Food Allergy

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Adverse reactions to foods

classically divided into food intolerances and food allergies.

Food intolerances are : non immunologicphysiologic responses and can include metabolic, toxic,pharmacologic, or other mechanisms.

Food allergies : immunologic responses and can be IgE mediated, non–IgE mediated, or mixed

FA Increase over the past ٣ decades, primarily in westernized/industrialized countries.

FA prevalence : rangefrom ١–١١% with regional variations.

The vast majority of food allergies are due to peanut, tree nuts, seeds, milk, egg, soy, wheat, fish, and shellfish, with regional variations in prevalence.

٨–١١% of children have food allergy, with ٢٫٤% having multiple food allergies .

Up to ٩% of children experience food allergic reactions in the first ٣ years of life

including :

approximately ٢٫٥% with cow's milk

allergy, ٢% with egg allergy

٢–٣% with peanut allergy.

“outgrow” milk and egg allergies, with approximately ٥٠% doing so by school-age.

In contrast, ٨٠–٩٠% of children with peanut, tree nut, or seafood allergy retain their allergy for life.

food allergy development *is influenced by*

genetics (HLA-DQ, filaggrin, interleukin ١٠, STAT٦, and FOXP٣)

environment

genome-environment interactions

Family and twin studies show that family history confers a ٢-to ١٠-fold increased risk

Skin exposure to foods in infantile eczema can lead to sensitization and allergy.

Decreased microbial exposure ("hygiene hypothesis"), decreased microbiome diversity, in the gastrointestinal (GI) tract, airway, and skin, influence allergic conditions,including food allergy.

Additional environmental factors with increased risk of food allergy:

reduced diversity of the diet

delayed introduction of allergenic foods

vitamin D deficiency

other factors.

Food Allergy :

cell-mediated immune mechanisms(in these patients Tregs and the microbiome of the gut mucosa,breaks down).

by IgE-mediated :Certain allergens generate food-specific IgE antibodies that bind to Fcε receptors on mast cells that induce vasodilation, smooth muscle contraction, and mucus secretion, ….

immediate hypersensitivity :

Skin :urticaria, angioedema, flushing, pruritus)

GI tract :oral pruritus, angioedema, nausea, abdominal pain, vomiting, diarrhea

Respiratory tract :nasal congestion, rhinorrhea, nasal pruritus, sneezing, laryngeal edema, dyspnea, wheezing,

Cardiovascular system : dysrhythmias, hypotension, loss of consciousness).

Activated mast cells, basophils,…. release several cytokines and activate other cells, such

as eosinophils and lymphocytes, leading to

prolonged “delayed,” inflammation :

Skin : pruritus, erythematous rash,

GI tract failure to thrive, early satietyسیری, abdominal pain, vomiting, diarrhea

OTHER MANIFESTATIONS OF GASTROINTESTINAL ALLERGY

- Gastroesophageal Reflux
- Infantile Colic
- Diarrhea
- Constipation

Respiratory tract : food-induced pulmonary hemosiderosis).

Mixed IgE and cellular responses to food allergens can also lead to chronic disorders : atopic dermatitis,, eosinophilic esophagitis (EoE), and eosinophilic gastroenteritis.

by food allergens penetrating the inflamed skin barrier, e.g., eczema, or GI barrier referred to as class ۱ food allergens (egg, milk, peanuts,tree nuts, seeds, fish, soy, and wheat account for ۹۰% of food allergies during childhood ,exposure and sensitization to these proteins often occur very early in life). Cell-mediated sensitivity typically develops to class ۱ allergens. (..... و مقاوم به هضم وحرارت وعلایم سیستمیک

food allergens that are partially homologous to plant pollens penetrating the respiratory tract referred to as ***class ٢ food allergens*** *(these allergens are typically vegetable, fruit, or nut proteins that are partially homologous to pollen proteins.*

seasonal allergic rhinitis from birch cross react with apples, cherries,pears ,…….

certain nuts, uncooked fruits, or vegetables provokes the pollen-food allergy syndrome (also called oral allergy syndrome).)

class ٢ food allergens continue

IgE-mediated hypersensitivity to certain uncooked or unprocessed plant-based

foodsAllergies that occurs in many older children

rapid onset of oral pruritus; tingling and angioedema of the lips, tongue, palate, and throat; and occasionally a sensation of pruritus in the ears

Symptoms are generally short-lived. local mast cell activation following contact with fresh raw fruit

At least ٣٠% of children with moderate to severe atopic dermatitis have IgE-mediated food allergies.

The younger the child and the more severe the eczema, the more likely food allergy is playing a pathogenic role in the disorder.

Atopic dermatitis is a risk factor for the development of food allergy rather than a result of food allergy.

Acute urticaria and angioedema are among the most common symptoms of food allergic reactions

may be very rapid, within minutes after ingestion (IgE-bearing) mast cells by food allergens that are absorbed and circulated rapidly throughout the body.

Chronic urticaria and. angioedema :

very rarely caused by food allergies.

Contact urticaria : perioral region of infants and young children, especially in those with eczema, when otherwise tolerated food causes , food exclusion is not generally needed, wiping the face during feeding or using a barrier ointment (such as petroleum jelly) in the perioral area before feeding.

- Perioral dermatitis is a contact dermatitis often caused by substances :

  in toothpaste, gums, lipstick, or medications.

- Perioral flushing is often noted in infants fed citrus fruits and may be caused by benzoic acid in the food. It may also occur in nursing infants.In both situations the effect is benign.

- *Respiratory food allergies are uncommon as isolated symptoms.*

١٠% of asthmatic patients have food-induced Respiratory symptoms.

- *Anaphylaxis*

DIAGNOSIS

thorough medical history

❑ *adverse food reaction:*

- ➢ Intolerance
- ➢ food allergic reaction :

  IgE-mediated or

  cell mediated response

Adverse Food Reactions

FOOD INTOLERANCE (NON–IMMUNE SYSTEM MEDIATED, NONTOXIC, NONINFECTIOUS)

Host Factors

Enzyme deficiencies—lactase (primary or secondary), sucrase/isomaltase, hereditary fructose intolerance, galactosemia, alcohol dehydrogenase deficiency

Gastrointestinal disorders—inflammatory bowel disease, irritable bowel syndrome, pseudoobstruction, colic

Idiosyncratic reactions—caffeine in soft drinks ("hyperactivity")

Psychologic—food phobias, obsessive/compulsive disorder

Migraines (rare)

Food Factors (Toxic or Infectious or Pharmacologic)

Infectious organisms—*Escherichia coli*, *Staphylococcus aureus*, *Clostridium perfringens*, *Shigella*, botulism, *Salmonella*, *Yersinia*, *Campylobacter*

Toxins—histamine (scombroid poisoning), saxitoxin (shellfish)

Pharmacologic agents—caffeine, theobromine (chocolate, tea), tryptamine (tomatoes), tyramine (cheese), benzoic acid in citrus fruits (perioral flare)

Contaminants—heavy metals, pesticides, antibiotics

Adverse Food Reactions

FOOD ALLERGY

IgE Mediated

Cutaneous—urticaria, angioedema, morbilliform rashes, flushing, contact urticarial

Gastrointestinal—oral allergy syndrome, gastrointestinal anaphylaxis

Respiratory—acute rhinoconjunctivitis, bronchospasm

Generalized—anaphylactic shock, exercise-induced anaphylaxis

Mixed IgE Mediated and Non–IgE Mediated

Cutaneous—atopic dermatitis, contact dermatitis

Gastrointestinal—allergic eosinophilic esophagitis and gastroenteritis

Respiratory—asthma

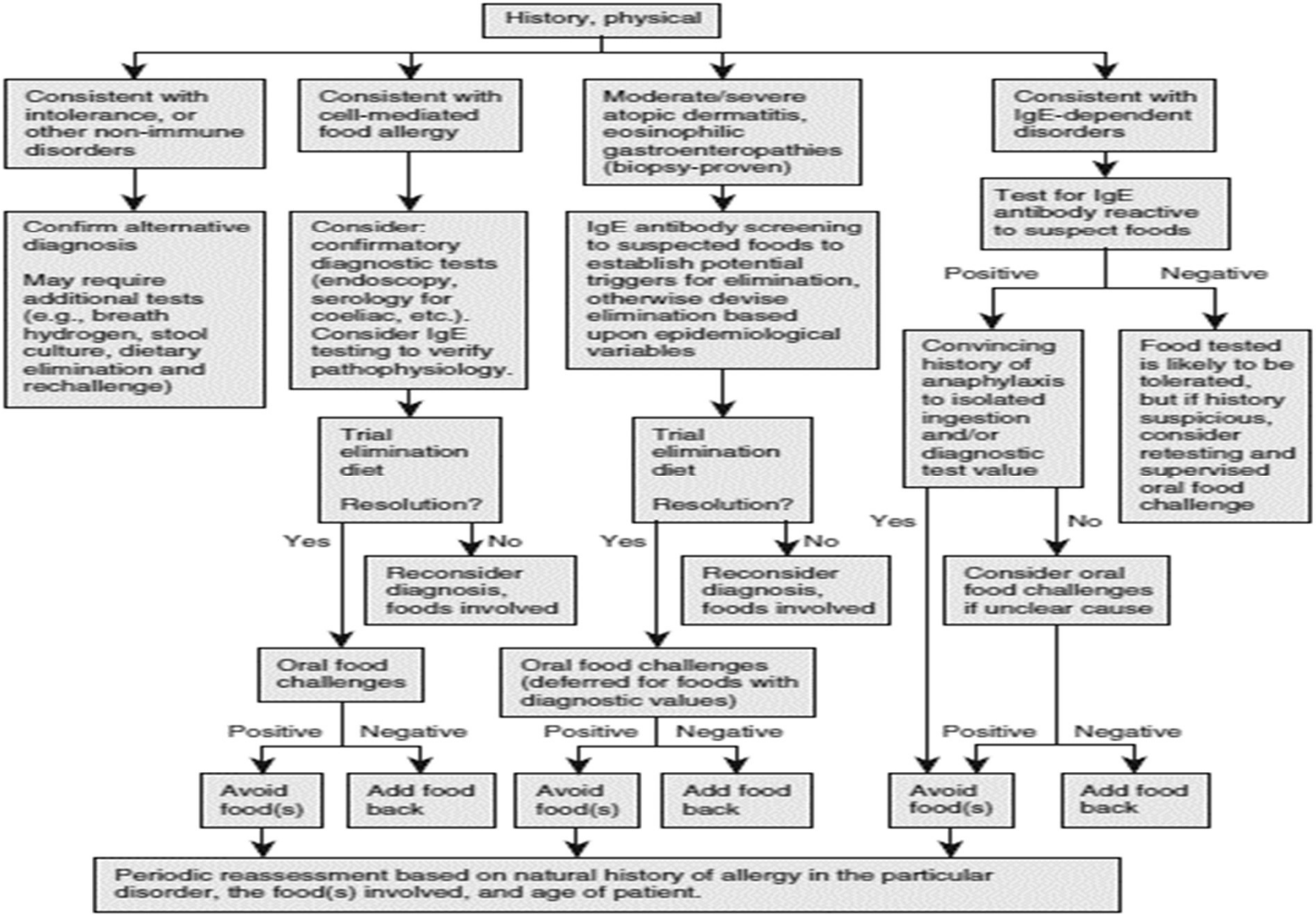
Non–IgE Mediated

Cutaneous—contact dermatitis, dermatitis herpetiformis (celiac disease)

Gastrointestinal—food protein–induced enterocolitis, proctocolitis, and enteropathy syndromes, celiac disease

Respiratory—food-induced pulmonary hemosiderosis (Heiner syndrome)

Unclassified



Algorithm for diagnosis of food allergy. *(From Sicherer SH. Food allergy. Lancet. 2002;360:701–710.)*

The following facts should be established:

(١) the food suspected of provoking the reaction and the quantity ingested

, (٢) the interval between ingestion and the development of symptoms, because most reactions occur within minutes to ٢ hours of ingestion

(٣) the types of symptoms elicited by the ingestion, which may suggest the pathophysiology

of the adverse reaction

(٤) whether ingesting the suspected food produced similar symptoms on other occasions because reproducibility is expected

(٥) whether other inciting factors, such as **exercise**, *are necessary*

- *serum food-specific IgE levels ≥١٥ kUA/L for milk (≥٥ kUA/L for children ≤١ year), ≥٧ kUA/L*

for egg (≥٢ kUA/L for children <٢ years), and ≥١٤ kUA/L for peanut are associated with a

>٩٥% likelihood of clinical reactivity to these foods in children with suspected allergy.

Evaluation of IgE-binding to specific digestion-resistant allergens that trigger reactions labile proteins unlikely to cause significant reactions in a food, termed molecular or component-resolved diagnostic (CRD) testing,can provide additional clinically relevant information.

Identification of sensitization to digestion-resistant proteins (components) in the foods correlates with a greater chance of systemic allergic reactions.

Examples of tests for digestion-resistant proteins include Cor a ٩ and Cor a ١٤ for hazelnut.

Ara h ٨ in peanut is a labile, birch pollen–related protein generally not associated with significant allergic reactions, and isolated sensitization to this component is typically associated with no or only mild oral reactions.

In the absence of a clear ***history of reactivity*** *to a food and evidence of food-specific IgE antibodies, definitive studies must be performed*

before

recommendations are made for avoidance or the use of highly restrictive diets that may be nutritionally deficient, logistically impractical, disruptive to the family, expensive, and/or a potential source of future feeding disorders.

IgE-mediated food allergic reactions are generally very food specific,

so the ***use of broad exclusionary diets****, such as avoidance of all legumes, cereal grains, or animal products, is* ***not warranted***

Clinical Implications of Cross-Reactive Proteins in IgE-Mediated Allergy

FOOD FAMILY	RISK OF ALLERGY TO ≥1 MEMBER (%; APPROXIMATE)	FEATURE(S)
Legumes	5–50	If allergic to peanut, 5-20% likelihood of allergy to other legumes (lupine, green bean, green pea, soy) If allergic to chickpea (garbanzo bean), >50% likelihood of allergy to lentil and/or pea.
Tree nuts (e.g., almond, cashew, hazelnut, walnut, Brazil)	15–33	Reactions are often severe
Fish	50	Reactions can be severe
Shellfish (crustaceans)	75 (other crustaceans) 50 (mollusks)	Reactions can be severe
Grains	20	Wheat shows cross-reactivity with barley and rye
Mammalian milks	90	Cow's milk is highly cross reactive to goat's or sheep's milk (92%) but not with mare's milk (4%)
Rosaceae (pitted fruits)	55	Risk of reactions to >3 related foods is very low (<10%); symptoms are usually mild (pollen food allergy syndrome)

When the earlier diagnostic modalities are not definitive, which is a common scenario, oral food challenges (OFCs), observed incremental feedings of a food performed under physician supervision,are useful in ruling out or confirming the presence of a food allergy.

no laboratory studies responsible for non–IgE and cell-mediated food reactions.

*OFCs are the only way to establish the diagnosis (for atopic dermatitis, **eosinophilic GI diseases**,and some forms of **contact dermatitis)***

*Before a food challenge is initiated, the **suspected food** should be **eliminated** from the diet for ١٠-١٤ **days** For IgE-mediated food allergy up to ٨ **weeks** for some cell-mediated disorders, such as EoE*

Some children with cell-mediated reactions to cow's milk do not tolerate hydrolysate formulas and must receive amino acid–derived formulas(neocate,….).

If symptoms remain unchanged despite appropriate elimination diets, it is unlikely that food allergy is responsible for the child's disorder.

TREATMENT

identification and elimination of foods responsible for food hypersensitivity reactions are the most established and validated management strategies for food allergies.

Complete elimination of common foods (milk, egg, soy, wheat, rice, chicken, fish, peanut, nuts) is very difficult because of their widespread use in a variety of processed foods.

Egg allergy is not a contraindication for vaccination with measles, mumps, rubella (MMR), or influenza vaccines, but remains a concern for the yellow fever vaccine where referral to an allergist is recommended.

Because many food allergies resolve, children should be reevaluated periodically by an allergist to determine whether they have lost their clinical reactivity.

oral, sublingual, and epicutaneous (patch) immunotherapy for the treatment (Immunotherapy) of IgE-mediated food allergies.

Immunotherapy is not typically curative but aims to provide temporary "desensitization," or an increase in the threshold of a food that can be consumed without triggering an allergic reaction. Success depends on continuous treatment exposure.

Combining OIT with anti-IgE treatment (omalizumab) or other biologic agents is under study and may improve safety or efficacy compared to OIT alone.

Furthermore, extensively heated milk or egg in baked products are tolerated by the majority of milk and egg–allergic children.

Regular ingestion of baked products with milk and egg may accelerate resolution of milk and egg allergy.

PREVENTION

It was once thought that avoidance of allergenic foods and delayed introduction to the diet would prevent allergy **but** *the opposite is probably true; delayed introduction of these foods may increase the risk of allergy, especially in children with atopic dermatitis.*

A trial of ***early introduction*** *of dietary peanut randomized ۶۴۰ infants age ۴-۱۱ months with* **severe eczema , egg allergy, or both** *to consume peanut until the age ۶۰ months* ***:Dramatically*** *decreased the development of peanut allergy among children at high risk for this allergy. Because :*

precedes the potential sensitization to peanut that can occur with environmental exposure to peanut via the inflamed,disrupted skin barrier seen in infants with eczema.

THUS:

Infants with severe eczema **or** *egg allergy in the first ۴-۶ months of life*

might benefit from evaluation for peanut- (If there is a positive peanut skin test response or serum peanut-specific IgE >۰٫۳۵ kUA/L do challenge test for them and if do not clinically reactive assist in promptly implementing appropriate ***early safe*** *peanut introduction at home.*

No evidence to support the practice of restricting the :

maternal diet during pregnancy

or while breastfeeding

or for delaying introduction of various allergenic foods to infants from atopic families.

Not supported the use of hydrolyzed infant formulas in cases where :

١. *breastfeeding cannot be continued for ٤-٦ months*

٢. after weaning to prevent eczema or food allergies in high-risk families.

Probiotic supplements in the third trimester and to the newborn infant may reduce the incidence and severity of eczema

Other potential influences on microbiome : mode of delivery (vaginal vs C-section),diet diversity, vitamin D supplementation, and household pet exposure.

infantile eczema increases the risk of allergic sensitization and food allergy :

١-aggressive treatment of infantile eczema

٢-skin preparations contain peanut or nut oils, which may sensitize young infants, especially those with cutaneous inflammation, such preparations should be avoided.

summarizes approaches to food allergy prevention.

Approaches to Prevention of Food Allergy

RECOMMENDED

Infant-safe forms of peanut, egg introduced around age 6 mo, not before 4 mo

- Other allergens may be introduced around this time as well
- Allergy testing before introduction not usually needed (see text)
- Infants with severe eczema or egg allergy may benefit from evaluation for early peanut introduction at 4-6 mo

Diverse infant diet

UNPROVEN/NOT RECOMMENDED

Hydrolyzed formulas

Maternal allergen avoidance during pregnancy or lactation

Purposeful delay in introducing allergens to infants

Non-IgE Gastrointestinal Food Allergy Disorders

Food protein–induced enterocolitis syndrome (FPIES):

- a non–IgE-mediated FA
- Can be confused with AGE
- Dehydration, lethargy, shock, bloody stool, anemia, hypoalbuminemia, transient methemoglobinemia

Food protein–induced enterocolitis syndrome (FPIES)

- onset between ۱ and ۴ hours after ingestion of foot
- Milk, soy, rice, wheat, egg, chicken, turkey, fish, pea
- Skin prick are not indicated
- confirmed with oral food challenge
- usually resolves by age ۳-۵ yr

Food protein–induced allergic proctocolitis (FPIAP)

- rectal bleeding, generally in children younger than ۲ months
- Cow's milk, soy, egg

- Significant cross-reactivity between soy and milk proteins, (۱۵%-۵۰%)

Food protein–induced allergic proctocolitis (FPIAP)

- Diagnosis is clinical; Blood-streaked stools, in a well baby, mild diarrhea
- Rarely anemia

- hydrolysate; resume/continue breastfeeding on maternal antigen restricted diet

- Reintroduction of the food at home in ٩-١٢ mo

FOOD PROTEIN–INDUCED ENTEROPATHY (FPE)

- often manifests in the ١st several mo of life
- Protracted diarrhea, often with steatorrhea and poor weight gain, vomiting in up to ۶۵% of cases, FTT, abdominal distention, early satiety, malabsorption. Anemia, edema, and hypoproteinemia occur occasionally
- Most common cause: **Cow's milk** in young infants, but soy, egg, wheat, rice, chicken, and fish in older children
- Treatment is Protein elimination
- Most cases resolve in ٢-٣ yr, reintroduce in home gradually advancing

EOSINOPHILIC ESOPHAGITIS (EoE)

- esophageal dysfunction and histologically by eosinophil-predominant inflammation
- rapid resolution of the symptoms is not achived by elimination diet
- symptoms do not always occur immediately after reintroduction of the foods
- aeroallergens may contribute to the development of EoE
- Antibiotic exposure in infancy conferred a ۶-fold increased risk of EoE (other factors: C/S, preterm birth, and formula exposure)

- there may be a genetic predisposition to the disease

EOSINOPHILIC ESOPHAGITIS (EoE)

- male-to female ratio of about ٣:١
- Prevalence of ٥٠ in ١٠٠٠٠٠ but ٣.٦% in aerodigestive referral center
- vomiting, regurgitation, nausea, epigastric or chest pain, globus, and decreased appetite(Less common symptoms: growth failure and hematemesis)

EOSINOPHILIC ESOPHAGITIS (EoE)

- Diagnosis with EsophagoGastroDuodenoscopy and eos count in mucosa of solely esophagus
- Due to PPI-Ree(علایم EOE دارند ولی با دارو خوب میشوند), a priod of ۸ wk aggressive acid supprssion perior to EGD is advised
- Skin prick testing (۵۰ -۷۰ % مثبت)
- Milk, soy, egg, wheat, nuts, fish, and shellfish are the most common foods involved

EOSINOPHILIC ESOPHAGITIS (EoE)

- Trial elimination of allergens or elemental diet (neocate)and clinical+histological monitoring
- Systemic corticosteroid
- aerosolized fluticasone or liquid budesonide
- Biologic agent anti IL-۵(reslizumab)

EOSINOPHILIC GASTRO ENTERITIS

- A constellation of symptoms attributable to the gastrointestinal tract with pathologic infiltration by eosinophils
- Clinical characteristics
- Nausea, vomiting, regurgitation
- Severe abdominal pain
- Diarrhea, protein-losing enteropathy
- Gastrointestinal bleeding
- Ascites
- Intestinal obstruction
- Peripheral eosinophilia (>۵۰%)

EOSINOPHILIC GASTROENTERITIS

- Elimination of pathogenic foods
- Elemental diet
- Corticosteroids (systemic)
- Immunomodulators
- Oral cromolyn sodium
- Montelukast
- Dopixant دوپیلوماب(IL ۱۳ ,IL۴ inhibitor)


FOOD ALLERGY

Thank You

For Your Attention