ADVERSE FOOD REACTIONS

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Disclosures

- I do not have any relevant financial or commercial interests to disclose.
- I do not intend to discuss an unapproved or investigative use of a commercial product/device in my presentation.

Learning objectives

- To identify the differences between IgE-mediated and non-IgE-mediated adverse food reactions
- Evaluation and management of IgE-mediated food allergy
- Evaluation and management of food protein-induced enterocolitis syndrome
- Evaluation and management of food protein-induced allergic proctocolitis
- Evaluation and management of eosinophilic esophagitis

Categories of adverse food reactions

- Food allergy: abnormal immunologic response to a food
  - May be IgE- and/or non-IgE-mediated
- Food intolerance: non-immunologic reaction to a food caused by a metabolic, pharmacologic and/or toxic mechanism
  - Examples: lactose intolerance, scromboid poisoning, sulfite sensitivity

https://utswmed.org/medblog/kids-food-allergies-can-affect-gi-tract-symptoms-parents-should-know/

Types of food reactions

- IgE-mediated:
  - **IgE-mediated hypersensitivity to food protein**
  - IgE-mediated hypersensitivity to food-associated carbohydrate
  - **Oral allergy syndrome**
- Non-IgE-mediated:
  - **Food protein-induced proctitis/proctocolitis**
  - Food protein-induced enteropathy
  - **Food protein-induced enterocolitis syndrome (FPIES)**
  - Food-induced pulmonary hemosiderosis (Heiner syndrome)
  - Celiac disease
- Mixed IgE and non-IgE-mediated:
  - Atopic dermatitis
  - **Eosinophilic gastrointestinal disorders (EGID)**

Slide courtesy of Tim Moran

Clinical Case #1

- A 6 month old full-term male presents to clinic for facial rash after ingesting peanut butter for the first time

Clinical Case #1

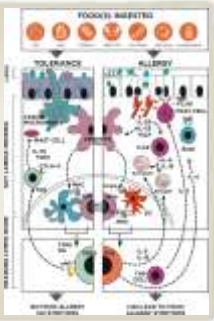
- PMH: History of eczema— controlled with topical corticosteroids
- PSH: none
- Family Hx: Dad has seasonal allergies and mom had eczema as a child
- Additional information pertaining to reaction:
  - *How much was ingested?*
  - *Was this the first exposure?*
  - *How quickly after eating the food did symptoms occur?*
  - *Any additional symptoms (hives, swelling, vomiting, diarrhea or respiratory)?*

Initial Allergy & Immunology clinic visit

- He was referred to our clinic after food panel was drawn with the following results:
  - *Peanut* sIgE 4.5 , *Egg white* sIgE 3.3, *Cow's milk* sIgE 5.5 , *Wheat* sIgE 2.1
  - *Cashew* sIgE 3.7 , *Pistachio* sIgE 2.4, *Pecan* sIgE 5.1, *Walnut* sIgE 6.3, *Hazelnut* sIgE 0.9, *Almond* sIgE 1.7
- On further history, he previously consumed egg and yogurt without issue (was instructed by PCP to stop eating these foods due to positive results) but he has never had wheat or tree nuts
- SPT was performed for further evaluation to peanut (8 mm), tree nuts (cashew 3 mm, pistachio 2 mm, pecan 4 mm, walnut 4 mm, hazelnut 3 mm and almond 5 mm) and wheat (3 mm)

IgE-mediated food allergy versus sensitization

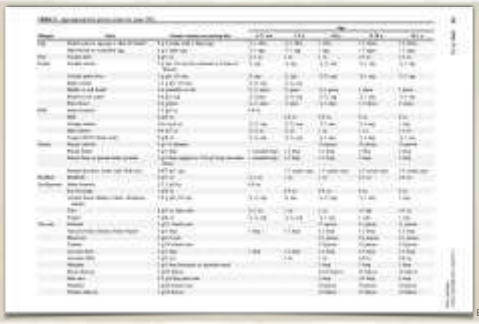
- Sensitization: presence of allergen-specific IgE bound mast cells to the offending allergen
  - Does not always result in an allergic disorder
- When sensitization and allergic clinical symptoms are both present, we diagnosis allergy.
- In patients with a food allergy, upon exposure to the offending allergen the mast cells with specific IgE bind to allergens causing local inflammation and allergic symptoms.



https://link.springer.com/article/10.1007/s12016-018-8710-3/figures/3

Next steps

- How would you advise the family?
  - Depending on comfort level of the family, I would recommend at home introduction to foods previously tolerated
  - If family was hesitant to reintroduce, then we would proceed with an in office challenge
  - For positive testing with foods that he has not consumed, we would schedule an in office challenge
  - I recommend continued avoidance of peanut with repeat testing in 1 year
    - EpiPen prescribed



Bird et al JACI 2009

Oral food challenge protocol

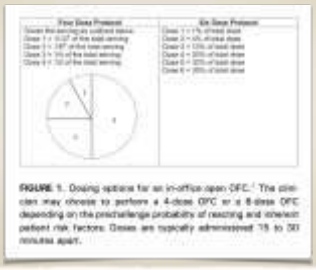


FIGURE 1. Dosing options for an in-office open OFC.[1] The clinician may choose to perform a 4-dose OFC or a 6-dose OFC depending on the prechallenge probability of reacting and inherent patient risk factors. Doses are typically administered 15 to 30 minutes apart.

Bird et al JACI 2009

Clinical Case #2

- An 8 month old full-term female who presented to the ER with numerous episodes of projectile vomiting and lethargy.
- Mom denies sick contacts and reports that she does not attend daycare.
- Mom reports giving her baby oatmeal a few hours prior to symptoms.

Additional history

- PMH: born full-term via SVD
- PSH: none
- Family hx: paternal cousin with celiac disease
- Developmental hx: age-appropriate
- Social history: lives with parents and older brother
- ROS: + vomiting, lethargy and decreased PO
- Immunizations: UTD

Hospital admission

- Laboratory evaluation:
  - CBC w/diff: WBC 14.4, Hgb 10.8, *Plt 491*
  - Stool occult blood: *negative*
  - GI pathogen panel: *none*
- She was discharged home from the ER after receiving fluids

Differential diagnosis

- Food protein-induced enterocolitis syndrome
- Infectious gastroenteritis
- Sepsis
- Food aversion
- Inborn errors of metabolism
- Neurologic disorders (cyclic vomiting)
- GERD
- Food protein-induced enteropathy
- Eosinophilic gastroenteropathies
- Celiac disease
- Immune enteropathies
- Obstruction problems

Initial Allergy & Immunology clinic visit

- A 12 month old female with well-controlled eczema presented to our clinic for an initial evaluation of repetitive projectile vomiting at 8 months old concerning for food protein-induced enterocolitis syndrome
- Parents introduced a variety of food into her diet without issue including green beans, pumpkin, banana, avocado, carrots, squash, cow's milk and soy
- Treatment plan:
  - Continue avoidance of rice and oatmeal.
  - Continue age appropriate food introductions.
  - Recommend skin testing for oat at 26 months old or older. If negative, proceed with at home introduction of oatmeal. If skin testing positive, proceed with in office food challenge to oatmeal.

Non-IgE mediated food reactions

- Generally present with delayed or chronic GI symptoms
- Severity can range from mild to severe
- Diagnosis is generally based on clinical findings
  - Reproducible clinical symptoms upon exposure to a food with resolution upon specific food avoidance
  - Food sIgE may be present, but symptoms are not consistent with immediate hypersensitivity reaction

FPIES Clinical presentation

- Usually presents in infancy
  - Early infancy: CM/soy (when introducing formula)
  - At 4-6 months: solid foods
  - Rare for adult onset (fish/shellfish)
- Incidence ranges 0.015-0.7%
- Slight male predilection (52 to 60%)
- Reports of FPIES in siblings of an affected child are rare
- Can present with chronic and/or acute symptoms

Table 1 Common food co-allergies in children with FPIES [1]

FPIES to	Clinical cross-reactivity/ co-allergy	Observed Occurrence*
Cow's milk	Soy	<10–40%
	Any solid food	<10%
Soy	Cow's Milk	<30–40%
	Any solid food	<10%
Solid food (any)	Another solid food	<44%
	Cow's milk or soy	<25%
Legumes*	Soy	<80%
Grains, rice, oats, etc*	Other grains (including rice)	about 30%
Poultry*	Other poultry	<40%

*Where a child already tolerates a food type in a particular group (e.g. beans), clinical reactions to other members of the **same** group (e.g. other legumes) are unlikely. Caution is warranted in interpreting these data as they were derived from single centers and from patient populations skewed towards the more severe phenotype of FPIES and may overestimate the actual risk of co-allergy

UpToDate

Infant food introduction guidelines

UpToDate

Acute FPIES management

UpToDate

Follow-up Allergy & Immunology visit

- Pt is now 30 months old and presented back to clinic to discuss next steps for possible oat reintroduction.
  - Introduced a variety of other foods including avocado, egg, peanut, tree nuts, vegetables and fruits
- Since she has been avoiding oat since she was 8 months old, evaluation for development of an IgE-mediated allergy prior to introduction of oat is warranted.
- Skin prick testing was negative to oat
- Plan to proceed with at home introduction of oat

Food protein-induced proctitis/proctocolitis

- Typically presents as rectal bleeding in otherwise healthy infant within the first few months of life
- Cow's milk and soy are most common triggers
- No specific laboratory testing
- Allergy testing NOT recommended
- Management is avoidance of trigger food
  - If breastfed, complete elimination of milk from mother's diet
  - If formula fed or no improvement with maternal elimination diet, then give extensively hydrolyzed formula
- Trigger foods can usually be gradually reintroduced at 1 year of age
  - If symptoms recur after reintroduction, wait 6 months and then try again

Oral allergy syndrome

- Oral allergy syndrome: form of contact allergic reaction that occurs upon contact of the mouth and throat with certain raw fruits and vegetables in individuals with allergic rhinitis.
  - Driven by cross-reacting allergens found in both pollen and raw fruits vegetables and some tree nuts in sensitized individuals.
- Cooked forms of fruit and vegetable are often tolerated because the proteins are distorted during the heating process
- Treatment: recommend avoidance of foods in the fresh form; some evidence that allergen immunotherapy can alter reactions

Clinical case #3

- 14 year old male with history of allergic rhinitis and eczema presents with poor weight gain and abdominal discomfort
- On further discussion, he reports limiting meats and starchy foods due to discomfort and feels that food gets stuck in his throat
- Family reports he does cut food into small pieces and takes longer than everyone else to eat

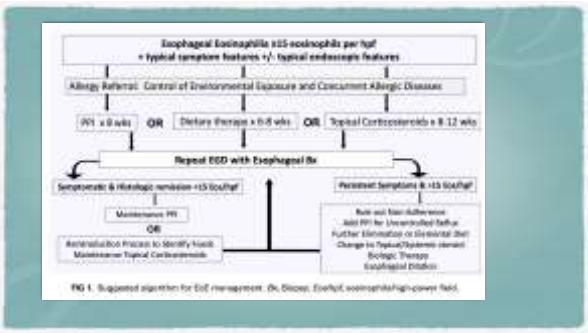
Eosinophilic esophagitis

- What are the symptoms?
  - Infants: GERD-like symptoms (reflux, feeding refusal, poor weight gain)
  - Children: abdominal pain, gagging/choking, growth delay, dysphagia, abdominal pain, food impaction
  - Young adults: dysphasia, heartburn, impaction, strictures
- Demographics:
  - occurs more often in school-aged boys with atopy
- Diagnostic criteria:
  - Presence of clinical symptoms of EoE
  - Esophageal biopsy ≥ 15 eosinophils/hpf

Eosinophilic esophagitis treatment

- Diet
- Oral medications
- Biologic

Photo courtesy of Allergic Living



Eosinophilic esophagitis diet

- Guided diet:
  - Allergy tests of foods that cause reactions are done by blood or skin prick
  - After the tests are done, the foods that cause a reaction may be removed from the diet.
- Non-guided diet:
  - Foods that cause EoE are taken out of the diet. Sometimes even when allergy tests are negative they are removed.
    - Milk, soy, egg, peanut/tree nut, wheat and seafood (6FED, 4FED or single food)
- Complete (Elemental Diet):
  - These formulas are pre-digested and "invisible" to the immune system. The formula has all the nutrition needed for growth and development. Often a large amount must be given (sometimes via feeding tube).

Eosinophilic esophagitis medications

- Anti-reflux medications (proton pump inhibitor)
- Topical steroids: swallowed Flovent® from an inhaler or drinking thickened Pulmicort® flavored with Splenda®
- The Food and Drug Administration (FDA) recently approved dupilumab (Dupixent) for treatment of adults and children 1 year and older who weigh at least 15 kg with eosinophilic esophagitis.
- These do not cure the disease but improve symptoms

References

- Bird, J. A., Leonard, S., Groetch, M., Assa'ad, A., Cianferoni, A., Clark, A., Crain, M., Fausnight, T., Fleischer, D., Green, T., Greenhawt, M., Herbert, L., Lanser, B. J., Mikhail, I., Mustafa, S., Noone, S., Parrish, C., Varshney, P., Vlieg-Boerstra, B., … Nowak-Wegrzyn, A. (2020). Conducting an Oral Food Challenge: An update to the 2009 adverse reactions to Foods Committee Work Group Report. *The Journal of Allergy and Clinical Immunology: In Practice*, *8*(1). https://doi.org/10.1016/j.jaip.2019.09.029
- Chetambath R, Panicker V. Clinical allergy and asthma management in adolescents and young adults. Boca Raton, FL: CRC Press; 2022.
- CM;, A. S. J. C. (n.d.). *IGE-mediated food allergy.* Clinical reviews in allergy & immunology. https://pubmed.ncbi.nlm.nih.gov/30370459/
- Dellon, E. S. (2012, July). *EOSINOPHILIC ESOPHAGITIS: Diagnostic tests and criteria.* Current opinion in gastroenterology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4591255/
- *Diagnosis of eosinophilic esophagitis.* Home. (n.d.). https://www.aap.org/en/patient-care/eosinophilic-esophagitis/diagnosis-of-eosinophilic-esophagitis/
- *Diagnosis and treatment of eosinophilic esophagitis. Journal of Allergy and Clinical Immunology. 2020;145:8.*
- *Oral allergy syndrome.* Windom Allergy Asthma and Sinus. (n.d.). https://www.windomallergy.com/meet-us/blog/oral-allergy-syndrome
- (n.d.). https://www.uptodate.com/contents/food-protein-induced-enterocolitis-syndrome-fpies
- https://www.mayoclinic.org/diseases-conditions/eosinophilic-esophagitis/diagnosis-treatment/drc-20372203https://www.allergicliving.com/2017/02/16/eoe-eosinophilic-esophagitis/