

IgE vs Non-IgE Mediated Food Allergies

Allergy-Immunology Review

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OBJECTIVES

- Know how to differentiate between food allergy vs food intolerance
- Recognize common food allergens in the pediatric population
- Be able to differentiate between IgE mediated vs non-IgE food allergies
- Know the benefits of skin-prick testing vs serum IgE antibody testing and the utility of allergy testing

Food Allergy

- **Definition: immunologically mediated pathologic response to a specific food protein**
- Prevalence: greatest in first years of life & decreases in adulthood
 - Higher in individuals with atopic disease i.e. atopic dermatitis or asthma

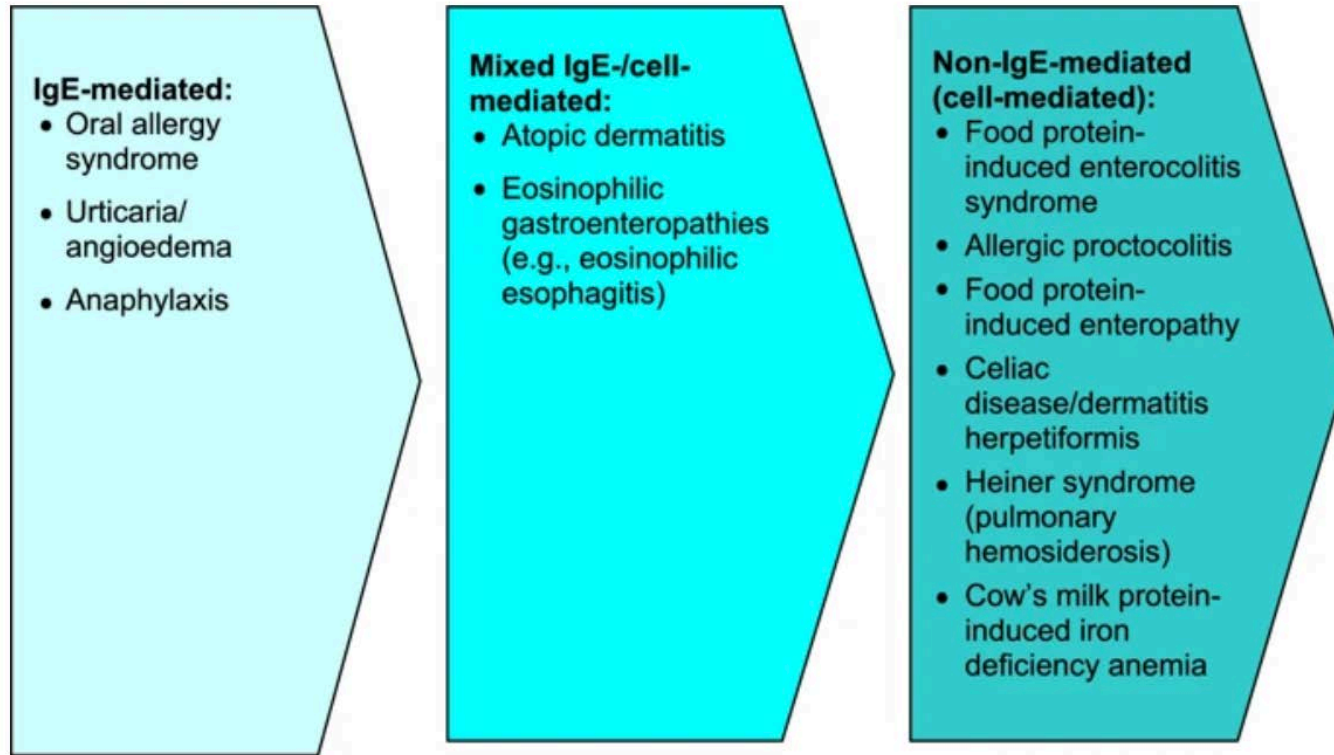
Allergy vs Intolerance

- Food allergy is an immunological response, which is distinct from other adverse food reactions
- Consider other etiologies
 - Food intolerance due to metabolic disorders e.g. lactase deficiency
 - Reactions to toxin contaminants in food
 - Reactions to pharmacologically active food components e.g. caffeine, tyramine in cheese

Common Food Allergens

- In children: milk, eggs, peanuts, fish, soybeans, wheat, tree nuts
 - In first 3 years of life, 85% of pediatric patients lose sensitivity to milk, eggs, soybeans, wheat
 - Peanuts & tree nuts cause the most severe allergic responses
- Compared to allergens in adults: peanuts, tree nuts, fish, shellfish
- Increased susceptibility to food allergies in infants likely due to immaturity of immune system

Fig. 1



Classification of Food Allergies

IgE vs Non-IgE Mediated Reactions

IgE mediated

- Rapid onset: within minutes of ingestion up to 2 hours following
- Symptoms
 - Skin: urticaria, angioedema
 - Respiratory: asthma, rhinitis
 - Gastrointestinal: abd pain, vomiting, diarrhea
 - Cardiovascular: hypotension
- Diagnostic tests: skin prick testing, serum IgE antibodies

Non-IgE mediated

- Delayed onset: hours to weeks after ingestion of food
- Symptoms
 - Skin: erythema, pruritis, eczema
 - Gastrointestinal: vomiting, diarrhea, abd pain
- Few non-invasive diagnostic tests available

Table 2 Signs and symptoms of food allergy

	IgE-mediated (immediate reactions)	Non-IgE-mediated (delayed/chronic reactions)
Skin		
Urticaria	✓	
Angioedema	✓	
Erythema	✓	✓
Pruritus	✓	✓
Ecematous rash/lesions	✓	✓
Respiratory		
Laryngeal edema	✓	
Rhinorrhea	✓	
Bronchospasm	✓	
Nasal congestion	✓	
Cough	✓	
Chest tightness	✓	
Wheezing	✓	
Dyspnea	✓	
Gastrointestinal		
Angioedema of the lips, tongue, palate	✓	
Oral pruritus	✓	
Tongue swelling	✓	
Vomiting	✓	✓
Diarrhea	✓	✓
Pain	✓	✓
Cardiovascular		
Presyncope/syncope	✓	
Hypotension	✓	
Tachycardia	✓	

IgE Mediated Food Allergy

- Pathophysiology:
 - Protein in food stimulates production of IgE antibodies, which bind basophils & mast cells – causing release of histamine, leukotrienes, prostaglandins
- Types of IgE mediated responses
 - Oral allergy syndrome
 - Cross reactivity between pollen allergy & certain raw foods e.g. melons, bananas, potatoes, carrots, apples
 - Fairly benign - pruritis & angioedema of oropharynx, throat & lips that resolves rapidly
 - Urticaria/Angioedema
 - Anaphylaxis
- Screening:
 - Maintain a diet diary
 - Allergy testing
 - Skin prick test
 - Serum food-specific IgE antibodies (e.g. RAST)
 - Oral food challenge

IgE mediated food allergy

Skin-prick testing

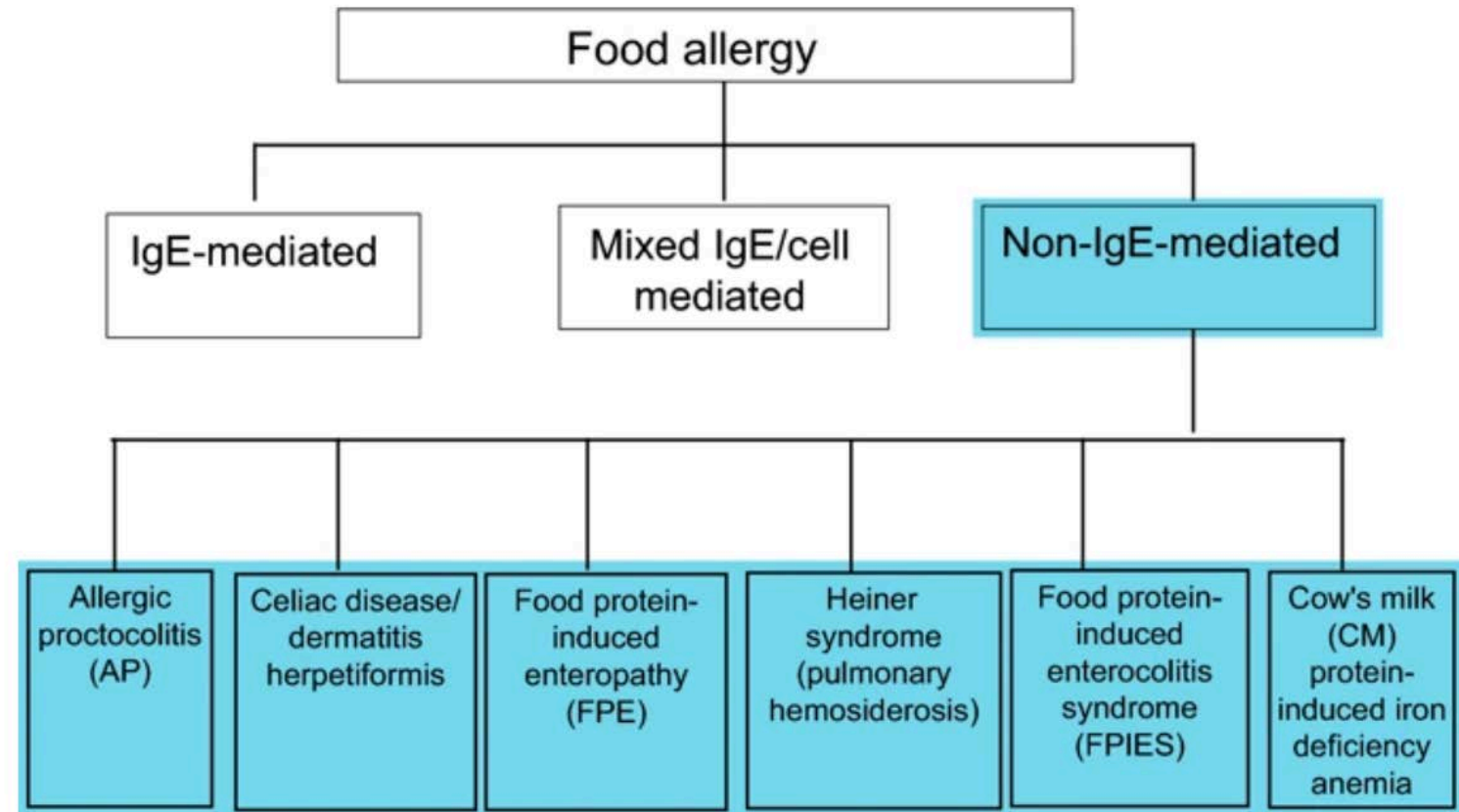
- More sensitive than blood test
- 60% of positive tests do not reflect a true symptomatic allergy (low PPV); however a negative test is useful to rule out an allergy
- Lower cost, faster results
- Withhold anti-histamine medications prior to testing

Serum IgE antibodies (e.g. RAST testing)

- There is no interference from anti-histamines or atopic dermatitis in obtaining samples
- Delayed results, higher cost

Non-IgE Mediated Food Allergy

Fig. 1



Classification of non-IgE-mediated food hypersensitivity

Non-IgE mediated food allergy

- **Food protein-induced enterocolitis syndrome (FPIES)**
 - Presentation: profuse emesis, diarrhea, failure to thrive
 - Presents at 6-12 mo
 - Symptoms occur 1-6 hrs after ingestion of food
 - Allergens: cow's milk protein, soy
- **Breast-milk-induced proctocolitis**
 - Presentation: mild symptoms, stools with mucus & blood streaks, normal to loose stools, otherwise healthy patient
 - Present within days of birth to 6 mo, occasionally in older children
 - Allergen: cow's milk protein, passed through breast milk
 - Common cause of rectal bleeding in infancy

Non-IgE mediated food allergy

- **Food protein-induced enteropathy (FPE)**
 - Presentation: non-bloody diarrhea, malabsorption, similar to Celiac disease but less common
 - Presents in first 9 mo
 - Allergens: cow's milk protein
- **Celiac Disease**
 - Gluten ingestion leads to small bowel villous atrophy
 - anti-TTG, anti-gliadin antibodies
 - Genetic predisposition
 - Can manifest at any age
 - Associated findings: dermatitis herpetiformis

Non-IgE mediated food allergy

- Screening:
 - Mild lab abnormalities
 - E.g. anemia, peripheral blood eosinophilia, hypoalbuminemia, hypoproteinemia, elevated serum IgE
 - Allergy testing not routinely recommended
 - Celiac disease: IgA-TTG, IgA levels, endomysium antibody
 - Endoscopy and biopsy may be required
- Treatment
 - Elimination of offending food from diet, or from maternal diet (in breastfed infants with cow's milk protein allergy)
- Prognosis is generally good
 - Cow's milk protein allergy typically resolves in early childhood

SUMMARY

- *A food allergy is an immune mediated response to a food protein, and is distinct from food intolerance*
- *IgE mediated food allergies are rapid in onset, and can be life threatening. Symptoms include urticaria, angioedema, asthma, hypotension. Treat with antihistamines & epinephrine.*
- *Skin prick testing is more sensitive than serum allergy testing. However both are reasonable options to screen for IgE mediated food allergies.*
- *Non-IgE mediated food allergies have delayed onset of symptoms. Common allergens include cow's milk protein and gluten (Celiac disease). There is low utility in obtaining serum IgE testing or skin prick testing.*

CITATIONS

1. Connors et al. Allergy Asthma Clin Immunol 2018, 14(Suppl 2):56
2. Sandra F. Braganza. Pediatrics in Review November 2003, 24 (11) 393-394; DOI: <https://doi.org/10.1542/pir.24-11-393>
3. Wasserman et al. Allergy Asthma Clin Immunol 2018, 14(Suppl 2):55