Objectives

- Identify an evidence-based approach to managing food allergy patients with both common and less common allergens
- Discuss how to screen for possible sensitivity to food additives and preservatives
- Describe a management approach for patients with multiple food allergies

Overview of Food Allergy

- An immunological response to primarily a food protein whose reactions can be severe or life-threatening.
- The allergic reaction results from the production of specific Immunoglobulin E (IgE) antibodies directed against food antigens.
- Food allergy is the most common cause of anaphylaxis either inside or outside of the Emergency Department.
- Must be differentiated from food intolerances and other adverse food reactions

Types of Adverse Food Reactions

- Nontoxic
  - Food Allergy
  - Food Intolerance
  - Other
- Toxic
  - Metabolic
  - Pharmacologic
  - Idiosyncratic
  - IgE & Non-IgE

Natural History

- Exposure
  - Generic Predisposition
  - Sensitization
  - Re-exposure
- Symptoms
**Food Allergy (FA) Prevalence is Increasing**
- Self-reported prevalence of FA is 8.96% children = 6.53% and adults = 9.72%
- Estimated that 1 children in every classroom of 25 children have FA
- Children with FA are more likely to have asthma or other allergic conditions than those without FA
- In the last 10 years, food-induced anaphylaxis hospitalizations has increased more than 3-fold.
- 170 foods have been identified as causing an IgE-mediated response

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**The Natural History of Peanut Allergy**
- Peanut allergy affects 1% of children
- There is a strong association between higher IgE levels and reaction severity.
- The annual incidence rate of accidental exposure for children with peanut allergy is 12.5%.
- Children and adolescents are at higher risk.

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**The Natural History of Milk Allergy**
- Research: in cohort of infants (n=293) with milk allergy, 90% resolved over 66 months of follow up.
- Baseline milk-specific IgE level, SPT wheal size, and AD severity were important predictors of the likelihood of resolution.

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**The Natural History of Egg Allergy**
- Medical records of 581 pts reviewed at pediatric allergy clinic for those outgrowing egg allergy
  - By age 4: 4%
  - By age 6: 12%
  - By age 10: 37%
  - By age 16: 68%
  - By age 18: 80%

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**8 Foods Cause 90% of IgE-Mediated Food Allergy**

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**Determining Severity of Reactions**

*What Matters Most*
- Consistent asthma
  - Amount ingested
  - Raw vs. cooked
- Co-ingestion of other foods
- Age
- Degree of sensitization
- Empty stomach
- Exercise

*Near Fatal Reactions*
- Asthma – especially severe on chronic corticosteroids
- Delayed use of epinephrine with reliance on Benadryl
- Alcohol consumption
Evidence-based Approach

- NIAID Food Allergy Guidelines: Guidelines for the Management and Diagnosis of Food Allergy in the United States
- DRAFT - Joint Task Force on Practice Parameters: Food Allergy: A Practice Parameter Update

Diagnostic Evaluation of Food Allergy

Prick Skin Testing

- Spork et al study in 3 yr olds (large cohort) prick testing & food challenge:
  - Peanut > 8mm over control
  - Cow’s milk > 8mm over control
  - Egg > 7mm over control
- Predictive accuracy approx. 95%
- ↑ specificity for reactions
- Studies have demonstrated that the wheal size and specific IgE level can be associated with the severity of reactions on oral challenge.
- Negative predictive accuracy of a properly performed prick test exceeds 99%

Lab Testing

- The comparability of skin testing and selected immunoassays is debatable.
- However, prior to a food challenge in a patient with a highly suggestive history and a negative in vitro test
  - Prick skin testing is advised

Testing

- Prick skin testing—systemic symptoms are rare:
  - Glycerinated
  - Fresh food extracts
  - Prick-prick test
- Positive predictive accuracy < .40% if 3mm greater than control criteria is used
Cross Reactivity and Food Allergen Groups

- When an allergic response is established toward a particular protein, presentation of a homologous form of that protein in another substance may also trigger an allergic response.
- Allergic reaction to multiple foods may follow initial sensitization caused by a food or nonfood allergen such as pollen.
- Food allergens are derived from just a few protein families.
- Over 70% identity in primary sequence is needed for cross-reactivity.

Cross Reactivity: Clinical Application

- Studies where a patient who is allergic to one member of a food family is challenged to all others in that food group are lacking.
- Decisions to avoid foods as a group may also be based upon concerns about cross-contact or misidentification of the allergens.
- Decisions can be individualized based upon clinical judgment, patient preference, nutritional considerations, and availability of safe foods.

Oral Allergy Syndrome

- Reactions occur because the proteins found in some fruits and vegetables are very similar to those found in pollen. These proteins can confuse the immune system and cause an allergic reaction or make existing symptoms worse.
- Cross-reactivity happens when the immune system thinks one protein is closely related to another.
- Most frequent reactions involve itchiness or swelling of the mouth, face, lip, tongue, and throat.
- Individuals react to different foods based on what type of seasonal allergies they are affected by.
- If a patient develops a pollen allergy prior to developing OAS, the reactions are less likely to be life threatening.

Eosinophilic Esophagitis

- Studies show complete food elimination as EoE’s most effective treatment.
- The drawbacks of an elemental diet have led to use of a 6-food elimination diet and skin prick test/atopy patch test-directed diet. Studies show that SPT may lead to better results.
- Spergel et al reported that 77% of 914 patients with EoE responded to diet modifications guided by SPT/APT plus empiric milk elimination compared with 45% of those on SPT/APT-based elimination alone.
- Fresh food SPT has been shown to identify food sensitivities not detected with commercial extracts.
Irritable Bowel Syndrome-Diarrhea Predominant

- In patients with AR, FA, or h/o atopic disease, the odds of IBS-D are 12.1, 2.9, and 4.6, respectively, compared with those who do not have these symptoms.
- Study: 203 patients who had undergone endoscopy and biopsies with immunostaining for mast cell tryptase were selected from the pathology department’s database.
- In comparison to patients with intestinal mast cell counts less than 5, patients with 5-19 mast cells/hpf have twice the probability of having IBS-D when controlling for atopic status.
- In patients with >19 mast cells/hpf, the presence of atopic disease quadrupled the odds of IBS-D.

Alpha-Gal Allergy

- Recent studies have linked the consumption of meat to an alpha-gal allergy, causing a reaction to red meat, which occurs after being bitten by a tick and may lead to anaphylaxis.
- The link is a sugar, commonly called alpha-gal, found in the meat of all non-primate mammals, including cows, pigs, sheep, and goats.
- Drs. Platts-Mills and Cunningham at the University of Virginia found that a tick bite (specifically the lone star tick, which is indigenous in the southeastern United States) is a cause, possibly the sole cause, of IgE production related to alpha-gal.
- The tick bite introduces alpha-gal into the skin of an individual, causing the creation of specific IgE in some people.
- If not exposed again through another tick bite, the allergy usually resolves within eight months to three years.

Food Additive Groups Known to Cause Reactions

- Antioxidants (such as BHA and BHT)
- Colors (food dyes)
- Emulsifiers and stabilizers (such as gums and lecithin)
- Solvent
- Glazing agents (such as stearic acid, beeswax, lanolin, esters)
- Preservatives (such as benzoates, nitrates, and sulfites)
- Flavoring and sweetening agents
- Thickeners

Patch Testing and IBS-D

- Patch testing may be useful in identifying the causative foods.
- Study: skin patch testing to common allergic foods and food additives on individuals with a history of or symptoms suggestive of IBS-D. Patch test-guided avoidance diets were used to determine whether avoidance alleviates IBS-D symptoms.
- Results: 20 of the 25 study participants showed at least one positive patch test result. Fourteen of the participants reported symptomatic improvement, ranging from slight to great, upon avoidance of the foods/food additives to which they reacted.

Allergic Reactions to Food Additives

- Food additives basic functions: make food safer by preserving it from bacteria and preventing oxidation
- Food additives are potential hidden allergens as everyone is exposed to them every day
- Among sensitive subjects, potential of allergic reaction to food additives is reported as 0.03-0.23%
- Some food additives may cause an allergic reaction by inhalation or by topical administration, but not just by ingestion

Testing for Allergy to Food Additives

- Patients with adverse reaction to food additives should be evaluated for sensitivity to annatto (yellow) and carmine (red) as they have been linked to anaphylaxis.
- There is also evidence that erythritol, guar gum, psyllium, carrageenan, lupine, pectin, gelatin, mycoprotein, and certain spices have caused anaphylaxis.
- Natural food additives and spices should be included in the work-up of patients with a history of unexplained anaphylaxis.
**Case Study: C. Gum**

- 39 year old female
- History of random and unanticipated tongue and throat swelling for 4 weeks, 3 episodes.
- Initial episode - ate cream pie (store bought) and developed swelling within 3 minutes.
- No hives or rash
- History of IBS-C

**Working diagnosis:** angioedema – suspect something ingested

**Lab work ordered:** ANA, liver enzymes, BUN, creatine, C4, ESR, total IgE level, UA, vitamin D level, thyroid studies, ssIgE levels for foods and food additives

- All lab work negative, except for Carrageenan Gum (+)
- Implemented avoidance diet of C. Gum
- At 3 month f/u: no incidences of angioedema on C. Gum avoidance. Patient also reported decreased IBS-C symptoms on avoidance diet.
- Patient declined re-challenge.

**Dust Mites and Food Allergy**

- House dust mites and storage mites are commonly found in grain, fishmeal, and dried fruit.
- Dust mite sensitive patients may react to a food that has been in extended storage and exposed to dust mites.

**Food Induced Allergic Rhinitis**

- The prevalence of food-induced allergic rhinitis appears to be less than 1 percent.
- Food reactions often lead to rhinitis symptoms without an immunologic nature.
- Although the role of food and fruits in developing allergic rhinitis is not clearly identified, in a very small percentage of patients, rhinitis is among the clinical manifestations of food allergy.

**Celiac Disease**

- Celiac disease (CD) is a chronic small intestine immune-mediated condition triggered by exposure to gluten in genetically sensitive individuals (DQ2+ or DQ8+).
- Gluten is a protein component found in wheat, barley, and rye (but not in oats).
- The gluten-free diet is currently the only available treatment for CD, although ongoing pharmacological and vaccine trials promise future alternatives.

**FPIES**

- Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated gastrointestinal food hypersensitivity that manifests as profuse, repetitive vomiting, often with diarrhea, leading to acute dehydration and lethargy or weight loss and failure to thrive if chronic.
- FPIES is elicited most commonly by milk and soy proteins; however, rice, oat, and other solid foods may also elicit FPIES.
- Certain FPIES features overlap with food protein-induced enteropathy and proctocolitis, whereas others overlap with anaphylaxis.
- Usually ST are negative for milk and soy.
**Experimental Approach:**

**Dust Mite Allergy and Shrimp Allergy**

- The presence of allergy to shrimp is currently a hypothetical contraindication to specific immunotherapy for house dust mites.
- **CASE STUDY:** A 15 year-old male presented with mild persistent asthma and rhinitis due to mites, and concomitant allergy to shrimps and seafood, with anaphylactic symptoms: urticaria, glottis oedema, asthma, enteritis.

**Skin Conditions Associated with Food Allergy**

**Low Nickel Diet**

- Nickel is present in most of the dietary items and food is considered to be a major source of nickel.
- Nickel when administered orally (600–3600 mg) as a single dose provoked hand eczema.
- Evidence cites improvement of dermatitis on a low nickel diet.
- Common sources of nickel foods: cereals, fish, canned vegetables, nuts, instant tea and coffee, dried peas.

**Role of Diet in Nickel Allergy**

- Nickel is a ubiquitous trace element and the commonest cause of metal allergy among people.
- Nickel allergy is a chronic, recurring problem; females are affected more commonly than males. Nickel allergy may develop at any age. Once developed, it tends to persist life-long.
- Nickel in the diet of a nickel-sensitive person can provoke dermatitis. Careful selection of foods with relatively low nickel concentrations can bring a reduction in the total dietary intake of nickel per day.

**CASE STUDY Results**

- The patient underwent SLIT extract for mites without any adverse events. The maintenance dose, regularly achieved, was 5 drops a day for 12 months, that is twice the recommended dose. This was done to achieve a high enough cumulative dose of tropomyosin, that was 146 μg.
- After 12 months the symptom/medication score decreased by approximately 40% and drug intake for asthma and rhinitis also decreased by 40%. At 12 months an oral challenge with a single shrimp was done, and it caused only an oral allergic syndrome, without systemic symptoms. In addition, the patient accidentally ate shrimps in small quantities at home, without any symptoms.
- After 12 months of SLIT the average diameter of skin prick test to shrimps was 5 mm; to *Dermatophagoides pteronyssinus* 10 mm; and to *Dermatophagoides farinae* 6 mm. Specific IgE to tropomyosin slightly increased to 33 KU/L, whereas no relevant change was seen in the remaining parameters.

**Foods that Contain Nickel**

- **High content (>0.5 mg/kg):** almond, asparagus, beans, buckwheat, chickpeas, cocoa powder, dark chocolate, fresh pears, hazelnut, herring, linseed, mussels, oat bran, oatmeal, onions, peanut, pistachio nuts, poppy seed, soy beans, soy flour, walnuts, wheat bran, yellow peas.
- **Medium content (0.1–0.5 mg/kg):** barley, black current, corn flour, eggs, garlic, horseradish, kale, milk chocolate, oysters, parsley, parsnip, raspberries, rice, rye, various mushrooms, yeast.
Balsam of Peru Diet

- Balsam of Peru, composed of a variety of components, is a fragrance found in foods such as alcohol, citrus fruits, chocolate, pickle vegetables, spices, and tomatoes that has been associated with systemic contact dermatitis.
- The diagnosis can be made by history and atopy patch testing but also may require dietary elimination or food challenge of the suspicious food or food components.
- Balsam of Peru is a well-known contact allergen that is one of the most prevalent in the United States. For some patients allergic to BOP, external avoidance of fragrance is not enough to eliminate their dermatitis.

Food-Dependent Exercise Induced Anaphylaxis

- FDEIA is a distinct condition in which anaphylaxis develops only if physical activity occurs within a few hours after eating a specific food. This disorder has been reported with a wide variety of foods.
- The foods most commonly implicated in food-dependent exercise-induced anaphylaxis include wheat, shellfish, tomatoes, celery, peanuts, and corn.

Management of Food Allergies

Allergenicity

Fruits and vegetables cause allergic reaction primarily if eaten raw, but may still cause reactions after being thoroughly cooked or having undergone digestion in the stomach and intestines.

Food Processing and Allergenicity

- The alteration of allergenicity of a protein during the manufacturing process may determine how provoking the food is
- The heating process of baking destroys the protein structure to which the child is sensitive
- For example, some egg sensitive children may be able to tolerate eggs in baked products, but not when eaten alone

Allergenicity of Oils

- Oils are commonly derived from soy, corn, peanut, and sesame
- They may range in their allergenicity depending on how much of the food protein is removed in process
- Consuming highly refined oils developed from major allergenic food sources does NOT appear to be associated with allergic response
- According to the FARE, “Studies show that most allergic individuals can safely eat peanut oil (not cold pressed, expelled, or extruded peanut oil - sometimes represented as gourmet oils).”
Cold Pressed vs. Cooked Oils?

- Cold pressed oils are obtained through pressing and grinding fruit or seeds with the use of heavy granite millstones or modern stainless steel presses.
- The temperature must not rise above 120°F (49°C) for any oil to be considered cold pressed.
- Cold pressed oils retain all of their flavor, aroma, and nutritional value - olive, peanut, and sunflower are among the oils that are obtained through cold pressing.
- Cold pressed oils are considered more risky for patients to consume due to their retention of more allergenic proteins.

Cross Contact Through Saliva

- Allergic reactions are possible via saliva exchange, including risks associate with sharing straws, cups and utensils.
- Discuss appropriateness of “peanut-free table” in school setting.
- “Allergic Kiss of Death” is NOT a myth.
- The safest strategy is that the family of the food allergic child also avoid the allergenic food.

Food Product Label

- Manufacturers must detail allergen information for top 8 food allergens (milk, eggs, fish, crustacean fish, peanuts, tree nuts, wheat, and soy).
- Manufacturers must list the specific nut (e.g., almond, walnut, cashew) or seafood (e.g., tuna, salmon, shrimp, lobster) that is used in the product.
- Products with precautionary labeling, such as “this product may contain trace amounts of allergen” should be avoided.

Are Patients Reading Food Labels?

- No.
- Hefle et al. (2007) demonstrated increasing numbers of FA consumers are NOT reading labels precautionary labeling and choosing to ingest products due to:
  - Their stated recognition of increase warnings and therefore not needing to rely on labels
  - FA consumers noting no reaction after ingestions
  - FA consumers presuming that advisory labeling is used for legal reasons only

Are Precautionary Labels Accurate?

- Current labeling laws relate only to intentionally added ingredients.
- Consumers must make risk assessments based on precautionary labeling.

Follow Up

- Allergies to milk, egg, wheat, soy generally resolve more quickly in childhood than peanut, tree nuts, fish and shellfish.
- Consider the natural course of allergies to specific foods when deciding upon frequency of food allergy follow-up evaluations.
The Future

- Component-resolved diagnostic testing to food allergen may be considered as in the case of peanut sensitivity, but it is not routinely recommended even with peanut sensitivity because the clinical utility of component testing has not been fully elucidated.

- Although immunotherapeutic approaches, e.g. such as oral immunotherapy, in clinical trials show promise, they are not ready for implementation in clinical practice at the present time due to inadequate evidence for therapeutic benefit over risks of therapy.