

*IN THE NAME OF GOD*

# **FOOD ALLERGY**

*Types and Clinical manifestations*

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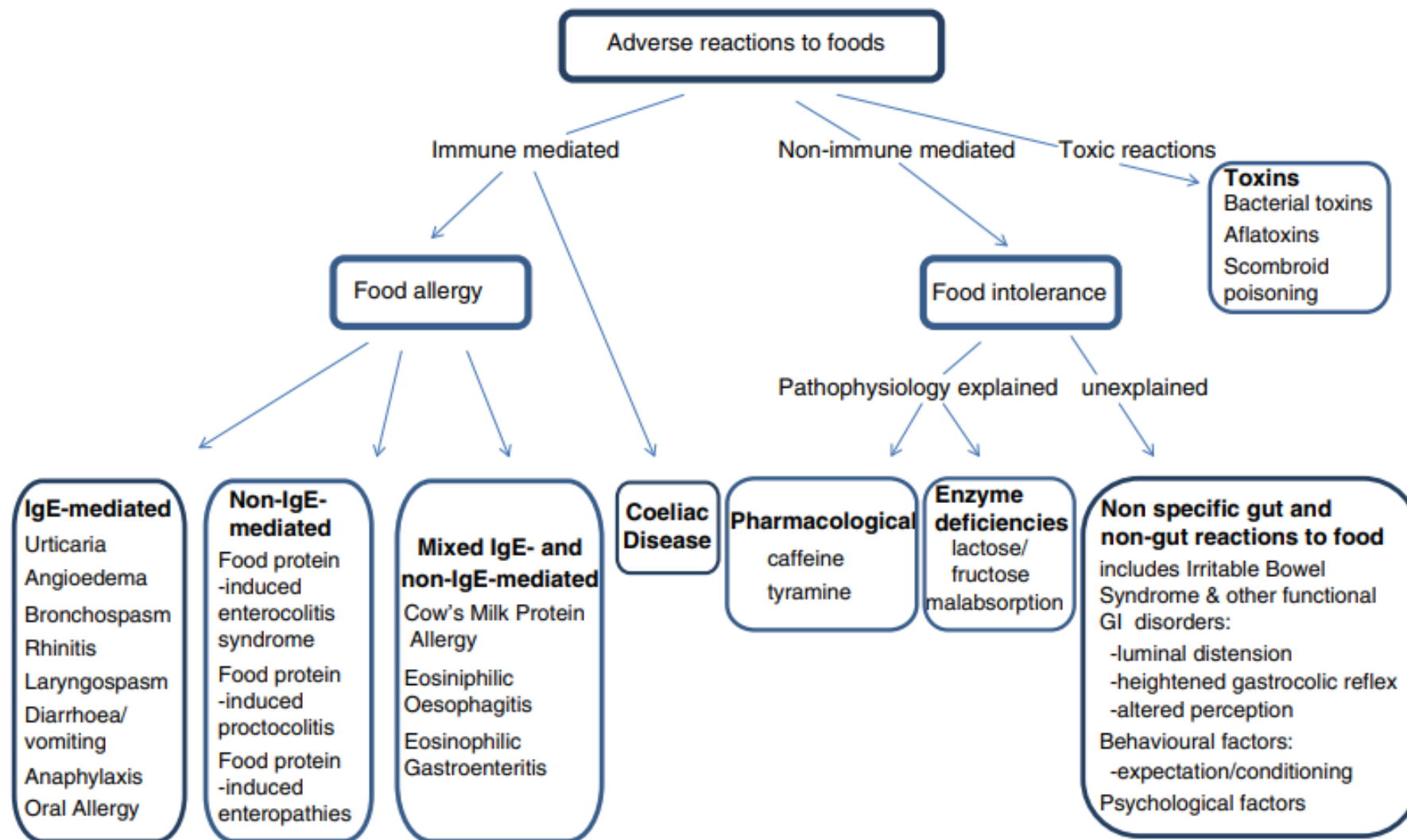
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# ADVERSE FOOD REACTION

*(Any untoward response to the ingestion of a food)*

- Immunologically mediated (food allergies)
- Nonimmunologic (Food intolerance)
- Toxic reactions





**Figure 1 |** Classification of adverse reactions to foods.

# PREVALENCE

- Up to one-third of parents/caregivers report adverse food reactions in their young children
- Food allergy occur in approximately 5 to 10 percent of young children.

Most food allergy is acquired in the first or second year of life

# NONIMMUNOLOGIC REACTIONS

*Nonimmunologic reactions to food are more common than true food allergies*

## **Gastrointestinal disorders**

- Nonceliac gluten sensitivity
- Gastroesophageal reflux
- Carbohydrate malabsorption
  - ✓ Lactase deficiency
  - ✓ Sucrose-isomaltase deficiency
- Irritable bowel syndrome
- Intolerance of short-chain fermentable carbohydrates (FODMAPs)
- Yeast overgrowth syndrome
- Pancreatic insufficiency (cystic fibrosis)
- Peptic ulcer disease
- Gallbladder disease

# NONIMMUNOLOGIC REACTIONS

## Intolerances Pharmacologic agents

- Caffeine Theobromine (tea, chocolate)
- Histamine and histamine-like compounds (berries, wine, fish, sauerkraut)
- Tryptamine (tomato, plum)
- Tyramine (aged cheeses, pickled fish)
- Serotonin (banana, tomato)
- Phenylethylamine (chocolate)
- Glycosidal alkaloid solanine (potatoes)
- Alcohol
- Flavorings and preservatives
  - ✓ Sodium metabisulfite
  - ✓ Monosodium glutamate

# NONIMMUNOLOGIC REACTIONS

## Neurologic reactions

- Auriculotemporal syndrome

## Psychologic reactions

- Food phobias
- Food aversions

## Accidental contaminations

- Pesticides
- Antibiotics (if allergy present)

# NONIMMUNOLOGIC REACTIONS

## Toxic reactions

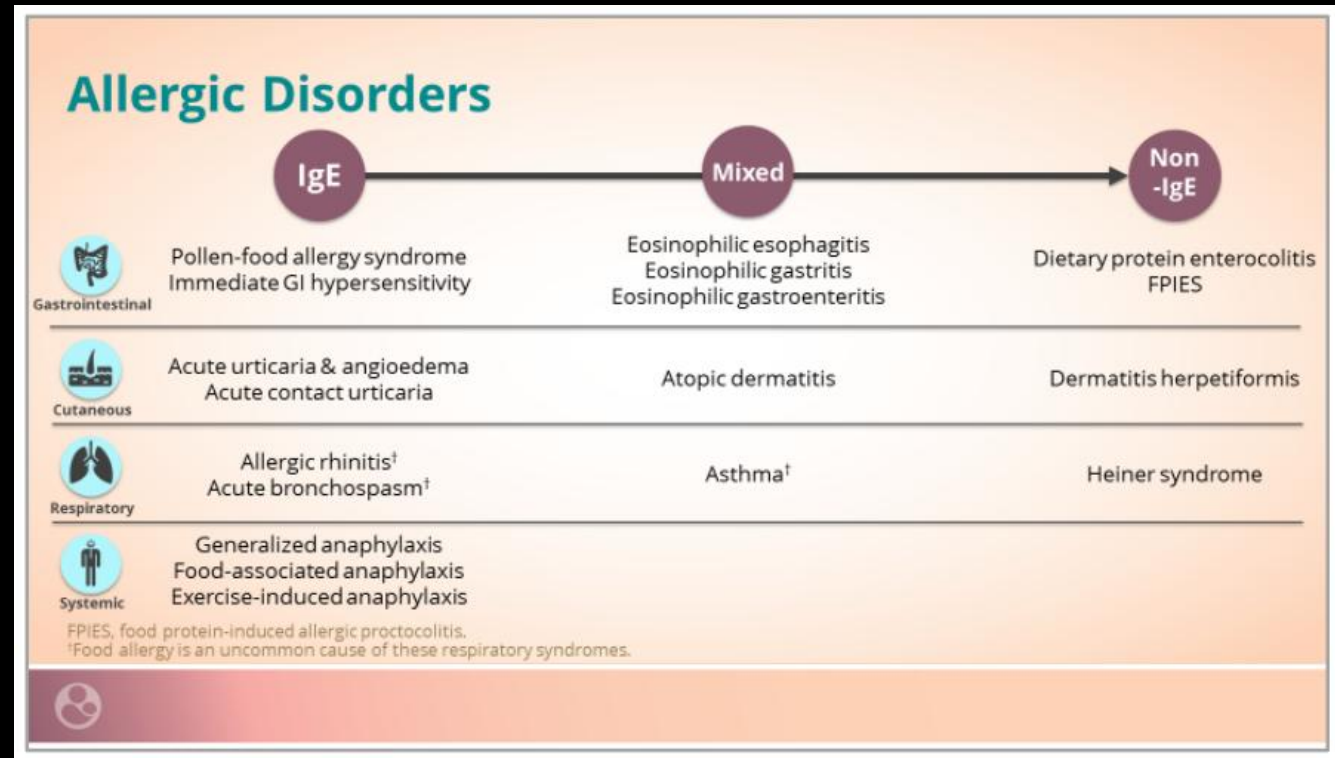
- Seafood
  - ✓ Scombroid poisoning (fresh tuna and mackerel)
  - ✓ Ciguatera poisoning (grouper, snapper)
  - ✓ Saxitoxin (shellfish)
- Other food poisoning
- Fungal toxins
- Bacterial toxins

# FOOD ALLERGIES

➤ IgE-MEDIATED REACTIONS

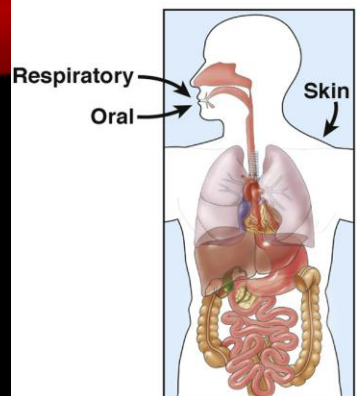
➤ NON-IgE-MEDIATED REACTIONS

➤ MIXED IgE AND NON-IgE-MEDIATED REACTIONS

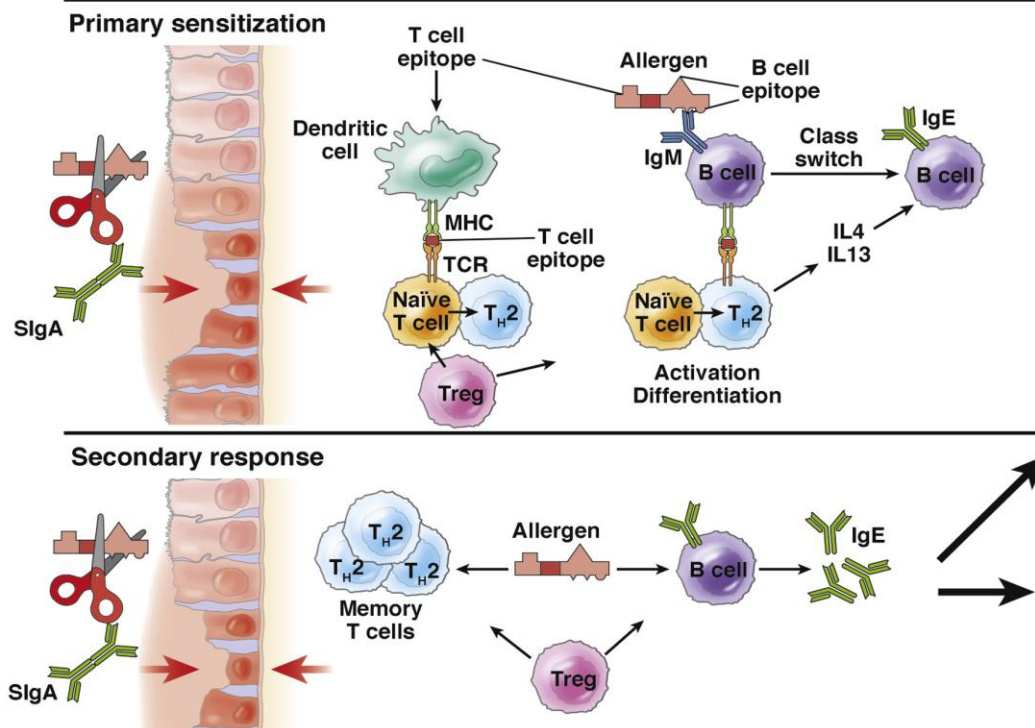
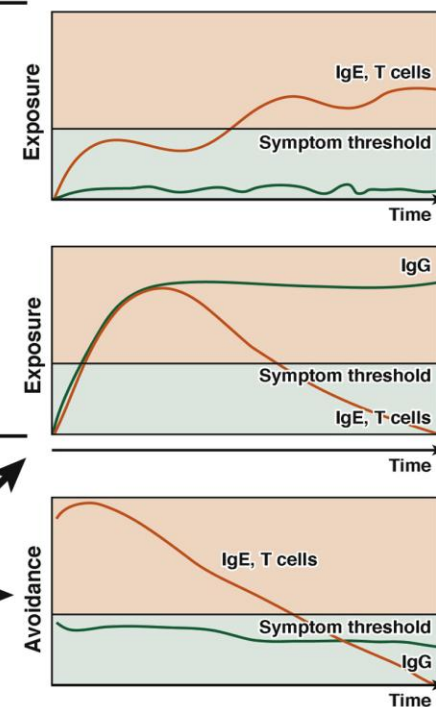
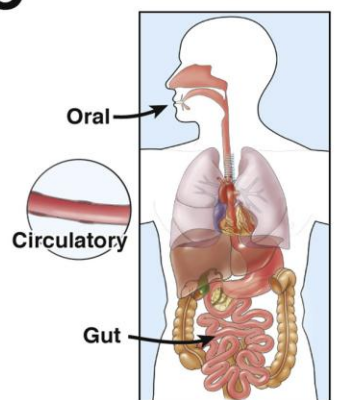


# IGE-MEDIATED REACTIONS

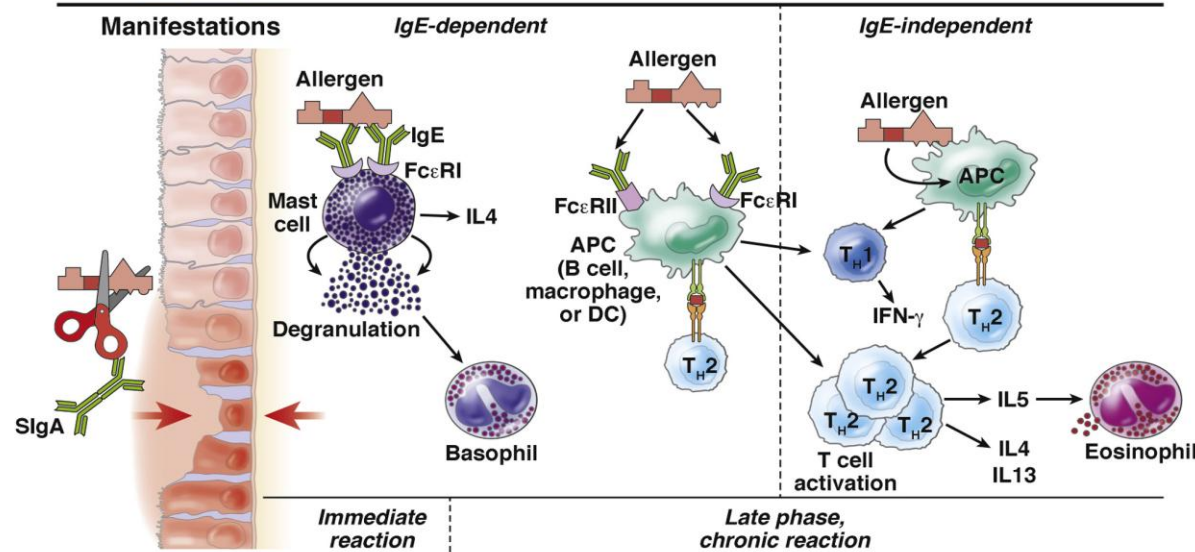
- *Rapid onset* (beginning within minutes to two hours from the time of ingestion).
- Most patients *react to one or two* specific foods/food groups, although an increasing number of patients react to multiple foods.
- Signs and symptoms are believed to be *caused by mediator release* from tissue mast cells and circulating basophils

**A**

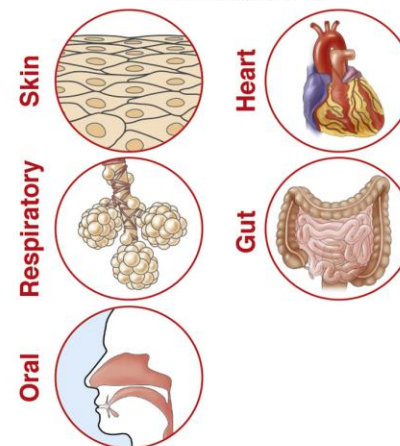
Sensitization and boosting of the secondary immune response by allergen contact

**B****C**

Repeated exposure



Sites of allergic manifestations



# IGE-MEDIATED REACTIONS

## ➤ Clinical manifestations

- **Dermatologic**: Pruritus, flushing, urticaria/angioedema, diaphoresis
- **Eyes** : Conjunctival injection, lacrimation, periorbital edema, pruritus
- **Respiratory tract** : Nose/oropharynx (sneezing, rhinorrhea, nasal congestion, oral pruritus, metallic taste), upper airway (hoarseness, stridor, sense of choking, laryngeal edema), lower airway (dyspnea, tachypnea, wheezing, cough, cyanosis)
- **Cardiovascular** : Conduction disturbances, tachycardia, bradycardia (if severe), arrhythmias, hypotension, cardiac arrest
- **Gastrointestinal** : Nausea/vomiting, abdominal cramping, bloating, diarrhea
- **Neurologic** : Sense of impending doom, syncope, dizziness, seizures

# URTICARIA AND ANGIOEDEMA

- The most common cutaneous manifestations
- Appear within minutes of ingestion of the food allergen.
- Food allergy may account for 20 percent of cases of acute urticarial
- Acute contact urticarial
  - ✓ Urticaria develops only on skin ( direct contact)
  - ✓ Common allergens, raw meats, seafood, raw vegetables and fruits, mustard, rice, and beer



# OROPHARYNGEAL SYMPTOMS

- Can occur in isolation or as part of a systemic reaction to a food
- Symptoms may occur in isolation because the allergy is mild, not much allergen was ingested, or the allergen is labile, as is seen in oral allergy syndrome.
- Tree nuts and peanuts can also cause isolated oral symptoms.



# ORAL ALLERGY SYNDROME

## (Pollen-food allergy syndrome)

- A form of **contact allergy** common in patients with allergic rhinitis to pollen.
- **Cross reaction** between **proteins of fresh, uncooked** fruits and vegetables (eg, profilins) and allergenic **pollen proteins**.
- Symptoms are confined **almost exclusively to the oropharynx** and include the immediate onset of pruritus, irritation, and mild swelling of the lips, tongue, palate, and throat
- Symptoms may be more noticeable during the associated **pollen season**
- **Anaphylaxis** has been reported



# RESPIRATORY TRACT SYMPTOMS

- Asthma and (allergic rhinitis and conjunctivitis) are **more common** in children with food allergy.
- In addition, conjunctival, nasal, and lower respiratory tract symptoms are **common in systemic** food allergic reactions (ie, anaphylaxis)
- **Isolated asthma in response to foods is rare.**
- An exception is occupational asthma for example **"Baker's asthma,"** caused by IgE-mediated allergy to **inhaled wheat proteins.**

# GASTROINTESTINAL SYMPTOMS

- Nausea, abdominal pain, abdominal cramping, vomiting, and/or diarrhea, are **more prominent features** in anaphylaxis **due to ingestion of a food allergen**.
- The term "**gastrointestinal anaphylaxis**" is used when gastrointestinal symptoms **occur in isolation**.
- Gastrointestinal symptoms **are rarely** the sole manifestations of a food-allergic reaction.
- More commonly, gastrointestinal symptoms occur in conjunction with involvement of **other target organs**.

# GASTROINTESTINAL SYMPTOMS

- The onset of symptoms (nausea, vomiting, abdominal pain) is generally **minutes to two hours** after ingestion of the offending food.
- Lower gastrointestinal symptoms, such as diarrhea, can begin two to six hours after ingestion.



# ANAPHYLAXIS

Anaphylaxis is **rapid in onset** and occasionally follows a **biphasic course**, with a **recurrence of symptoms hours** after the initial onset.

## Anaphylaxis signs and symptoms

### Signs and symptoms of anaphylaxis

Dermatologic - Pruritus, flushing, urticaria, angioedema

Eyes - Conjunctival injection, lacrimation, pruritus, periorbital edema

Nose - Sneezing, rhinorrhea, nasal congestion

Upper airway - Glossal/pharyngeal edema, metallic taste, hoarseness, stridor, sense of choking

Lower airway - Dyspnea, tachypnea, wheezing, dry and repetitive cough, cyanosis

Gastrointestinal/abdominal - Nausea, vomiting, crampy pain, diarrhea, uterine contractions (women)

Cardiovascular - Hypotension, tachycardia (or sometimes bradycardia), palpitations, lightheadedness, syncope

Neurologic - Sense of impending doom

# FOOD-DEPENDENT, EXERCISE-INDUCED ANAPHYLAXIS

- Anaphylactic response that occurs only if the patient exercises or exerts himself or herself within two to four hours of ingestion of food.
- In adolescents and young adults, although they can occur in patients of any age
- Common foods include wheat, celery, and seafood.
- The food can be ingested in the absence of exercise without development of symptoms.
- Menstruation, nonsteroidal antiinflammatory drugs (NSAIDs), alcohol, elevated body temperature, acute infections, and antacids , may increase the risk .

# COMMON CULPRIT FOODS

IgE-mediated food allergy occurs most often in association with certain foods, although any food has the potential to cause allergy.

- ✓ peanut, tree nuts (eg, cashew, walnut, etc)
- ✓ fish,
- ✓ shellfish,
- ✓ cow's milk (hereafter referred to as "milk"),
- ✓ hen's egg (hereafter referred to as "egg"),
- ✓ wheat,
- ✓ soy, and
- ✓ seeds (particularly sesame)

## Food Allergies

- In the United States, 3 million children are affected by food allergies
- Food allergy is most common in infants and children
- Eight food groups account for 90% of all food allergies in the United States

### Eight Most Common Food Allergens



NIAID-Sponsored Expert Panel, J Allergy Clin Immunol. 2010;126(5 Suppl):S1-S58.

*Allergies to fresh fruits and vegetables are common but usually less severe*

# IGE-MEDIATED REACTIONS

- A patient may present with only one or two or virtually all of them.
- In children, a **classic presentation** is **vomiting and urticarial**.
- **Extragastrintestinal** symptoms are **common** and may be the **only symptoms** present.



# NON-IGE-MEDIATED REACTIONS

subacute and/or chronic symptoms and typically isolated to the gastrointestinal tract and/or skin

- Food protein-induced enterocolitis syndrome (FPIES;entire gastrointestinal tract)
- Food protein-induced enteropathy (small bowel)
- Food protein-induced proctitis and proctocolitis(rectum and colon)
- Food-induced pulmonary hemosiderosis (heiner syndrome)

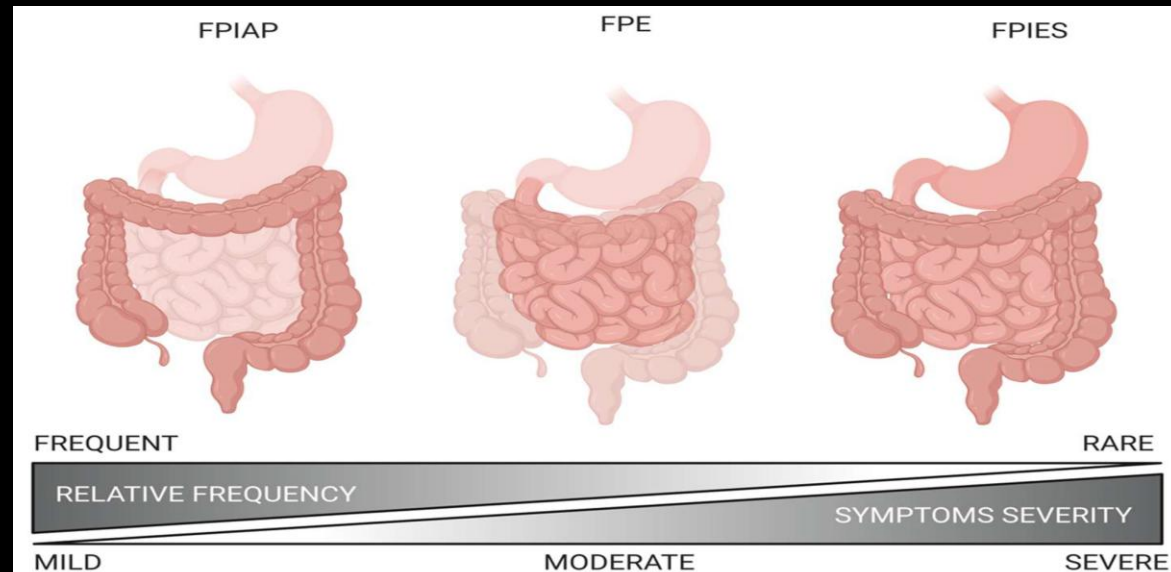
# FOOD PROTEIN-INDUCED PROCTITIS/PROCTOCOLITIS

- Passage of **blood-tinged stools and mucus** in an otherwise **healthy infant** without an anal fissure
- The most common trigger is **cow's milk in the mother's diet**, although it can also occur in formula-fed infants.
- **Typically presents between two and eight weeks** of age and **resolves in a few days** with complete elimination of the offending protein.



# FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME (FPIES)

- **Sicker** in appearance with lethargy and pallor .
- **Watery stools** with mucus or grossly bloody diarrhea .
- **Intermittent vomiting** in the chronic setting but can be severe and can lead to dehydration.
- **Malabsorption**, Poor weight gain/failure to thrive is common.
- **Laboratory abnormalities** ( hypoalbuminemia, anemia, and leukocytosis).



# FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME (FPIES)

- FPIES is uncommon in exclusively breastfed infants.
- Cow's milk and soy are the most common triggers in infants and children, although many other food protein triggers have been reported.
- FPIES in older children and adults is rare and typically presents a milder syndrome of nausea, protracted vomiting, and cramping several hours after ingestion.
- There are several reports of shellfish as a causative food in adults.
- Symptoms of FPIES resolve several weeks to a month to start to see an improvement.
- If the causative food is later reintroduced, there is a characteristic delayed onset (approximately two to four hours)

# PROTEIN-INDUCED ENTEROPATHY

Findings are similar to patients with FPIES who are regularly ingesting a causative food (eg, chronic vomiting and diarrhea, failure to thrive)

## **Celiac disease**

- Known as gluten-sensitive enteropathy
- Immune-mediated inflammatory disease

# NON-IGE-MEDIATED REACTIONS

## Dermatitis herpetiformis

- ✓ Exclusive non-IgE-mediated food allergy
- ✓ Up to one-quarter of adult patients with celiac disease
- ✓ Itchy papular vesicular eruption usually located symmetrically on the extensor surfaces of the elbows, knees, buttocks, sacrum, face, neck, trunk, and occasionally within the mouth



# NON-IGE-MEDIATED REACTIONS

## Food-induced pulmonary hemosiderosis (Heiner syndrome)

- ✓ Rare syndrome in infants
- ✓ Recurrent pneumonia with pulmonary infiltrates, hemosiderosis, iron deficiency anemia, and failure to thrive.
- ✓ Cow's milk is the most common causative food, with pork and egg also being reported
- ✓ Elimination of the offending food results in resolution.

# MIXED IGE AND NON-IGE-MEDIATED REACTIONS

typically isolated to the gastrointestinal tract and/or skin

- Atopic dermatitis
- Eosinophilic esophagitis (EoE)
- Eosinophilic gastroenteritis

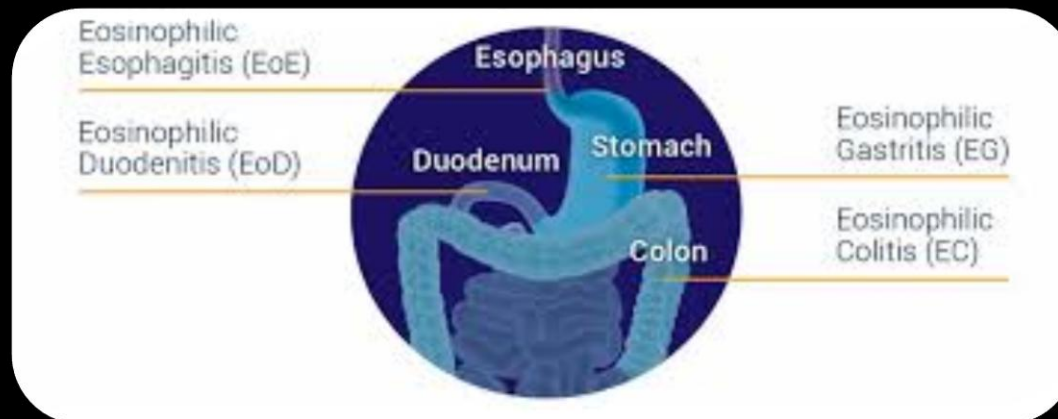
# ATOPIIC DERMATITIS (ECZEMA)

- Food allergies may exacerbate atopic dermatitis and flare of the patient's atopic dermatitis (increased erythema and pruritus of eczematous lesions).
- The flare occurs **within minutes to a few hours if the reaction** is IgE mediated but may **take hours to days** if the reaction is non-IgE mediated.
- The elimination of suspected food allergens **improves** symptoms **within a few weeks**.
- Repeated exposure exacerbates skin symptoms.



# EOSINOPHILIC GASTROINTESTINAL DISORDERS

- **Eosinophilic infiltration** of various segments of the intestinal tract on biopsy.
- Chronic symptoms are typical if the food trigger is consumed regularly.
- Symptoms are intermittent but can be delayed by hours to days if the food trigger is eaten infrequently.
- Allergic sensitivities to food and/or environmental allergens



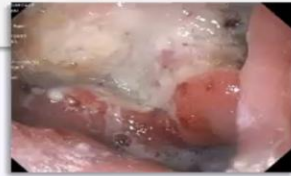
# EOSINOPHILIC ESOPHAGITIS

- In patients of any age presenting with **esophageal symptoms**
  - ✓ ( Infants and young children )feeding disorders and failure to thrive
  - ✓ (older children) dysphagia, vomiting, food impaction and abdominal pain
- **Failure to respond** to antacids and antireflux therapies
- May have other atopic diseases
- **Cow's milk, egg, soy, corn, wheat, and beef**

# EOSINOPHILIC GASTROENTERITIS

- Can present at any age with abdominal pain, nausea, diarrhea, malabsorption, and weight loss
- In infants, it may present as outlet obstruction with postprandial projectile vomiting that can mimic pyloric stenosis
- In adolescents and adults, it can mimic IBS.
- Approximately one-half of patients have allergic disease, such as defined food sensitivities, asthma, eczema, or rhinitis.

## Eosinophilic Gastroenteritis: Treatment Options Based on Severity of the Disease

| Mild                                                                                                                                            | Moderate                                                                                                                                                                | Severe                                                                                                                                                                                                                   | Severe + Concern for HES                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• Trial of PPI</li><li>• Trial of topical crushed budesonide</li><li>• Empiric elimination diet</li></ul> | <ul style="list-style-type: none"><li>• Trial of PPI + Trial of topical crushed budesonide with cromolyn</li><li>• Trial of PPI with Empiric elimination diet</li></ul> | <ul style="list-style-type: none"><li>• Trial of PPI plus</li><li>• Oral corticosteroids</li><li>• Elemental diet</li><li>• Biologic therapy</li><li>• Surgical consultation for non-healing ulcers/strictures</li></ul> | <ul style="list-style-type: none"><li>• Hematology consult for evaluation of HES</li><li>• Additional diagnostic imaging such as CT scan</li></ul> |
|                                                              |                                                                                    |                                                                                                                                     |                                                                                                                                                    |

# Comparison of IgE- and Non-IgE-mediated Food Allergies

|                                                               | IgE-mediated food allergy                                                                                                   | Mixed IgE or non-IgE-mediated food allergy                            |
|---------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| <b>Prevalence in children</b>                                 | More common, about 6%                                                                                                       | Rare, <1%                                                             |
| <b>Typical organ systems involved in symptom presentation</b> | Symptoms across broad range of organs, including oral, respiratory, cardiovascular, cutaneous, and gastrointestinal systems | Symptoms usually isolated to gastrointestinal system                  |
| <b>Timing after oral intake</b>                               | Usually seconds to minutes (within 2 hours)                                                                                 | Usually hours to days                                                 |
| <b>Severity</b>                                               | May proceed to anaphylaxis                                                                                                  | Variable, life-threatening is rare but can occur (eg, FPIES)          |
| <b>Pathogenesis</b>                                           | Type 1 immune hypersensitivity (IgE-mediated)                                                                               | Cell-mediated immune hypersensitivity                                 |
| <b>Examples</b>                                               | Peanuts, tree nuts, seafood, milk                                                                                           | Eosinophilic esophagitis, food protein-induced enterocolitis syndrome |



Ruffner MA, Spergel JM. *Ann Allergy Asthma Immunol*. 2016;117(5):452-454.  
 Wrobel JP et al. *Aust Fam Physician*. 2008;37(4):222-226.

THANK YOU



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