Food Allergy Diagnosis and Management

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No notes.
Presented by

Insert presenter name here

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Note: Speaker can insert their name above.
Learning objectives

• Identify patients who should be evaluated for food allergy
• Select appropriate tests to diagnose food allergy
• Formulate a food allergy management plan
• Discuss potential treatments for food allergy
What is a food allergy?

• Food allergy is an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.

• This reaction can be IgE-mediated, non IgE-mediated or mixture of both that results in clinical symptomatology.

Food allergies are adverse immune reactions to food proteins that can lead to a range of symptoms.

The exposure with clinical reaction is the key point here. Food Allergy Testing determines sensitivity, and does not diagnose food allergy.
Immunologic food reactions

**IgE-Mediated**
- Systemic allergic reaction (Anaphylaxis)
- Oral Allergy Syndrome
- Eosinophilic esophagitis (EoE)
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

**Non IgE-Mediated**
- Food Protein-Induced Enterocolitis (FPIES)
- Protein-Induced Enteropathy
- Eosinophilic proctocolitis
- Dermatitis herpetiformis
- Contact dermatitis

The key disorders to point out are:

- **FPIES** – Generally presents in infancy and is characterized by delayed vomiting 2-3 hours post ingestion.
  - Milk is the most common trigger in children, followed by soy.
  - FPIES can also be triggered by solid foods – rice and oat are the most common triggers for solid food FPIES.

- **EoE** – Chronic, immune/antigen-mediated esophageal disease.
  - Characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.
  - Most common trigger in children is milk.
  - Younger children most often present with vomiting, growth failure and food refusal.
  - For older patients, dysphagia, impaction and heartburn are more often reported.

IgE-mediated food allergy

- IgE-mediated food allergy reaction often occurs within minutes to 2 hours of ingesting a food
- Reactions can range from mild to severe (anaphylaxis)
- Symptoms include:

<table>
<thead>
<tr>
<th>Category</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous</td>
<td>urticaria, angioedema, pruritus, flushing, rash</td>
</tr>
</tbody>
</table>
| Respiratory    | upper airway → rhinitis, stridor, hoarseness, sneezing  
|                | lower airway → cough, wheeze, dyspnea, cyanosis   |
| Cardiovascular | vasodilation, tachycardia, arrhythmia, hypotension, shock |
| Gastrointestinal | swelling of lips/tongue, palatal itch, nausea, vomiting, abdominal cramps, diarrhea |
| Neurologic     | anxiety, headache, seizure, LOC               |

This talk will focus on IgE-mediated food allergies.
Oral Allergy Syndrome or Pollen-Food Allergy Syndrome

- The reaction is due to cross reactivity with the fruit, vegetable, seed or nut with a corresponding pollen
- Symptoms are generally mild and limited to the oropharynx
- In rare cases, systemic reactions can occur
- Management: avoidance of the raw food, but cooked versions are well-tolerated

Oral allergy syndrome is also an IgE-mediated allergy that is due to cross-reacting, homologous proteins between pollens and food proteins. Symptoms are triggered by fresh fruits and vegetables. Commonly associated foods with birch tree pollen are shown in the figure.

Symptoms are mild, and localized to the oropharynx; typical symptoms include lip/mouth itching, and swelling. However, systemic reactions can occur. In a study of 706 patients with OAS, 2.1% of individuals experienced anaphylaxis. [Ortolani C, Pastorello EA, Farioli L, et al. IgE-mediated allergy from vegetable allergens. Ann Allergy 1993 Nov;71(5):470-6.]

Management
Patients are advised to avoid the raw fruits and/or vegetables that trigger symptoms. Heating the food allergens that trigger OAS denatures the relevant protein, therefore-cooked forms of the foods are generally well tolerated. The degree of clinical reactivity can have seasonal variations.
“Food Intolerance”

- Term that encompasses non-Immune food reactions.

- Complaints variable and can include fatigue, brain fog, GI complaints.

- Often delayed symptoms hours to days post consumption

- Example: lactose intolerance is due to inability of the body to break down lactose milk sugar leading to increase bloating and GI pain.
Epidemiology of Food Allergy

Going forward, this presentation will focus on IgE-mediated food allergies that are not oral allergy syndrome.
Epidemiology of Food Allergy

- Estimated 8% of children and 10% of adults in the US are food allergic
- Food allergy prevalence is increasing among children (18% increase from 1997-2007).
- Food allergy reactions are common
  - 42% of children with food allergy report at least 1 lifetime food allergy-related visit to the ED
  - 19% of children with food allergy report at least 1 food allergy-related ED visit in the last year.
- Estimated cost of food allergy is ~$25 billion annually
- Similar trends are seen in other countries across the world

Surveys of the US population suggest that 8% of children and 10% of adults in the US are food allergic. Prevalence of food allergy appears to be increasing over time.

Food allergic individuals are at risk for allergic reactions – many children with food allergies have needed emergency medical attention to treat food-related allergic reactions. Similar data exists for adults with food allergy.

Food allergy carries a significant financial burden on patients, families and society, with the estimated cost of food allergy nearing $25 billion per year in the US.

Similar trends for food allergy are reported by other countries as well.
Similar to data on ED visits for food allergic reactions, increased hospitalizations for food allergy have been reported in recent years.

This bar graph shows the prevalence of hospital discharges with diagnosis of food allergy from late 1990’s to mid 2000’s.
Estimated Prevalence in US Children

<table>
<thead>
<tr>
<th>Food Allergy</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Food Allergy</td>
<td>7.6%</td>
</tr>
<tr>
<td>Peanut</td>
<td>2.2%</td>
</tr>
<tr>
<td>Tree nut</td>
<td>1.2%</td>
</tr>
<tr>
<td>Milk</td>
<td>1.9%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>1.3%</td>
</tr>
<tr>
<td>Egg</td>
<td>0.9%</td>
</tr>
<tr>
<td>Fin fish</td>
<td>0.6%</td>
</tr>
<tr>
<td>Wheat</td>
<td>0.5%</td>
</tr>
<tr>
<td>Soy</td>
<td>0.5%</td>
</tr>
<tr>
<td>Sesame</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

An estimated 39.9% of food allergic children have multiple food allergies.

The most common food allergens causing reactions in children include:

- milk
- egg
- peanuts
- tree nuts
- wheat
- soy
- fish, and
- shellfish

Sesame is increasingly an issue as well.

In this study, the prevalence in children of peanut allergy has increased in 2018 to 2.2%. The same group in 2011 was 2.0%, and in 2008 Sicherer et al.’s had an estimated 1.4%.
The majority of children outgrow their allergy to milk, egg, wheat and soy. However, allergies to peanut, tree nuts, fish and shellfish often persist into adulthood.

Therefore, the most common food allergens for adults are peanut, tree nuts, fish and shellfish.

For some individuals, food allergies do not develop until adulthood.
Diagnosis of IgE-Mediated Food Allergy

No notes.
Diagnosis of Food Allergy begins with the History

- Symptoms within minutes to a few hours of ingesting a food, especially if it is reproducible

- Symptoms can include
  - Skin – itching, hives, flushing, swelling (Most common)
  - Mouth – itching, swelling lips and/or tongue
  - Throat – itching, tightness/closure, hoarseness
  - GI – immediate vomiting, diarrhea, cramps
  - Lung – wheezing, cough, shortness of breath
  - CV – hypotension, tachycardia

History is the most important factor in the diagnosis of food allergy. Symptoms of IgE-mediated food allergy generally develop quickly, within minutes to 2 hours after ingestion. If a specific allergen has triggered symptoms on multiple occasions, then the suspicion for allergy to that food is high.

Allergy symptoms are variable and can affect any body system. Skin symptoms are most commonly seen, though are not seen with every allergic reaction. Symptoms can also affect the mouth, throat, gastrointestinal tract, lung and cardiovascular system.
Associating allergen exposure and symptoms

- Timing of ingestion and onset of symptoms
- Type and quantity of food that triggered the reaction
- Prior exposures to the trigger or related foods
- Association of additional factors such as exercise and concurrent medications

Information regarding timing of ingestion to the onset of symptoms, types of signs and symptoms, type and quantity of food that triggered the reaction, prior exposures to the trigger or related foods, and association of additional factors such as exercise and concurrent medications should be obtained.

A history of symptoms with exposures to the triggering food and lack of symptoms with exclusion of the food is highly suggestive of allergy. Based on the history, selected foods are evaluated by skin prick testing or serum specific IgE testing.
Unlikely to be Food Allergy

• Hives that last more than a few hours (especially over 24 hours) or recurrent over several days
• Reactions that occur only sporadically when the patient eats the food (not every exposure)
• Headaches (migraines), hyperactivity, mood changes
• Chronic nasal congestion or rhinorrhea

Approximately 20% of people believe they have food allergy, but only about half have true allergies.

Here are some examples of concerns that are unlikely to be food allergy.

• Food allergy reactions generally do not manifest as hives that persist for many hours or multiple days, without repeat allergen exposure.
• Food allergies are reproducible such that every exposure to the allergen trigger should trigger symptoms, though the exact symptoms or severity of symptoms may vary with each exposure.
• Headaches, hyperactivity, mood changes, chronic nasal congestion or rhinorrhea are unlikely to be signs of food allergy.
Pathophysiology: Definition

- **Pathophysiology**: IgE production in response to allergen exposure, allergen cross-links IgE on surface of mast cells and basophils leading to release of mediators

Binding of food allergens by specific IgE on effector cells, such as basophils and mast cells, leads to degranulation and mediator release (i.e. histamine, tryptase, cysteinyl leukotrienes, prostaglandin D$_2$), causing a variety of symptoms seen in allergic reactions.
Diagnostic Testing

- Both skin prick testing and specific allergen IgE are tools to show IgE mediated sensitivity to a particular food.

- They do not predict severity of reactions or the dose of allergen that could trigger reactions.

If the history and physical examination are consistent with IgE-mediated food allergy, skin prick testing and/or serum allergen-specific IgE testing can be performed to support the diagnosis.

Both tests provide an indication of the likelihood of allergic reaction with exposure to the food allergen. The results of these tests do not predict the severity of reactions that may occur as a result of allergen exposures.

These tests have high negative predictive values (NPV >95%), so negative tests largely exclude a specific IgE-mediated food allergy.
NIAID Guidelines for the diagnosis of food allergy

- **Guideline 4**: The EP recommends performing an skin prick test to assist in the identification of foods that may be provoking IgE-mediated food-induced allergic reactions, but the skin prick test alone cannot be considered diagnostic of food allergy.

- **Guideline 7**: The EP recommends specific IgE tests for identifying foods that potentially provoke IgE-mediated food-induced allergic reactions, but alone these tests are not diagnostic of food allergy.

While these are useful tests, we know that they are not perfect. The positive predictive value (PPV) is <50% for these tests, therefore a positive test in isolation without a clinical history is not diagnostic for food allergy. Test results need to be taken in the context of history, as cross-reactivity between proteins can give positive IgE test results that may not be clinically relevant.
Oral Food Challenge

• The current gold standard for the diagnosis of food allergy is a Double Blind Placebo Controlled Food Challenge

• These must be performed at centers that comfortable with handling anaphylaxis.

• Reasons for food challenges
  – 1. Determine whether the wrong food is suspected as the cause of symptoms.
  – 2. Prove that a food is NOT the cause of symptoms.
  – 3. Verify whether a patient has outgrown food allergies.
  – 4. Discover the degree of sensitivity.

• The decision to undergo food challenge is a combination of history and diagnostic testing (SPT/immunoCAP)**

When history and skin prick/IgE testing do not provide a diagnosis with high certainty, a food challenge should be performed. Because of the risk for severe allergic reaction (anaphylaxis) during food challenges, this procedure should be performed in settings where medical staff and equipment are readily available.

The gold standard for the diagnosis of food allergy is a double-blind, placebo-controlled oral food challenge – the allergen in question is gradually fed in increasing doses under medical supervision.

**Among children with peanut-specific IgE levels of less than 5kUA/L, 77% tolerated peanut at food challenge if their peanut allergy diagnosis was made on the basis of sensitization only, whereas none of the patients who had confirmed history of reacting to peanut with similar peanut-specific IgE levels passed a food challenge.
### Additional diagnostic tests: Component testing

- Assess IgE binding to individual proteins within a food
- May increase diagnostic accuracy
- May provide indicators for severity or persistence of allergy
- Example: peanut components

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Protein characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ara h 1</td>
<td>Seed storage protein, stable to heating, major allergen</td>
</tr>
<tr>
<td>Ara h 2</td>
<td>Seed storage protein, stable to heating, major allergen</td>
</tr>
<tr>
<td>Ara h 3</td>
<td>Seed storage protein, stable to heating, major allergen</td>
</tr>
<tr>
<td>Ara h 6</td>
<td>Ara h 2 homologue</td>
</tr>
<tr>
<td>Ara h 8</td>
<td>Bet v 1 (birch tree pollen) homologue; heat labile</td>
</tr>
<tr>
<td>Ara h 9</td>
<td>Lipid transfer protein, associated with more severe symptoms as well as oral symptoms in the Mediterranean area</td>
</tr>
</tbody>
</table>

Recent advances in the identification of relevant allergens, and the development of recombinant proteins now allow us to assess IgE binding to individual proteins within a food. This is known as **component testing**.

The hope is that this testing may have increased sensitivity and specificity, and thus diagnostic accuracy. This may assist in the decision-making process to decrease the need for food challenges. And, perhaps provide prognostic information regarding the severity or persistence of the food allergy.

Peanut protein components that are currently available for testing by diagnostic laboratories are listed. Some studies suggest that having elevated IgE levels to specific components are more predictive of allergy, however, there is no consensus at this time for how these tests should be interpreted or cutoff levels.
Unproven tests for Food Allergy

- These are **not** recommended in the evaluation of food allergy.
  - IgG testing
  - Provocation-neutralization testing
  - ALCAT
  - Electrodermal testing
  - Applied kinesiology

These tests are not proven or disproven for food allergy diagnosis. Given the lack of scientific support for these tests, patients should be counseled against pursuing these tests, as well as the potential risks of dietary modification based on these tests.
Management of Food Allergy

No notes.
Avoidance

- Currently, there are no FDA approved therapies for the treatment of food allergies

- Guidelines recommend avoidance of allergens and treatment for any suspected allergic reactions.

- Patients and Parents/Families of patients should be provided education and resources to aid in avoidance.
  - Education and resources on supplementation may be needed depending on the types and numbers of foods to be avoided
    - e.g. vitamin D and calcium in milk allergic infants

These recommendations are in line with the current “Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAD-Sponsored Expert Panel”.

Education on avoidance measures can be found on the ACAAI website (acaai.org) for those wishing to know more information.
Label reading

- **Food Allergen Labeling and Consumer Protection Act (FALCPA)**
  - Passed by the US Congress in 2004
  - Identifies 8 major food allergens estimated to account for 90% of reactions
    - Milk, egg, peanut, tree nuts, soy, wheat, fish, and shellfish
    - Sesame is under consideration for being added
  - These allergens must be listed in **bold** letters underneath the ingredient list
  - Food labeling laws differ around the globe:
    - EU includes top 8 allergens + sesame, celery, mustard, lupine, and mollusks
    - Canada includes top 8 allergens + sesame, mustard, and mollusks

Currently, the FDA is seeking input on sesame allergy (prevalence and severity) in order to decide whether this should be included as the 9\textsuperscript{th}.

The food allergen should also be listed in the ingredients, however the name may be different (such as casein instead of “milk”). Thus, the labeling in bold letters below the ingredients is meant to be as clear as possible.
Precautionary Labeling

- Precautionary labeling includes statements such as “may contain”, “processed in a facility with”, “made on equipment with”, etc.
- Use of precautionary labeling is voluntary
- FALCPA does not currently regulate precautionary labeling disclaimers
- Whether avoidance of products with these disclaimers is warranted is debatable
  - While the risk of reaction to these products is likely low, there is some risk

Some researchers have tried to establish thresholds, such as the eliciting dose that would cause 10% of allergic patients to react. This would help to better define how to label these products. However, thresholds have not yet been defined.
Precautionary Labeling

- Studies have examined protein content in packages with these labels and found detectable levels of allergen in packaged products that contain precautionary labels.

- Allergens were also detectable in some products that did not have allergen labeling or precautionary labeling on the package.

<table>
<thead>
<tr>
<th></th>
<th>Precautionary Label</th>
<th>No allergen declared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>10.2%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Egg</td>
<td>1.8%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Peanut</td>
<td>4.5%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Understand that the levels of detection of allergen in these products is arguably lower than the threshold of reaction for >95% of patients. Thus, a discussion of the risks and benefits of avoiding these foods is good to have with patients and families so that they can understand their risks.
Cross-contact/Cross-contamination

- Can occur anywhere along the food preparation chain
- Can occur at home or at outside eating establishments
  - Allergen can be transferred by shared cooking equipment such as cutting boards, knives, pans, grills, fryers
  - When eating out, patients should communicate their allergies to relevant staff and co-diners
    - Request tables to be cleaned with soap and water or commercial wipes
- Higher risk areas
  - Buffets or self-serve
  - Asian restaurants, bakeries, ice cream shops for nut-allergic patients
  - Seafood restaurants for patients allergic to fish and shellfish

Cross-contamination can occur on farm equipment, in processing facilities, inside the restaurant, at home, etc. There are no studies that examine each of these situations specifically.
Even with avoidance, reactions occur
- Reaction rate ~ 0.81 reaction/year in children ages 3-15 months in one multicenter study

Patients and Parents/Families should be provided with a written emergency action plan that should detail
- The patients’ allergies
- How to assess allergic reactions
- How to treat allergic reactions

The Fleischer study followed 512 children, ages 3-15 months, at enrollment with milk and/or egg allergy at 5 sites (New York, NY; Baltimore, MD; Little Rock, AR; Denver, CO; and Durham, NC).

2/3 were sensitized to peanut. They followed them on averaged 35 months. A total of 1171 reactions were reported by 367 (71.7%) subjects.
Examples of action plans can be found and downloaded freely

- [https://college.acaai.org/sites/default/files/Resources/anaphylaxisactionplan.pdf](https://college.acaai.org/sites/default/files/Resources/anaphylaxisactionplan.pdf)
- [https://www.aap.org/anaphylaxis](https://www.aap.org/anaphylaxis)

Here are examples of action plans that are available for download.
Here is one example of an emergency plan. This one is from the American Academy of Pediatrics.
Treatment for Acute Reactions

- Patients at risk for anaphylaxis should be prescribed auto-injectable epinephrine
  - Epinephrine is the 1st line treatment for anaphylaxis
  - In the United States, auto-injectable epinephrine is available in:
    - 0.1 mg (trade name only)
    - 0.15 mg (trade name and generic)
    - 0.3 mg (trade name and generic)
      - Patients weighing > 25 kg should be switched to the 0.3 mg dose
  - Epinephrine should be injected IM into the outer thigh (vastus lateralis)
  - Most retrospective studies suggest that early administration is key

IM > SubQ in time-to-onset and peaks. Vastus lateralis > deltoid. Every guideline on this topic states that epinephrine is the first line treatment for anaphylaxis.
Given that there is no contraindication to epinephrine, it is not unreasonable to state that any time that there is doubt or concern, it is better to give the epinephrine.

The reason to call 911 after giving epinephrine is NOT because epinephrine can be dangerous. It is because if the reaction were that severe, the patient should be monitored for resolution or sequelae.
Mild Reaction can be Treated with Antihistamines

<table>
<thead>
<tr>
<th>For Mild Allergic Reaction</th>
<th>Monitor Child</th>
</tr>
</thead>
<tbody>
<tr>
<td>What to look for</td>
<td>What to do</td>
</tr>
<tr>
<td>If child has had any mild symptoms, monitor child.</td>
<td>Stay with child and:</td>
</tr>
<tr>
<td>Symptoms may include:</td>
<td>• Watch child closely.</td>
</tr>
<tr>
<td>• Itchy nose, sneezing, itchy mouth</td>
<td>• Give antihistamine (if prescribed).</td>
</tr>
<tr>
<td>• A few hives</td>
<td>• Call parents and child’s doctor.</td>
</tr>
<tr>
<td>• Mild stomach nausea or discomfort</td>
<td>• If more than 1 symptom or symptoms of severe allergy/anaphylaxis develop, use epinephrine. (See “For Severe Allergy and Anaphylaxis.”)</td>
</tr>
</tbody>
</table>

- Example antihistamine doses:
  - cetirizine (0.25 mg/kg up to 10 mg)
  - diphenhydramine (1 mg/kg up to 50 mg)

**Antihistamines should not be given in lieu of epinephrine for anaphylaxis**

It is important to make families and patients aware of the fact that this is not to be used in place or before epinephrine for any concerning reaction.
Anaphylaxis Preparedness Questionnaire

This is a tool that providers can use to assess how prepared their patients are to manage allergic reactions. This can be completed by patients/parents and then reviewed with the health care provider.
Management of Food Allergies in the School Setting

- There are numerous resources to help educate patients and school personnel
  - [https://www.cdc.gov/healthyschools/foodallergies/index.htm](https://www.cdc.gov/healthyschools/foodallergies/index.htm)
- All 50 states have a law in place to either allow or require schools to have “stock epinephrine”
  - To see your state’s status and law:
    - [https://www.foodallergy.org/education-awareness/advocacy-resources/advocacy-priorities/school-access-to-epinephrine-map](https://www.foodallergy.org/education-awareness/advocacy-resources/advocacy-priorities/school-access-to-epinephrine-map)

Local practitioners can work with their states and school systems to better understand how it is being done locally.
How to Handle the Classroom and Cafeteria

- There are no set guidelines for these situations
- Current CDC “voluntary guidelines” provide tips for schools and parents
  - Special seating arrangements can be considered when age and circumstance appropriate (e.g., during meal times, birthday parties)
  - Staff and students should wash their hands and clean surfaces to reduce the risk of exposure to food allergens
  - The importance of not sharing food

*There is no one size fits all for all schools and all families

Different schools and school districts take different measures to decrease risk of allergen exposure for food allergic students in schools. There are no mandated guidelines for school management, but the CDC does provide some guidance.
Allergen Free Tables and Schools?

- Very few studies so limited data available:
  - Self-designated peanut-free schools and schools banning peanuts from being served in school or brought from home reported allergic reactions to nuts.
  - Policies restricting peanuts from home, served in schools, or having peanut-free classrooms are not associated with lower epinephrine administration rates.
  - Schools with peanut-free tables, compared to without, had lower rates of epinephrine administration
    - incidence rate per 10,000 students 0.2 and 0.6, respectively
  - One must consider the social stigma of isolation of “allergen free tables”

*And remember, peanut is only one of the many allergens out there.

This is from one group of public schools in Massachusetts.
- No actual intervention studies.
- Unclear how it is in other states, school systems, private vs public, etc.
Airlines

• Every airline has their own policy regarding travelers with food allergies
  – Families should be counseled to understand these policies, that they differ amongst airlines and that policies can change
• The only data on risk-mitigation come from self-reported, retrospective studies. The following have been reported to lower risk in one study:
  – Requesting a buffer zone, announcement to not eat peanut, or peanut-free meal
  – Wiping tray table
  – Bringing own food
  – Avoiding use of airline blanket/pillow


There are no intervention studies. All data is self-reported. There is no outcomes data on whether or not airline policies actually make a difference.
Risks and Route of Exposures

• Route of exposure is an important concept for families and patients to understand
• Severe reactions generally occur as a result of oral exposure to allergen
• With the majority of allergens, risks of severe reaction to inhalation of vapors or casual skin contact are low.
  – Studies have shown that even in severely allergic patients, peanut butter when near a patient, or even wiped on the skin, does not lead to concerning reactions.¹
  – In addition, peanut allergen can only be detected in the air during active peanut shelling. It can not be detected immediately after shelling is stopped.²
  – The one exception to this may be when the allergen is being cooked or fried, especially with fish or shellfish allergens

In the Simonte article, they masked peanut butter by smell and look, and applied peanut butter versus soy butter on the skin, and had children inhale the fumes. All had anaphylaxis by history or peanut IgE>50. None had respiratory or systemic reaction. Some had redness, itching, or wheal/flare locally with peanut butter.

Johnson article used ELISA to measure detectable peanut protein in air and ground with various scenarios. The air while shelling peanuts could detect very low levels in one sample, but the ground could not.
Prevention of Food Allergy

- New guidelines on timing of peanut introduction have been put out by the National Institutes of Health\(^1\)
  - Guidelines are based on the first randomized controlled study of early introduction of allergen for the prevention of food allergy
  - The Learning Early about Peanut Allergy (LEAP) trial\(^2\)
    - Peanut introduced to high-risk infants at 4-11 months of age
    - Consumption group continued ingestion of peanut at least 3 times/week for 60 months

<table>
<thead>
<tr>
<th></th>
<th>Peanut Consumption Group</th>
<th>Peanut Avoidance Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanut Allergy at 60 months of age</td>
<td>1.9%</td>
<td>13.7%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>


The NIH guidelines and updates are specific to peanut allergy. The Du Toit article is the “LEAP” article.

In the LEAP article, the effect was much greater in those that actually ate peanut 3 times per week (the per-protocol analysis), than in all comers who were randomized (the intention-to-treat analysis).
The current infant feeding guidelines address 3 groups of infants:

- For infants with severe eczema and/or egg allergy, the recommend is to strongly consider evaluation of peanut allergy.
- For infants with mild-moderate eczema, recommendation is to introduce peanut containing foods around 6 months of age in age-appropriate forms.
- For infants with no history of eczema or food allergy, peanut containing foods can be introduced in an age-appropriate manner and in accordance with family preferences and cultural practices.
For Infants with Severe Eczema and/or Egg Allergy

Severe eczema or egg allergy or both

Peanut sIgE

- <0.35
  - Risk of reaction low. Over 90% will have (c) SPT to peanut.
  - Options: a) Introduce peanut at home; b) Supervised feeding in the office (based on provider/parental preference)
  - Refer to specialist for consultation/SPT protocol

- ≥0.35
  - Risk of reaction varies from moderate to high.
  - Options: a) Supervised feeding in the office; b) Graded OFC in a specialized facility

Peanut Skin Prick Test

- 0-2 mm
  - Risk of reaction low. (95% will not have peanut allergy).
  - Options: a) Introduce peanut at home; b) Supervised feeding in the office (based on provider/parental preference)

- 3-7 mm
  - Risk of reaction varies from moderate to high.
  - Options: a) Supervised feeding in the office; b) Graded OFC in a specialized facility

- ≥8 mm
  - Infant probably allergic to peanut.
  - Continue evaluation and management by a specialist

This is meant to help primary care providers. They can order the peanut-specific serum IgE in their patients if they feel comfortable doing this. This should be done as early as possible (ideally 4-6 months of age) so that if negative, they can start the introduction, and if positive, they can be referred to an allergist.
Early Introduction Notes

- A practical guide on how to introduce peanut can be found on the ACAAI website https://acaai.org/news/new-guidelines-show-how-introduce-peanut-containing-foods-reduce-allergy-risk
- ACAAI joint venture with the National Peanut Board: https://preventpeanutallergies.org
- Early introduction may also be of benefit for egg
- More studies are needed to determine whether early introduction of other allergens could be of benefit in high-risk populations
- Or if early introduction in the general population is beneficial


There are more than 1 egg intro studies, and meta-analysis suggest it to be beneficial.

The EAT trial (Perkins et al.) suggested that early intro of foods was not beneficial in general/breastfed population (although it may have decreased allergy rates to peanut and egg in the per-protocol analysis).
Food Allergy Treatment

No notes.
Treatment for Food Allergy

- While there are no approved therapies for food allergy, current research is showing efficacy of immunotherapy for food allergies
  - Immunotherapy for food allergy works similar to "allergy shots"
  - Current research has shown immunotherapy can be effective for different foods using various routes of exposure

Older studies suggest that allergy shots could actually work for food allergies (specifically peanut), but the adverse effects were too great to continue as a primary treatment option.
Routes of Immunotherapy for Food Allergy

- **Oral immunotherapy (OIT)**
  - Ingesting increasing amounts of the food over time until a target “maintenance dose”
  - Daily oral dosing, dose increases occur under medical supervision

- **Epicutaneous immunotherapy (EPIT)**
  - Patch containing the food protein is placed on the skin daily
  - Fixed amount of allergen on the patches

- **Sublingual immunotherapy (SLIT)**
  - Holding a small volume of liquid with the allergen under the tongue
  - Daily dosing

For EPIT, there is only one company that has a device for this that is currently being studied. Realize that OIT is currently being practiced off label by allergists around the country.

SLIT has not progressed to the point of having a product that is being tested for the goal of an FDA approved product.
Example of Oral Immunotherapy Schedule

This is meant to give an example of how the up-dosing is done in most studies. The rush build up is rarely used, and only in small studies.

For now, maintenance is likely to be life-long.
Efficacy of Immunotherapy

• Data to date suggest that the efficacy of OIT > SLIT > EPIT
  – No studies have directly compared treatment approaches

• These effects are likely due to dose differences:
  EPIT (250mcg) < SLIT (2.5mg) < OIT (300mg)

• There have been randomized, double-blind, placebo-controlled Phase 3 studies examining EPIT and OIT for peanut immunotherapy

There is some thought that EPIT efficacy increases with time on therapy as well.
Adverse Events

• Data suggests that safety of EPIT > SLIT > OIT

• Oral immunotherapy¹
  – GI symptoms the most common (abdominal pain, vomiting)
  – Followed by oral itching
  – 11.6% from the active group withdrew due to adverse events

• Epicutaneous immunotherapy²
  – Local skin reactions the most common
  – 1.7% from the active group withdrew due to adverse events


This is Phase III data for OIT and EPIT. It is important to note that there are no studies that directly compare OIT and EPIT.
Goals and Roles of Therapy

- Goals of immunotherapy may differ between physicians and families and from one patient to another
  - Some families simply want a “safeguard” from accidental ingestions.\(^1\)
  - Others may want a cure for the food allergy.
- With OIT, a small portion of subjects who complete the therapy achieve “sustained unresponsiveness”\(^2,3\)
  - However, this has not been assessed for EPIT and SLIT
- Because the therapies differ and goals of patients/families differ, a shared decision making approach will need to be used if multiple therapies become available.


The Greenhawt article interviewed families who enrolled in one of the EPIT or OIT studies. The Burks article was Egg OIT and published in NEJM. The Vickery article was peanut OIT.

Sustained unresponsiveness was defined by tolerating a set dose (greater than at baseline) after stopping therapy for up to 2 months.

As of 1/10/19, EPIT removed their FDA application and peanut OIT has not filed application.
Other Therapies Under Investigation

- Adjuvants to immunotherapy are being tested in hopes of improving efficacy and/or safety
  - Examples include anti-IgE therapy and probiotics
- Anti-IgE therapy has also been studied as a mono-therapy for peanut allergy
- Other approaches include vaccines using modified peanut proteins, anti-cytokine therapy, Chinese herbal therapy, combination therapies

The Wood article examined omalizumab given prior to, and at the first part of an OIT protocol.

The Tang article compared OIT plus probiotics to placebo OIT and placebo probiotics. It did **NOT** compare OIT to OIT+probiotics

The Leung article examined an anti-IgE monotherapy which was an older drug (not omalizumab), however omalizumab will be studied as a monotherapy in the future.

The Begin article was on multi-food OIT, which has only been reported out of a single center. There are no good data on multi-food OIT to date.
Take-home points

No notes.
Summary

• Food allergy affects up to 10% of the US population
• Diagnosis relies on history, with testing providing supportive information
• Allergen avoidance, education, and preparation for emergencies are the mainstays of current management
• Several new therapies are in clinical trials

No notes.
Approach to patients presenting with concern for food allergy

- If history & time course is highly suspicious for a food allergy, recommend avoidance of identified triggers.

- Targeted testing can be performed to only suspected foods (panel testing should **NOT** be done).

- Provide guidance for allergen avoidance, prescribe epinephrine auto-injector and educate on management of allergic reactions

- Refer to Allergy for assistance in confirming the diagnosis and counseling

Take home points:

- A detailed history of allergen exposure and reaction is important.
- A dietary history is necessary as well - if the patient is eating the food without reactions, he/she is by definition not allergic to that food, so do not test tolerated food.
- Indiscriminate testing results in false positives and results in unnecessary food avoidance and burden/stress on the patient/family.
Additional Resources

- For Patients: https://acaai.org/allergies/anaphylaxis
- Patient Video: Introducing peanut-containing foods to prevent peanut allergy
- Early Peanut Introduction Partnership Website
- COLA: Update on Food Allergy

References


No notes.