THE NUTS AND BOLTS OF FOOD ALLERGY

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LEARNING OBJECTIVES

1. Discuss the epidemiology, natural history and prevalence of food allergy.
2. Describe important aspects of history required to evaluate patients with adverse reactions to foods
3. Educate on interpretation of skin testing and in vitro testing in the evaluation of food allergy
4. Briefly discuss other allergic conditions, such as atopic dermatitis and oral allergy syndrome
5. Review the acute and long term management of food allergic patients
6. Discuss the appropriate indications for referral to an allergist

DEFINITIONS

• **Food allergy**: any adverse health effect caused by a specific immune response (immune-mediated) that occurs reproducibly on exposure to offending food

• **Food allergens**: specific components (proteins) of food that cause specific immune reactions

TYPES OF IMMUNOLOGIC FOOD REACTIONS

<table>
<thead>
<tr>
<th>IgE-mediated</th>
<th>Mixed IgE/Non IgE</th>
<th>Non-IgE Mediated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic (anaphylaxis)</td>
<td>Eosinophilic Esophagitis (EoE)</td>
<td>Food Protein-Induced Enterocolitis (FPIES)</td>
</tr>
<tr>
<td>Oral Allergy Syndrome</td>
<td>Eosinophilic Gastritis</td>
<td>Food Protein-Induced Enteropathy or Proctocolitis</td>
</tr>
<tr>
<td>Asthma/Rhinitis</td>
<td>Eosinophilic Gastroenteritis</td>
<td>Dermatitis herpetiformis</td>
</tr>
<tr>
<td>Urticaria</td>
<td>Atopic dermatitis</td>
<td>Contact dermatitis</td>
</tr>
</tbody>
</table>


IGE-MEDIATED FOOD ALLERGY

- IgE-mediated food allergy involves release of mediators from mast cells and can induce reactions and anaphylaxis
- Diagnosis of immune-mediated food allergy requires both clinical symptoms upon exposure to the offending food, as well as positive testing


SYMPTOMS

- Cutaneous
  - flushing, urticaria, angioedema, pruritis, atopic dermatitis
- Gastrointestinal
  - abdominal pain, nausea, vomiting, diarrhea
- Respiratory
  - cough, wheezing, shortness of breath, laryngeal edema
- Cardiovascular
  - hypotension, arrhythmias, tachycardia
- Neurological
  - syncope, lightheadedness
**ORAL ALLERGY SYNDROME**

- **Oral Allergy Syndrome**: patients develop symptoms (itchy mouth and throat, tingling) following ingestion of certain foods
  - Plant proteins cross-react with airborne allergens
  - Birch: apple, potato, pear, carrot, celery
  - Ragweed: melon, banana, avocado


**ATOPIC DERMATITIS**

- **Atopic Dermatitis**: Chronic inflammatory skin disorder that causes pruritis and can lead to lichenification and/or secondary infections
  - Infants: face, extensor surfaces
  - Older children/adults: flexor surfaces, neck, upper trunk
  - Food allergy can play a role in 10-30% of patients

Sticherer B, et al. JACI 1999; 104:S114-118
American Academy of Dermatology (www.aad.org)

**PREVALENCE OF FOOD ALLERGY**

- True prevalence can be difficult to measure
- Approximately 6% of children, 4% of adults
- Largely over-reported by the public - up to 25%
- According to 2013 study by CDC, food allergies among children increased by 50% between 1997 and 2012
- So why are food allergies on the rise?
  - "Hygiene hypothesis"
  - Epigenetics

RISK FACTORS

- Family history
- Atopic dermatitis
- Other allergic conditions

- Up to 75% of patients with food allergy have evidence of another allergic condition

Lam JJ, et al. Allergy, Asthma & Clinical Immunology 2008; 4: 144-149

PREVALENCE OF FOOD ALLERGY

<table>
<thead>
<tr>
<th>Food</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow’s Milk</td>
<td>2.5%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Peanut</td>
<td>2.0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Egg</td>
<td>1.5%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Tree nut</td>
<td>0.5%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Wheat</td>
<td>0.4%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Soy</td>
<td>0.4%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>0.1%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Finned Fish</td>
<td>0.1%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Sesame</td>
<td>0.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Overall</td>
<td>6%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

Sicherer SH, Sampson HL. J Allergy Clin Immunol 2010; 125; S116-S25
NATURAL HISTORY OF FOOD ALLERGY

- Most common foods are peanut, treenuts, milk, egg, soy, wheat, fish, shellfish
  - Sesame on the rise
  - Anything containing proteins can be an allergen source
- Most children with milk, soy, egg and wheat allergy will eventually tolerate the food
- Outgrowing peanut and tree nut significantly less
- Shellfish/fish allergy can be later onset

Sastre J. Clinical and Experimental Allergy, 2010;40:896-904

WHEN TO SUSPECT FOOD ALLERGY?

- Any local or systemic reaction following ingestion of food
- Infants with moderate to severe atopic dermatitis
- Infants with persistent atopic dermatitis despite appropriate therapy
- Patients with eosinophilic GI disease
- Patients with enterocolitis


Which of the following is most useful in diagnosing food allergy?

a) Skin prick testing
b) Serum-specific IgE testing
c) Clinical history
d) None of the above
Which of the following is most useful in diagnosing food allergy?

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d) None of the above

CLINICAL HISTORY

• Obtain detailed history of reaction:
  • Symptoms
  • Timing
  • Amount of food
  • Route of exposure (ingestion, contact, inhalation)
  • Raw vs. cooked; Baked vs. whole

Boyce J, et al. JACI 2010;126:S1-14

CLINICAL HISTORY

• Previous tolerance
• Presence of risk factors
• Introduction of other high risk foods
• Concurrent exercise, meds, alcohol
PHYSICAL EXAM

• Assess for other disorders, especially comorbid allergic conditions

• Physical Exam findings may include:
  ▪ Conjunctivitis, allergic shiners
  ▪ Nasal turbinate hypertrophy, nasal polyps, post nasal drainage
  ▪ Atopic dermatitis/eczema
  ▪ Urticaria, angioedema
  ▪ Wheezing, cough

Boyce J, et al. JACI 2010;126:S1-48

DIAGNOSTICS

• Skin Prick Testing (SPT)
• Allergen Specific Serum IgE (sIgE) Testing
• Food elimination
  ▪ Can be useful in non IgE-mediated FA and EoE
• Oral food challenges
  ▪ Gold standard

Not recommended:
• Patch testing
• Allergen IgG panels
• Applied kinesiology/muscle response testing

• Intradermal tests
• Hair analysis
• Electrodermal testing


SKIN PRICK TESTING

• Skin prick testing (SPT):
  ▪ Diluted allergen is applied on the surface of the skin and area of test is observed for 15 minutes
  ▪ Measures IgE bound to cutaneous mast cells by causing mast cell degranulation on surface of the skin which causes local reaction
  ▪ Measure wheal and flare
  ▪ Wheal ≥ 3 is considered positive test
  ▪ Larger skin tests do not necessarily correlate with severity
SKIN PRICK TESTING
- Indicates presence of IgE antibody but does not always correlate with reactivity
- Interpret results using skin testing and history
- Sensitivity: ~90%
- Specificity: ~50%
- A negative skin prick test can essentially exclude IgE mediated food allergy 95%


SERUM IGE TESTING
- Detects food-specific IgE antibodies in the serum
- Presence reflects sensitization which does not always correlate with clinical allergy
- Sensitivity: ~90%
- Specificity: ~50%
- Using specified 95% predictive values, they can often be more useful than SPT
- Broad serum IgE panels are not recommended


SERUM IGE TESTING
- Food-Specific sIgE levels and clinical reactivity
**ORAL FOOD CHALLENGE**

- Double blind placebo controlled food challenge is the gold standard for diagnosis of food allergy
- Single-blind or open-food challenges may also be done
- If no reaction (negative challenge) then FA can be ruled out
- If SPT or sIgE testing negative but history highly suggestive = perform oral food challenge

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**SERUM COMPONENT TESTING**

- Each allergen source contains multiple allergenic proteins (components)
- Component testing helps to identify whether sensitization is due to primary allergen, or cross-reactivity
- Helps to evaluate risk of reaction on exposure, and sometimes severity
- Available and widely used for peanut, milk, egg; Other foods the clinical utility remains unclear

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**MANAGEMENT OF FOOD ALLERGY**

- Dietary avoidance if allergy is confirmed
  - Complete vs. Partial avoidance
  - Elemental/Amino Acid formulas
- Epinephrine auto-injector
- Nutritional counselling
- Education on reading food labels
- Cross-contamination risk
- Periodic re-evaluation and follow up testing
- Food Allergy Action Plan

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Sastre J. Clin and Exper Allergy, 2010; 40:896-904
Sampson HA. J Allergy Clin Immunol 2004;113:805-19
FOOD ALLERGY ACTION PLAN
• Should be renewed annually by physician
• Discuss and educate when to administer epinephrine based on patient’s history of severity
• Helps physician, family, school nurse, daycare staff be more informed
• FARE (Food Allergy Research & Education) Website: www.foodallergy.org

TREATMENT OF ACUTE FOOD-INDUCED ALLERGIC REACTIONS
• IM Epinephrine is first-line therapy for anaphylaxis
  “Epi first, Epi fast”
• Other medications used:
  ▪ Antihistamines (Benadryl)
  ▪ Corticosteroids (Solumedrol, Prednisone)
  ▪ Albuterol
  ▪ Supplemental O2
  ▪ IV fluids
  ▪ Recumbent position
• Must call 911 or seek hospital care for monitoring after administering Epi
• Milder reactions can be treated with antihistamines, with monitoring. If progression of symptoms then treat with Epi

EPINEPHRINE AUTOINJECTORS

Images courtesy of Mylan, Kaleo, Impax
CASE #1

• 1 y/o female presents for follow up on labs
• HPI: She has mild eczema, and parents are concerned about food allergy. She is using hydrocortisone 1% cream as needed for eczema, which seems to be helping her skin, but still gets breakouts.

• A serum IgE panel to foods was completed, which showed low level positives to peanut, milk, egg, wheat, and soy.

CASE #1

Lab findings:  Reference range < 0.35 kU/L

Peanut IgE 0.57 kU/L
Cow’s milk IgE 0.37 kU/L
Egg white IgE 0.84 kU/L
Wheat IgE 0.37 kU/L
Soy IgE 1.25 kU/L
Total IgE was not completed

She and her parents come to you for follow up on labs and to discuss findings and next steps.

What do you want to know? What do you do next?

CASE #1

• Obtain detailed history regarding exposure to the questionable positive foods

• Skin care, skin care, skin care
  • “Soak and smear”
  • Wet wraps
  • Bleach baths

• Referral to allergist if needed
CASE #1 - DETAILED HISTORY

• She has eaten cow’s milk, egg white, wheat, and soy products without any obvious worsening dermatitis, or any other signs or symptoms of anaphylaxis
• They had eliminated milk, egg, wheat, and soy after reading a food allergy blog and there was no change in patient’s symptoms
• They have never introduced peanuts or other nuts because were scared to do so
• Patient is also exposed to animal dander (dog) at home

CASE #1 - PLAN

• Continue eating milk, eggs, wheat, soy without restriction
• Referred to allergist for evaluation of peanut allergy
• Continue skin care
• Epipen Jr. ??

CASE #1 – ALLERGY CONSULT

• Skin prick testing done to nut panel was negative
• Advised to continue skin care
• Okay to introduce peanut
• Patient also had low level positive to dog dander on skin prick testing
  • Discussed allergen avoidance
  • More likely to be responsible for this patient’s eczema
CASE #2

- 13 month old male presents to your pediatric clinic
- HPI: Patient was eating breakfast a few days ago, and was eating scrambled eggs, pancakes, and avocado. Initially had perioral hives, which quickly spread all over his body and he also had one episode of vomiting, cough, and wheezing
- He was given 1/4 tsp Benadryl and within 30 minutes, symptoms resolved
- PMH also positive for mild eczema, currently well controlled
- They have since avoided eggs (all forms) and avocado. He had previously ingested cow’s milk without issues

CASE #2 - PLAN

- Advised to avoid all forms of egg, avocado
- Epipen Jr. at all times, and education on anaphylaxis
- Serum IgE testing completed:
  - Egg white 15.60 kU/L
  - Avocado < 0.35 kU/L
- Refer to allergist?

CASE #2 – ALLERGY CONSULT

- Records, labs, and history reviewed
- Patient had previously tolerated baked egg in most baked goods (cakes, cookies)
- Continue avoidance of whole egg products
- Okay to continue egg baked into goods
- Plan follow up and repeat labs in 6 months
FOOD INTRODUCTION

• For low risk infants, introduce foods between 4-6 months of age
• New data (LEAP study) suggests early introduction in high risk infants may reduce risk of allergy
• If patient has moderate to severe eczema or another food allergy, consider referral to allergist

PREVENTING FOOD ALLERGY

LEAP Study:
• 640 children between 4-11 months of age who were determined to be “high risk” for peanut allergy
• Randomized to either consume or avoid peanut until age 5
• Results:
  • Avoidance group: 17% of kids were allergic
  • Consumption group: Only 3% of kids were allergic (~80% reduction)
• Findings suggest early introduction of peanut in high-risk infants can prevent development of allergy

LEAP-ON study:
• Follow up of LEAP study
• Looked to see if participants who had consumed peanut for more than four years were protected long-term when they stopped eating peanut
• Followed 556 of the original children in LEAP study
• Results:
  • 4.8% of original peanut consumers were allergic
  • 18.6% of original peanut avoiders were allergic
• Study reassures that eating peanut-containing foods as part of normal diet will be safe

WHEN TO REFER TO ALLERGIST?

- Moderate to severe eczema/difficult to control
- Unknown causative food
- Positive IgE testing (food panel) prior to food introduction
- Food specific IgE is negative in a child/adult with suspected history
- High risk patients with moderate to severe eczema or other known food allergy
- Atopic families to identify risk
- Evaluation of food triggers in EoE or enterocolitis
- For known food allergy diagnosis and ongoing follow up and development of tolerance

ROLE OF THE ALLERGIST

- Identify causative food(s)
- Education, education, education!
  - Reactions/anaphylaxis
  - Appropriate treatment
  - Emergency action plan
  - Regular follow up to update status
  - Up-to-date prescriptions and review technique
  - Resource for patients, families, schools, and primary providers

RESOURCES FOR CLINICIANS

- Local allergist
- American Academy of Allergy, Asthma and Immunology (AAAAI) – www.aaaai.org
- American College of Allergy, Asthma and Immunology (ACAAI) – www.acaai.org
- FARE (Food Allergy Research Education) – www.foodallergy.org
KEY POINTS

• Clinical history is the most important tool in diagnosing food allergy
• Broad serum IgE food panels are not recommended
• Testing can have false positives and unnecessary avoidance may be harmful
• Refer to allergist when appropriate, or anytime!

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