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Food Protein induced Enterocolitis

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Introduction

- A number of gastrointestinal disorders in children have been attributed to immunologic reactions to dietary proteins.
- The entire gastrointestinal tract can be affected, from the mouth to the rectum.
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Classification And Terminology

Immunologic reactions to dietary proteins may be classified as:

- **IgE-mediated**
- **Non-IgE-mediated**
- **Mixed**

Food protein-induced gastrointestinal disease in childhood

Disorder	Target	IgE-mediated?	Symptoms
Immediate hypersensitivity	Systemic	Yes	Rapid onset of nausea, abdominal pain, vomiting, and/or diarrhea; often with hives and wheezing
Oral allergy syndrome	Oral	Yes	Mild tingling or angioedema of the lips or oropharynx; occasional sensation of tightness in the throat

Food protein-induced gastrointestinal disease in childhood

Disorder	Target	IgE-mediated?	Symptoms
Eosinophilic esophagitis	Esophagus	No; T cell-mediated	Gastroesophageal reflux, dysphagia, abdominal pain, or lack of histologic response to acid suppression; $\pm$ esophageal strictures
Eosinophilic gastroenteritis	Stomach, small bowel	No; T cell-mediated	Recurrent abdominal pain, intermittent vomiting, failure to thrive, or weight loss; $\pm$ ascites

Food protein-induced gastrointestinal disease in childhood

Disorder	Target	IgE-mediated?	Symptoms
Food protein-induced allergic proctocolitis	Rectum, sigmoid colon	No	Gross or occult blood in stool; otherwise, typically asymptomatic
Food protein-induced enteropathy	Small bowel	No	Diarrhea or steatorrhea, abdominal distension, failure to thrive, nausea, or vomiting
Food protein-induced enterocolitis syndrome (FPIES)	Small bowel, colon	No	Protracted vomiting and diarrhea ($\pm$ blood), dehydration, shock, or failure to thrive

IgE: immunoglobulin E.

Courtesy of Alan M Lake, MD.

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INTRODUCTION

- Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated gastrointestinal food hypersensitivity that manifests as profuse, repetitive vomiting, sometimes with diarrhea, leading to dehydration and lethargy in the acute setting, or chronic, watery diarrhea with intermittent vomiting, leading to weight loss, failure to thrive, dehydration, and metabolic derangements in a chronic form.
- This disease primarily affects infants.
- It is most commonly caused by cow's milk (CM) or soy protein, although other foods can be triggers

INTRODUCTION

- Most of GI immunologic disorders affect a specific region of the gastrointestinal tract, such as eosinophilic esophagitis (EoE), eosinophilic gastritis, food protein-induced enteropathy, enterocolitis, or proctocolitis.
- FPIES has some features that overlap with the other non-IgE-mediated gastrointestinal allergic disorders, food protein-induced enteropathy, and proctocolitis.

INTRODUCTION

- The diagnosis is based upon the presence of consistent clinical features with improvement following withdrawal of the suspected causal protein.
- Affected children are often misdiagnosed as having acute viral gastrointestinal illness or sepsis, delaying diagnosis of FPIES for many months.
- An oral food challenge (OFC) is sometimes performed to confirm the diagnosis or to determine resolution of the food allergy.
- Treatment consists of elimination of the food trigger(s) from the diet, periodic reassessments for resolution, and managing acute emergencies.

EPIDEMIOLOGY

- Non-IgE-mediated and mixed gastrointestinal immune reactions to cow's milk (CM) proteins are estimated to account for up to 40 percent of CM protein hypersensitivity in infants and young children.
- FPIES represents the severe end of the spectrum of food protein-induced gastrointestinal diseases in infants and is far less common than proctocolitis.
- The incidence ranges from 0.015 to 0.7 percent.
- There is a slight male predilection (52 to 60 percent) in FPIES.
- Reports of FPIES in siblings of an affected child are rare.

EPIDEMIOLOGY

- In Spain, FPIES was reported to affect 0.7 percent of infants younger than 12 months in a single-center, unselected, population-based birth cohort (n = 1142).
- CM, hen's egg (HE) yolk, and fish were the most common triggers.

EPIDEMIOLOGY

- A population-based survey of food allergies in the United States was estimated to affect 0.51 percent (95% CI 0.42-0.62) of the US population under the age of 18 years and 0.22 percent (95% CI 0.17-0.28) of adults (18+ years), with an overall prevalence of **0.28 percent** (0.24-0.33 percent).

EPIDEMIOLOGY

- As in prior reports, most patients had an acute presentation (78 percent), and CM, soy, oat, rice, potato, and HE were common triggers.
- The mean age of diagnosis was 6.8 months

PATHOGENESIS

- FPIES is triggered by non-IgE-mediated food hypersensitivity.
- However, the exact underlying mechanisms of FPIES are not clearly understood.
- It is postulated that ingestion of food allergens causes local inflammation mediated by T cells, leading to increased intestinal permeability and fluid shift.
- However, baseline intestinal absorption was normal in a group of infants with FPIES confirmed by oral food challenge (OFC) [20].
- Activated peripheral blood mononuclear cells, increased tumor necrosis factor (TNF) alpha, and decreased expression of transforming growth factor (TGF) beta receptors in the intestinal mucosa may be involved in the intestinal inflammation

PATHOGENESIS

- Systemic food-specific IgE antibodies (determined by serum food-specific IgE and/or skin prick test) are not detected in the majority of patients with FPIES.
- However, up to 25 percent of children have evidence of specific IgE to the FPIES-inducing food.
- Intestinal mucosal IgE may facilitate the antigen uptake and local intestinal inflammation, but this requires further study.

PATHOGENESIS

- A decrease in serum food-specific immunoglobulin G4 (IgG4) antibody and an increase in serum food-specific immunoglobulin A (IgA) levels were noted in one study.
- A subsequent study found that both casein-specific IgG4 and IgA antibodies were significantly decreased in cow's milk (CM) FPIES.

PATHOGENESIS

- Profiling of whole blood by mass cytometry demonstrated activation of cells of the innate immune system (monocytes, neutrophils, natural killer cells, and eosinophils) in addition to T lymphocytes after food challenge in children with FPIES.
- This activation was not observed in children who had outgrown FPIES.

PATHOGENESIS

- **Untargeted serum metabolomics identified 34 metabolites that were significantly increased following a symptomatic food challenge, in particular, steroids in the corticosteroid and androgen (pregnenolone and progestin) families, inosine, and metabolite of serotonin (5-hydroxylindoleacetate).**

PATHOGENESIS

- In a small study, plasma metabolic profiles were different among patients with cow's milk allergy (CMA), with significantly lower concentrations of various fatty acids and higher concentrations of primary metabolites such as amino acids in CM FPIES compared with IgE-mediated CMA.

Food triggers

- Although CM and soy protein have traditionally been reported as the most common triggers in young infants, more studies now indicate that solid foods, such as rice, oat, hen's egg (HE), and fish, are also triggers.

Milk and soy

- The most common food triggers in FPIES are CM and soy (classic FPIES), with reactions occurring to infant formula during the first months of life.
- While several studies have shown that over 50 percent of infants with FPIES react to both foods, none of the 44 infants diagnosed with CM FPIES in a birth cohort study in Israel showed sensitivity to soy.
- Globally, CM remains the single most common FPIES trigger.

Milk and soy

- CM FPIES in exclusively breastfed infants is rare, suggesting a protective role of breastfeeding that may be attributed to predigested and partially processed food allergens as well as presence of TGF-beta and IgA in mother's milk.
- Only a few cases of exclusively breastfed infants with CM FPIES have been reported in the literature, and there are no reports in the literature of soy FPIES in exclusively breastfed infants.
- FPIES to goat's milk was reported in an Italian series.

Solid foods

- FPIES may be induced by solid food, including grains (rice, oats, barley, corn, wheat); meat and poultry (beef, chicken, turkey); HE (egg white and egg yolk); vegetables and fruit (white potato, sweet potato, squash, string beans, avocado, mushroom, banana, apple, tomato); legumes (peanut, green peas, lentils); tree nuts; seafood (fish, crustaceans, molluscs); seeds (sesame); and the probiotic *Saccharomyces boulardii*.

Solid foods

- Among infants with solid-food FPIES in one series, 80 percent reacted to more than one food, 65 percent were previously diagnosed with CM and/or soy FPIES, and 35 percent were breastfed.
- Infants with early-onset FPIES and reactions to fruits or vegetables are at higher risk for reacting to multiple food triggers

Cereal grains

- Rice and oat are the most common solid foods inducing FPIES.
- In one case series, rice was responsible for 46 percent of FPIES episodes requiring hospitalization.
- Children with rice-induced FPIES were more likely to have multiple food sensitivities and severe symptoms requiring intravenous fluid resuscitation compared with children with CM- or soy-induced FPIES.
- Those with a history of FPIES to one grain have an approximately 40 to 50 percent chance of developing FPIES to other grains.
- However, wheat FPIES has not been reported in infants with oat or rice FPIES

Egg

- HE is among the common triggers of FPIES.
- The reported frequency of infantile HE FPIES is approximately 11 percent in Australia and the US and up to 36 percent in Turkey.
- In an Italian multicenter study, among 61 children with HE FPIES, 47 (77 percent) tolerated cooked HE at the mean age 30.2 (range: 7 to 120) months; of them, 32 (68.1 percent) tolerated raw HE at a food challenge done at a mean age 43.9 (range: 18 to 120) months.
- In Japan, a marked increase in HE FPIES incidence was observed over the five-year period from 2014 to 2019, coinciding with changes in infant feeding practices resulting in earlier introduction of HE into infants' diet.

Seafood

- In Spain, Italy, and Greece, fish are the most common solid food triggers in infantile acute FPIES, likely reflecting the local dietary patterns.
- Fish FPIES in infants and young children has less favorable prognosis than other foods.
- In a single-center study in Spain, only 3 of 16 patients (18.7 percent) became tolerant by mean age 4.5 years.

Seafood

- In older children and adults, fish and shellfish are the most common triggers of FPIES.
- In adults with seafood FPIES, overall 60 percent react to a single food group.
- Fifty percent with fish FPIES react to a shellfish (crustacean or mollusk), 40 percent with crustacean FPIES react to a mollusk, and 55 percent with mollusk FPIES react to crustacean and/or fish

Peanut

- Peanut was an uncommon trigger for acute FPIES, generally representing less than 2 percent of cases in large series.
- However, more recent reports have highlighted the possibility of increasing incidence of infantile peanut FPIES.
- One retrospective, single-center study identified 14 cases of peanut FPIES from 2017 to 2019 compared with no cases in the same institution between 2001 and 2011.

Peanut

- Possible association with early introduction remains speculative in the absence of a comparison group without early introduction, requiring a prospective or case control study.
- Pediatricians and allergy specialists should consider acute FPIES in the differential diagnosis of adverse reactions to peanut in infancy.

Multiple-food FPIES

- The reported proportion of patients with single- versus multiple-food FPIES varies widely, between 40 to 80 percent depending upon the study population and methodology.
- In general, higher rates of multiple-food FPIES are reported from studies based upon the surveys among caregivers compared with studies based upon data from allergy practices.

Multiple-food FPIES

- In a small subset of infants and children, three or more triggers were documented in 9 to 18 percent.
- Compared with FPIES due to two or fewer triggers, patients with multiple triggers were more likely to develop food aversion (43.2 versus 16.9 percent) and to have poor weight gain (21.6 versus 6.6 percent).

Multiple-food FPIES

- The patients with multiple triggers frequently reacted to HE, soy, grains (oat, rice, wheat, and barley), vegetable (sweet potato, legume), fruits (avocado, banana), and turkey but were less likely to have shellfish-related FPIES

Clinical features of food protein-induced enterocolitis syndrome (FPIES)

Chronic	Acute
Signs and symptoms	
Intermittent, chronic vomiting Chronic, watery diarrhea with blood/mucus Lethargy Pallor Dehydration Abdominal distension Weight loss Failure to thrive	Repetitive vomiting every 10 to 15 minutes, onset 1 to 3 hours after ingestion (> 90%) Diarrhea, onset approximately 5 hours after ingestion (< 50%) Lethargy (70%) Pallor (70%) Dehydration Hypotension (15%) Hypothermia (25%) Abdominal distension
Laboratory findings	
Anemia Hypoalbuminemia Elevated white count: - Left shift - Eosinophilia Metabolic acidosis Methemoglobinemia Stool-reducing substances Negative IgE test to the trigger food in most cases	Elevated neutrophil count Thrombocytosis Metabolic acidosis Methemoglobinemia Fecal leukocytes and eosinophils Frank or occult fecal blood Increased carbohydrate content in stool Elevated gastric juice leukocytes Negative IgE test to the trigger food in most cases
Radiologic features*	
Air-fluid levels	Air-fluid levels

IgE: immunoglobulin E.

* Radiologic studies are not recommended for the diagnosis of FPIES, since there is no

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Signs and symptoms	
Intermittent, chronic vomiting	Repetitive vomiting every 10 to 15 minutes, onset 1 to 3 hours after ingestion (> 90%)
Chronic, watery diarrhea with blood/mucus	Diarrhea, onset approximately 5 hours after ingestion (< 50%)
Lethargy	Lethargy (70%)
Pallor	Pallor (70%)
Dehydration	Dehydration
Abdominal distension	Hypotension (15%)
Weight loss	Hypothermia (25%)
Failure to thrive	Abdominal distension
Laboratory findings	

Laboratory findings	
Anemia	Elevated neutrophil count
Hypoalbuminemia	Thrombocytosis
Elevated white count:	Metabolic acidosis
- Left shift	Methemoglobinemia
- Eosinophilia	Fecal leukocytes and eosinophils
Metabolic acidosis	Frank or occult fecal blood
Methemoglobinemia	Increased carbohydrate content in stool
Stool-reducing substances	Elevated gastric juice leukocytes
Negative IgE test to the trigger food in most cases	Negative IgE test to the trigger food in most cases
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* Radiologic studies are not recommended for the diagnosis of FPIES, since there is no radiographic finding that is pathognomonic for FPIES. A few older studies, involving infants with possible FPIES symptoms including chronic diarrhea, rectal bleeding, and/or failure to thrive, reported air-fluid levels, nonspecific narrowing and thumb printing of the rectum and sigmoid, and thickening of the plicae circulares in the duodenum and jejunum with excess luminal fluid. Intramural gas has also been rarely documented, potentially leading to a misdiagnosis of necrotizing enterocolitis (NEC).

CLINICAL FEATURES (Age of onset)

- Symptoms of classic FPIES usually begin in early infancy, within one to four weeks following introduction of cow's milk (CM) or soy protein.
- In extreme cases, symptoms may begin within the first days of life.
- The first description of the disorder included nine infants who presented with severe vomiting and diarrhea, developing an average of 11 days after birth (range 4 to 27 days).
- In the Israeli birth cohort previously discussed, all 44 infants with CM FPIES presented with symptoms within the first six months of life.

CLINICAL FEATURES (Age of onset)

- Delayed introduction of CM or soy in breastfed infants may result in later onset.
- The mean age at onset of solid-food FPIES tends to be later than that of CM and soy FPIES, typically presenting when these foods are first introduced between the ages of four to seven months.
- The development of FPIES upon introduction of foods after one year of age is rare, although onset of a non-IgE-mediated gastrointestinal food hypersensitivity similar to FPIES, most commonly triggered by shellfish, fish, and/or hen's egg (HE), has been observed in older children and adults.

Chronic versus acute presentation

- The disease typically presents in two phases.
- The initial presentation of CM- or soy-induced FPIES in infancy is that of a chronic disease while the food antigen is ingested on a regular basis.
- This can be followed by an acute phase if the antigen is removed from the diet and subsequently reingested, with symptoms occurring approximately two hours after ingestion and lasting several hours.

Chronic versus acute presentation

- An acute presentation is also seen when the antigen is ingested intermittently.
- Young infants with FPIES due to CM- and/or soy-based formulas usually have a chronic presentation, whereas solid-food FPIES can have an acute or chronic presentation depending upon the frequency of ingestion of the offending food.
- In a retrospective review of 203 patients with FPIES, 180 had reported acute, 8 chronic, and 15 both acute and chronic FPIES.

Chronic versus acute presentation

- Oat (34.5 percent), rice (29.6 percent), and CM (19.2 percent) were the most common food triggers in acute FPIES, whereas, in chronic FPIES, 87 percent of cases were caused by CM and 21 percent by soy.
- The median age of onset of acute FPIES was older, 6.0 (interquartile range [IQR]: 5.0 to 7.0) months compared with the median age of onset of chronic FPIES of 0.4 (IQR: 0.0 to 1.7) months.

Chronic versus acute presentation

- Nearly all patients present with vomiting, which is projectile, repetitive in the acute presentation, and intermittent in the chronic setting, and are commonly pale and ill appearing.
- Overall, approximately 75 percent of infants with FPIES appear seriously ill, and 15 percent develop hypotension and require hospitalization.
- Other symptoms that can occur in both the chronic and acute presentations include diarrhea, abdominal distention, dehydration, pallor, and lethargy.

Chronic versus acute presentation

- In acute FPIES, repetitive emesis usually begins within 1 to 4 hours and diarrhea within 2 to 10 hours (mean onset 5 hours) of ingestion.
- Patients with acute presentations tend to be sicker and may develop pallor, hypotonia, hypotension/shock, and/or hypothermia.
- Failure to thrive/poor weight gain (<10 g/day in young infants), weight loss, anemia, hypoproteinemia, and hypoalbuminemia are seen in patients with chronic FPIES, who might need a longer period of food avoidance for symptom resolution (days to weeks).

Feeding and growth issues

- In a retrospective review of 203 patients with FPIES, 23.3 percent reported food aversion, and, compared with patients without food aversion, they were more likely to have multiple food triggers (36.4 versus 14.2 percent), have a wheat trigger (13.6 versus 2.1 percent), and have a family history of food allergy (45.4 versus 28.4 percent).

Feeding and growth issues

- Patients with poor weight gain compared with normal weight gain were more likely to have chronic FPIES (31.6 versus 10.2 percent), multiple food triggers (42.1 versus 16.8 percent), and triggers of CM (42.1 versus 18.6 percent) and banana (26.3 versus 5.4 percent).

Feeding and growth issues

- The risk of developing food aversion was higher in patients with FPIES triggered by three or more foods compared with patients with FPIES with one or two food triggers (adjusted odds ratio [OR] 3.07, 95% CI 1.38-6.82).
- The risk of poor weight gain was higher in FPIES triggered by CM (adjusted OR 3.41, 95% CI 1.21-9.63) and banana (adjusted OR 7.63, 95% CI 2.10-27.80).

Atypical FPIES

- Some patients with FPIES have mixed immunologic reactions to the food(s) causing their FPIES symptoms.
- Up to 25 percent of infants and children fulfilling the clinical diagnostic criteria for FPIES have or develop IgE antibodies to the trigger food.
- These patients are referred to as having atypical FPIES because the disorder is primarily considered a cell-mediated allergy.

Atypical FPIES

- They tend to have a more protracted course of FPIES and have the potential for developing symptoms of IgE-mediated allergy (eg, anaphylaxis) in addition to FPIES.
- In one study, for example, 7 of 17 children with CM-induced FPIES who developed CM IgE positivity progressed to immediate allergic reactions ranging from mild symptoms to anaphylaxis

Atopic disease

- FPIES is associated with atopic comorbidities.
- Approximately 30 percent of infants with FPIES develop atopic diseases, such as atopic dermatitis (25 to 65 percent), asthma (3 to 20 percent), or allergic rhinitis (20 percent).
- In one study, 39 percent of the children with FPIES had concurrent sensitization (positive IgE test) to other foods.
- Family history of atopic diseases is present in 40 to 80 percent of patients, including a family history of food allergy in approximately 20 percent.

Laboratory and radiographic findings

- The common laboratory and radiographic findings are reviewed below and summarized in the table.
- Most of these studies are not performed as part of the initial diagnostic evaluation for FPIES, although some may have been performed as part of the evaluation for the patient's presenting symptoms (eg, vomiting and diarrhea, failure to thrive).

Laboratory findings	
Anemia	Elevated neutrophil count
Hypoalbuminemia	Thrombocytosis
Elevated white count:	Metabolic acidosis
- Left shift	Methemoglobinemia
- Eosinophilia	Fecal leukocytes and eosinophils
Metabolic acidosis	Frank or occult fecal blood
Methemoglobinemia	Increased carbohydrate content in stool
Stool-reducing substances	Elevated gastric juice leukocytes
Negative IgE test to the trigger food in most cases	Negative IgE test to the trigger food in most cases
Radiologic features*	
Air-fluid levels	Air-fluid levels

IgE: immunoglobulin E.

* Radiologic studies are not recommended for the diagnosis of FPIES, since there is no radiographic finding that is pathognomonic for FPIES. A few older studies, involving infants with possible FPIES symptoms including chronic diarrhea, rectal bleeding, and/or failure to thrive, reported air-fluid levels, nonspecific narrowing and thumb printing of the rectum and sigmoid, and thickening of the plicae circulares in the duodenum and jejunum with excess luminal fluid. Intramural gas has also been rarely documented, potentially leading to a misdiagnosis of necrotizing enterocolitis (NEC).

Diagnosis

- The diagnosis of FPIES is based upon the history, constellation of typical clinical symptoms with clinical improvement following withdrawal of the suspected causal protein, exclusion of other etiologies, and, if necessary, results of an oral food challenge (OFC).

Diagnosis

- There are no laboratory and radiographic findings specific to FPIES.
- However, obtaining a complete blood count with differential during an acute presentation may be useful in that an elevated white blood cell count with a left shift is suggestive of FPIES or sepsis.
- In addition, an elevated methemoglobin level in a child that appears ashen, gray, or cyanotic and very ill also suggests the diagnosis of FPIES.

Oral food challenge

- OFC is the gold standard for diagnosis of FPIES.
- However, infants do not usually require confirmatory challenges for initial diagnosis if they have a classic history and symptoms resolve after removal of the offending food from the diet.

Oral food challenge

- Clinician-supervised OFCs are necessary, however, if the history is unclear and a specific food trigger has not been identified, if the time course symptoms are atypical (eg, severe emesis within minutes of food ingestion in the absence of food-specific IgE), or if the child has persistent symptoms on an allergen-restricted diet, with the goal in this case of identifying the relevant food(s) and avoiding unnecessary food restrictions.

Oral food challenge

- An OFC for FPIES is generally considered a high-risk procedure.
- In a patient with prior severe FPIES reactions, an OFC should be conducted in a setting where intravenous access can be secured, rapid fluid resuscitation given if a reaction occurs, and prolonged observation can occur if necessary.
- An inpatient setting is the most appropriate for FPIES OFCs.

Differential diagnosis

- The differential diagnosis of FPIES is extensive and includes food-allergic disorders, infectious diseases, intestinal obstruction due to anatomic or functional etiologies, severe gastroesophageal reflux disease, and metabolic, neurologic, and cardiac diseases.
- A comprehensive differential diagnosis is presented in the table

Differential diagnosis of food protein-induced enterocolitis syndrome (FPIES)

Allergic
Food protein-induced proctocolitis
Food protein-induced enteropathy
Eosinophilic gastroenteropathies
Anaphylaxis
Nonallergic
Infectious
Sepsis
Viral gastroenteritis
Bacterial enteritis (<i>Salmonella</i> , <i>Shigella</i> , <i>Campylobacter</i> , <i>Yersinia</i>)
Parasites
Gastrointestinal disorders
Hirschsprung disease
Intussusception
Volvulus
Gastroesophageal reflux disease
Pyloric stenosis
Other
Metabolic disorders
Neurologic disorders
Heart defects
Necrotizing enterocolitis

Food protein-induced proctocolitis

- This benign, transient condition typically begins in the first few months of life with blood-streaked stools.
- These infants are well appearing and thriving, unlike the typical infant with FPIES.
- Over one-half of infants with proctocolitis are exclusively breastfed.
- Mild anemia and, rarely, hypoalbuminemia may be present.
- Eosinophilic infiltration of colonic biopsies is prominent, and peripheral blood eosinophilia is occasionally seen.

Food protein-induced enteropathy

- This non-IgE-mediated inflammatory response to food causes small bowel injury, leading to malabsorption, intermittent vomiting, diarrhea, failure to thrive, and, rarely, bloody stools.
- It is similar to celiac disease (also known as gluten-sensitive enteropathy), although less severe.
- Clinical manifestations seen in FPIES that are not typically seen in patients with food protein-induced enteropathy are lethargy, pallor, dehydration, abdominal distension, hypotension, and hypothermia.

Food protein-induced enteropathy

- Food protein-induced enteropathy is usually induced by CM protein and is most likely to occur in infants fed unmodified (nonformula) CM prior to nine months of age.
- It has also been described in response to other foods, including soy, hen's egg (HE), rice, poultry, fish, or shellfish.
- In some cases, the onset coincides with an episode of gastroenteritis.

Food protein-induced enteropathy

- Anemia and hypoalbuminemia may be present but not methemoglobinemia or acidemia, which can also help differentiate it from FPIES.
- The diagnosis is suspected based upon the clinical features and is confirmed by endoscopy with biopsy of the proximal small intestine that demonstrates patchy villous atrophy with a cellular infiltrate.
- Celiac disease should be specifically excluded by antibody testing (typically IgA antibodies to tissue transglutaminase [IgA-tTG]) and histologic features.

Food protein-induced enteropathy

- The histopathologic features of food protein-induced enteropathy are similar to those of celiac disease (villous blunting, intraepithelial lymphocytes, and crypt hyperplasia) but are generally less severe.
- Food protein-induced enteropathy is managed by strict elimination of the offending protein, just as celiac disease is managed by elimination of gluten.
- The disorder generally resolves spontaneously after two years of age.

Eosinophilic gastrointestinal disorders

- Eosinophilic esophagitis (EoE) and eosinophilic gastroenteritis are mixed pathophysiology disorders.
- Sensitization to food allergens is more common in the eosinophilic gastrointestinal disorders than in FPIES, with approximately one-half of patients having detectable food-specific IgE antibodies.
- Disease onset ranges from a few days of age to adulthood.

Eosinophilic Gastrointestinal Disorders

- Symptoms are usually chronic, evolving over days to weeks following food exposure, and may include nausea, vomiting, poor appetite, early satiety, abdominal pain, and diarrhea with blood or mucus.
- The course is insidious, chronic, and not characterized by acute episodes of severe, repetitive vomiting or lethargy.
- Difficulty swallowing and food impaction may be the presenting symptom in teenagers and adults with EoE.

Management

- **Management consists of elimination of the offending food from the diet and an emergency treatment plan for acute episodes due to accidental exposures.**

Dietary Elimination

- The triggering food(s) should be completely eliminated from the diet.
- A casein hydrolysate-based (hypoallergenic) formula is recommended in the infant with cow's milk (CM) FPIES if breastfeeding is not possible or the infant is exclusively formula fed due to frequent concomitant CM and soy FPIES.
- In the rare case of FPIES in the nursing infant, the mother should completely eliminate the triggering food(s) from her diet.

Dietary elimination

- Infants presenting with chronic symptoms due to CM or soy usually improve within 3 to 10 days of switching to a casein hydrolysate-based formula with or without temporary intravenous fluids.
- Approximately 10 to 20 percent may require an amino acid-based formula.
- Many children with IgE-mediated cow's milk allergy (CMA) and hen's egg allergy (HEA) can tolerate these allergens in baked goods.

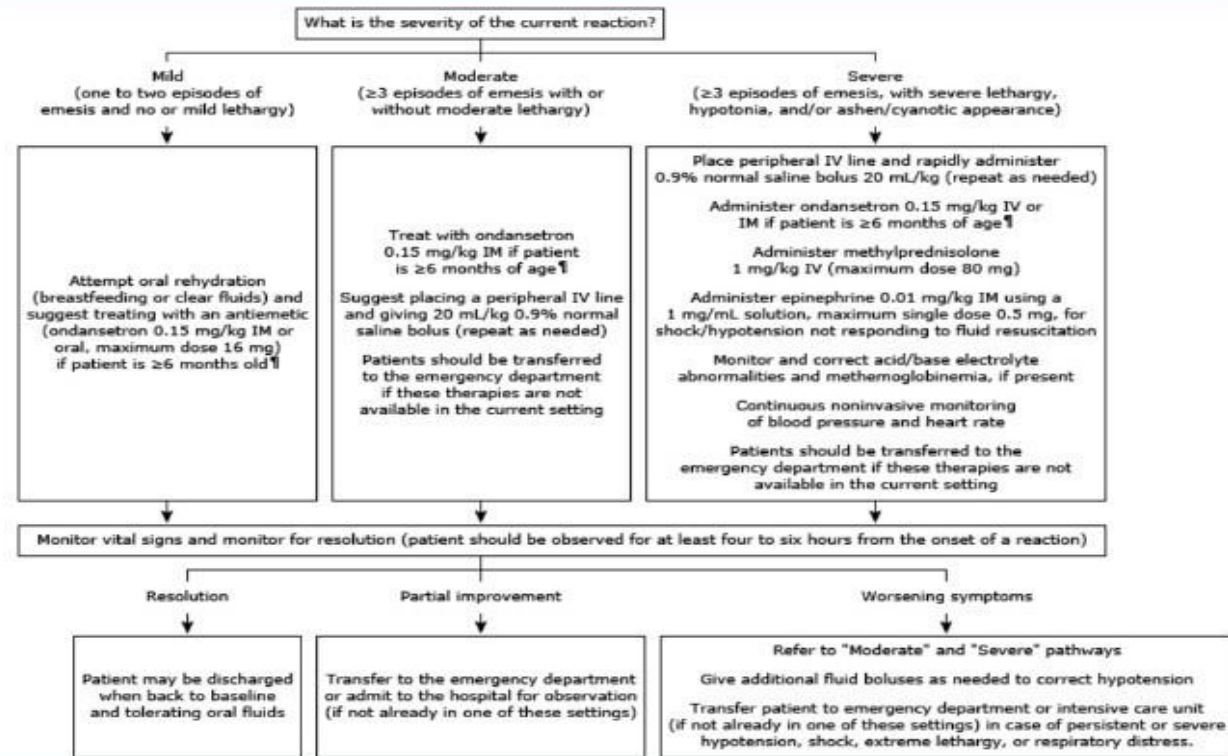
Introduction of new foods

- Introduction of green vegetables and then fruits at four to six months of age instead of cereals is suggested because approximately one-third of infants with CM or soy FPIES develop solid-food FPIES and reactions to rice and other grains represent the most common types of solid-food FPIES .
- Introduction of CM and soy in these infants may be attempted after one year of age (preferably under clinician supervision) if there is no prior history of reactivity to these foods.

Emergency treatment plan

- In general, the child should be taken to the ED for evaluation and intravenous fluid administration if the episode is severe, manifesting with multiple episodes of projectile emesis, lethargy, and a pale or ashen appearance.
- Most patients with severe disease are also treated with a glucocorticoid.
- Ondansetron is used to control emesis in children over six months old with moderate-to-severe symptoms.

Management of acute FPIES episode at a medical facility*



FPIES: food protein-induced enterocolitis syndrome; IM: intramuscular; IV: intravenous; ECG: electrocardiogram.

* Medical facilities include outpatient clinics/medical offices, emergency departments, and inpatient units (regular and intensive care).

¶ ECG changes, including dose-dependent QT interval prolongation, have been observed with ondansetron use. Thus, a baseline and post-dose ECG is suggested in at-risk patients (eg, those with underlying heart disease and/or uncorrected electrolyte abnormalities).



NATURAL HISTORY

- Cow's milk (CM) and soy FPIES resolve in a majority of patients by age three years.
- However, patients with solid-food FPIES may have a more protracted course.
- Factors associated with a slower acquisition of tolerance include concomitant detectable food specific IgE and older age at both initial episode and diagnosis.
- Age at resolution of FPIES for a particular food also varies by population.
- An oral food challenge (OFC) is used to determine if FPIES has resolved.



Thank you for attention

کوه پوشیده از شقایق – یکانات مرند