Food Allergy
Diagnosis and Management

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Adverse Food Reactions

IgE Mediated
- Anaphylaxis
- Oral Allergy Syndrome
- Latex Fruit Syndrome

Immunologic Reactions
- Celiac Disease
- Dermatitis herpetiformis
- Allergic Colitis
- Asthma

Mixed IgE/Non IgE
- Eosinophilic Esophagitis
- Eosinophilic Gastroenteritis
- Atopic dermatitis
- Asthma

Non IgE Mediated
- Celiac Disease
- Dermatitis herpetiformis
- Allergic Colitis
- FPIES
- Contact Dermatitis

Toxic Reactions
- Scombroid
- Ciguatera
- Lactose Intolerance
- Aversion
- Tyramine
- Metabisulfites
Food allergy is an adverse health effect arising from specific immune response that occurs reproducibly upon exposure to a food.

Oral tolerance (or lack of) is a key concept.

There are different types of food allergy based on different immune mechanisms.

The best way to identify an IgE mediated reaction is to assess the time interval between ingestion of food and onset of symptoms - < 2 hours.
A 30 y.o. woman with recurrent hives w/o any other symptoms for 6 months without obvious trigger has a food allergen panel which is positive for milk. Pick the true statement:

A. She’s likely allergic to milk and should avoid it.

B. Food allergen panels should generally not be ordered.

C. Because milk is a staple food she should be desensitized.

D. Skin testing should be used to supplement the blood test.

E. Patients with recurrent hives often have an occult food allergen which requires careful history and testing to uncover.
Recurrent typical hives over several week without an obvious food trigger = chronic idiopathic urticaria.
1. Recurrent hives
2. Over several weeks
3. No historical trigger

Chronic Idiopathic Urticaria
Food Allergy

• 2% of dietary protein is absorbed and disseminated throughout the body in intact form.

• In certain patients ‘oral tolerance’ fails to develop and food allergy results.

• Food allergy is rarely the cause for recurrent episodes of hives and swelling. These patients are generally diagnosed with ‘chronic idiopathic urticaria’.

• About 50% of skin tests for foods are false positive.
## Overview of Food Allergy

### TABLE I. Prevalence of food allergies in the United States

<table>
<thead>
<tr>
<th>Food</th>
<th>Young children</th>
<th>adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>2.5%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Egg</td>
<td>1.3%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Peanut</td>
<td>0.8%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>0.2%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Fish</td>
<td>0.1%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>0.1%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Overall</td>
<td>6%</td>
<td>3.7%</td>
</tr>
</tbody>
</table>
IgE Mediated Food Allergy

• Diagnosis is based on the combination of an appropriate history of reaction after a food along with a positive test for specific IgE to that food.

• **History + Test = Diagnosis**

• The time interval between ingestion of the food and onset of symptoms is almost always $\leq 2$ hours.

• 95% of IgE mediated food allergy is associated with the following 8 foods: peanut, tree nut, seafood, egg, milk, and soy.
IgE Mediated Food Allergy

• Symptoms are the same as for any anaphylactic reaction:
  • **Skin** – Hives, flush, angioedema, itching
  • **Pulmonary** – wheeze, shortness of breath, chest tight
  • **GI** – nausea, vomiting, diarrhea
  • **Nasal and ocular** – rhinorrhea sneezing
  • **Cardiovascular** – low BP – collapse/LOC
IgE Mediated Food Allergy

• Treatment = avoidance and portable epinephrine kit.
• There are 3 epinephrine syringes available which come in 3 strengths – 0.10, 0.15 and 0.3 mg.
• Epinephrine should be used for any reaction that involves more than a few hives.
• Any reaction can potentially progress to a fatal reaction.
• Risk factors for a fatal reaction:
  • prior severe reactions
  • poorly controlled asthma,
  • delay in administration of epinephrine
Food Allergy - Testing

• The skin prick test and blood allergy test both measure the presence of specific IgE.

• Because the skin test detects IgE bound to the surface of the mast cell whereas the blood test detects free IgE – they may occasionally be discordant.

• The term “RAST” is outdated.

• Skin testing is generally more accurate, quicker, and less expensive.

• Avoid food allergy panels.
Food Allergy - Testing

• Positive testing denotes sensitization – not necessarily allergy.

• Measurement of serum total IgE is of little value.

• Intradermal testing should be avoided for food testing.

• Testing with the fresh food is occasionally helpful - OAS.

• Probability curves that will predict the results of a food challenge are based on the results of specific IgE testing.
Serology Predicts Risk of Reaction

![Graph showing the relationship between decision level (kU/L) and probability for Peanut.](image-url)
Evaluation of Food Allergy

Strong clinical story and positive skin test $\rightarrow$ Avoidance

Weak clinical story and positive skin test $\rightarrow$ Specific IgE

If specific IgE is high $\rightarrow$ Avoidance

If specific IgE is low $\rightarrow$ Consider food challenge.

If after clinical history, skin test, and specific IgE the situation is still unclear consider component testing.
Component Testing

- Food allergens/reagents are made up of many individual proteins – 10-15.

- Measuring levels of IgE to these individual proteins can help identify truly allergic patients – as opposed to those who are just sensitized.

- Peanut allergen is composed of Ara H1 through Ara H9.

- Patients with high level sensitivity to Ara H1 or Ara H2 often have true anaphylaxis.

- Patients with mostly sensitivity to Ara H8 or 9 often have cross reaction from grass sensitivity.
Food Allergy – Tests that we shouldn’t order.

- IgG food antibodies.
- Provocation-Neutralization tests.
- Due to the lack of evidence to support its use, many organizations, including the American Academy of Allergy, Asthma & Immunology, the Canadian Society of Allergy and Clinical Immunology and the European Academy of Allergy and Clinical Immunology have recommended against using IgG testing to diagnose food allergies or food intolerances / sensitivities.
Oral Food Challenge

• A food challenge is very helpful to confirm that a patient has outgrown their allergy.

• The double blind placebo controlled food challenge (DBPCFC) is the gold standard; although a single blind challenge or open feeding maybe helpful if negative – or objectively positive.

• If the patient only develops *subjective symptoms* then it may be necessary to proceed to a DBPCFC.
Oral Food Challenge

• The food in question will need to be eliminated for 2 weeks prior.

• Prior to the challenge FEV1 must be > 70%.

• The first dose is a sub-threshold dose which is then tripled every 20 minutes until a serving size portion has been ingested.

• Food challenges prevent unnecessary dietary avoidance (if negative) & enhance compliance with elimination diet (if positive).
Food Allergy - Milk

• Milk is most common food allergy in children.
• 80% will outgrow by their 5\textsuperscript{th} birthday.
• Children with milk allergy tend to consume less calcium and protein and have been found to have lower height for age percentile.
• Consultation with a nutritionist may be helpful.
• 95% percent will tolerate an extensively hydrolyzed formula – whereas partially hydrolyzed formulas will cause allergy symptoms in 1/3 – ½ of patients with milk allergy.
Food Allergy - Milk

- In general partially hydrolyzed formulas are not considered hypoallergenic – ½ might tolerate.
- Skin testing with the formula and ingestion of the first dose in the physicians office may be wise.
- IgE mediated – follow skin or blood test until challenge is appropriate.
- Non-IgE mediated (other than FPIES) – every 6-12 months a gradual reintroduction is appropriate.
What percentage of children with egg allergy (IgE) will tolerate ingestion of egg in a baked good?

A. 1%
B. 5%
C. 20%
D. 70%
E. 98%
Food Allergy - Egg

• 50 - 80% of children with egg allergy may tolerate eggs in extensively baked goods.

• Ingesting cooked eggs may actually speed the resolution of egg allergy - OIT.

• There is no longer a recommendation about delaying introduction of egg.
Food Allergy - Egg

• One observational study suggests that introduction of egg at 4 – 6 months of age results in a lower rate of allergy compared with introduction at 12 months.¹

• For quality of life, nutritional, and possibly immunologic reasons, it is often helpful to perform a “brownie challenge” for patients with egg (or milk) allergy.

1. JACI 2010 vol 126; 807-13
**Flu Vaccine/Egg Allergy**

- Influenza vaccine (along with yellow fever and rabies vaccine) may contain small amounts of egg protein.

- For patients with egg allergy the risk benefit ratio falls in favor of them receiving the vaccine.

- Risk of anaphylaxis has been falling as egg protein levels in vaccine have been falling.

- Current recommendation is:
  - prior rxn = hives – give any flu vaccine
  - prior rxn = anaphylaxis – give any flu vaccine in an inpatient or outpatient setting.
Shrimp allergy is a relative contraindication for the administration of radiographic contrast media?

A. True
B. False
IgE Mediated Food Allergy

Natural History

- Milk – 80% outgrow by 5\textsuperscript{th} birthday.
- Egg – 60% outgrow by age 10.
- Soy – 50% outgrow by age 6.
- Shellfish – 1% outgrow per year.
- Peanut – 20% outgrow allergy lifetime.
- Tree nuts – 20% may outgrow long term.

*Lower specific IgE levels and smaller skin prick test results tend to predict that a patient is outgrowing their allergy.*
Delayed Anaphylaxis

• Certain patients in the mid-Atlantic States have been noted to have delayed onset of anaphylaxis 4 – 6 hours after consumption of mammalian meat (beef, pork, and lamb).

• Patients in the same region have had anaphylaxis to Cetuximab with the first exposure.

• Both of these groups of patients have been noted to have antibodies to galactose-\(\alpha\)-1,3 galactose (alpha-gal).

• Testing for antibodies to alpha-gal has been suggested prior to treatment with cetuximab.

• Development of these antibodies is thought to be related to tick exposure.
Oral Allergy Syndrome

• Certain fruits, vegetables, and nuts contain antigens that cross react with airborne pollen.

• First sensitized to pollen experience oral symptoms upon ingestion of relevant fruits.

• Patients experience itching and burning of the mouth immediately on ingestion of the fruit/nut.

• Anaphylaxis is rare in this setting.

• Heating or processing the fruit will often eliminate the symptoms.

• Immunotherapy to pollen may improve symptoms.
The Latex-Fruit Syndrome

• About 40% of patients with latex allergy will react (usually anaphylaxis) to certain cross reactive fruits.

• The most commonly reported fruits are avocado, banana, chestnut, and kiwi.

• The syndrome should be discussed in patients with latex allergy and skin testing considered.

• The main risk groups for latex allergy are atopic patients, children with spina bifida, health care workers, and patients with multiple surgeries.
Which of the following regarding peanut allergy is false?

A. Cross reactivity with pea is about 5%.
B. 20% of children will outgrow peanut allergy.
C. Cross reactivity with lupine is high.
D. Current recommendation is to avoid until age 3.
E. It is safe for a child with severe peanut allergy to touch peanuts.
Food Allergy - Peanut

• Accounts for about half of food related fatalities.
• 20% of patients will outgrow peanut allergy.
• The typical patient reacts at about 1/3 of a peanut kernel.
• A sibling of a peanut allergy patient is at increased risk.
• Peanut is a bean (legume) and may cross react with other legumes. (5%)
Food Allergy - Peanut

- Lupine is a legume that has high cross reactivity with peanut.

- Most peanut allergic patients do not have tree nut allergy, but may often choose to avoid it based on risk of cross contamination.

- ‘Cold pressed’ or gourmet peanut oil should be avoided. Highly refined peanut oil is ok for allergic pts to eat.

- High risk areas include Asian restaurants, bakeries, and ice cream parlors.
Food Allergy - Peanut

• 4% of children who outgrow peanut allergy experience a recurrence; this is more common in children who did not put this back into their diet.

• Parents often express concern about casual contact with peanuts.

• Simonte et al had 30 children with severe peanut allergy have peanut butter smeared on their arm – no one reacted.¹

• Children with higher levels of sensitivity do exist but they are uncommon.

# Food Allergy – Fatalities

Table I. Food fatalities 2001-2006

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (y)</th>
<th>M/F</th>
<th>Date</th>
<th>Culprit</th>
<th>Asthma</th>
<th>Previous history</th>
<th>Food</th>
<th>Location</th>
<th>Timely epinephrine</th>
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<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>M</td>
<td>3/11/2001</td>
<td>Nuts</td>
<td>Yes</td>
<td>Yes</td>
<td>Nut bowl</td>
<td>Restaurant</td>
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<td>2</td>
<td>16</td>
<td>M</td>
<td>5/9/2001</td>
<td>Walnut</td>
<td>Yes</td>
<td>Yes</td>
<td>Chinese food</td>
<td>School, cooking class</td>
<td>Probably</td>
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<td>3</td>
<td>9</td>
<td>M</td>
<td>5/18/2001</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Cookie</td>
<td>School outing</td>
<td>No</td>
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<tr>
<td>4</td>
<td>24</td>
<td>F</td>
<td>11/26/2001</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Chinese food</td>
<td>Home</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>F</td>
<td>10/30/2001</td>
<td>Nut meats</td>
<td>Yes</td>
<td>Yes</td>
<td>Candy</td>
<td>Home of friends</td>
<td>No</td>
</tr>
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<td>6</td>
<td>16</td>
<td>M</td>
<td>11/5/2002</td>
<td>Milk</td>
<td>Yes</td>
<td>Yes</td>
<td>Bread</td>
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<td>7</td>
<td>31</td>
<td>M</td>
<td>12/13/2002</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Catered food</td>
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<td>8</td>
<td>50</td>
<td>M</td>
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<td>Yes</td>
<td>Cookie</td>
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<td>No</td>
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<tr>
<td>9</td>
<td>12</td>
<td>F</td>
<td>3/14/2003</td>
<td>Peanut</td>
<td>Unk</td>
<td>Unk</td>
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<td>10</td>
<td>18</td>
<td>M</td>
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<td>Unk</td>
<td>Wrap</td>
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<td>M</td>
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<td>Yes</td>
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<td>Restaurant</td>
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<tr>
<td>13</td>
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<td>M</td>
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<td>Yes</td>
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<td>Yes</td>
<td>Cookie</td>
<td>Home of friends</td>
<td>No</td>
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<tr>
<td>15</td>
<td>21</td>
<td>F</td>
<td>10/9/2003</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Brownie</td>
<td>College</td>
<td>No</td>
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<tr>
<td>16</td>
<td>18</td>
<td>M</td>
<td>1/20/2004</td>
<td>Shrimp roll</td>
<td>Yes</td>
<td>Unk</td>
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<td>17</td>
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<td>Baked clam</td>
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<td>Yes</td>
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<tr>
<td>19</td>
<td>17</td>
<td>F</td>
<td>4/6/2004</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Peanut butter</td>
<td>Camp</td>
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<tr>
<td>20</td>
<td>34</td>
<td>F</td>
<td>5/29/2004</td>
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<td>Unk</td>
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<td>Thai dish</td>
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<tr>
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<td>8/1/2004</td>
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<td>Unk</td>
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<td>22</td>
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<td>Milk</td>
<td>Unk</td>
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<td>Milk</td>
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<td>Yes</td>
</tr>
<tr>
<td>23</td>
<td>22</td>
<td>F</td>
<td>10/29/2004</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Dessert</td>
<td>Restaurant</td>
<td>No</td>
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<tr>
<td>24</td>
<td>14</td>
<td>F</td>
<td>1/22/2005</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Egg roll</td>
<td>Restaurant</td>
<td>No</td>
</tr>
<tr>
<td>25</td>
<td>36</td>
<td>M</td>
<td>3/21/2001</td>
<td>Peanut</td>
<td>Yes</td>
<td>Yes</td>
<td>Brownie</td>
<td>Work</td>
<td>No</td>
</tr>
</tbody>
</table>
Table 4. Strategies for Dining out with Peanut Allergy

Identify the diet request as a life-threatening allergy, not just a preference
Avoid Asian restaurants, ice cream shops, and bakeries
Identify the individual(s) in the restaurant who are responsible for the ingredients
Remind the restaurant personnel about issues of cross-contamination and hidden peanut
Avoid buffets
Be wary of desserts, especially ice creams and baked goods
Be wary of multi-ingredient, mixed items (stews, sauces dressing, sauces, soups, chili)
If there is an error, hold the dish and have the management bring a newly prepared order
If the patron is uncomfortable in trusting the establishment, leave
Food Allergy Prevalence

- Why is food allergy becoming more common?
- Prior prevention strategies focused on avoidance during pregnancy – nursing – and early life.
- It now appears that early oral exposure is beneficial – oral tolerance.
- Topical exposure appears to be a risk factor for allergy.
- Studies randomizing high risk children to exposure at 4-6 months vs usual care show 90% reduction in peanut allergy.
Prevalence of Peanut Allergy

Peanut Protein Consumption 8 - 14 month

United Kingdom: 0 g/week  
Israel: 7.1 g/week  

p < 0.001

Prevalence of Peanut Allergy in Children 4 - 18 yrs

United Kingdom: 1.85%  
Israel: 0.17%  

p < 0.001
LEAP Study

A Intention-to-Treat Analysis

SPT-Negative Cohort (N=530)

- Avoidance Group: 13.7%
- Consumption Group: 1.9%

P < 0.001

SPT-Positive Cohort (N=98)

- Avoidance Group: 35.3%
- Consumption Group: 10.6%

P = 0.004

Severe eczema
or
egg allergy
or
both

Peanut sIgE*

< 0.35
Risk of reaction low (more than 90% will have (-) SPT to peanut).
Options:
 a) Introduce peanut at home  
 b) Supervised feeding in the office (based on provider/parental preference)

≥ 0.35
Refer to specialist for consultation/SPT protocol

Peanut skin prick test (SPT)

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 oral food challenge in a specialized facility

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

Oral Immunotherapy

- LEAP study showed that even sensitized but non-allergic children benefit from peanut introduction.
- What if truly allergic children gradually ingest peanut?
- Subcutaneous immunotherapy for peanut failed.
- Oral immunotherapy (OIT) has been tried with significant success.
Oral Immunotherapy

• **Desensitization** - a state where patients may ingest the allergenic food if they maintain daily (or regular) exposure to the allergen.

• **Sustained unresponsiveness** - the ability to truly eat the allergic food intermittently only.

• OIT is able to achieve desensitization about 75% of the time but true tolerance about 50% of the time although it is not clear how durable this response is.

• Standard care at the current time is to only allow patients to eat the food if they maintain regular dosing.
FIG 2. Patterns of response to the food OIT.
Thank You!

Questions?