Guideline-Based Care of Infants With Food Protein-Induced Enterocolitis Syndrome A Case-Based Program



Pediatric Nutrition

CONTINUING EDUCATION FOR CLINICIANS

Presented by

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Faculty Disclosures

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Clinical Trial Regeneron

Speaker Danone, Nestlé, Thermofisher

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Learning Objectives



Identify an infant with a convincing history of food protein-induced enterocolitis syndrome (FPIES)



Optimize the nutritional management of an infant with FPIES



Summarize new areas of research in FPIES



Have you provided care to a patient with FPIES in your clinical practice?



Diagnosing FPIES



Food Protein-Induced Enterocolitis Syndrome

- FPIES is a non-IgE, cell-mediated food allergy that manifests as delayed, repetitive vomiting after ingestion (sometimes with diarrhea), primarily in infants. [1]-[3]
 - One of several immunologic reactions to dietary proteins
- FPIES can lead to shock and dehydration.
- Chronic FPIES can lead to failure to thrive.
- Pathophysiology is poorly understood.
- **FPIES** awareness remains low.



Nowak-Węgrzyn A, et al. J Investig Allergol Clin Immunol. 2017;27:1-18.
 Nowak-Węgrzyn A, et al. J Allergy Clin Immunol. 2015;135:1114-24.

^{3.} Nowak-Wegrzyn A, et al. J Allergy Clin Immunol Pract. 2020;8:24-35.

Natural History: Prevalence and Food Triggers

- FPIES may be more common than once thought^[1]:
 - Cumulative incidence of FPIES in infants est. 0.015%–0.7%
 - Prevalence in US infants 0.51%
- Onset typically occurs during the first year of life [a][2]
- Diagnosis may be missed due to [1]-[2]
 - Symptoms appear 1–4 hours after food ingestion
 - Lack of typical allergic skin and respiratory symptoms
 - Food triggers perceived to be hypoallergenic (oat, rice, fruits, vegetables)
 - No biomarkers; clinical diagnosis
- a. Seafood-induced FPIES may start in adulthood



Common Food Triggers

Study (country)	N=	Median Age of First FPIES	Median Age of Diagnosis	Most Common Food Triggers
Lemoine et al. 2022 (France)	179	5.8 months	n/a	Cow's milk (60.3%), hen's egg (16.2%), fish (11.7%)
Lee et al. 2021 (Australia)	168	5 months	9 months	Rice (45%), cow's milk (30%), soya (13%)
Blackmann et al. 2019 (US)	74	5 months	11 months	Grains (88%), rice (53%), cow's milk (49%), vegetables (43%), banana (24%), avocado (16%)
Alonso et al. 2019; PREVALE study (Spain)		0.7% <1-year old	n/a	Cow's milk (50%), fish (37.5%), egg yolk (12.5%)



^{1.} Lemoine A, et al. Clin Transl Allergy. 2022;12:e12112.
2. Lee E, et al. Pediatr Allergy Immunol. 2021;32:742-749; Mehr S, et al. J Allergy Clin Immunol. 2017;140(5):1323-1330.
3. Blackman AC, et al. Ann Allergy Asthma Immunol. 2019;122:407-411.
4. Alonso SB, et al. J Allergy Clin Immunol. 2019;143:430-433.

Natural History: Resolution

- Generally favorable prognosis
- Self-limiting disorder of childhood
- Majority outgrow FPIES by age 3–5 years
- Atypical FPIES (positive skin or blood test for food IgE) tends to be more persistent



FPIES Clinical Phenotypes

- FPIES phenotype depends on dose and frequency of food allergen ingestion.
- Phenotype provides guidance for diagnosis and management.

Phenotypes influenced by		
Age of onset	infancy	older children, adults
Severity	mild-to-moderate	severe
Timing and duration of symptoms	acute (symptoms resolve in 24 hrs)	chronic (resolution may take days to weeks)
Detectable s-IgE to food trigger	lgE negative (typical)	IgE positive (atypical)



Chronic vs Acute Presentation: Determined by frequency and dose of the ingested food

Acute FPIES	Chronic FPIES	
Emesis onset 1–4 hours after ingestion	Emesis intermittent but progressively worsening	
Repetitive emesis	Watery diarrhea	
Pallor	Poor growth / FTT	
Dehydration	Dehydration, metabolic acidosis	
Lethargy progressing	Lethargy, pallor, abdominal distension	
Hypovolemic shock in 15% of cases	Hypovolemic shock after a period of days to weeks	

FTT, failure to thrive.



FPIES Phenotypes (continued)

Acute

- Ingestion following a period of avoidance (at least several days)
- Onset of emesis: 1–4 hours
- 6–8 hours later: diarrhea
- Lethargy, limpness, 'septic' appearance
- 15% with methemoglobinemia
- Onset: usually <12 months
- Symptoms resolve within 24 hrs
- Cow's milk, soy, oat, rice, vegetables
 - Fish/Shellfish: more common in children and adults

Chronic

- Onset of symptoms: first 1–3 months of life
- Young infants fed continuously with milk or soy formulas
- Watery diarrhea
- Mucous, blood in stools
- Intermittent emesis
- Low albumin and total protein
- Failure to thrive, poor growth
- Symptoms resolve within days– weeks, may require TPN
- · Cow's milk, soy

TPN, total parenteral nutrition.



The JOURNAL of ALLERGY and CLINICAL IMMUNOLOGY

REVIEWS AND FEATURE ARTICLE | VOLUME 139, ISSUE 4, P1111-1126.E4, APRIL 01, 2017

International consensus guidelines for the diagnosis and management of food protein-induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology

Anna Nowak-Wegrzyn, MD, PhD, Mirna Chehade, MD, Marion E. Groetch, MS, RDN, et al. Published: February 03, 2017

- First international evidence-based consensus guidelines
 - 9 countries represented
- Recommendations
 - Epidemiology and diagnosis
 - Specific diagnostic criteria for acute and chronic FPIES
 - Guidance on managing FPIES emergencies and long term



Acute FPIES diagnostic criteria



1 Major criterion + 23 Minor criteria

Vomiting in 1-4 hrs, and absence of skin and respiratory sxs

>1 episode to the same food

Repetitive emesis to another food

Lethargy

Pallor

Emergency room visit

Need for intravenous fluids

Diarrhea in 24 hrs (5–10 hours)



Diagnostic criteria for patients with possible chronic FPIES

The most important criterion for chronic FPIES diagnosis is resolution of the symptoms within days following elimination of the offending food(s) and acute recurrence of symptoms when the food is reintroduced, onset of vomiting in 1-4 hours, diarrhea in 24 hours (usually 5-10 hours).

Without confirmatory challenge, the diagnosis of chronic FPIES remains presumptive.



FPIES Differential Diagnosis

Most common differential diagnosis	Other non-IgE mediated food allergic disorders	
Acute viral gastroenteritis	Eosinophilic esophagitis (EoE)	
Sepsis	Food protein-induced allergic proctocolitis (FPIAP)	
Anaphylaxis	Food protein-induced enteropathy (FPE)	
Intestinal obstruction		
Necrotizing enterocolitis (NEC) ^[a]		
 a. Abdominal distension and pneumatosis intestinalis may be seen in FPIES and in NEC; peripheral blood eosinophilia is more common in FPIES. 		



Distinguishing FPIES, FPIAP, and FPE

	Main clinical features
FPIES	Delayed repetitive vomiting, pallor, lethargy
FPIAP	Benign blood in stool, baby thriving Average age at onset lower: 2 months vs 4-6 months in FPIES, no acute symptoms upon food ingestion
FPE	Chronic diarrhea, malabsorption, low weight gain, no acute symptoms upon food ingestion

FPIAP, food protein-induced allergic proctocolitis; FPE, food protein enteropathy.



Diagnostic Strategies

- Understanding FPIES specific features
 - No diagnostic tests or biomarkers, currently
 - Chronic FPIES is usually a diagnosis of exclusion
- Recognize pattern of clinical symptoms
- FPIES may be missed due to
 - Absence of typical allergic symptoms (eg, urticaria, wheezing)
 - Delayed onset (1–4 hours) in relation to food ingestion
 - Unusual food triggers: rice, oat, sweet potato, considered hypoallergenic foods for IgE-mediated food allergy



Diagnosing FPIES, Acute and Long-Term Management, and Optimizing Nutritional Management



Case Study 1—Diagnosing FPIES

Isabella, a 5-month-old girl, has had her third feeding of oats, along with bananas, and is having symptoms. She presents in the emergency room with repetitive, forceful projectile vomiting that started 3 hours after her last meal. She is not itching, coughing, or wheezing; however, she is lethargic and pale, and looking very unwell, and is found to be hypotensive.

She was breastfed without any symptoms, on a regular, unrestricted maternal diet, and has recently begun feeding with oatmeal.

What are the signs and symptoms upon presentation that will help to diagnose Isabella?



What are the signs and symptoms upon presentation that will help to diagnose this patient?

- A. Lack of allergic skin symptoms
- B. Lethargy
- C. Onset of projectile, repetitive emesis within 1–4 hours following feeding
- D. All of the above <



Case Study 1—Explanation

Acute FPIES typically starts during the first year of life, with acute symptoms appearing 1-4 hours after food ingestion. Note, a child can experience a reaction after 2 or more feedings from an offending food until the full phenotype is displayed. The International Consensus Guidelines for the Diagnosis and Management of FPIES, published in 2017, provides specific recommendations and diagnostic criteria for acute and chronic FPIES. [1] Because she was breastfed without symptoms, and she did not develop violent vomiting until her third feeding with oatmeal, within 2 hours, a careful history and review of symptom pattern can help guide a diagnosis.

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Treatment Strategies & Management

- According to 2017 FPIES Guidelines... eliminate food trigger(s)
 - Food avoidance risks nutritional deficiencies in long term
 - Involve registered dietitian
 - Introduce food without unnecessary delays
- Acute management of FPIES emergencies
- Long-term management of FPIES



Acute Management

- Severe reaction—Have emergency treatment plan
 - Go to the Emergency Department
 - Call 911
 - Child needs fluids to recover
- Mild reaction
 - Can manage at home, except in a child with prior severe FPIES reaction to the trigger food



Oral Food Challenge: What Clinicians Need to Know

- OFC is usually not necessary for diagnosis but can be used if history is not clear or doesn't meet diagnostic criteria for acute FPIES
- Acute FPIES can be reliably diagnosed based on diagnostic criteria
- Clinician-supervised OFC is necessary to evaluate for FPIES resolution
- Keep infant/child away from food until challenge is done



Oral Food Challenge (continued)

- At-home OFCs are generally not recommended, given the potential for severe reactions
- Intravenous fluids must be available for rehydration, if needed
 - If mild, attempt oral rehydration by breastfeeding or with clear fluids
- Recommended to be done at centers with expertise in managing food allergy and performing oral food challenges
- Consider OFC between 6–24 months or longer from the most recent reaction, depending on nutritional and social importance of food

OFC, oral food challenge.



Case Study 2—Selecting foods for introduction

This same infant, Isabella, now 10-months old is fed with a hypoallergenic formula along with apples, pears, and avocado. Five month earlier she had an acute reaction while being fed oatmeal and bananas. Her mother says her daughter remembers the taste and is refusing to eat any cereal or bananas, creating nutrition concerns about getting enough iron, specifically vitamin B, without cereal grains in her diet. The baby is generally suspicious of any new foods. The parents were also traumatized by the acute FPIES reaction, so they were apprehensive about trying new foods.

What is the next step to help the parents provide the necessary nutritional requirements for this young infant?



What is the next step to help the parents provide the necessary nutritional requirements for this young infant?

- A. Tell the parents not to worry and to keep offering a variety of solid foods
- B. Offer a food challenge to oats
- C. Provide a short list of possible new foods and specific instructions for gradual introduction at home or under supervision in the office
- D. Recommend starting introduction with peanut to prevent development of peanut allergy



Case Study 2—Explanation

It is common for infants and their caregivers to experience difficulties following an acute FPIES episode, just as described in this case. [1],[2] While the apprehension is justified, it is very important to encourage and support introduction of new solid foods to develop feeding skills and to maintain a nutritionally complete diet. [3] The effective support entails:

- Acknowledging the concerns while providing reassurance that most children react to only 1 food and that with every month, the risk of FPIES to a new food decreases gradually;
- 2. Explaining why timely introduction of solids is important;
- 3. Providing specific instructions for gradual home introduction, including the selection of the foods generally considered to be a low risk for the initial introduction (eg, cauliflower, broccoli, parsnip, etc); [4]

^{1.} Maciag MC, et al. J Allergy Clin Immunol Pract. 2020;8:1702-1709.

^{2. 2.} Bartnikas LM, et al. Ann Allergy Asthma Immunol. 2021;126:489-497.

^{3.} Su KW, et al. J Allergy Clin Immunol. 2020;145:1430-1437.e11.

^{4.} Groetch M, et al. Ann Allergy Asthma Immunol. 2021;126:124-126.

Case Study 2—Explanation (continued)

- 4. If needed, offering a supervised food challenge to introduce 1 or 2 new foods in the office;
- 5. Deferring introduction of potentially cross- and co-reactive foods, such as other cereal grains (eg, rice, barley, wheat in the case of our patient) until several other new foods have been tolerated; [1]
- 6. Providing a specific plan for managing acute FPIES reactions. [2]

Infants with FPIES are at high risk to develop other allergic comorbidities, including IgE-mediated food allergy, atopic dermatitis, allergic rhinitis, asthma, eosinophilic esophagitis. [3]-[5]

While risk for peanut allergy is of concern, especially in an infant with FPIES and atopic dermatitis, peanut is not an optimal food for the initial introduction in this setting due to the challenging texture and the recognition of high allergenicity in terms of IgE-food allergy.

Nowak-Węgrzyn A, et al. J Allergy Clin Immunol. 2017;139:1111-1126.e4.
 Leonard SA, et al. Ann Allergy Asthma Immunol. 2021;126(5):482-488.e1.

^{3.} Cianferoni A, et al. Allergy. 2020;75(6):1466-1469. doi: 10.1111/all.14148.

^{4.} Nowak-Wegrzyn A, et al. J Allergy Clin Immunol. 2019;144(4):1128-1130. Ruffner MA, et al. J Allergy Clin Immunol Pract. 2020;8(3):1039-1046.

Long-term Management of FPIES

- Eliminate food trigger(s) from diet
- Periodic reassessment for tolerance (every 6–24 months)
- Attention to feeding skills
- Timely introduction of complementary solid foods
- Provide emergency plan for potential acute reaction (see resources)
- Be aware of issues associated with long-term management:
 - Avoidance
 - Breastfeeding



Long-term Nutritional Management

- Nutritional management is most important (once diagnosed)
- Long-term management of food avoidance
 - Potential for nutritional deficiencies
- Anticipatory guidance of complementary feeding
 - Unnecessary delay of solid food introduction, how to reduce this risk



Nutritional Daily Management

- No need to avoid traces or foods with "may contain" labels
- Avoid baked milk/egg (unless tolerance to baked products is documented by a challenge, or is frequent at large ingestions)
- Consider dietary consult
- Be aware of co-reactivity (eg, milk-soy, rice-oat)
- Introduce solids in a timely manner
- Monitor growth



Management While Breastfeeding

FPIES can happen in exclusively breastfed infants, although rare

- Do not restrict maternal diet unless infant is symptomatic (acute or chronic), or is not thriving
- Majority are asymptomatic and thriving during breastfeeding
- Rarely have acute or chronic symptoms been reported in breastfed infants, attributed to foods in maternal diet
- Maternal dietary avoidance vs stopping
- Substitute for breast milk: Hypoallergenic formula is recommended if the trigger is thought to be cow's milk
 - Extensively hydrolyzed casein or amino-acid formula [up to 40%]



Selecting Safe Nutritional Alternatives

Ages and Stages	Lower-risk foods ^[a]	Moderate-risk foods ^[a]	Higher-risk foods [a]
 4-6 months (per AAP, CoN) If developmentally appropriate, and safe and nutritious foods are available: Begin with smooth, thin, purees and progress to thicker purees Choose foods high in iron Add vegetables and fruits 	Broccoli, cauliflower, parsnip, turnip, pumpkin	Squash, carrot, white potato, green bean (legume)	Sweet potato, green pea (legume)
 6 months (per WHO) Complementary feeding should begin no later than 6 months of age In breastfed infant, high-iron foods or supplemental iron (1 mg/kg/day) is suggested by 6 months of age Continue to expand variety of fruits, vegetables, legumes, grains, meats, and other foods as tolerated 	Blueberries, strawberries, plum, watermelon, peach	Apple, pear, orange	Banana, avocado

a. Risk assessment is based on the clinical experience and the published reports of FPIES triggers. AAP, CoN, American Academy of Pediatrics, Committee on Nutrition; WHO, World Health Organization.



Selecting Safe Nutritional Alternatives

Ages and Stages	Lower-risk foods [a]	Moderate-risk foods ^[a]	Higher-risk foods [a]
 8 months of age or when developmentally appropriate Offer soft-cooked and bite-and-dissolve textures around 8 months or as tolerated by infant. 	Lamb, fortified quinoa cereal, millet	Beef, fortified grits and corn cereal, wheat (whole wheat and fortified), fortified barley cereal	Higher iron foods: Fortified, infant rice and oat cereals.
 12 months of age or when developmentally appropriate Offer modified tolerated foods from the family table: chopped meats, soft cooked vegetables, grains, and fruits. 	Tree nuts and seed butters [a] (sesame, sunflower, etc)	Peanut, other legumes (other than green pea)	Milk, soy, poultry, egg, fish

a. Risk assessment is based on the clinical experience and the published reports of FPIES triggers.



Case Study 3— Timing of Reintroduction of Offending Food

Our case infant is now a toddler at 1.5 and ready to enter daycare. Her parents are returning to their offices after working from home during Covid. They worry about what will happen if she grabs oat cereal from another child, picks it up from a table, or is fed oats incidentally.

When is the optimal time to reintroduce the food that has triggered FPIES?



When is the optimal time to reintroduce the food that has triggered FPIES?

- A. It is recommended to re-try food reintroduction every 3–6 months
- B. Not sooner than 24 months from the most recent reaction
- C. When the child is older than 3 years
- D. Depends on the nutritional and social importance of the food, as well as the severity of the past reaction





Case Study 3—Explanation

The decision to reintroduce the FPIES trigger is made empirically because there are no biomarkers to guide the timing. [1] It is a shared decision between the caregivers and the physician, taking into consideration the nutritional and social importance of the food. Usually, foods that are dietary staples, such as cow's milk, egg, or wheat, tend to be reintroduced sooner than foods that are not as prevalent in the diet, eg, sweet potato, or fruits.

In one approach, food can be re-tried within 6–24 months following the most recent reaction. Generally, the more severe the most recent reaction was (especially to small amount of the food), the more worried and more apprehensive the caregivers / patients are to re-try the food, which leads to a more deferred reintroduction.

New Areas of Research in FPIES



Immune Mechanisms Underlying FPIES Reactions

- FPIES associated with systemic innate immune activation in absence of a detectable antigen-specific antibody or T-cell response; mechanism of specific food recognition by the immune system remains unclear
- Berin et al. 2021 study to identify immune mechanisms underlying FPIES reactions by proteomic and flow cytometric analysis of peripheral blood
 - N=23; 184 protein markers analyzed
- Special type of inflammation in FPIES
- Insight into acute reactions
- Only goes up during acute reaction
- Results demonstrate a unique IL-17 signature and activation of innate lymphocytes in FPIES



FPIES in Adults!

- FPIES can also start in adulthood
- Seafood most often the cause
- Guidelines did not focus on adults, who may (or appear to) have a different clinical presentation than children.
- Delay in diagnosis!
 - Adult FPIES is often mistaken for food poisoning
- Need to advance our understanding of FPIES in adults



Characteristics in Children vs Adults

Characteristics	Children	Adults	
Sex	Male > Female	Female > Male	
Food trigger	Cow's milk, soy	Seafood, crustaceans	
Onset (range)	1-4 h	3 min-6.5 h	



Peanut FPIES

- Early peanut introduction may contribute to peanut-induced FPIES
- Small study (n=32) 2017 Wu et al.^[1]
 - Higher incidence of peanut-induced FPIES (12.5%) in atopic infants with early peanut introduction
 - FPIES to peanut is uncommon; only 1.9% of all FPIES cases
- Early introduction of nuts is important; however, it can be a potential risk factor for FPIES <<cli>inicians need to be aware>>
- Continue to introduce peanut and egg early, as benefits outweigh risk for FPIES
- Be aware of a potential FPIES diagnosis



Unmet Needs-I

- Laboratory biomarker
- Standardized food challenge procedure
 - Accessibility for oral food challenges primarily at large academic centers
 - IV access
 - Prolonged observation
- Burden of FPIES for families
 - QoL of caregivers and feeding children
 - Impact on families who stop working or move for family support
 - Financial burden—Out-of-pocket costs for FPIES



Unmet Needs-II

- Define genetics
- Identify risk factors
- Prevention strategies
- Therapies for acute reactions and to accelerate resolution



Federal-Funded Research is Lacking

- Lack of federally funded research is an impediment
- First NIH workshop to be held June 2022
 - NIH recognizing FPIES as a public health topic
- In addition to pathophysiology research there is interest in microbiome and FPIES.
- Epidemiology of FPIES is needed to study its natural history



Key Takeaways



Suspect acute FPIES in infants with projectile emesis starting 1–4 hours after food ingestion. Acute FPIES typically is more dramatic than chronic FPIES, which develops over time.



Suspect chronic FPIES in young infants with dramatic presentation (dehydration, metabolic acidosis, shock).



- Empower caregivers to introduce new foods without delay.
- Pay attention to nutritional status.
- Provide clearly outlined plan for managing acute reactions.
- Monitor for tolerance development.



Resources

- FPIES.org https://www.fpies.org
- FPIES Guidelines https://www.fpies.org/fpies-guidelines/
- FPIES Emergency Room Letter example
 https://www.fpies.org/wp-content/uploads/2017/12/IFPIES-ER-Letter.pdf
- Help track frequency of FPIES occurrence
 - o ICD-10 code: K52.2

https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Management/finances-coding/FPIES-Codes-ICD-10.pdf





Food Protein-Induced Enterocolitis Syndrome for ICD-10

K52.2 is a new, approved ICD-10 code for Food Protein-Induced Enterocolitis Syndrome (FPIES). FPIES is a non-IgE gastrointestinal food hypersensitivity that manifests as delayed, profuse vomiting, often with diarrhea, acute dehydration, and lethargy. The most common triggers are milk and soy, but any food, even those thought to be hypoallergenic (e.g., rice and oat), can cause an FPIES reaction.

According to the International Association for Food Protein Enterocolitis (IAFFPE), hundreds of patients suffer from FPIES, a rare non-IgE form of food allergy. The new code K52.2 will take effect when ICD-10 implementation is completed in 2015. The new code is the result of advocacy efforts by the International Association for Food Protein Enterocolitis, a lay organization and partner of the AAAAI.



Questions?

Please type your question into the *Ask a Question* box and hit send.



Understanding Food Allergies in Infants and Children: The Symptoms, Diagnoses, and Management

pnce.org/Food-Allergies

The Intestinal Microbiome and the Developing Immune System



Alessio Fasano, MD Professor of Pediatrics Harvard Medical School

Wednesday, May 25

Noon Eastern 11:00 AM Central 10:00 AM Mountain 9:00 AM Pacific

pnce.org/Microbiome-2

Guideline-Based Care of Infants with Food Protein-Induced Enterocolitis Syndrome A Case-Based Program



Anna Nowak-Wegrzyn, MD, PhD Professor of Pediatrics NYU Grossman School of Medicine

Thursday, May 26

1:00 PM Eastern Noon Central 11:00 AM Mountain 10:00 AM Pacific

pnce.org/FPIES-Cases-2

The Probiotic LGG and Its Benefits to the Immune System



Fayez K. Ghishan, MD Professor, Pediatric Gastroenterology and Nutrition University of Arizona Health Sciences

Tuesday, May 31

2:00 PM Eastern 1:00 PM Central Noon Mountain 11:00 AM Pacific

pnce.org/LGG-2

Made possible through educational grants from Mead Johnson Nutrition.



FPIES in Exclusively Breastfed Infants (Italian Study)

Exclusively Breastfed Cases	Presentation	Methemoglobin level		
2-month-old infant	Persistent vomiting and diarrhea; presented to ED in septic-like condition	Labs showed significant increase in methemoglobin (13%)		
Resolution: When breastfeeding suspended, diarrhea improved, and vice versa when maternal milk was reintroduced. An amino acid-based formula allowed a complete normalization of the symptoms.				
3-month-old infant	3-days history of persistent vomit and diarrhea	Raised level of methemoglobin (7%)		
An esophagogastroduodenoscopy wa Resolution: Maternal exclusion diet a function.	s performed; biopsies showed eosinophilion nd an amino acid-based formula allowed a	infiltration of the duodenal mucosa. rapid regularization of the bowel		

- Research showed majority of cases initially diagnosed as gastroenteritis or sepsis
 - 5 cases of acute or chronic FPIES with cow's milk most frequently involved food
 - Methemoglobin was never tested
- Again, FPIES in exclusively breastfed infants is rare, but should be considered in exclusively breastfed babies.
- The evaluation of methemoglobin can simplify the diagnostic process.



Adults FPIES From Crustacean Ingestion

Characteristics	N=19	% or IQR
Sex: Female / Male	13/6	68% / 32%
Average age of onset (y)	34.3	20.5-52.5
Type of crustacean with reaction Shrimp Lobster Crab	18 6 5	94.7% 31.6% 26.3%
Symptoms Emesis Abdominal pain Diarrhea	19 7 8	100% 36.8% 42.1%
Average duration of symptoms (h)	9.4	2.0-9.75
Average number of reactions	4.8	3-6
History of atopy	3	15.8%

