• Measures have been taken, by the Utah Department of Health, Bureau of Health Promotions, to ensure no conflict of interest in this activity
Food Allergy

Rafael Firszt, M.D.
Pediatric Allergy and Immunology
University of Utah
Objectives

• Review epidemiology of food allergies
• Describe what is a food allergy and how do we recognize it?
• How do we manage food allergies with emphasis on resources for schools
Case – Siena, 12 m/o

• Vomiting and urticaria on face, trunk and arms within minutes of eating first piece of birthday cake.
• Parents gave Benadryl and called pediatrician.
• Siena was taken to ER. Symptoms resolved within 45 minutes. No further problems.
Siena’s PMH

• Breastfed until 6 m/o and then transitioned to Similac.
• 50\textsuperscript{th} %ile for height and weight.
• No dietary restrictions for mother
• History of eczema
  – Topical corticosteroids
  – Emollients
Food Allergy is Common

• Perception by public: 20-25%
• Confirmed allergy (oral challenge)
  – Adults: ~4%
  – Infants/Children: 6-8% (~1/4 million births)
• Specific Allergens
  – Dependent upon societal eating pattern
  – Milk (infants)- 2.5%
  – Peanut/nuts in general population- 1.4%
• Increased by 20% in past 10 years, PN allergy has tripled
Figure 2. Percentage of children under age 18 years who had a reported food or digestive allergy in the past 12 months, by age group: United States, 1997–2007

1Statistically significant trend.
SOURCE: CDC/NCHS, National Health Interview Survey.

Prevalence
Food Allergy is *Burdensome*

- Peanut, tree nut, & shellfish allergy are rarely outgrown

- Accidental reactions are common
  - 55% of peanut-allergic children experienced reactions following accidental ingestion within a 5 year period
  - Peanut is often a hidden ingredient, esp. in ethnic foods
  - Labels can be misleading “may contain”
  - Contamination can occur during processing, preparation or serving
Food Allergy is *Burdensome*

- Peanut allergy has a negative effect on the quality of life of children and their families
  - Anxiety, fear, frustration, and sadness reported frequently
  - Environmental restriction: school, daycare, restaurants, camp/vacation, etc.
  - Social and educational isolation / disruption

- Parent Quality of Life scores for both food allergy and atopic dermatitis rank lower than diabetes, ventilator-dependent/tracheostomy, and autoimmune disease
Food Allergy is **Burdensome**

Figure 3. Percentage of children under age 18 years with asthma or other reported allergic conditions in the previous 12 months, by reported food allergy status: United States, 2007

- **Asthma**
  - With food allergy: 29.4%
  - No food allergy: 12.4%

- **Eczema or skin allergy**
  - With food allergy: 27.2%
  - No food allergy: 8.1%

- **Respiratory allergy**
  - With food allergy: 31.5%
  - No food allergy: 8.7%

*Source: CDC/NCHS, National Health Interview Survey.*
Food allergy can be severe

- Small quantities are sometimes enough to provoke fatal reactions
- IgE measurements are not predictive of reaction severity
- 30,000 food-related anaphylactic reactions are treated each year in US EDs,
  - Peanut accounts for > 80% of these
Adverse Food Reactions

- **Adverse food reaction** - generic term referring to any reaction following the ingestion of a food
  - **Food intolerance** - result of non-immunologic mechanism
    - Ex: Lactose Intolerance
  - **Food allergy** - reaction presumed to be the result of an abnormal immunologic response following the ingestion of a food
    - Spectrum of IgE-, non-IgE, and mixed mechanisms
# Adverse Food Reactions

## Non-Immunologic

<table>
<thead>
<tr>
<th>Toxic / Pharmacologic</th>
<th>Non-Toxic / Intolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial food poisoning</td>
<td>Lactase deficiency</td>
</tr>
<tr>
<td>Heavy metals poisoning</td>
<td>Galactosemia</td>
</tr>
<tr>
<td>Scromboid fish poisoning</td>
<td>Pancreatic insufficiency</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Gallbladder disease</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Liver disease</td>
</tr>
<tr>
<td>Histamine</td>
<td>Panic, anxiety</td>
</tr>
<tr>
<td>Tyramine in aged cheeses</td>
<td>Gustatory rhinitis</td>
</tr>
<tr>
<td>Citrus fruits/tomatoes</td>
<td>Auriculotemporal syndrome</td>
</tr>
</tbody>
</table>

Spectrum of Food Allergy

**IgE-Mediated**
- Oral Allergy Syndrome
- Anaphylaxis
- Urticaria
- Asthma

**Non-IgE Mediated**
- Eosinophilic esophagitis
- Eosinophilic gastroenteritis
- Atopic dermatitis
- Protein-Induced Enterocolitis
- Eosinophilic proctitis

## Most Common Allergens

### TABLE I. Prevalence of food allergies in the United States

<table>
<thead>
<tr>
<th>Food</th>
<th>Young 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>
<tr>
<td>Overall</td>
<td>6%</td>
<td>3.7%</td>
</tr>
</tbody>
</table>

Pathophysiology

Sensitization

Antigen

Peanut-Specific T cell

Th1

IFN-γ

IL-4

IL-5

IL-13

B

Th2

IgE

Mast Cell

Re-exposure

Cytokines

Histamines

Leukotrienes
Pathophysiology

- **Food allergens are Proteins!** or glycoproteins

- Epitopes can be linear (Type 1) or conformational (Type 2)
  - Type 1: Linear = persistence / severity
    - Generally resistant to denaturation by acid, proteases, & heat
  - Type 2: Conformational
    - Pollen-Food Allergy Syndrome
    - Outgrown
    - Tolerate baked eggs/milk
### Oral Allergy Syndrome

- Oral pruritus, rapid onset, IgE-mediated, rarely progressive
- Usually fresh fruits and vegetables
- Heat labile: cooked forms, no reaction
- Cause: cross reactive proteins pollen/food

<table>
<thead>
<tr>
<th>Pollen</th>
<th>Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birch</td>
<td>Apple, apricot, carrot, cherry, kiwi, plum</td>
</tr>
<tr>
<td>Ragweed</td>
<td>Banana, cucumber, melon, watermelon</td>
</tr>
<tr>
<td>Grass</td>
<td>Cherry, peach, potato, tomato</td>
</tr>
</tbody>
</table>
Name the allergens

- Eggs
- Milk
- Peanut
- Wheat
The Food Allergy Conundrum

- Food
  - Sensitized
    - No IgE
    - Re-exposure
      - Clinical reaction
  - No reaction
How do we deal with this problem?

I. Diagnosis
II. Management
III. Research
Approach to Diagnosis *History*:

- Food suspected to have provoked the reaction
- Quantity of the suspected food
- Time between ingestion and development of symptoms
Medical History

• Description of symptoms provoked – GI, respiratory and skin

• Similar symptoms when food was eaten on other occasions

• Other factors (eg, exercise) necessary to provoke reaction

• Time since last reaction
Diagnostic Strategies: IgE-Mediated Food Allergy

• Skin prick tests/Lab tests for food-specific IgE
  – Indicates presence of IgE antibody NOT clinical reactivity (~50% false positive)
  – Essentially excludes IgE antibody (>95%)
  – Panels/broad screening should NOT be done without supporting history because of high rate of false positives

• Gold standard – Food Challenge
Diagnosis: Laboratory Evaluation

• Suspect non-IgE-mediated
  – Consider biopsy of GI tract, skin
• Suspect non-allergic, consider:
  – Breath hydrogen
  – Sweat test
  – Endoscopy
Lab Evaluation – Not Useful

- Patch testing for non-IgE mechanisms
  - Might change in the future with more research
- ID skin test with food
  - Risk of systemic reaction & not predictive
- Unproven/experimental tests
  - Provocation/neutralization, cytotoxic tests, applied kinesiology, hair analysis, IgG₄
If the patient can eat the food without a reaction, the number doesn’t matter!
When do we typically challenge?

When skin testing is negative or
When IgE values fall below 50%PPV:

### TABLE III. Predictive values of selected food allergens*

<table>
<thead>
<tr>
<th>Food</th>
<th>Mean age 5 y ~50% react†</th>
<th>Mean age 5 y ~95% react‡</th>
<th>Age ≤2 y ~95% react</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg</td>
<td>2</td>
<td>7</td>
<td>2§</td>
</tr>
<tr>
<td>Milk</td>
<td>2</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Peanut</td>
<td>2/5¶</td>
<td>14</td>
<td>–</td>
</tr>
</tbody>
</table>

¶Value is 2 kIU/L for those with and 5 kIU/L for those without a clear history of peanut allergy.
Management: Current Standard of Care

- No active treatment available (for now)
- Complete avoidance of specific food trigger
- Ensure nutritional needs are being met
- Education
- Anaphylaxis Emergency Action Plan if applicable
  - most accidental exposures occur away from home
- Serial history / IgE measurements, with challenges as indicated
What is Anaphylaxis?

- Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.
- AAAAI: “killer allergy”
There is no universally accepted definition of anaphylaxis

- Underresearched, underdiagnosed and undertreated
- Broadly defined as an acute allergic reaction involving ≥ 2 organ systems &/or SBP < 100
- Skin findings most common, but main causes of death are airway obstruction & shock
- Rapid progression can occur without cutaneous findings & is a marker of severity
  - ↑ vascular permeability: > 50% extravasation within 10 minutes
Anaphylaxis is highly likely when any one of the following three criteria are fulfilled:

1. Acute onset of an illness (minutes to hours) with involvement of the skin and/or mucosal tissue and respiratory compromise and/or reduced blood pressure.

2. Symptoms involving two or more organ systems (skin/mucosal, respiratory, cardiovascular, GI) that occur rapidly after exposure to a likely allergen for that patient.

3. Reduced BP following exposure to a known allergen for that patient.

Food Anaphylaxis

- Occurs within minutes (< 120) of ingesting food
- Can be associated with postprandial exercise
- Peanut is the leading cause of anaphylaxis in children and accounts for > 80% all-cause anaphylaxis mortality
- Delayed administration of epinephrine is associated with fatal outcomes
- Other risk factors include asthma, lack of insight
### Table I. Group 1

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Food</th>
<th>Asthma</th>
<th>Prior history</th>
<th>Food</th>
<th>Location</th>
<th>Epinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>M</td>
<td>Brazil nut</td>
<td>No</td>
<td>No</td>
<td>Mixed nuts</td>
<td>Home</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Cake</td>
<td>Friend's home</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>M</td>
<td>Pecan</td>
<td>Yes</td>
<td>Yes</td>
<td>Dip</td>
<td>Country club</td>
<td>Unknown</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Egg roll</td>
<td>Restaurant</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>18</td>
<td>M</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Candy bar</td>
<td>School</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>F</td>
<td>Walnut</td>
<td>Yes</td>
<td>Yes</td>
<td>Candy</td>
<td>School</td>
<td>Late</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>M</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Mexican food</td>
<td>Restaurant</td>
<td>Late</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Candy</td>
<td>Home</td>
<td>Late</td>
</tr>
<tr>
<td>9</td>
<td>17</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Snack mix</td>
<td>Video store</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Cookie</td>
<td>Home</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>20</td>
<td>M</td>
<td>Walnut</td>
<td>Yes</td>
<td>Yes</td>
<td>Veggie burger</td>
<td>Friend's home</td>
<td>Late</td>
</tr>
<tr>
<td>12</td>
<td>14</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Peanut sauce</td>
<td>Home</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>14</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Peanut butter contamination</td>
<td>Camping trip</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>18</td>
<td>F</td>
<td>Nut</td>
<td>Yes</td>
<td>Yes</td>
<td>Dessert</td>
<td>University cafeteria</td>
<td>Late</td>
</tr>
<tr>
<td>15</td>
<td>19</td>
<td>M</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Cookie</td>
<td>College dorm</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>21</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Cake</td>
<td>Banquet</td>
<td>Late</td>
</tr>
<tr>
<td>17</td>
<td>20</td>
<td>M</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Chinese food</td>
<td>College dorm</td>
<td>Late</td>
</tr>
<tr>
<td>18</td>
<td>28</td>
<td>F</td>
<td>Brazil nut</td>
<td>Yes</td>
<td>Yes</td>
<td>Ice cream</td>
<td>Restaurant</td>
<td>Yes</td>
</tr>
<tr>
<td>19</td>
<td>18</td>
<td>M</td>
<td>Pistachio</td>
<td>Yes</td>
<td>No*</td>
<td>Nuts</td>
<td>College camp</td>
<td>Yes</td>
</tr>
<tr>
<td>20</td>
<td>33</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Peanut sauce</td>
<td>Restaurant</td>
<td>Late</td>
</tr>
<tr>
<td>21</td>
<td>20</td>
<td>F</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Peanut</td>
<td>Camp</td>
<td>No</td>
</tr>
</tbody>
</table>

*History of reaction to peanut but not to pistachio.
Management: Dietary Elimination

- Hidden ingredients in restaurants/homes
  - Especially ethnic cuisines, desserts and buffets
- Labeling issues ("spices", changes, errors)
  - "may contain" = does contain
- Cross contamination (shared equipment)
- Seeking assistance
  - Food allergy specialist
  - Registered dietitian: (www.eatright.org)
  - Food Allergy & Anaphylaxis Network (www.foodallergy.org; 800-929-4040) and
  - Utah Food Allergy Network (www.utahfoodallergy.org)
Peanut Allergy Guidance

• Must ingest for severe reaction
• Touch - may cause localized allergic reactions
• Not generally aerosolized
• Smell - not life-threatening symptoms

Management: Emergency Treatment of Anaphylaxis

• Epinephrine: drug of choice
  – High risk: (1) previous systemic reactions, (2) significant asthma, (3) peanut, tree nut, fish and shellfish
  – Self-administered epinephrine readily available at all times
  – If administered, seek medical care IMMEDIATELY
  – Train patients, parents, contacts: indications/technique

• Antihistamines: secondary therapy only: WILL NOT STOP ANAPHYLAXIS

• Written Anaphylaxis Emergency Action Plan
  – Schools, spouses, caregivers, mature sibs / friends

• Emergency identification bracelet
Epinephrine Pearls

- Dose: 0.01mg/kg (max 0.3mg) of a 1:1000 w/v (1mg/mL) solution given IM
- 1:10 000 is generally not used
  - IV / cardiac monitor in place
- Consensus guidelines generally favor IM administration, preferably in vastus lateralis
- Route of administration has not been shown to affect mortality
- **Almost all anaphylaxis mortality is associated with a delay in epinephrine administration**
Anaphylaxis Pearls

- ABCs
  - Secure edematous airway early
  - $O_2$ and $\beta$-agonists
- 0.3mL (0.01 mg/kg) 1:1000 epinephrine IM
- H1 antihistamines (Benadryl 1mg/kg IV/IM) +/- H2 antihistamines
- Supine position & volume resuscitation
  - May require up to 7L crystalloid
- Glucagon 20-30 $\mu$g/kg (max 1-2mg) IM/IV q5 min for refractory shock c $\beta$-blockers / ACE-I
- Arrest rhythm usually PEA/asystole: move quickly to high-dose epi and continue CPR
ANAPHYLAXIS MANAGEMENT

ACUTE TREATMENT, HEALTHCARE SETTING

ASSESSMENT
- airway
- breathing
- circulation
- orientation
- skin*
- weight*

TREATMENT
- epinephrine
- oxygen
- IV fluids
- supine position**
- 911***

TREATMENT, IF NEEDED
- ADDITIONAL EPINEPHRINE
- ANCILLARY MEDICATIONS
  - β2-agonist (inhaled)
  - H1-antihistamine
  - H2-antihistamine
  - glucocorticoid
  - other vasopressor
  - glucagon
- OTHER
  - CPR and ACLS
  - rapid volume expansion

LONG-TERM RISK REDUCTION, COMMUNITY SETTING

EMERGENCY PREPAREDNESS
- epinephrine autoinjector
- Anaphylaxis Emergency Action Plan (www.aaaai.com)
- medical ID

ASSESS/TREAT COMORBIDITIES
- asthma
- cardiovascular disease
- mastocytosis
- other

ASSESS NEED FOR CO-MEDICATIONS
- nonselective β-blockers
- other

ALLERGEN AVOIDANCE
- www.foodallergy.org
- www.latexallergyresources.org
- www.aaaai.org
- www.acaai.org

IMMUNOMODULATION
- allergen-specific
  - immunotherapy with insect venom
  - desensitization to β-lactam antibiotics, NSAIDs, other
- allergen non-specific
  - idiopathic anaphylaxis: consider glucocorticoid treatment
1. Unscrew the yellow or green cap off of the EpiPen® or EpiPen® Jr carrying case and remove the EpiPen® or EpiPen® Jr auto-injector from its storage tube.

2. Grasp unit with the black tip pointing downward.

3. Form fist around the unit (black tip down).

4. With your other hand, pull off the gray safety release.

5. Hold black tip near outer thigh.

6. Swing and jab firmly into outer thigh until it clicks so that unit is perpendicular (at a 90° angle) to the thigh. (Auto-injector is designed to work through clothing.)

7. Hold firmly against thigh for approximately 10 seconds. (The injection is now complete. Window on auto-injector will show red.)

8. Remove unit from thigh and massage injection area for 10 seconds.

9. Call 911 and seek immediate medical attention.

10. Carefully place the used auto-injector (without bending the needle), needle-end first, into the storage tube of the carrying case that provides built-in needle protection after use. Then screw the cap of the storage tube back on completely, and take it with you to the hospital emergency room.
MYTH: Prior Episodes Predict Future Reactions

• No predictable pattern
• Severity depends on:
  – Sensitivity of the individual
  – Dose of the allergen
  – Other factors (e.g. food matrix effects, exercise, concurrent medications, asthma control)
• Must always be prepared for an emergency
Natural History

What is Siena’s prognosis?

- Depends on food & immunopathogenesis
- Majority of soy and wheat resolve by school age
- Cow’s milk resolution – 64% by 12 y/o
- Egg resolution – 68% by 16 y/o
  - Declining/low levels of specific-IgE predictive
  - IgE binding to conformational epitopes predictive
- Peanut – typically lifelong (20%)
Prevention

*Siena’s parents ask about risk for future children...*

- 2010 Food Allergy Guidelines for at-risk infant
  - Exclusive breast feeding >4 months (no allergy benefit thereafter) decreases the “cumulative incidence of atopic dermatitis and CMA in the first 2 years of life.”

Food Allergy Programs for Schools

• “How to C.A.R.E. for students w food allergies: what educators should know”
• Free, interactive online course
  – Basic facts about food allergies
  – Avoiding the allergens
  – Recognizing symptoms
  – Enacting emergency protocols
• Collaborative effort from many organizations
• www.allergyready.com
Food Allergy Programs for Schools

- Food Allergy Management and Education Program for Schools
- Free online program
- Goals:
  - Provide schools with components of a school-based food allergy program
  - Promote best practice
- Online toolkit that provides targeted educational information for every staff member
  - Admin, teachers, food services, paraprofessionals, custodial staff, parents and students
- www.stlouischildrens.org