Food Allergy

Mark A. Posner, M.D.
FAAAAI, FACAAI
Senior Partner, Allergy &Asthma Specialists, P.C.

Immunologic (Allergic) Adverse Food Reactions

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

Mixed IgE/Non IgE
- Eosinophilic esophagitis (EoE)
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

Non-IgE Mediated Cell-Mediated
- Food Protein-Induced Enterocolitis
- Food Protein-Induced Enteropathy
- Food Protein-Induced Proctocolitis
- Dermatitis herpetiformis
- Contact dermatitis

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

Learning objectives

- Describe diverse manifestations of food allergy
- Describe prevalence of food allergy
- Explain natural history of food allergy
- Describe strategies for food allergy prevention
- Develop rational approach to diagnosis of food allergy
- Examine avoidance strategies for various environments
- Appraise treatment of acute allergic reactions including anaphylaxis
- Summarize future therapies for food allergy

IgE-Mediated Food Allergy Presentation

Cutaneous
- Flushing, hives, angioedema, eczema

Gastrointestinal
- Abdominal cramping, nausea, vomiting, diarrhea

Respiratory
- Rhinitis, laryngeal edema, wheezing, coughing

Cardiovascular
- Hypotension, tachycardia, arrhythmias

Central Nervous System
- Lightheadedness, syncope

Food Allergy

- **Food allergy**: an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.
- **Food allergens**: specific components of food recognized by allergen-specific cells and eliciting specific immune reactions resulting in characteristic symptoms.

Sampson HA, et al. J Allergy Clin Immunol 2014;134:1016-25

Mixed IgE/ Non-IgE-Mediated Food Allergy

Eosinophilic Esophagitis, Gastritis, Gastroenteritis
- Vomiting, nausea, abdominal pain, diarrhea, failure to thrive, weight loss, dysphagia, food impaction

Atopic Dermatitis
- Itchy, erythematous papulo-vesicular rash localized to flexor areas, in infants rash can be generalized; chronic lesions-hypertrophy, lichenification, hyperpigmentation

Non IgE-Mediated Food Allergy Presentation

Food Protein-Induced Allergic Proctitis/Proctocolitis
- Gross blood in stool ± other symptoms, usually well-appearing infant

Food Protein-Induced Enterocolitis Syndrome (FPIES)
- 2-4 hours after ingestion: repetitive projectile vomiting ± diarrhea that can lead to severe dehydration, onset usually in the 1st year of life

Celiac Disease
- Diarrhea, steatorrhea, malabsorption, abdominal distention, flatulence, ± nausea & vomiting, failure to thrive, oral ulcers

Prevalence of Food Allergy

- Perception by public: 20-25%
- Confirmed allergy: Adults: 2-3.5% and infants/young children: 6%
- Specific Allergens: Geographical and cultural variations
- Prevalence higher in those with: atopic dermatitis, pollen allergies, latex allergy
- Prevalence increasing – 18% increase between 1997-2007

Branum AM, Lukacs SL. Pediatrics 2009;124:1549-55.

Routes of Exposure

- Ingestion: most relevant in systemic reactions, severity depends on amount and form of food [raw vs./ cooked]
- Inhalation: possible with foods that have been aerosolized; e.g. steamed milk, cooked fish/shellfish, fried eggs; respiratory symptoms or anaphylaxis with severe allergy
- Contact: skin - usually local reactions, such as hives or redness; mucous membranes: in young children skin contact on the hands may lead to mucosal contact by rubbing eyes

Simonte S, et al. JACI 2003;112:180-2.

Estimated Prevalence of Food Allergy

Food	Children (%)	Adults (%)
Cow's milk	2.5	0.3
Egg	1.5	0.2
Wheat, Soy	0.4	0.3
Peanut	2.0	0.6
Sesame	0.1	0.1
Tree nut	0.5	0.6
Crustacean	0.1	2.0
Fish	0.1	0.4
Overall	**6**	**2-3.5**

Sicherer SH, Sampson HA. J Allergy Clin Immunol 2010;125:S116-125.

Non-Immunologic Adverse Food Reactions

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

Sicherer SH, Sampson HA. J Allergy Clin Immunol 2006;117:S470-475.

Prevalence of Food Allergy

Disorder	Food Allergy Prevalence
Anaphylaxis	**35-55%**
Pollen-food allergy syndrome	**25-75% in pollen-allergic**
Atopic dermatitis	**37% in children (rare in adults)**
Urticaria	**20% in acute (rare in chronic)**
Asthma	**5-6%**
Chronic rhinitis	**Rare**

Sicherer SH, Sampson HA. J Allergy Clin Immunol 2010;125:S116-125.

Natural History

- ~ 80% of milk, soy, egg, wheat allergy remit by teenage years
  - Declining/low levels of specific-IgE predictive
  - Milk and egg: tolerance to extensively heated proteins precedes development of tolerance to unheated
- High likelihood of developing further allergic disease: other foods >30%; allergic rhinitis >90%; asthma 50 – 90%
- Non-IgE-mediated GI allergy[e.g., allergic proctocolitis, FPIES]: Infant forms resolve in 1-3 years; toddler/adult forms more persistent

Wheat Allergy

- Prevalence in children 0.4%[1]
- Cross-reactivity with other grains (rye, barley, oat, grasses): 20%
- Associated with exercise-induced anaphylaxis[2]
- 65% resolution by age 12 years[1]

[1]Keet CA, et al. Ann Allergy Asthma Immunol 2009;102:410-15.
[2]Morita E, et al. Allergol Int 2009;58:493-8.

Milk Allergy

- Most common food allergy in children: Prevalence 2-3% of infants
- Usually develops in the first 6-12 months
- Symptoms: eczema, hives, wheezing, anaphylaxis, colic, GE reflux (10%), bloody diarrhea. NOT isolated nasal congestion and mucous.
- 37% outgrown by age 12 yrs; 79% outgrown by age 16 yrs

Skripak JM, et al. J Allergy Clin Immunol 2007;120:1172-7.

Peanut Allergy

- Prevalence has more than tripled, from 0.4% in 1997 to 1.4% in 2008
- Onset of symptoms usually by age 2 yrs; 75% of reactions may occur with first exposure
- The food allergy most commonly associated with anaphylaxis
- 150 deaths / year, predominantly from peanut and tree nut anaphylaxis
- ~20% peanut allergy resolution; relapse rate ~ 9%;

Skolnick H, et al, J Allergy Clin Immunol 2001;107:367-74. Skripak JM, Wood RA. Pediatr Allergy Immunol 2008;19:368-73. Burks AW. Lancet 2008;371:1538-46. Sicherer SH, Sampson HA. J Allergy Clin Immunol 2007;120:491-503. Fleischer DM, et al. J Allergy Clin Immunol 2004;114:1195-201

Egg Allergy

- Second most common in children: Prevalence 1.3%
- Usually develops in the first 6-24 months
- Present in influenza and yellow fever vaccines; (not present in MMR or Varicella)
- 80% risk of allergic rhinitis and asthma at age 4 yrs for infants with egg allergy and eczema[1]
- Over 70% of children may tolerate extensively heated egg[2]
- 48% outgrow by age 12 yrs; 68% outgrown by age 16 yrs[4]

[1] Tariq SM, et al. Pediatr Allergy Immunol 2000;11:162-7.
[2] Lemon-Mule H, et al. J Allergy Clin Immunol 2008;122:977-83.
[3] Ando H, et al, J Allergy Clin Immunol 2008;122:583-8
[4] Savage JH, et al. J Allergy Clin Immunol 2007;120:1413-7

Tree Nuts, Seeds, Seafood

- Tree nut allergies usually develop ages 1-7 yrs or as adults; fish: in late childhood and adulthood; shellfish: adulthood in 60%
- Allergies to tree nuts, seeds, fish and shellfish are typically lifelong
- Resolution: 10% tree nut allergies[1]; rare for seafood
- Favorable prognostic factors[2]: decreasing serum IgE levels over time; resolution of atopic dermatitis; reduction of skin prick test wheal diameter

[1]Fleischer DM. Curr Allergy Asthma Reports 2007;7:175-181. [2]Boyce, JA et al. J Allergy Clin Immunol. 2010 Dec;126(6 Suppl):S1-58

Food Additives and Colorings

- Food additives and colorings derived from natural sources that contain proteins may induce allergic reactions.
- Examples: turmeric, annatto seed, and insects (e.g., carmine)
- Chemical additives and colorings [e.g., tartrazine (yellow # 5)] are not likely to cause IgE-mediated food allergy.
- Sulfites are added to foods as preservative, anti-browning agent, or bleaching effect. In sensitive persons, sulfites may induce asthma (though this is *not* a food allergy).

Gultekin F, Doguc DK. Clin Rev Allergy Immunol. 2013;45:6-29

Allergy Prevention

- Exclusive breastfeeding is recommended for 4-6 months of age to reduce risk of cow's milk allergy and atopic dermatitis (AD) in first 2 years and reduce wheezing in first 4 years
- For infants at high-risk who cannot be exclusively breastfed for first 4-6 months, hydrolyzed formula may prevent AD
- Maternal avoidance diets during pregnancy and lactation are not recommended based on current data; more research is *needed regarding maternal avoidance of* peanut.

Fleischer DM et al. J Allergy Clin Immunol: In Practice. 2013;1:29-36

Spices

- A spice is any part of a plant that is used for the purpose of seasoning or flavoring food.
- Spices may be obtained from bark, leaves, seeds, roots, buds, fruit or other part of the plant. An herb is usually obtained from the leafy part of a plant. Most people use the terms spice and herb interchangeably.
- Spice allergy is rare: between 5-10 people/10,000 adults
- Examples: celery, cumin, coriander, fennel, cloves, anise

Chen JL, Bahna SL. Annals of Allergy Asthma Immunol, 2011, 107: 199

Introduction of Complementary Foods

- Complementary foods, including cow's milk protein (except for whole cow's milk), egg, soy, wheat, peanut, tree nuts, fish, and shellfish, can be introduced between 4-6 months of age
- New data suggest that early introduction of highly allergenic foods (e.g. peanut) may reduce the risk of food allergy
- If a patient has difficult to control moderate-severe AD or a food allergy, referral to an allergist for possible testing is *recommended before introduction of highly allergenic foods*

Fleischer DM et al. J Allergy Clin Immunol: In Practice. 2013;1:29-36
Du Toit G, et al. N Engl J Med. 2015; 372: 803-13

Food Allergy Prevention

Diagnosis of Food Allergy

Evaluation: History & Physical Exam

- History: very important
  - Symptoms, timing, amount, raw vs. cooked food, reproducibility, treatment, and outcome
  - Concurrent exercise, medications, alcohol
- Diet details / symptom diary
- Physical exam: assess for other disorders
- Identify general mechanism
  - Allergy vs. intolerance; IgE vs. non-IgE mediated

Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58.
Sampson HA, et al. JACI 2014; 134(5):1016-25.e43

Molecular Diagnosis of Food Allergy

- Major allergens identified in certain foods
- Birch cross-reactive allergens: Ara h 8 in peanut, Cor a 1 in hazelnut-mild oral symptoms or no symptoms upon ingestion, consider challenge
- Storage seed proteins: Ara h 1, 2, 3 in peanut, Cor a 9 and 14 in hazelnut-associated with systemic reactions, recommend strict avoidance, defer challenge

Sicherer SH, Wood RA. JACI in Practice 2013;1:1-13.
Sampson HA, et al. JACI 2014; 134(5):1016-25.e43

Evaluation of Food Allergy

- Suspect IgE-mediated:
  - Panels/broad screening should NOT be done without supporting history because of high rate of false positives.
  - Skin prick tests (prick with fresh food if pollen-food syndrome); *In vitro* tests for food-specific IgE
  - Oral food challenge
- Suspect non-IgE-mediated, consider: Biopsy of gut, skin
- Suspect non-immune, consider referral for:
  - Hydrogen breath test, Sweat test, Endoscopy

Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58; Sampson HA, et al. JACI 2014; 134(5):1016-25.e43

Unproven/Experimental Tests

- Intradermal skin test with foods
  - Risk of systemic reactions and death; high false positive rate
- Atopy patch testing with foods
  - No standardized reagents; No significant enhancement in diagnostic accuracy compared with skin prick testing
- Provocation/neutralization, cytotoxic tests, applied kinesiology (muscle response testing), hair analysis, electrodermal testing, food-specific IgG or IgG_4 (IgG "RAST")

Lockey RF. Allergy Proc 1995;16:293-6.
Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58.
Sampson HA, et al. JACI 2014; 134(5):1016-25.e43

Evaluation: Interpretation of Laboratory Tests

- Positive skin prick test or food-specific IgE
  - Indicates presence of IgE antibody NOT clinical reactivity
  - ~90% sensitivity; ~50% specificity
  - ~50% asymptomatic sensitization
  - Larger skin tests/higher sIgE levels correlate with increased likelihood of reaction but not severity
- Negative skin prick test or food-specific IgE
  - Essentially excludes IgE antibody (>95% specific)

Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58; Sampson HA, et al. JACI 2014; 134(5):1016-25.e43
Sampson and Ho. J Allergy Clin Immunol 1997;100:444-51. Sampson HA, J Allergy Clin Immunol 2001, 891-96. Celik-Bilgili S, et al. Clin Exp Allergy 2005;35:268-73.

Evaluation: Elimination Diets & Food Challenges

- Elimination diets (1-6 weeks) most useful for chronic disease (eg. AD, GI syndromes)
  - Eliminate suspected food(s) or
  - Prescribe limited "few food" diet or
  - Elemental (free amino acid) diet
- Oral food challenge – MD supervised, emergency meds available
  - Open
  - Single-blind
  - Double-blind, placebo-controlled (DBPCFC)-gold standard
  - Usually full serving of food administered in divided, increasing doses over 1 hour, followed by observation

Nowak-Wegrzyn A, et al. JACI 2009;123:S365-83.
Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58.
Sampson HA, et al. JACI 2014; 134(5):1016-25.e43

Diagnostic Approach: Suspicion of IgE-Mediated Allergy

- If test for food-specific IgE is
  - Negative: reintroduce food*
  - Positive: food avoidance recommended
- If elimination diet is associated with
  - No resolution: reintroduce food*
  - Resolution
    - Open / single-blind challenges to "screen"
    - DBPCFC for equivocal open challenges

** Unless convincing history warrants supervised challenge*

Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58.
Sampson HA, et al. JACI 2014; 134(5):1016-25.e43

General Principles of Management

- Avoidance of the food allergen
- Ensure nutritional needs for children are met
- Education
- Written individualized healthcare plans (IHP) and emergency action plans (EAP)
- Quick access to emergency medications including self-injectable epinephrine (SIE)

Boyce JA, et al. J Allergy Clin Immunol 2010;126:S1-S58.

Diagnostic Approach: Non-IgE-Mediated Disease or Those with Unclear Mechanism

- Elimination diets (may need elemental amino acid-based diet)
- Physician-supervised Oral Food Challenges
  - Timing/dose/approach individualized for disorder
    - Enterocolitis syndrome can induce shock
    - Eosinophilic gastroenteritis may need prolonged feedings before symptoms develop
  - Blinded challenges may be necessary
  - May require ancillary testing (endoscopy/biopsy)

Sampson HA. JACI 2004;113:805-19.
Sicherer SA. JACI 2005;115:149-56.
Järvinen KM, Nowak-Węgrzyn A. JACI in Practice 2013;1(4):317-22.

Dietary Elimination

- ***Complete avoidance*** (e.g. peanut) vs. ***partial avoidance*** (e.g. avoid whole egg but eat baked egg products if tolerant)
- **FALPCA**[1] (effective 1/1/06) requires labeling for the 8 major food allergens.
- ***Advisory warning labels*** (May contain…, Processed in a facility…). For peanut, <10% of products had peanut.[2]
- ***Cross contact issues:*** share equipment, fried foods

[1]Food Allergen Labeling and Consumer Protection Act of 2004 (P.L. 108-282) (FALCPA)
[2]Allen KJ, et al WAO Journal 2014;7:10

Management of Food Allergy

Hypoallergenic Infant Formulas for Cow's Milk Allergy (CMA)

- ***Soy based formulas*** For IgE-CMA, soy co-allergy is 0-14%[1]. For non-IgE CMA, soy co-allergy 0%[2] to 60%[3].
- Partial hydrolysates (e.g. Good Start, Peptamin Jr, Pediasure Peptide) are *not recommended* for CMA
- ***Extensively hydrolyzed formulas*** (EHF) Alimentum, Nutramigen, Pregestimil: >90% tolerance in IgE-CMA
- ***Elemental amino acid based formulas*** (Neocate, Elecare, PurAmino): CMA,FPIES intolerant of EHF, EoE

[1]Katz Y, et al. JACI 2010;126:77-82. [2]Katz Y, et al. JACI 2011;127:647-53.
[3]Sicherer SH, et al. J Pediatr 1998; 133: 214–219

Management: Emergency Treatment of Anaphylaxis

- Epinephrine: drug of choice
  - Have 2 doses of self-injectable epinephrine available as 12% of children, 17 % of adults require >1 dose
  - Emergency transport to hospital to monitor for possible biphasic (late phase) anaphylaxis
- Antihistamines: WILL NOT STOP ANAPHYLAXIS
- *Written Anaphylaxis Emergency Action Plan*
- Emergency identification bracelet

Simons FE, JACI 2010;125(2 Suppl 2):S161-81. Kim JS, et al. JACI 2005; Jul;116(1):164-8. Rudders S, et al. Pediatrics 2010;125:e711-8. Rudders S et al. Allergy Asthma Proc. 2010;31:308-16

Emergency Action Plan (EAP)

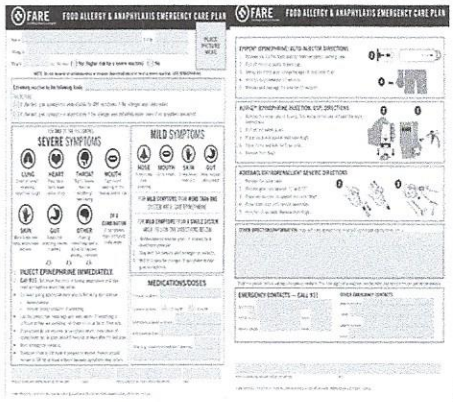
- Reviewed annually by physician.
- Recommendation for when to administer epinephrine based on patient's history and risk factors for fatal anaphylaxis and activation of emergency medical services.
- The IHP and EAP are collaborative efforts of the physician, family, school nurse and school staff.

Young MC, et al. JACI 2009;124:175-82. Sicherer SA, Mahr T. Pediatrics 2010;126:1232-39.

Respond Quickly!

- Administer epinephrine quickly
- Activate EMS – 911
- Then, call emergency contacts

Images provided by: EpiPEN – Mylan, 2015. Adrenaclick – Impax Labs. Auvi-Q - Sanofi



With permission from FARE. Download from www.foodallergy.org

Management of Food Allergies in Schools

Individualized Health Care Plans (IHP)

- Preventive proactive plan for day-to-day management
- Recommendations on avoidance measures for the classroom, snack and lunch periods and other school environments including school bus, sports, trips.
- Guidelines for access to epinephrine and designating staff responsible for administration of epinephrine and implementation of the emergency action plan.

Young MC, et al. JACI 2009;124:175-82. Sicherer SA, Mahr T. Pediatrics 2010;126:1232-39. Simonte SJ, et al. JACI 2003;112:180-2.

Managing Food Allergies in Restaurants and Travel

- Always declare your food allergies to the restaurant staff. When traveling avoid eating airline food; bring your own food.
- Inspect seating for residual food from previous passengers; clean seat and table.
- Some airlines do provide additional accommodations when requests are made in advance of travel.
- Always have epinephrine auto-injector for quick access!

Food Allergy Research and Education www.foodallergy.org

Future Therapies for Food Allergy

In clinical trials:

- Oral immunotherapy (OIT) for milk, egg, peanut, multiple food combinations
- OIT in combination with anti-IgE
- Sublingual immunotherapy (SLIT)
- Epicutaneous (patch) immunotherapy for milk, peanut
- OIT with baked milk, egg for milk and egg allergy
- Chinese Herbal Formula (FAHF-2)
- Anti-IL5 for treatment of eosinophilic esophagitis

Nowak-Wegrzyn A, Sampson HA. JACI 2011;127:558-73. Lieberman JA, Nowak-Wegrzyn.
Curr Allergy Asthma Rep 2012;12:55-63. Berin MC. Curr Pediatr Rep 2014;2:119-26.

Epicutaneous Immunotherapy

- Patch applied daily in microgram amounts
- Side effects minimal (skin irritation)
- Efficacy similar to SLIT
- Appears less effective older than 11 years of age

Immunotherapy Goals

- Desensitization- increasing the threshold of reactivity to specific allergens.
  - low level protects against accidental ingestion
  - high level allows consumption of normal amts
- Tolerance-permanent immunologic change, either naturally or via immunotherapy. Reflected by "sustained nonresponsiveness", the ability to pass a food challenge off therapy

Oral Immunotherapy

- Initial dose escalation in office (mcgs to mgs)
- Build up phase (office) over several months
- Maintenance phase (hundreds of mgs to few grams) culminating in an OFC
- More likely to give high level desensitization
- Mild to moderate reactions (mainly abdominal) in up to 5% of doses but 24% of patients required epinephrine
- 2.7% pts at risk of developing EoE

Sublingual Immunotherapy

- Allergens applied daily under tongue
- Maintenance doses range from mcgs to mgs
- Side effects are minimal (oropharyngeal itching) and infrequent < 5%
- Efficacy limited to low level desensitization and must be continued
- No anaphylaxis recorded

Role of the Allergist

- Identification of causative food, risk of anaphylaxis and education on elimination diet.
- Education on the signs and symptoms of allergic reactions and anaphylaxis, and appropriate treatment including correct technique of using epinephrine auto-injector.
- Assist in formulation of IHP and EAP, particularly for child-care and educational settings.

Young MC, et al. JACI 2009;124:175-82.

Role of the Allergist

- Regular follow-up to update status of food allergies and possible development of tolerance, and to update prescriptions for epinephrine and review technique of auto-injector use.
- Be a resource for not only patients and families, but for schools, the community and primary physicians.

Young MC, et al. JACI 2009;124:175-82.