What is a Food Allergy?

- An adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food
- Also known as a food hypersensitivity
  - Autoimmune disease
    - Elicits an abnormal immune response to a harmless food substance
      - Antibodies are released to fight the allergen
    - Allergen is usually a protein

Adverse Food Reactions

Immunologic

IgE-Mediated (most common) → **Non-IgE Mediated** Cell-Mediated

- Systemic (Anaphylaxis)
- Oral Allergy Syndrome
- Immediate gastrointestinal allergy
- Asthma/rhinitis
- Urticaria
- Morbilliform rashes and flushing
- Contact urticaria
- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis
- Protein-Induced Enterocolitis
- Protein-Induced Enteropathy
- Eosinophilic proctitis
- Dermatitis herpetiformis
- Contact dermatitis

Sampson H. J Allergy Clin Immunol 2004;113:805-9, Chapman J et al. Ann Allergy Asthma & Immunol 2006;96:S51-68.

What is Food Allergies (*and what is not*)?

Adverse Food Reaction
"any untoward reaction to food"

Food Allergy
"IgE and non-IgE mediated immunologic reaction"

Food Intolerance
"any adverse reaction due to nonimmunologic mechanism"

Prevalence of Food Allergies

- Children: 6-8%
- Adults: 2-3%
- Is there an increase in prevalence?
  - >1-2% but less than 10%
  - Self reported is higher (12% *vs* 3% in children)
  - US National Health Survey: prevalence increased in children 0-17 from 3.4% in 1997-1999 to 5.1% in 2009-2011
  - Peanut allergy 0.4% in1997 to 1.4% in 2008

Chafen et al. JAMA 2010;303:1848
Rona et. al. JACI. 2007 Sep;120(3):638

Food Allergy Rates in USA

Prevalence	Children	Adults
Milk	2.5%	0.3%
Egg	1.5%	0.2%
Peanut	1%	0.6%
Tree nuts	0.5%	0.8%
Fish	0.1%	0.4%
Shellfish	0.1%	2%
Wheat/Soy	0.4%	0.3%
Sesame	0.1%	0.1%
Overall	5%	3-4%

Boyce et al. JACI 2010;126:S1

Risk Factors and Comorbidities

Risk Factors

- Male sex in children
- Blacks
- Asian ethnicity
- Atopic disease
- Family hx: 7x increase in risk of peanut allergy if parent or sibling peanut allergic
  - 64% likelihood if twin allergic
- Birth order: 1st child with higher risk
- ? Hygiene theory

Comorbid diseases

- Atopic dermatitis
  - 35-70%
- Asthma
  - 34-49%
- Allergic rhinitis
  - 35-40%
- Eosinophilic esophagitis
  - 15-43% with IgE sensitization

What are the symptoms of food allergy?

Symptoms of Food Allergy

Skin (80-90%)
- Hives
- Swelling
  - Lip, tongue, throat
- Pruritus
- Flushing
- Eczema flare

Gastrointestinal (40%)
- Cramps
- Nausea
- Vomiting
- Diarrhea

Respiratory (60-70%)
- Itchy, watery eyes
- Runny nose
- Stuffy nose
- Sneezing
- Coughing
- Difficulty swallowing
- Chest tightness
- Wheezing

Cardiovascular (30%)
- Tachycardia
- Hypotension
- Cardiac arrest

How is food allergy diagnosed?

Diagnosis

- Detailed history and physical
  - Symptoms: typical allergic symptoms (skin, GI, resp)
  - Timing: within 4 hours of ingestion to symptoms
  - Reproducibility (repeat consumption without symptoms excludes food allergies)
  - Associated factors: exercise, asthma
  - Identify "allergy" vs "intolerance"
- Tests for specific IgE to a food
  - Skin tests with extracts and fresh food
  - Serum tests
- Oral food challenge: demonstrate that IgE sensitization is responsible for the clinical reaction

Interpretation of Laboratory Tests for Food Allergies

- Positive prick test or serum IgE tests
  - Indicates presence of IgE antibody NOT clinical reactivity (~50% false positive)
  - Overall positive predictive accuracy is < 50 %
- Negative prick test of serum specific IgE
  - Essentially excludes IgE antibody
  - Negative predictive accuracy >95%
- Skin test
  - Preferred for accurate dx
  - Avoid allergic food
  - Avoid unnecessary avoidance

Food Allergy

- Diagnosis is based on the medical history, supported by identification of specific IgE antibodies to the incriminated food allergen and confirmed by challenge

Diagnosing food hypersensitivity disorders: IgE-mediated

- Identification and relationship with the food: Medical history
- To identify specific IgE: Skin tests/serum specific IgE
- To demonstrate that IgE sensitization is responsible for the clinical reaction: Controlled challenge tests
- Diagnosis is based on the medical history, supported by identification of specific IgE antibodies to the incriminated food allergen and confirmed by challenge

What Foods Cause Allergic Reactions?

Food Allergies

Major allergenic foods (>85% of food allergy)

Children: milk, egg, soy, wheat, peanut, tree nuts

Adults: peanut, tree nuts, shellfish, fish, fruits and vegetables

Prevalence of Clinical Cross Reactivity

Food Allergy	Risk of Reaction to another Food in Family
Fish	50%
Shellfish	75%
Tree Nut	15-40%
Grain	25%
Legume	5%

Important Food Pairs

Cashew and Pistachio

Pecan and Walnut

Almond and Hazelnut

Lentil and Chickpea

Sampson et al. JACI 2014;134:1016

Tree nut allergy

- 1.8 million Americans
- Among the leading causes of fatal and near-fatal reactions to foods
- Tree nuts = walnuts, almond, hazelnuts, coconuts, cashews, pistachios, and Brazil nuts
- Tend to have a lifelong allergy
- Hidden sources: Salads and salad dressing, barbecue sauce, breading for chicken, pancakes, meat-free burgers, pasta, honey, fish dishes, pie crust, mandelonas (peanuts soaked in almond flavoring), mortadella (may contain pistachios)

Fish and shellfish allergy

- 2.3% of Americans
- Salmon, tuna, and halibut
- Avoid all varieties
- Lifelong
- Avoid seafood restaurants
- Asian restaurants-fish sauce
- Read ingredient lists
- Avoid areas where fish is being handled or cooked

- Hidden Sources: Salad dressing, Worcestershire sauce, bouillabaisse, imitation fish or shellfish, meatloaf, barbecue sauce (some are made from Worcestershire)

Wheat allergy

- Common in children
- Often confused with celiac disease
- IgE-mediated response to wheat protein
  - May tolerate other grains
- Symptoms range from mild to severe

- Sources: baked goods (wheat flour), pasta, sauces thickened with flour, cereals, crackers

- Substitute with amaranth, barley, corn, oat, quinoa, rice, rye, tapioca

Natural History

- Cow milk
  - IgE: 42% by 8 years, 79% by 16 years
  - Non-IgE: all tolerant by age 5
- Egg: 37% by 10 years, 68% by 16
- Soy: 69% by 10 years
- Wheat: 29% by 4 years, 65% by 12 years
- Peanut: 20% of children become tolerant
- Tree nut: 9% of children become tolerant

- Adult food allergies persist

Skripak et al, J Allergy Clin Immunol 2007;120:1172-7
Savage et al, J Allergy Clin Immunol 2007;120:1413-7

Persistence of Food Allergies

- An earlier age at diagnosis
- Presence of other comorbid allergic diseases (eg, allergic rhinitis, asthma, and eczema)

- What predicts tolerance
  - Low sIgE at diagnosis
  - Reduction in sIgE
  - Skin test?

Pollen-Food Syndrome or Oral Allergy Syndrome

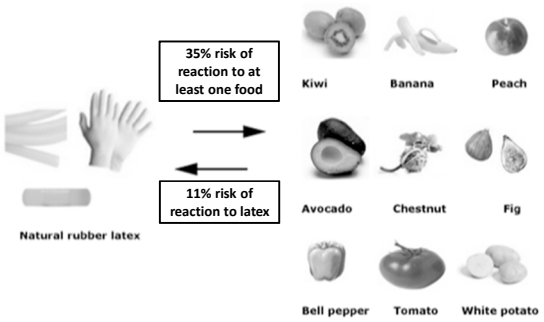
- Rapid onset mouth itching, burning, swelling caused by fresh fruits and vegetables in individuals with allergic rhinitis
- Cause: cross reactive proteins pollen/food
- Key foods: raw fruits and vegetables
- Allergens: Profilins and pathogenesis–related proteins
  - Heat labile (cooked food usually OK)

Class 2 Allergens/Oral Allergy Syndrome

Cross-reactivity between airborne and food allergens

Pollen	Cross-Reactive Foods
Birch	Apple, Peach, Plum, Pear, Cherry, Apricot Carrot, Celery, Parsley, Soybean, Peanut, Hazelnut
Ragweed	Cantaloupe, Honeydew, Watermelon, Cucumber, Zucchini, Banana
Mugwort	Celery, Carrot, Parsley, Bell Pepper, Black Pepper, Garlic, Onion, Mustard, Cabbage, Broccoli

Class 2 Allergens/Latex-Fruit Syndrome



Food Additives

- Sulfites
  - Triggers asthma
- Annatto
  - Coloring from achiote seeds
- Carmine
  - Red coloring from insect
- Natural food additives

Food Dependent Exercise induced anaphylaxis

- Anaphylaxis after eating a particular food or any food prior to exercising
  - Wheat
  - Celery
- Able to exercise without a problem if don' t eat 4 hours prior
- Able to eat incriminated food if don't exercise
- Not reproducible
- Treatment: avoidance of food 4 hours prior to exercise, epi

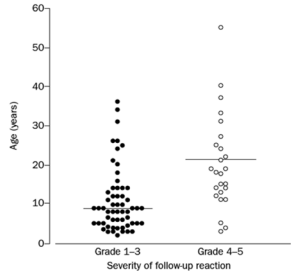
What treatment is available?

Food Allergy: Treatment

- Epinephrine: 0.3 mL of 1:1000 IM
- Antihistamines
  - Benadryl 25 – 50 mg every 4-6 hours
  - Non-sedating antihistamines
- Corticosteroids
  - 1-3 days depending on severity
- Monitor for severe or biphasic reactions
- Educate on avoidance in the future
- Support groups

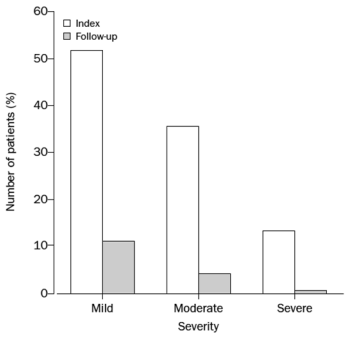
How Effective is Education?

Severity of Reactions



Ewan et al. Lancet 2001;357:111

Severity of Reaction After Education



Ewan et al. Lancet 2001;357:111

Fatal Food Anaphylaxis

- Frequency: ~ 150 deaths / year
- 2nd-4th decade of life
- Clinical features:
  - Biphasic reaction can contribute –initially better, then recurs
  - Cutaneous symptoms may not be present
  - Respiratory symptoms prominent
- **Risk factors:**
  - **Underlying asthma – Delayed epinephrine**
  - **Symptom denial – Previous severe reaction**
  - **Adolescents, young adults**
- History: known food allergen
- Key foods: ***peanuts and tree nuts dominate (~90% of fatalities)***, fish,crustaceans
- Most events occurred away from home

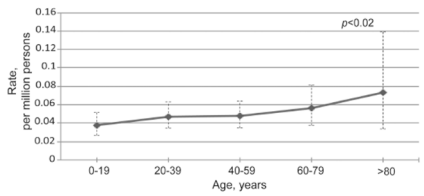
Bock et al. JACI 2001;107:191.

Fatal Food Anaphylaxis

- 100 deaths a year
- Highest risk foods:
  - Peanut, tree nut, seafood
- Clinical features
  - Cutaneous manifestations may be absent
  - Respiratory symptoms predominate
- Risk factors
  - Asthma
  - Symptom denial
  - Delay in epinephrine use
  - Previous serious reaction
  - adolescents

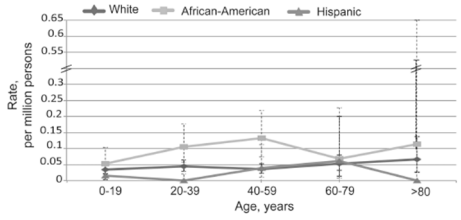
Fatal Food Anaphylaxis

- 6.7% of fatal anaphylaxis in the US between 1999 and 2010 were secondary to foods



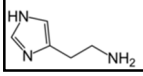
Jerchow et al. JACI 2014;134:1318

Fatal Food Anaphylaxis by Race



Scromboid Poisoning (Histamine Fish Poisoning)

- Histamine fish poisoning (HFP) is a chemical intoxication which occurs after eating fish of the dark meat varieties including tuna, kahawai, mackerel, bonito, butterfly kingfish, anchovies
- Symptoms similar to anaphylaxis
- Histamine is commonly the result of high temperature spoilage (>21° C), and often occurs if dead fish remain in set nets during warm sea temperatures, or improper or delayed refrigeration.
- Histamine is not destroyed by freezing, cooking, smoking, curing or canning.
- Should be considered in a patient who regularly eats fish, without a previous reaction



What to Do With Egg Allergy and Flu Vaccine?

- Influenza vaccine is prepared in embryonated eggs
- Exceptions:
  - Recombinant influenza vaccine (RIV3, Flublok)
  - Cell culture based inactivated vaccine (ccIIV3, Flucelvax)
- Of 4,172 egg allergic patients (513 with severe allergic reaction)
  - No anaphylaxis
- Joint Task Force on Practice Parameters of the AAAAI and ACAAI:
  - No special precautions are required for the administration of influenza vaccine to egg allergic patient no matter how severe the egg allergy
  - Normal precautions (1/1000,000 can have allergic reaction)
  - Be prepared to treat that

Des Roches et al. 2012;130:1213

CDC Guidelines

- History of hives only can receive influenza vaccine
  - IIV or trivalent recombinant influenza vaccine (RIV3)
  - Observe for >30 mins afetr
  - Administered by HCP who is familiar with potential food allergy
- History of severe symptoms
  - RIV3 if >18
  - IIV by physician with experience in management of anaphylaxis

Food Allergy vs Food Intolerance

- Reactions to food consist of a variety of reactions to food or food additive ingestion
- Usually not allergenic and caused by food intolerance
  - Symptom-inducing food properties
  - Metabolic disorders
  - Bacterial food contamination
- Consider lactose or gluten avoidance
- low FODMAP (fermentable oligo-, di- and monosaccharides and polyols

Food Intolerance: FODMAP Diet

F	Fermentable		
O	Oligosaccharides	Fructans, galacto-oligosaccharides	Wheat, barley, rye, onion, leek, white part of spring onion, garlic, shallots, artichokes, beetroot, fennel, peas, chicory, pistachio, cashews, legumes, lentils, and chickpeas
D	Disaccharides	Lactose	Milk, custard, ice cream, and yogurt
M	Monosaccharides	"Free fructose" (fructose in excess of glucose)	Apples, pears, mangoes, cherries, watermelon, asparagus, sugar snap peas, honey, high-fructose corn syrup
A	And		
P	Polyols	Sorbitol, mannitol, maltitol, and xylitol	Apples, pears, apricots, cherries, nectarines, peaches, plums, watermelon, mushrooms, cauliflower, artificially sweetened chewing gum and confectionery

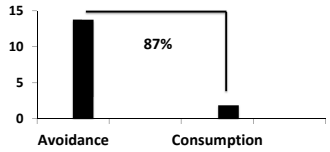
- Elimination for 4-6 weeks and then slow reintroduction
- Consider evaluation by a dietician

Doc, can we prevent food allergies in our child?

- Maternal avoidance diet?
  - Current evidence doesn't support dietary restrictions during pregnancy and lactation
- How about breast feeding?
  - Breast feeding for at least 4 months prevents or delays occurrence of atopic dermatitis, cow milk allergy
- Use of probiotics?
- Early introduction of allergenic foods

LEAP Study

Children (4-11 months) at risk for food allergy → Peanut consumption or avoidance till 5 years of age → Avoidance group had 5x higher likelihood of peanut allergy



Recommendation: recommend introduction of peanut early on in life between ages 4-6 months

Du Toit New Engl J Med 2015;372:813

Unproven Tests

- Allergen specific IgG
- Cytotoxicity assays
- Applied kinesiology
- Provocation neutralization
- Hair analysis

Future Treatment: Immunotherapy

- Sublingual immunotherapy (SLIT)
- Oral Immunotherapy (OIT)
- Contact of an antigen induces tolerance
- Patient is given increasing amounts of the allergen

- Conclusion: may be effective during therapy (for egg, milk and hazelnut) but there is no evidence for long-term tolerance
- Not ready for clinical use

Sampson et al. JACI 2014;134:1016

Conclusions

- Prevalence of food allergy may be increasing
- Diagnosis depends on appropriate history and tests (sIgE in serum and/or skin tests)
- Broad panel testing is not recommended as positive test alone is not diagnostic (50% false positive)
- Epidemiologic risk factors and history can identify those at risk for severe reaction
- Treatment: Strict avoidance and appropriate treatment of anaphylaxis