________

______ BEE STING ALLERGY ______ FIRE ANT ALLERGY ______ ANAPHYLAXIS

The above-listed patient should have access to injectable epinephrine at all times due to a life-threatening allergy. The prescribed Epipen, Twinject or Adrenaclick should be kept in a cool, dark place and should be refilled annually. Patients should carry a small amount of antihistamine with the injector in the event of an accidental ingestion. Patients under 45-50 lbs. should have available a 0.15 mg (Jr.) dose; patients over 45-50 lbs. should have the 0.30 mg dose.

Should an allergic ingestion or bee sting occur, follow these steps:

1. Locate your Epipen, Twinject, Adrenaclick.

2. Take an antihistamine immediately. Preferably, this should be Zyrtec or Benadryl, which have the quickest onset of action.

Suggested dose of Benadryl: ____________ Zyrtec: ____________

3. Get around other people, who can assist you if your reaction progresses.

AT THE FIRST SIGN of any symptoms of severe hives and swelling, difficulty swallowing, speaking, or talking, throat swelling, severe wheezing, cough, shortness of breath, or if collapse occurs, immediately inject Epipen, Twinject or Adrenaclick into the upper outer thigh of the patient and hold for 10 seconds (see back page for diagram). Epinephrine must be given in the muscle for quickest absorption. If the reaction is worsening after 10 minutes or so, administer a second dose if available. The patient should then be taken to the ER for further evaluation. A follow-up appointment with Dr. Greene or Pulcini should be scheduled soon thereafter to review what happened. Remember, it is only necessary to give the rescue epinephrine (Epipen, Twinject, Adrenaclick) if the reaction is progressing in a serious manner as described above, for simple itching or mild hives, no further action is necessary. Often, only an antihistamine will be needed.

Remember, stings and accidental ingestions happen when you least expect them, so be prepared. Have your Epipen, Twinject or Adrenaclick close by at all times.
Forms of Rescue Epinephrine

**EpiPen® (epinephrine) Auto-Injector Directions**

- First, remove the EpiPen® (epinephrine) Auto-Injector from the plastic carrying case
- Pull off the blue safety release cap
- Hold orange tip near outer thigh (always apply to thigh)
- Swing and firmly push orange tip against outer thigh. Hold on thigh for approximately 10 seconds.
- Remove EpiPen® (epinephrine) Auto-Injector and massage the area for 10 more seconds.

**Auvi-Q™ (epinephrine injection, USP) Directions**

Remove the outer case of Auvi-Q. This will automatically activate the voice instructions.

- Pull off RED safety guard.
- Place black end against outer thigh, then press firmly and hold for 5 seconds.

**Adrenaclick® 0.3 mg and Adrenaclick® 0.15 mg Directions**

- Remove GREY caps labeled “1” and “2.”
- Place RED rounded tip against outer thigh, press down hard until needle penetrates. Hold for 10 seconds, then remove.
Future Food Allergy Treatments

- **Sublingual immunotherapy (SLIT)**
  - Concept that contact of an antigen with the oral mucosa/gut-associated lymphoid system leads to induction of oral tolerance
- Has been associated with success for kiwi, hazelnut, peach, cow’s milk and peanut
- SLIT in Peanut – RPCT – Active Peanut SLIT ingested more peanut during OFC than controls (1710 vs 85 mg)
- **Side effects:** Mostly oropharyngeal
  - Median peanut specific IgE decreased in active groups
  - Limitation: maximal dose administered in SLIT limited by small volumes – so maybe more challenging than OIT
Oral Immunotherapy

- **Randomized Controlled Trials:**
  - **Peanut OIT:** Active Peanut OIT showed increased peanut consumption compared to Placebo OIT (5000 vs 280 mg)
  - **Milk OIT:** 20 children with milk allergy (target dose 500 mg, increased milk reaction threshold to 5100 mg in OIT compared to placebo)
  - **Egg OIT:** 27.5% passed 10 g OFC at 24 months after being off therapy for 4-6 weeks and continued egg ad lb for 30-36 months and considered to have “sustained unresponsiveness”
Baked in Foods (Cow’s Milk, Egg)

• Up to 70% of children with egg or cow’s milk allergy can safely consume the extensively heated proteins, with reduction in Th-2 type immune response and accelerated tolerance (compared to natural history cohort of patients with milk allergy)

• Questions remain about effective dose, degree of heating, role of food matrix, ability of heated proteins to induce lasting tolerance
Peanut Oral Immunotherapy

- **Consortium of Food Allergy Research Trial**
  - 40 children/adults given daily peanut or placebo SLIT – Multi-centered study
  - After 44 weeks – 5 gram OFC to peanut and compared groups
  - 70% of peanut SLIT responders passed but only 15% of placebo
  - 11,000 peanut SLIT doses – 63% symptom free, excluding oral-pharyngeal symptoms – 95% symptom free
  - Conclusion: Most achieved ‘modest level of desensitization’
  - Limitations: Patients with anaphylaxis were excluded, 40% of patients with peanut SLIT reported problems with oral-pharyngeal itching (so was it truly blinded)

- **Oral Immunotherapy Trials in Private Practice – Group Dallas**
  - OIT to 150 patients - graded dosing over time at home
  - Results: 111/150 able to tolerate 8 peanuts - considered protective for usual accidental peanut ingestion
  - Reactions: Epinephrine given 8/10,000 doses.

Pro/Con: Is oral peanut immunotherapy ready

• **Pro:**
  – Accidental reactions are ~10% annually and 1-2% require Epinephrine
  – Only 20% chance of outgrowing

• **Con:**
  – Reactions occur during treatment, no longitudinal studies in patients with anaphylaxis, appears to induce desensitization not tolerance
  – Anaphylaxis, progression to EoE, timing of dose (menstruation, food consumption)

• **Summary:**
  – Equipoise: not certain if the benefits outweigh the risks
Other Future Immuno-modulatory Approaches

- Humanized monoclonal IgE (Omalizumab)
  - 2 small studies – shown that in patients with Omalizumab they had higher reaction threshold to peanut on OFC.
  - Other studies show as adjunct with OIT reduced side effects (time to reach daily maintenance)
- Chinese Herbal Therapy
  - In mouse model herbal formula of 9 Chinese herbs
  - Showed reduction in IL-5 levels – phase II studies
- Immune-modulating adjuvants
- Probiotics
- T lymphocyte manipulation to induce tolerance
Prevention of Food Hypersensitivities

- 2010 National Institute of Allergy and Infectious Diseases (NIAID) Guidelines for Diagnosis and Management of Food Allergies 2015 guidelines
- Maternal diet during pregnancy and lactation.
  - Not recommend restricting maternal diet during pregnancy or lactation as a strategy for preventing the development or clinical course of FA.
- Breast-feeding.
  - The committee recommends that all infants be exclusively breast-fed until 4 to 6 months of age
- Timing of introduction of allergenic foods to infants.
  - The committee suggests that the introduction of solid foods should not be delayed beyond 4 to 6 months of age including potentially allergenic foods

LEAP Trial Information

- 500 infants at high risk for peanut
  - Consumption Group:
  - Avoidance Group:

- Age 5 peanut challenge (prevalence of peanut allergy)
  - Consumption Group: 3.2%
  - Avoidance Group: 17.2%

- Excluded 10% of children with SPT > 4 mm

LEAP Trial Information

• Further sub-analysis
• Age 5 peanut challenge - prevalence of peanut allergy
  – Non-sensitized (negative SPT)
    • Consumption: 1.9%
    • Avoidance: 13.7%
  – Mild Sensitized (SPT 1-4 mm)
    • Consumption Group: 10.6%
    • Avoidance Group: 35.3%

Should we recommend introduction of peanuts to all infants before they reach 11 months?
Persistence of Food Hypersensitivities

Peanut Allergy

- Most studies report around 20% of children allergic to peanuts outgrow response.
- However, recurrence rate among children who tolerate peanut was 7.9 in 2005 study by Fleischer et al, so even resolution may not be permanent.

Summary of Studies:

- 80-85% of young children with milk and egg allergies outgrow (develop clinical tolerance) in first 5-10 years of life but it varies on history of their reactions. In addition, peanut allergy is likely to be a lifelong disorder in most children.

Food Allergy: Medcalf, Sampson and Simon 2008
Food Allergy Research & Education (FARE)

- National: [www.foodallergy.org](http://www.foodallergy.org)
- Local: Food Allergy and Asthma Support Group – SAFE of Greenville
  - Contact: Donna Frank, dlfrank71@yahoo.com
  - Facebook: [www.facebook.com/SAFEofGreenvilleSC](http://www.facebook.com/SAFEofGreenvilleSC)
  - Support Meetings: Thursday May 7th and Oct 1st at 9am Panera Bread at Shoppes at Greenridge
  - Saturday August 22nd: 9am FARE WALK at Heritage Park in Simpsonville Please register online at: [www.foodallergywalk.org/upstate2015](http://www.foodallergywalk.org/upstate2015)
Patient Advocacy – Label Change

- Food Allergen Labeling and Consumer Protection Act
  - Effective January 1, 2006, mandated that foods containing milk, eggs, fish, crustacean shellfish, peanuts, tree nuts, wheat, and soy must declare the food in plain language on the ingredient list or via:
    - Foods must have the word “Contains” followed by the name of the major food allergen (milk, wheat, or eggs for example)

- Such ingredients must be listed even if they are present in colors, flavors, or spice blends.
- Manufacturers must list the specific nut or seafood that is used (e.g., almond, walnut, cashew; or tuna, salmon, shrimp, or lobster).
- Role of May contain or processed at a plant that processes (voluntary)
### Old Label

<table>
<thead>
<tr>
<th>Nutrition Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serv. Size</strong> 1 tbsp (15mL)</td>
</tr>
<tr>
<td><strong>Servings about 20</strong></td>
</tr>
<tr>
<td><strong>Calories</strong> 10</td>
</tr>
<tr>
<td><strong>Fat Cal.</strong> 0</td>
</tr>
<tr>
<td><strong>%DV</strong></td>
</tr>
<tr>
<td><strong>Amount/Serving</strong></td>
</tr>
<tr>
<td>Total Fat</td>
</tr>
<tr>
<td>Sat. Fat</td>
</tr>
<tr>
<td>Cholest.</td>
</tr>
<tr>
<td>Sodium</td>
</tr>
</tbody>
</table>

Not a significant source of vitamin A, vitamin C, calcium and iron.

**INGREDIENTS:** WATER, SALT, HYDROLYZED SOY PROTEIN, CORN SYRUP, CARAMEL COLOR, POTASSIUM SORBATE (PRESERVATIVE).

ConAgra Foods. Questions and Comments? Please contact us at La Choy’s Consumer Affairs, P.O. Box 57078, Irvine, CA 92619-7078. La Choy is a registered trademark of Conagra Brands, Inc. Copyright 2002 ConAgra Brands, Inc. When writing, please send code from top of cap. PRODUCED IN U.S.A.

### New Label

<table>
<thead>
<tr>
<th>Nutrition Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serv. Size</strong> 1 tbsp (15mL)</td>
</tr>
<tr>
<td><strong>Servings about 30</strong></td>
</tr>
<tr>
<td><strong>Calories</strong> 10</td>
</tr>
<tr>
<td><strong>Fat Cal.</strong> 0</td>
</tr>
<tr>
<td><strong>%DV</strong></td>
</tr>
<tr>
<td><strong>Amount/Serving</strong></td>
</tr>
<tr>
<td>Total Fat</td>
</tr>
<tr>
<td>Sat. Fat</td>
</tr>
<tr>
<td>Cholest.</td>
</tr>
<tr>
<td>Sodium</td>
</tr>
</tbody>
</table>

Not a significant source of vitamin A, vitamin C, calcium and iron.

**INGREDIENTS:** WATER, SALT, HYDROLYZED SOY PROTEIN, CORN SYRUP, CARAMEL COLOR, POTASSIUM SORBATE (PRESERVATIVE), CONTAINS: SOY

ConAgra Foods. Questions and Comments? Please contact us at La Choy’s Consumer Affairs, P.O. Box 57078, Irvine, CA 92619-7078. La Choy is a registered trademark of Conagra Brands, Inc. Copyright 2002 ConAgra Brands, Inc. When writing, please send code from top of cap. PRODUCED IN U.S.A.
Case #1

• 17 year old WF who has allergic rhinitis complains of oral itching with certain foods – specifically fresh apples, peaches and plums – but also now some complaints with peanuts.

• She is fine with apple juice, peach cobbler and peanut butter
Case #1 Cont.

This patient:

A: Has severe seasonal allergies to tree pollen
B: May have improvement of symptoms with pollen immunotherapy
C: Usually does not require an injectable Epinephrine
D: May have similar symptoms with fresh vegetables
E. All of the above
Case #1: of Food Hypersensitivity – GI

Oral Allergy Syndrome

- **Pathogenesis:**
  - An IgE-mediated allergic reaction, usually limited to the oropharynx, which occurs upon ingestion of certain fresh fruits, nuts or vegetables in pollen-sensitized individuals.

- **Clinical symptoms:**
  - Pruritus and/or “Tingling” of the lips, tongue, palate, and throat
  - ± Edema of the lips, tongue and/or sensation of throat tightening

- **Treatment:**
  - Avoidance of fresh, raw or dried form of foods
  - Patients are usually able to ingest cooked forms of the foods because the responsible allergens are heat labile
  - Rarely providers prescribe injectable Epinephrine
**Cross-reactivity patterns in pollen-food allergy syndrome**

<table>
<thead>
<tr>
<th>Birch</th>
<th>Rosaceae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td>Peach</td>
</tr>
<tr>
<td>Plum</td>
<td>Pear</td>
</tr>
<tr>
<td>Cherry</td>
<td>Apricot</td>
</tr>
<tr>
<td>Almond</td>
<td></td>
</tr>
<tr>
<td>Carrot</td>
<td>Celery</td>
</tr>
<tr>
<td>Parsley</td>
<td>Caraway</td>
</tr>
<tr>
<td>Fennel</td>
<td>Coriander</td>
</tr>
<tr>
<td>Aniseed</td>
<td></td>
</tr>
<tr>
<td>Soybean</td>
<td>Peanut</td>
</tr>
<tr>
<td>Fabaceae (old Leguminosae)</td>
<td></td>
</tr>
<tr>
<td>Hazelnut</td>
<td></td>
</tr>
<tr>
<td>Betulaceae</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ragweed</th>
<th>Cucurbitaceae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cantaloupe</td>
<td>Honeydew</td>
</tr>
<tr>
<td>Watermelon</td>
<td>Zucchini</td>
</tr>
<tr>
<td>Cucumber</td>
<td></td>
</tr>
<tr>
<td>Banana</td>
<td>Musaceae</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mugwort</th>
<th>Apiaceae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celery</td>
<td>Carrot</td>
</tr>
<tr>
<td>Parsley</td>
<td>Caraway</td>
</tr>
<tr>
<td>Fennel</td>
<td>Coriander</td>
</tr>
<tr>
<td>Aniseed</td>
<td></td>
</tr>
<tr>
<td>Bell pepper</td>
<td></td>
</tr>
<tr>
<td>Black pepper</td>
<td></td>
</tr>
<tr>
<td>Garlic</td>
<td>Onion</td>
</tr>
<tr>
<td>Solanaceae</td>
<td></td>
</tr>
<tr>
<td>Piperaceae</td>
<td></td>
</tr>
<tr>
<td>Liliaceae</td>
<td></td>
</tr>
</tbody>
</table>

**Typical patterns of cross-reactivity between pollens and fruits and vegetables. Individual foods are grouped by their taxonomical families.**

Component Resolved Diagnostics

• Component-resolved diagnostics – using recombinant DNA to identify a patient’s specific IgE reactivity to specific recombinant allergenic proteins rather than the whole allergen

• Studies evaluating the usefulness of CRD are relatively small and mostly centered on peanut, so far
Component Resolved Diagnostics

- Measurement of specific peanut components
  - Ara h 2, Ara h 1, Ara h 3—correlate strongly with severe systemic reactions to peanut
  - Ara h 9 – moderate risk of severe reactions to peanut
  - Ara h 8 – low risk of severe reactions and maybe due to cross-reactivity with other sources (birch pollen)
- Also available for: cow’s milk, egg
**Case #2**

- 23 yo WM reported 2 episodes of anaphylaxis
- First reaction occurred while laying in bed around 1 am and had returned from dinner with friends (had consumed alcohol, Roast Beef, Pimento Cheese Burger, Potatoes Salad with nuts - including Macadamia nut) a few hours before. Also had taken 4 Aspirin pills that day.

- He reported leg itching, then diffuse hives, abdominal pain/ emesis. Brought to ER, reported "I couldn't breathe" and treated with Epinephrine, IVF, Oxygen and observed x 4-6 hours then discharged home. He reports consuming all those foods on a regular basis and takes Aspirin on average 2 per day (due to back pain).

- Upon further questioning this patient reports distant history of tick bites and is an avid meat eater - beef, venison.
Case #2 Cont.

- Second episode again around 12 AM he noted back itching (hives) quickly spread diffusely. Was brought to ER and given Epinephrine, Benadryl and IVF. He also had shortness of breath and hand/feet swelling. This occurred while watching TV in bed but without alcohol. He did have a headache and took 4 Excedrin that day. He had consumed for dinner about 4 hours prior: bacon burger, peanuts, some fries with barbecue sauce, blue cheese. Again he reports consuming those foods on a regular basis.

- This patient most likely suffered anaphylaxis due to what?
  - A. Aspirin
  - B. Macadamia Nut
  - C. Beef
  - D. Alcohol
Red Meat Allergy

- He is referred to an allergist who performs skin testing and RAST/Blood testing
- Results indicate: Lamb 2.58 ku/L - Class 2. Beef IgE 4.45 ku/L - Class 3. Total IgE 160 ku/L - ref <114.
- **Galactose-alpha-1,3galactose (Alpha Gal)** IgE* 12.60 H <0.35 kU/L
- Reported first in 2009 - patients with IgE antibodies to galactose-alpha-1,3-galactose are at risk for delayed anaphylaxis, angioedema, or urticaria following consumption of beef, pork, or lamb.
- So elevated/positive alpha-gal patients need to avoid all red meat - including **beef, pork, lamb, venison**.
- They are often ok with chicken, turkey.
- Patient cautioned over other factors that may decrease threshold for anaphylaxis – alcohol, NSAIDs, trained how to use injectable EpiPen and advised on diet
Red Meat Allergy

• A bite from the Lone Star tick can cause people to develop an allergy to red meat, including beef and pork.
• This specific allergy is related to a carbohydrate called alpha-gal and is best diagnosed with a blood test.
• Although reactions to foods typically occur immediately, in the instance of allergic reactions to alpha-gal, symptoms often take several hours to develop. Owing to the significant delay between eating red meat and the appearance of an allergic reaction, it can be a challenge to connect the culprit foods to symptoms.
• The Lone Star tick is found predominantly in the Southeast from Texas, to Iowa, into New England
Case #3

- A 6 month old BF was initially breastfed and supplemented with a cow’s milk–based formula. From birth she had issues with increased gas and appeared uncomfortable. She also had recurrent vomiting, which typically would occur soon after eating, and intermittent bloody streaks in her stool.

- Her symptoms did not improve when a short trial of soy formula was given at 2 weeks of age.

- At 3 weeks of age she was prescribed ranitidine and formula was changed to a casein hydrolysate–based formula with resolution of vomiting and improvement in her symptoms.

- At 4 months of age she was given soy formula and within 1 hour developed repetitive vomiting, became lethargic and pale, and her parents described her as nonresponsive. EMS contacted brought to ED and treated with oral rehydration. Her brother had had diarrhea around the same time, and it was thought that the infant’s symptoms could be secondary to viral gastroenteritis.

- Patient referred to an allergist, and food allergy testing was performed. She had negative skin testing to milk, soy, and egg and specific IgE (RAST) was undetectable to milk, soy, egg, wheat, and peanut.
Case #3

• Due to the negative test results, family advised to slowly reintroduce soy into her diet at home. She was given a bottle with 1 oz of soy formula and 7 oz of casein hydrolysate–based formula and did not complete the bottle.
• Within 2 hours, she developed repetitive vomiting but was not pale or lethargic and she recovered within 1 hour. She did not have any shortness of breath, rash, or angioedema with any of these reactions.
• Her diet currently includes hydrolyzed casein formula, grains (rice, wheat and oat), fruits and vegetables, and chicken.

• This infant suffers from:
  A. Severe GERD
  B. Soy Intolerance
  C. Soy Protein Allergy
  D. FPIES - Food protein–induced enterocolitis
FPIES

• FPIES is a non–IgE-mediated gastrointestinal food hypersensitivity thought to be cell-mediated

• Incidence
  – Cow’s milk FPIES ~0.34% in the first year of life compared with 0.5% for IgE-mediated cow’s milk allergy.

• Presentations:
  – Typically before 6 months of age in formula-fed infants with repetitive emesis, diarrhea, dehydration, and lethargy 1 to 5 hours after ingesting

• Diagnosis:
  – Based on Clinical grounds – very rare in breastfeed babies
  – Most common cow’s milk, soy can be other foods (rice, oats, potato).
FPIES

- **Treatment:**
  - Casein hydrolysate–based formula and avoid specific foods (often soy and milk)
  - Physician-supervised food challenge to milk or soy at approximately 2 years of age. (with IV access).
  - Usually outgrown by school age. Although management remains avoidance of the offending food, observations that natural history varies for different foods has redefined the timing of reintroduction
Reasons for Referral

- Persons who have limited their diet based upon perceived adverse reactions to foods or additives.
- Persons with a diagnosed food allergy.
- Atopic families with, or expecting, a newborn who are interested in identifying risks for, and preventing, allergy.
- Persons who have experienced allergic symptoms in association with food exposure.
- Infants with recalcitrant gastroesophageal reflux or older individuals with recalcitrant reflux symptoms, particularly if they experience dysphagia.
- Infants with gastrointestinal symptoms including vomiting, diarrhea (particularly with blood), poor growth, and/or malabsorption whose symptoms are otherwise unexplained.
Role of the Allergist

- Identification of causative food
- Institution of elimination diet
- Education on food avoidance
- Development of an Anaphylaxis Emergency Action Plan
- Prevention of other allergies
- Follow-up to ascertain tolerance
Summary and Conclusions

• IgE & non-IgE-mediated food allergy conditions exist – many are intolerances
• The history and physical are paramount
• Elimination diets, skin testing, in vitro assays, and food challenges all have roles in diagnosis
• Avoidance, education, and preparation for emergencies are the pillars of current management
• Periodic rechallenge to monitor tolerance as indicated by history, allergen, and level of food-specific IgE is an important part of ongoing care
Questions?