

“Dying to Eat That”: Evaluation and Management of Food Allergies in ChildrenA Presentation for the 3rd Annual SPAP Conference

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After participating in this lecture, attendees should be able to:

- Realize the enormous burden of allergic disease and the impact it has on patients' quality of life
- Review the pathophysiology of the allergic response
- Identify the signs and symptoms of adverse reactions to foods
- Review the diagnostic testing options for food allergies
- Discuss treatment options for food allergies
- Identify promising advances in the evaluation and management of adverse reactions to foods

Presentations of Allergic Disease and “The Allergy or Atopic March”

- Atopic dermatitis
- Adverse reactions to foods
- Allergic rhinitis
- Allergic asthma

The Impact of Allergic Disease

- Allergic disease is the 6th most common chronic disease in the United States, and one of the most common chronic diseases in children
- One-half of all US citizens test positive for one or more allergens
- Allergic diseases significantly alter quality of life affecting employment, sleep, learning and cognitive ability

Pathophysiology of the Allergic Response

- Sensitization – via gut mucosa, cutaneous exposure, or aerosolized allergens
- Production of IgE
- IgE-antigen complexes bind to mast cells and basophils
- Release of chemical mediators (histamine, tryptase, chemotactic factors, cytokines, platelet-activating factor, and others) that produce effects on the target organs

Food Allergies: (some of the) Statistics

- Affects 6-8% of children, 2% of adults
- Food intolerances or adverse reactions are more common than IgE-mediated allergies
- 35% of children with atopic dermatitis have food allergy
- Food allergies are responsible for @150 deaths per year in US

- Most children allergic to milk, egg, wheat and/or soy will lose their sensitivity by 3-5 years of age, approximately 20% of children with peanut allergy will lose their sensitivity during childhood

Food Allergies: The Definition(s)

- IgE-mediated reactions to food
 - Urticaria, angioedema, rhinitis, bronchospasm, gastrointestinal symptoms, anaphylaxis, all with rapid onset after ingesting, touching or inhaling food
- Non-IgE-mediated immunologic reactions
 - Food-induced enterocolitis (breast-milk colitis), celiac disease, dermatitis herpetiformis
- Non-immunologic reactions
 - Adverse reactions to toxins, lactose intolerance, ingestion of foods with pharmacologically active substances

Food Allergies: On the Rise

- Hygiene hypothesis
- Reduction and change in fatty acid consumption
- Reduced dietary antioxidants
- Vitamin D deficiency/excess
- Exposure before ingestion
- Immaturity of the gut barrier
- Use of medications such as antacids

Food Allergy: The “Big 8” Most Common Foods

- Milk
- Egg
- Peanut
- Tree nut
- Soy
- Wheat
- Fish
- Shellfish

Diagnosis of a Food Allergy: A Targeted History The Most Important Tool

- Description of symptoms for each suspected food
- Timing from ingestion to symptom onset
- Number of occasions
- Approximate quantity of food observed to produce the symptoms
- Any associated factors such as exercise

Food Allergy: Signs in Four Target Organs

- Skin: Acute urticaria < 120 minutes after exposure, angioedema
- GI: Nausea, vomiting, cramping, diarrhea
- Resp: Rhinitis, wheezing
- CV: Anaphylaxis, hypotension

Food Allergy Signs: Anaphylaxis

- National Institute of Allergy and Infectious Diseases and Food Allergy and Anaphylaxis Network (FAAN):
 - “A serious allergic reaction that is rapid in onset and may cause death.”
- At least two organ systems or hypotension
 - Low systolic BP for children is defined as less than 70 mmHg from 1 month to 1 year, less than (70 mmHg + [2 x age]) from 1 to 10 years, and less than 90 mmHg from 11-17 years
- Biphasic pattern

Patients More Likely to Experience Anaphylaxis

- Past history of anaphylaxis
- Concomitant respiratory symptoms/asthma
- Reactions after ingestion of peanuts, tree nuts, or seafood

Food Allergies: Diagnostic Testing

- Skin prick testing
 - negative test more helpful than positive one
- Allergen-specific IgE antibody
 - CAP-RAST, ImmunoCap
 - Higher specificity, higher reliability
- Oral challenges
 - Open challenges
 - Double-blind, placebo-controlled challenges

Food Allergies: Skin Prick Testing (SPT)

- Uses commercial extracts of stable food proteins
- Negative saline control and positive histamine control
- Wheal diameter of 3 mm or larger than that produced by saline control are considered positive
- High rate of false-positives
- Patient must be free of antihistamines for 72 hours prior to testing

Food Allergy Diagnostic Testing: sIgE Specific Antibody Testing

- Food allergen-specific IgE levels (kUA/L) with PPV 95%

▪ Egg	7
▪ Milk	15
▪ Peanut	14
▪ Fish	20
▪ Soy	65
▪ Wheat	80
- Possibly reactive if levels less than values above but greater than 0.35
- Unlikely reactive if level 0.35 or less

When are sIgE tests preferred to SPT's?:

- In patients with eczema or dermatographism
- In patients who are unable to stop taking their antihistamine medication
- When there is a risk of developing a severe reaction upon performing a SPT, especially in allergens such as peanut

- Performing SPTs may sensitize a patient to an allergen he/she has not yet been exposed to
- Serum-IgE is quantitative and the pattern of decline may predict who will eventually outgrow the allergy and may help determine if food challenge should be attempted

Oral Food Challenges

- Double-blind, placebo-controlled oral food challenges (DBPCFCs) are the gold standard for the diagnosis of food-related disorders
 - Used when the diagnosis is unclear
 - Lack of clinical reaction by history
 - Negative SPT with positive history
 - sIgE > 0.35 but less than 95% PPV and a negative history
- Used to determine when re-introduction into the diet is safe based on decreasing levels of sIgE or length of time since last reaction

Oral Food Challenges

- Escalating doses of protein administered every 15 minutes until reaction or pre-determined tolerance level is achieved such as 4 g in children < 5 yrs and 8 g in children \geq 5 yrs
- Time-consuming, risk of potentially life-threatening reactions
- Must be carried out in a controlled setting with proper supervision

Food Allergies: Management

- Referral to allergist for initial testing and monitoring
- Dietary management and aggressive avoidance
 - May need referral to dietician
- Allergy Action Plan with Epi-Pen Jr or Epi-Pen for home use with instructions
- Allergy identification cards, jewelry, tags
- Therapy if accidental exposure occurs

Food Allergies: Reading Food Labels

- Milk proteins
 - Casein, caseinates, rennet casein
 - Whey
 - Lactalbumin, lactoglobulin, lactulose
- Egg proteins
 - Albumin, albumen
 - Meringue
 - Lecithin
- Recent survey found 42 different statements:
 - “May contain ...”
 - “Made on the same equipment with ...”

Managing Food Allergy: Food Allergen Labeling and Consumer Protection Act (FALCPA)

- Effective January 2006
- Mandates that foods containing any of the Big 8 allergens must declare the allergen in plain English in one of the following ways:
 - List allergens in ingredient list
 - Provide “Contains...” statement, separate from ingredient list

- List common names in parentheses in ingredient list (albumin [egg])
- Ingredients must be listed even if they are present in colors, flavors, spice blends
- Does not address “May contain...” or “Packaged in a facility that processes...” statements

Allergy Action Plan

- Food Allergy and Anaphylaxis Network www.foodallergy.org
 - Downloadable allergy action plans
 - Guidelines for schools, camps

Allergy Identification Items

- Tags
- Shirts
- Lunch bags
- Jewelry

Food Allergy Management: Mild to Moderate Post-Exposure Reactions

- Antihistamines
 - Diphenhydramine 1-2 mg/kg PO q 6 hrs, max 50mg/dose
- Corticosteroids
 - Prednisolone 1-2 mg/kg/day in one or two divided doses for 3-5 days
- Inhaled Beta-Agonists
 - Albuterol 2.5 mg in 3 ml saline nebulized or in MDI

Food Allergies: Severe Reactions and Anaphylaxis Management

- Oxygen
- IV fluids
- Epinephrine 0.01 ml/kg (1:1000) IM q10-20 min
- Additional medications
 - Diphenhydramine 1-2 mg/kg IM/IV
 - Ranitidine 1.5 mg/kg IM/IV
 - Corticosteroids
 - 2 mg/kg Methylprednisolone IV
- Diagnostic testing not usually helpful, may order
 - IgE specific antibodies
 - Serum tryptase (produced by mast cells)
 - Serum or urine histamine

Epinephrine Dosing

- 1:1000 dilution contains 1 mg/ml
- Weight calculated dosage 0.01 mg/kg and repeated if necessary
- Intramuscular Injection

> 12 years	0.3-0.5 mg	0.50 ml of 1:1000
6-12 years	0.25 mg	0.25 ml of 1:1000
6 mo to 6 yrs	0.12 mg	0.12 ml of 1:1000
Under 6 months	0.05 mg	0.05 ml of 1:1000
- Auto-injectors
 - < 25 kg 0.15 mg
 - > 25 kg 0.30 mg

Food-Anaphylaxis Fatalities

- FAAN Network maintains a registry of fatalities (63 cases recorded through 2006)
- Most deaths occur in persons known to have a food allergy (most often peanut/tree nuts)
- Most common sources of foods were restaurant menu items and packaged foods
- Only a few of these persons (10%) had self-injectable epinephrine available

After a Trip to the ER

- 2004 study conducted by Emergency Medicine Network (Clark S, Bock SA, Gaeta TJ, *et al.* Multicenter study of emergency department visits for food allergies. *J Allergy Clin Immunol* 2004; 113:347-352)
- Retrospective chart review of 678 patients in the ER with diagnosis of food-related allergic reaction (50% of these were anaphylactic/severe)
- 40% received instruction to avoid allergen
- 16% received a prescription for self-injectable epinephrine
- 12% received referral to allergist

Food Allergies: Management in Special Settings

- 85-90% of fatal or near-fatal reactions occur away from home after unintentional ingestion in a person known to have food allergy and there is delay in epinephrine administration
- Schools
- Childcare settings
- Restaurants
- Hospitals
- Summer camps
- Public transportation (airlines)

Food Allergies: Managing Food Allergy in Schools

- Increased supervision during meals and snacks
- Allergy-free tables
- No sharing of food, utensils, containers
- Regular cleaning of tables, toys
- Avoid the use of food for crafts and rewards
- Require labels on all food brought into school
- School staff training
- Accessible Epinephrine

Food-Pollen Allergy (or Oral-Allergy Syndrome)

- Rapid onset of itching and swelling of lips, mouth, oropharynx after eating RAW fruits or vegetables
- IgE to various pollens can cross react with proteins in fruits and vegetables and cause local mast cell degranulation
- May have to test skin with raw foods
- Managed by avoidance of raw, but OK with cooked foods

Exercise-Induced Food Allergy

- Symptoms include pruritus, urticaria, angioedema, wheezing, anaphylaxis occurring during or after exercise when the food allergen is eaten prior to exercise
- The food or exercise alone does not produce the allergic reaction
- Common in adolescents
- Wheat-containing products are often implicated, but any food can cause a reaction
- Management includes avoiding offending foods 12 hours prior to exercise, pre-exercise treatment with antihistamines, avoid exercising alone, carrying EpiPen and antihistamine

Food Allergies: Emerging Therapies

- Dietary manipulation including early exposure to promote tolerance
- The use of probiotics in pregnancy and early infancy
- Decreasing intestinal permeability to food proteins
- Desensitization with sublingual allergen immunotherapy (cow's milk, egg, peanut)
- Engineered proteins for immunotherapy
- Anti-IgE antibody medication (Omalizumab/Xolair)
- Anti-cytokine therapy
- Sublingual epinephrine tablets

Oral Immunotherapy: Cow's Milk

- Study by Longo, *et al.* (*J Allergy Clin Immunol* 2008;121:343-7)
 - 60 children with severe cow's milk allergy (reacted to under 0.8 ml milk and had serum IgE > 85 kUA/L)
 - 30 underwent 10-day in-hospital rush protocol to 20 mL tolerance, and then gradual progression at home to 150 mL
 - After 1 year:
 - 11 (36%) children achieved tolerance to 150 mL or more
 - 54% tolerated 5 to 150 mL
 - 3 children could not achieve 5 mL
 - Untreated controls had no increase in tolerance over the year
 - Almost all children had a reaction during the protocol
 - Overall, milk IgE levels declined in the treatment group
 - Similar studies have been reported with peanut, egg, hazelnut
- Northwestern Peanut Protein Study

Pack It Up and Take It Home

- Children often present with the signs and symptoms of allergic reactions following ingestion of one or more of the following foods: milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish.
- Clinicians must be able to identify the cutaneous, upper and lower respiratory tract, gastrointestinal, and anaphylactic presentations of allergic disease.
- Management of allergic reactions consists of allergen avoidance and prompt administration of antihistamines, corticosteroids and epinephrine.

Selected References and Resources

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- Kids with Food Allergies <http://www.kidswithfoodallergies.org>