

FPIES

Sterling Slocum, DO

Allergist

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Lets Talk About... FPIES

- FPIES overview
- Phenotypes
- Demographics
- Proposed mechanisms
- Food Triggers
- Diagnosis
- Treatment
- Resources
 - ED letter
 - Food introduction guidance

Food Protein-Induced Enterocolitis Syndrome (FPIES) Overview

- Non-IgE, cell mediated food hypersensitivity manifesting as severe, delayed gastrointestinal symptoms which can lead to dehydration and lethargy in the acute setting
 - The underlying pathophysiology is not well understood
 - First described in 1960's, and over the past 2 decades the literature on FPIES has blossomed and it is now diagnosed with increased frequency
- 51% of patients react on their first exposure to a food, 14% on 2nd exposure, 11% after 2 tolerated exposures and 24% after 3 or more tolerated exposures
- Triggers can include all foods:
 - Milk, Soy (although Soy is less common than originally thought)
 - Grains (Rice & Oat), those with FPIES to one grain have 40-50% chance of having other grain triggers (although wheat is an uncommon trigger even with other grains)
 - Egg (egg yolk)
 - Seafood- most common trigger in older children and adults
 - Nuts- Peanut represents < 2% of triggers, however is becoming more prevalent with early peanut introduction in infants.
- Prevalence is likely more than reported 0.015-0.7%, with slight male predominance in children with onset <12 months of age,, and a more female predominance in adults

Phenotypes

- Chronic FPIES

- Occurs when trigger food is ingested on a regular basis (most common with CM or Soy FPIES in infants that are exclusively formula fed), often presents in the first months of life after formula introduction
 - Intermittent but progressive vomiting and diarrhea, not clearly temporally related to feedings as it is gradual, difficult to identify it as a food trigger
 - Often present with FTT, lethargy, irritability, dehydration, metabolic derangements, and even shock in severe cases
 - Symptoms resolve within days after elimination of the offending food, and acute recurrence with reintroduction

- Acute FPIES

- Dramatic, repetitive vomiting 1-4hrs after ingestion of a trigger food. Can be followed by watery diarrhea about 5-10hrs after ingestion and can persist for up to 24hrs.
 - Are well and thriving between episodes, but during acute episodes can presents with acute hypovolemia and shock
 - Often diagnosed in infants 6-12months, but adult onset FPIES has been reported
 - Adult onset FPIES: rare, most often triggered by seafood, female predominance

- Atypical FPIES: FPIES + allergic sensitization to trigger food (+ SPT and/or sIgE)

- Up to 25% of patients have or develop IgE antibodies to their trigger food
- Tend to have a more protracted course of FPIES, and carry the risk of anaphylaxis

Demographics - Children

TABLE II. Sociodemographic characteristics and comorbidities in children and adults

Characteristic	% among those with FPIES (95% CI)	% among those without FPIES (95% CI)	P value
Children			
Race/ethnicity			
Asian, non-Hispanic	8.1 (4.2-15.1)	3.2 (2.8-3.7)	.02
Black, non-Hispanic	16.3 (10.5-24.3)	13.2 (12.3-14.2)	
White, non-Hispanic	44.1 (34.9-53.8)	52.9 (51.3-54.4)	
Hispanic	27.8 (19.4-38.2)	24.1 (22.5-25.7)	
Multiple/other	3.7 (1.7-8.1)	6.7 (6.1-7.3)	
Country of origin			
Born in the United States	95.8 (87.6-98.7)	97.8 (97.4-98.1)	.26
Sex			
Female	47.7 (38.5-57.2)	48.9 (47.8-50.0)	.81
Age (y)			
<1	1.1 (0.5-2.7)	5.4 (4.8-5.9)	.15
1	5.6 (3.1-10.1)	4.9 (4.4-5.3)	
2	8.6 (4.5-15.8)	5.7 (5.2-6.3)	
3-5	16.7 (9.9-26.8)	16.2 (15.5-17.0)	
6-10	30.9 (23.1-39.9)	27.8 (26.9-28.8)	
11-13	20.1 (14.4-27.3)	16.6 (15.9-17.4)	
14-17	17.0 (11.3-25.0)	23.4 (22.4-24.4)	
Household income (\$)			
<25,000	16.8 (10.2-26.5)	16.1 (14.9-17.3)	.85
25,000-49,000	20.0 (12.5-30.4)	22.2 (20.9-23.5)	
50,000-99,999	34.5 (26.6-43.3)	31.1 (29.7-32.5)	
100,000-149,000	20.3 (13.6-29.1)	19.2 (18.0-20.5)	
≥150,000	8.4 (4.4-15.6)	11.4 (10.3-12.7)	
Physician-diagnosed comorbid atopic conditions†			
Current			
IgE-mediated food allergy*	65.3 (55.2-74.2)	7.3 (6.9-7.8)	<.001
Lifetime			
Asthma	25.2 (18.5-33.4)	12.1 (11.3-13.0)	<.001
Atopic dermatitis/eczema	9.6 (5.8-15.5)	5.9 (5.3-6.5)	.06
Allergic rhinitis	32.6 (24.4-42.0)	12.7 (11.9-13.5)	<.001
Insect sting allergy	5.0 (2.8-9.1)	2.2 (1.9-2.6)	.007
Latex allergy	8.9 (5.3-14.6)	1.0 (0.8-1.2)	<.001
Medication allergy	6.9 (4.1-11.4)	4.1 (3.7-4.6)	.06
Urticaria	3.4 (1.0-7.3)	0.5 (0.4-0.6)	<.001

Demographics - Adults

Adults			
Race/ethnicity			
Asian, non-Hispanic	5.0 (2.4-10.2)	3.9 (3.6-4.1)	
Black, non-Hispanic	13.8 (7.6-23.7)	11.7 (11.3-12.1)	
White, non-Hispanic	53.2 (41.2-65.0)	64.9 (64.2-65.6)	.18
Hispanic	24.4 (14.6-37.9)	15.5 (14.9-16.1)	
Multiple/other	3.6 (1.2-9.8)	4.1 (3.8-4.4)	
Country of origin			
Born in the United States	87.1 (77.0-93.1)	91.6 (91.2-92.0)	.18
Sex			
Female	53.5 (41.5-65.1)	51.7 (51.0-52.4)	.77
Age (y)			
18-29	32.3 (22.4-44.2)	21.4 (20.8-22.1)	
30-39	20.5 (12.8-31.4)	17.0 (16.5-17.4)	
40-49	16.6 (8.6-29.4)	16.8 (16.3-17.3)	.1
50-59	8.9 (4.5-16.9)	18.0 (17.6-18.5)	
60+	21.7 (13.1-33.6)	26.8 (26.2-27.4)	
Household income (\$)			
<25,000	19.7 (12.2-30.2)	16.6 (16.2-17.1)	
25,000-49,000	24.5 (16.0-35.5)	21.9 (21.4-22.5)	
50,000-99,999	29.6 (19.7-41.9)	30.9 (30.3-31.5)	.75
100,000-149,000	19.9 (11.3-32.7)	19.6 (19.0-20.2)	
≥150,000	6.3 (2.4-15.3)	10.9 (10.4-11.5)	
Physician-diagnosed comorbid atopic conditions†			
Current			
IgE-mediated food allergy*	42.5 (31.6-54.3)	10.7 (10.3-11.1)	<.001
Lifetime			
Asthma	37.4 (26.7-49.5)	12.2 (11.8-12.7)	<.001
Atopic dermatitis/eczema	22.3 (13.8-34.0)	6.7 (6.4-7.0)	<.001
Allergic rhinitis	31.1 (21.5-42.7)	21.4 (20.9-22.0)	.047
Insect sting allergy	10.1 (4.5-21.0)	3.8 (3.6-4.1)	.01
Latex allergy	13.1 (7.0-23.2)	2.3 (2.1-2.5)	<.001
Medication allergy	17.6 (9.4-30.5)	13.4 (13.0-13.9)	.38
Urticaria	16.0 (8.5-28.1)	0.8 (0.7-1.0)	<.001

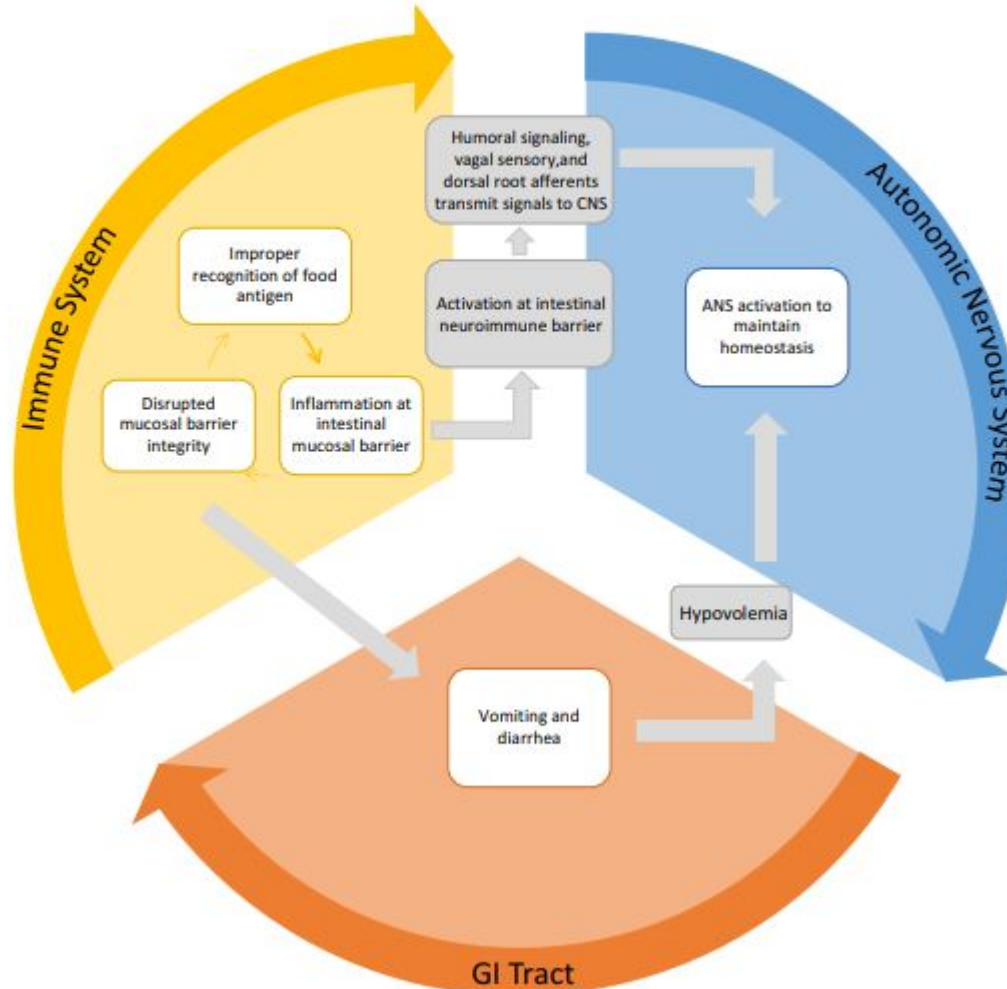
Adult vs Childhood Onset FPIES

Comparison of Childhood-Onset and Adult-Onset FPIES

Demographics and clinical characteristics	Adults	Children
Typical age of onset	35 y of age	2-7 mo of age
Sex distribution	More females	Slight male predominance
Frequency of specific symptoms	Abdominal pain > vomiting > diarrhea	Vomiting > pallor > lethargy > diarrhea > hypotension
Risk of hypotension	Not reported	5%-15%
Metabolic acidosis	Not reported	More common in chronic FPIES
Major food triggers	Shellfish, fish, cow's milk, wheat, egg	Cow's milk, rice, soy, oat, egg, fish, vegetables
Natural history	Does not progress to anaphylaxis on rechallenge	Remission, usually resolves by school age
Prick skin tests	Negative	Positive in 5%-25% in cow's milk or rarely with other foods
Serum-specific IgE	Negative	2%-12% in atypical FPIES
Specific biomarkers	None	None

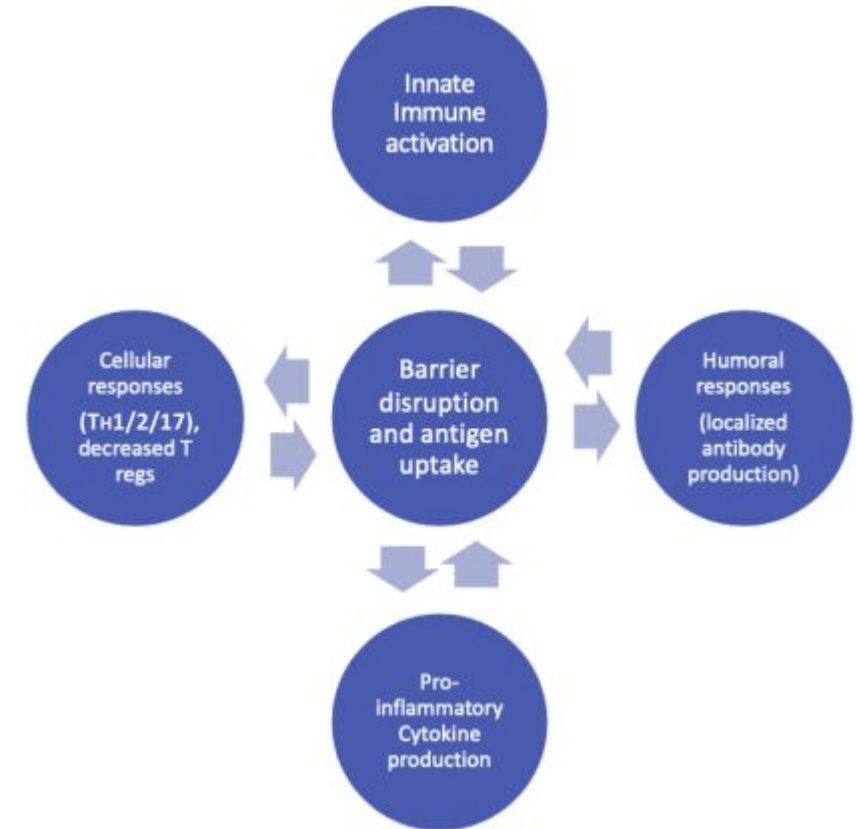
Proposed immune mechanisms for acute FPIES

N.V. Hoffmann et al. / Ann Allergy Asthma Immunol 126 (2021) 498–505



Proposed immune mechanisms for acute FPIES

- Direct effect of TNF-alpha on GI barrier disruption and lymphocyte activation
- Elevated CRP and Platelets during an FPIES reaction indicate an acute inflammatory process is occurring
 - Increased CRP level is associated with delayed tolerance of a specific FPIES food trigger
- Negative correlation of eosinophilia and tolerance
 - Is eosinophilia protective?
- Decreased Treg cells □ TH2 predominance



Mature gut

Tregs, IL-10

IFN- γ (TH1)

TGF- β 1 and
receptors

Immature gut

IL-4 (TH2)

Cytotoxic
T-cells, ?Eos

TNF- α

Tolerance

FPIES

The 4 major or “classic” FPIES Triggers in the US

Cow's Milk



Soy Milk

VS



Oats vs Rice



- ~50% co-reactive before 1y- debatable
- FPIES to soy does not appear to be related to FPIES to other legumes
- “Non-Solid Food FPIES”

- ~40% co-reactive
- Association with wheat and corn have been suggested but unlikely

Other FPIES Triggers

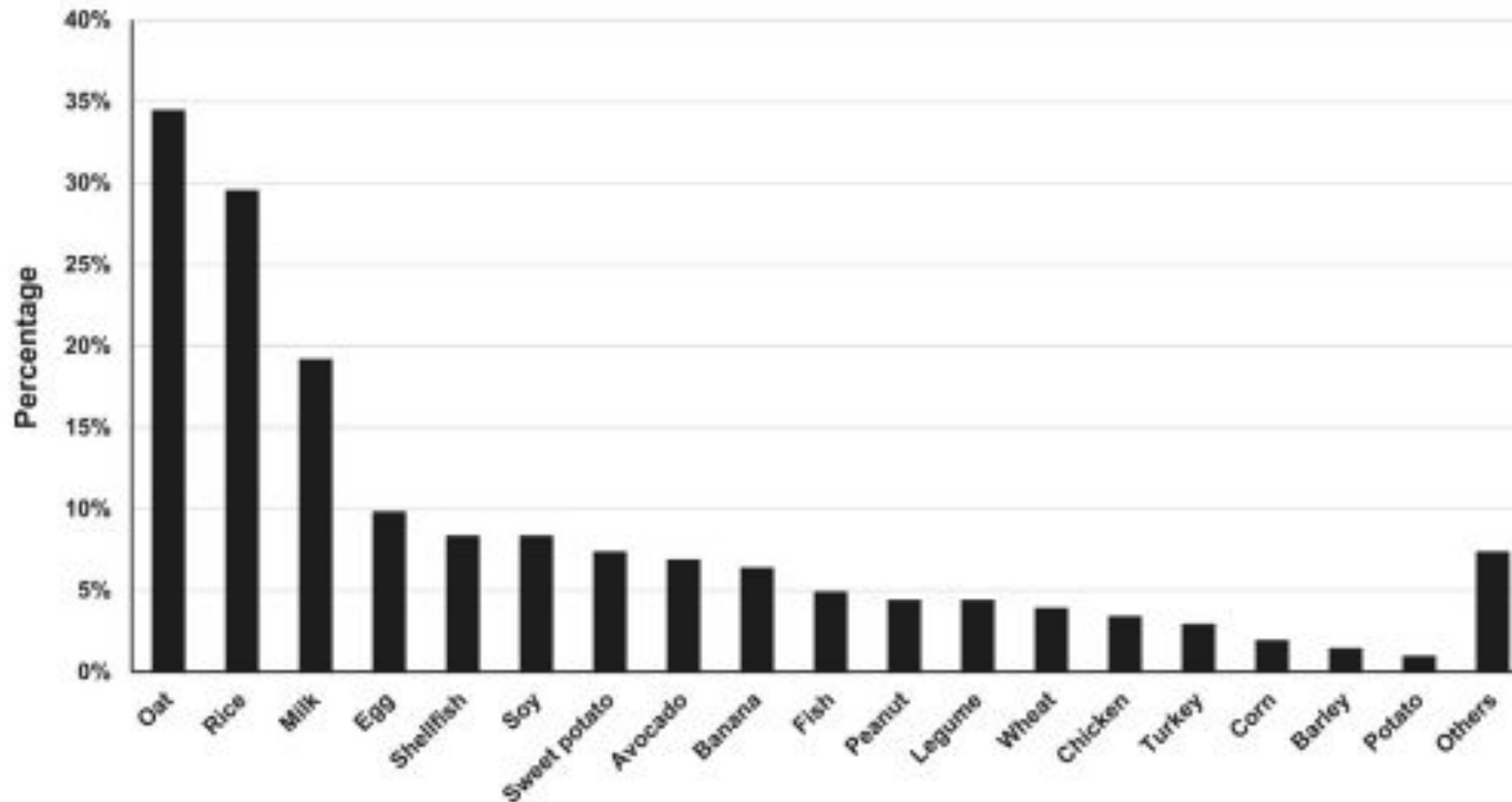


FIG 1. Foods causing FPIES, expressed as a percentage of patients with FPIES reaction to the trigger food.

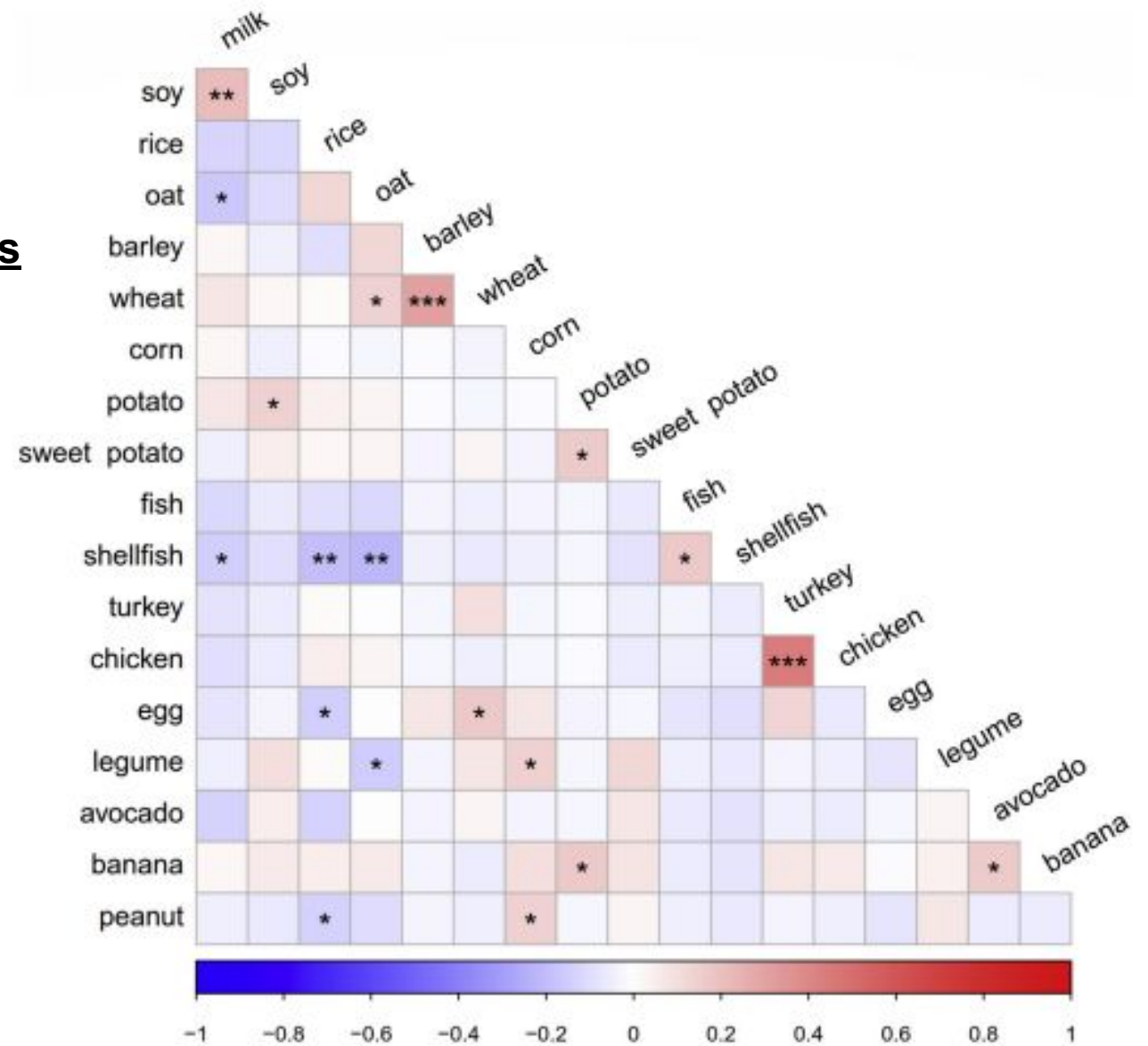
Food Associations

- Positive Correlations

- Milk- Soy???
- Rice-Oat
- Wheat-Barley
- Wheat-Egg
- Sweet Potato- Potato
- Potato-Soy
- Potato-Banana
- Shellfish-Fish
- Chicken-Turkey
- Banana-Avocado
- Corn –Legume
- Peanut-Corn

- Negative Correlations

- Oat-Milk
- Shellfish
- Milk, Rice, Oat
- Egg-Rice
- Legume- Oat
- Peanut- Rice



(*P < .05; ** P < .01; *** P < .001)

Diagnosis

- Diagnosis: based on clinical features with improvement following withdrawal of the suspected trigger food
 - Often the diagnosis is delayed as it is often initially misdiagnosed
 - OFC can both confirm diagnosis and resolution of the food allergy
- Food specific IgE levels are often undetectable of the trigger food, only ~25% are sensitized with Atypical FPIES

Acute FPIES

Major criterion:

Vomiting in the 1- to 4-hour period after ingestion of the suspect food and the absence of classic IgE-mediated allergic skin or respiratory symptoms

Minor criteria:

1. A second (or more) episode of repetitive vomiting after eating the same suspect food
2. Repetitive vomiting episode 1 to 4 hours after eating a different food
3. Extreme lethargy with any suspected reaction
4. Marked pallor with any suspected reaction
5. Need for emergency department visit with any suspected reaction
6. Need for intravenous fluid support with any suspected reaction
7. Diarrhea in 24 hours (usually 5 to 10 hours)
8. Hypotension
9. Hypothermia

The diagnosis of FPIES requires that a patient meets the major criterion and at least 3 minor criteria.

If only a single episode has occurred, a diagnostic oral food challenge should be strongly considered to confirm the diagnosis, especially since viral gastroenteritis is so common in this age group. Further, while not a criteria for diagnosis, it is important to recognize that acute FPIES reactions will typically completely resolve over a matter of hours compared with the usual several-day time course of gastroenteritis. The patient should be asymptomatic and growing normally when the offending food is eliminated from the diet.

Signs and Symptoms of Acute FPIES

- 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

	Acute
Laboratory findings	
	- 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

Treatment

- Elimination of food trigger
- Anticipatory guidance, complementary feeding
- Periodic reassessments for resolution
- Management acute reactions with Zofran

Anticipatory Guidance: Nutritional Considerations

- Children with 3 or more FPIES triggers are at increased risk for food aversion and poor weight gain

M. Groetch et al. / Ann Allergy Asthma Immunol 00 (2021) 1–8

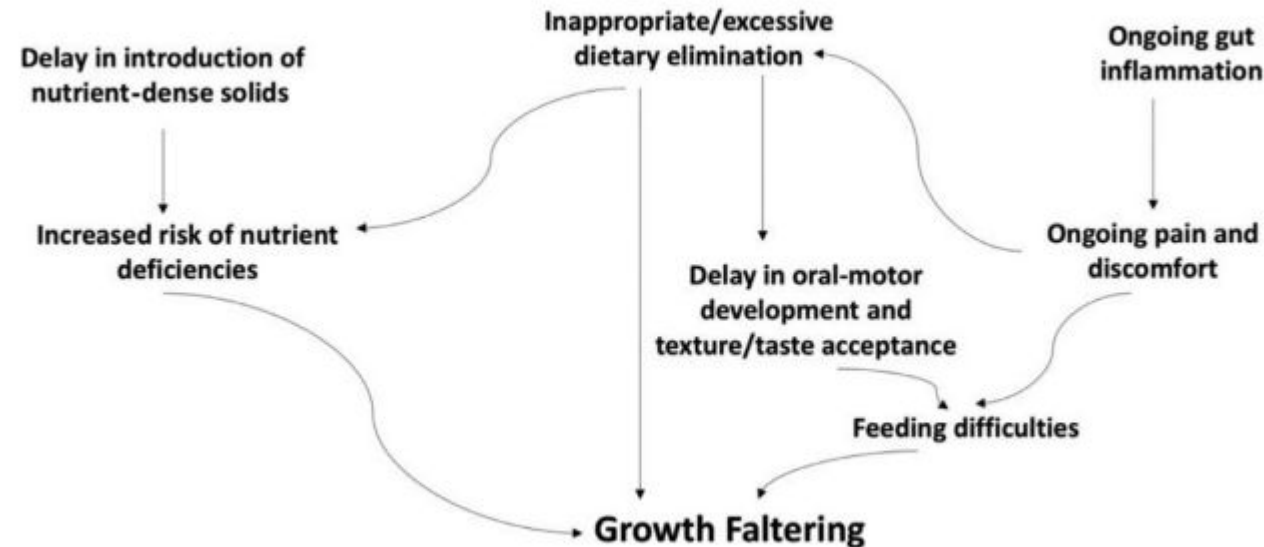


Figure 1. Potential contributing factors to growth faltering in FPIES. FPIES, food protein-induced enterocolitis syndrome.

Anticipatory Guidance: Nutritional Considerations

Table 3

Practical Tips on Prevention and Treatment of Vitamin and Mineral Deficiencies

Tips of prevention of vitamin and mineral deficiencies	Tips on correcting vitamin and mineral deficiencies
• Ensure baseline supplementation, as suggested by country-specific guidelines • Provide guidance on foods that are rich in iron and other essential micronutrients in breastfed infants • Give advice on fortified foods (ie, cereals) when appropriate • Avoid oversupplementation in a child where no deficiency is suspected • Monitor patient frequently to ensure that complementary foods have been introduced in a timely manner	• Consider nutritional biomarkers in particular in children with growth failure, ongoing/frequent diarrhea, and vomiting • Provide targeted supplementation for the nutrient that is deficient • Understand potential gastrointestinal adverse effects of supplements (ie, iron) • Understand interaction between supplemented micronutrients (ie, copper and zinc) • Monitor supplementation to ensure supplements are stopped when required • Assess and address causes of deficiency

Abbreviation: FPIES, food protein-induced enterocolitis syndrome.

Anticipatory Guidance: Nutritional Considerations

- **Cow's milk or soy** = avoid the other until 12 months old □ exclusively breastfeed or trial of extensively hydrolyzed formula
 - If react to EHF □ elemental formula
- **Grains**- consider avoiding some other monocots (oat and rice, +/- wheat)
 - Can introduce dicots (e.g., buckwheat, quinoa) and corn
- **Chicken or turkey** = avoid all poultry
- **Fish**...probably not all varieties are triggers
 - Maybe OFCs recommended to differentiate?
 - ~50% co-reactivity with shellfish
- **Lactation**- Avoidance of FPIES triggers is not recommended for mom, unless convincing/reproducible reactions to breast milk
- Precautionary Allergen Labeling (PAL) is safe!

Anticipatory Guidance: Feeding Plan

M. Groetch et al. / Ann Allergy Asthma Immunol 00 (2021) 1–8

WHAT to feed your baby (as tolerated and advised by your baby's doctor) ^(73b)		FOODS BASED ON RISK AS FPIES TRIGGER ^{a (8)}			
Food Group	Daily Servings for 6-12 months of age	Food group	Lower risk	Moderate risk	Higher risk
Milk & dairy	Continue breastfeeding on demand (or formula feeding) while introducing complementary foods. Serve up to ¼- ½ cup dairy foods such as plain yogurt.	Milk and alternatives	Breast milk, hypo-allergenic formula For cooking only in infants: Fortified coconut, flax, hemp milk		Milk, soy, pea, oat and rice beverages
Grains	1/2 - 1 ounce ½ ounce daily should be fortified with iron and zinc for the breastfed infant. Otherwise choose whole grain options.	Meat, fish, poultry	Lamb, beef, pork, bison		Fish, poultry
Meats & proteins	3/4 - 3 ounces Serve a variety of meat, poultry, eggs, fish, nuts and seeds.	Other protein foods	Tree nuts, seeds	Peanut	Soy, egg
Fruits and vegetables	1/8-1/2 cup each Serve a variety of dark green, red, orange and other vegetables and fruits.	Grains	Quinoa, millet, amaranth	Wheat, corn	Rice, oat
The amounts listed in this table are approximate <i>amounts to serve</i> so caregivers know how to provide nutrition in a balanced, diverse, and proportional manner. These amounts are NOT a prescription on <i>how much your baby should eat</i> as each baby is unique.		Vegetables	Broccoli, cauliflower, parsnip, turnip, beet	Squash	Pea, sweet potato
		Fruit	Blueberries, raspberries, plum, peach, strawberry, watermelon		Avocado, banana

RESPONSIVE FEEDING HOW to feed your baby:

Responsive feeding means honoring your baby's hunger and satiety cues. Babies are usually very good at letting you know when they are hungry and when they have had enough to eat.

Feeding goes best when caregivers serve a balance of healthy foods from each food group, while allowing the baby to decide how much to eat at each feeding.

Progressively advance the textures of food ⁽⁵⁸⁾ as skill appropriate (age estimates):

6 months:
Begin complementary feeding

6-9 months:
Smooth purees to soft foods (lumpy, mashed, finger foods)

9-12 months:
Chopped and firm finger foods

Anticipatory Guidance: Outgrowing FPIES

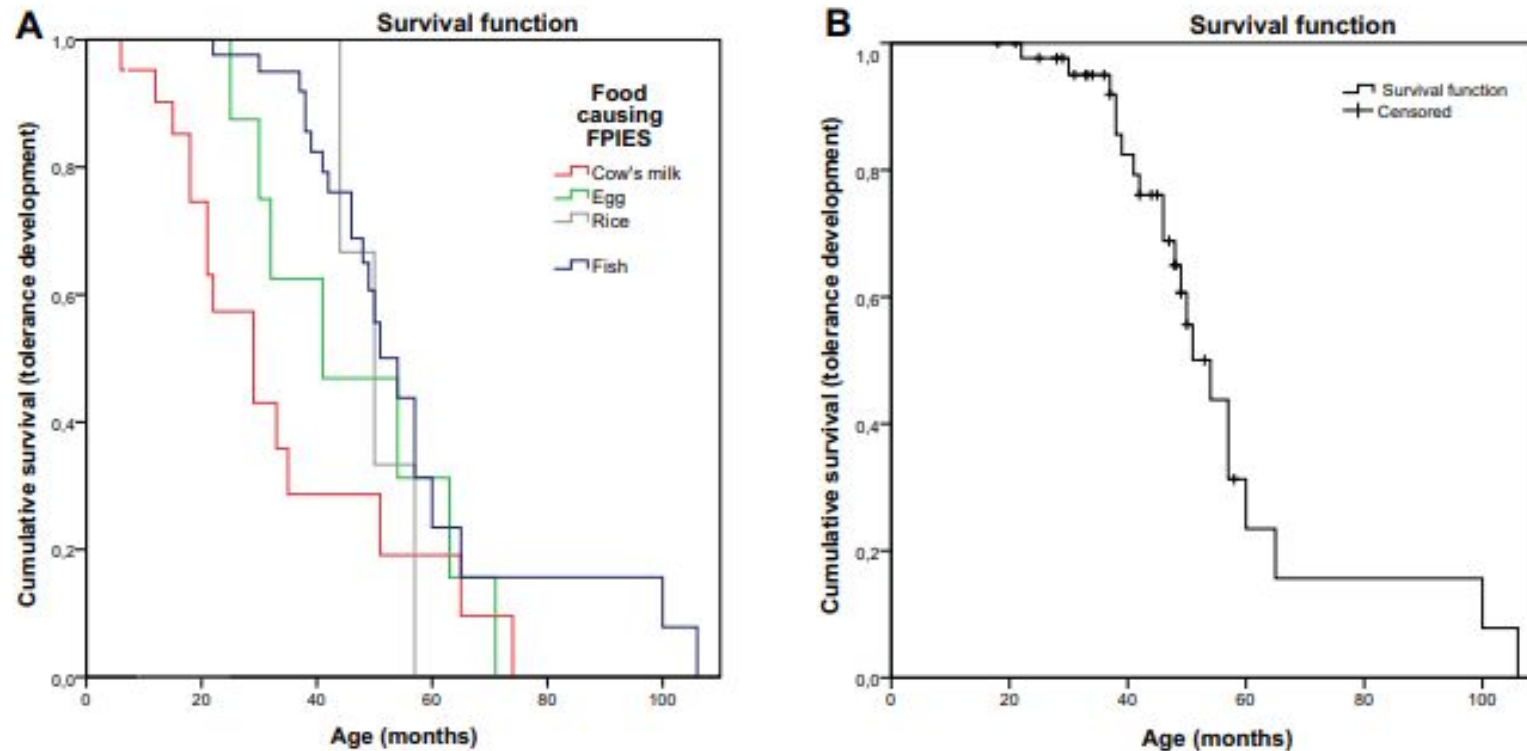
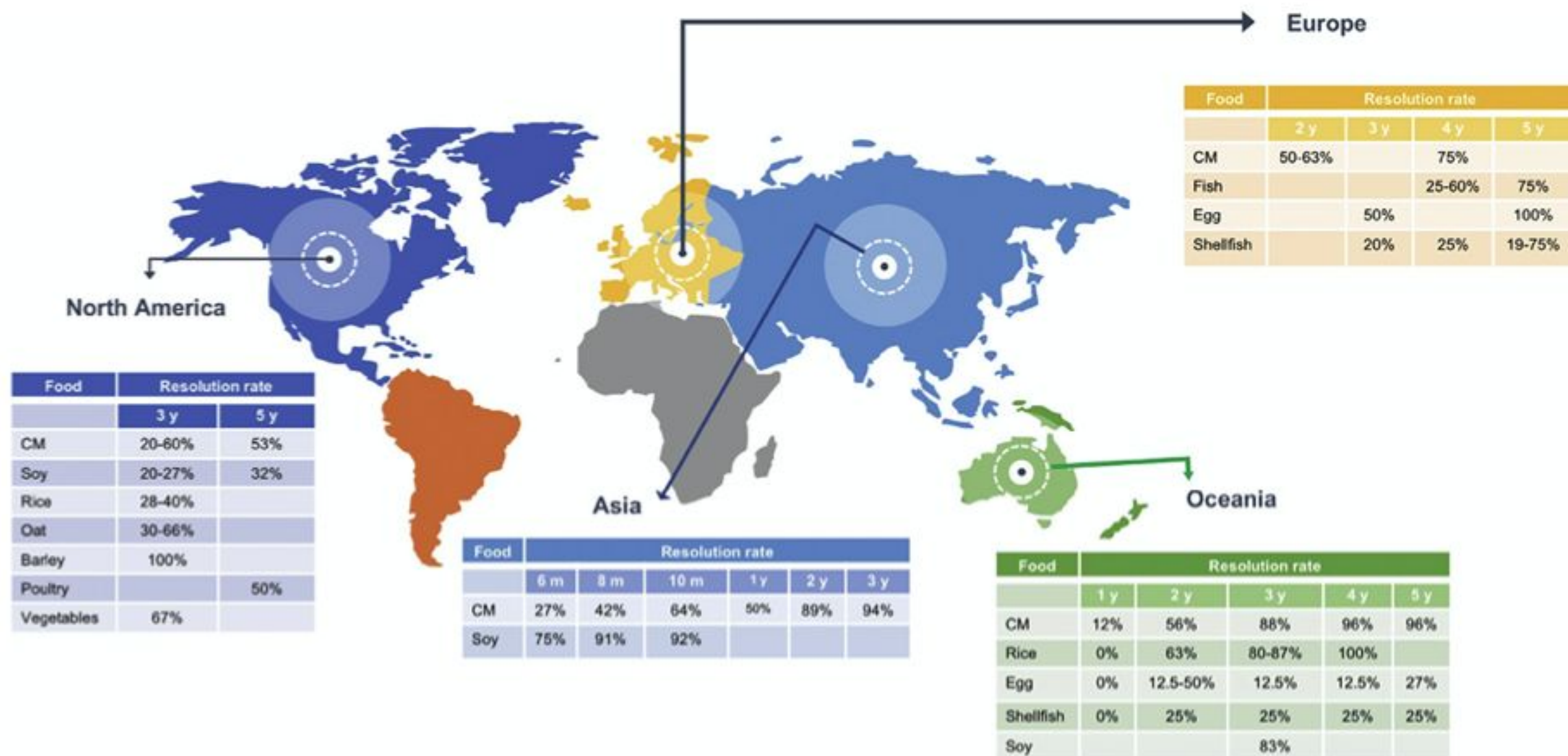


FIGURE 1. Kaplan-Meier estimate of survival showing tolerance development over time to the different culprit foods (A) and to any food (B) in a cohort of 81 children with FPIES from Barcelona, Spain.

TABLE E1. Kaplan-Meier estimate of survival showing tolerance development over time to the different culprit foods in a cohort of 81 children with FPIES from Barcelona, Spain

Culprit food	25th centile (95% CI)	50th centile (95% CI)	75th centile (95% CI)
Any food	33 (26.1-39.9)	50 (45-55)	60 (52.1-67.9)
Fish	46 (37.6-54.4)	54 (46.9-61.1)	60 (49.5-70.5)
Cow's milk	18 (12.8-23.2)	29 (17.2-40.8)	51 (27.8-74.2)
Egg	30 (21.6-38.4)	41 (15.3-66.7)	63 (47-79)
Rice	44	50 (40.4-59.6)	57
Corn	7	7	9



Periodic Reassessments for Resolution with OFC

- Recommend OFC at least 12-18months since last FPIES reaction
 - Sooner with Baked Milk/Egg?
- SPT of the allergen prior to the FPIES OFC, even if negative at time of FPIES diagnosis

Modified FPIES OFC Protocol:

- 0.06 to 0.6 grams of food protein per kg of body weight (usually 0.3)
 - Divided into 3 equal doses over 30min (=Q10min?)
- Max dose = 3g of protein, or 10g of total food weight, or 100mL
 - *Or maybe a standard, age-appropriate serving?*
- Wait 4-6h,
 - Give more if started low or total was less than a full serving
- PIV recommended
- *(NO LABS Recommended)*

Alternative FPIES OFCs

A modified oral food challenge in children with food protein-induced enterocolitis syndrome

Simona Barni¹  | Lucrezia Sarti¹ | Francesca Mori¹ | Lucia Liotti² | Neri Pucci¹ | Elio Novembre¹

¹Allergy Unit, A. Meyer Children's Hospital, Florence, Italy

²Pediatric Unit, Hospital of Senigallia, Senigallia, Italy

- FPIES symptoms are delayed
 - Why give several doses within 1 hour?
 - Unless evidence of sensitization
 - The first dose alone should be enough to trigger a reaction
- Full dose = 0.3g/kg (no max)
 - Give 25% then wait 4h
 - If tolerated, give remainder, and watch some more...
 - ~1/3 (n=19) = positive
 - All after the 25% dose
 - In 1-4h

An observed serving dose may not be necessary following a standard divided-dose FPIES oral food challenge

Mariam W. Guenther, MD^a, Maria Crain, CPNP^b, Christopher P. Parrish, MD^a, and J. Andrew Bird, MD^a



- 0.06 to 0.6 g/kg
 - Divided into 3 equal doses
 - Given over 30min
 - *Max dose = standard serving*
- All reactions occurred after the initial divided doses, within 2-3h
- PIV at provider discretion

Barni S, et al. CEA 2019, 49:1633-6.
Bird JA, et al. JACI IP, 2020: 8:1462-4

FPIES OFC – Key Points

WHEN TO CONSIDER?

- Unable to meet diagnostic criteria
 - Mixed reaction – possible AD flare?
 - Don't meet 3 minor criteria
- Too many foods to count!
 - To confirm reaction
 - Guide introduction
- 6-12m from last reaction
 - >18 months of age

BEING PREPARED

- SPT and/or sIgE prior to OFC
- Ondansetron
- PIV?
- IV fluids
- Staff available

What About Egg or Milk in Baked Goods?

TABLE I. Characteristics and allergic reactions of children with food protein–induced enterocolitis syndrome to milk, who participated in oral food challenge (OFC) of baked milk

Sex	Atopic background (atopic dermatitis, IgE-mediated food allergy, recurrent wheezing)	Age at last allergic reaction, mo	Reaction characteristics	Time from milk exposure to reaction, h	Treatment of last allergic reaction	Hospital admission	Age at baked milk OFC, mo	Time from last reaction to baked milk OFC, mo	Results of baked milk OFC
M	—	1	Restlessness, vomiting, diarrhea	1-3	—	—	12	11	Pass
F	—	19	Vomiting, lethargy	3-6	—	—	22	3	Pass
F	—	6	Vomiting, pallor	1-3	—	—	8	2	Fail
F	—	8	Vomiting, pallor	1-3	—	—	14	6	Pass*
M	—	3	Vomiting, lethargy	1-3	+	+	8	5	Fail
F	Atopic dermatitis	10	Vomiting, lethargy	1-3	+	+	12	2	Pass
F	—	6	Vomiting, lethargy	1-3	—	—	11	5	Pass
F	—	9	Vomiting, pallor	1	—	—	12	3	Pass
M	—	3	Vomiting, pallor, ER visit	1-3	+	+	10	7	Pass
M	—	2	Vomiting, pallor, ER visit	1-3	+	+	10	8	Fail
M	—	13	Vomiting, lethargy	1-3	+	—	14	1	Pass
F	—	12	Vomiting, pallor, ER visit	1-3	+	—	18	6	Pass

FPIES Management Algorithm: COVID Adjustments

**Severe past FPIES
reaction:
prolonged
hospitalization and
support**

- Food that caused past severe reaction was definitely ingested OR shows signs of FPIES reaction:
- Activate emergency services (EMS) or go to the emergency department (ED) by private car if prolonged waiting time for ambulance
- If available, immediately administer ondansetron orally for patients older than 6 months, 0.15 mg /kg, max dose 8 mg; may repeat once if patient vomited within 10 minutes after the first dose

**Moderate past
FPIES reaction:
intravenous
hydration in the
ED or hospital**

- Food that caused past moderate reaction was definitely ingested OR shows signs of FPIES reaction:
- If available, immediately administer ondansetron orally for patients older than 6 months, 0.15 mg /kg, max dose 8 mg; may repeat once if patient vomited within 10 minutes after the first dose
- If symptoms appear:
 - Go the ED by private car and wait outside, enter ED only if symptoms worsen, e.g., continued forceful emesis, lethargy, signs of dehydration
 - Attempt oral rehydration with clear liquids or breast milk, small amount, e.g., ice chips or 1 teaspoon 20 min after vomiting episode, advance as tolerated; monitor for dehydration (tears, saliva, wet diapers) while in the car
 - If initial symptoms are severe (lethargy, unresponsiveness, floppy, dusky appearance) activate EMS or go to the ED by private car if prolonged waiting time for ambulance

**Mild past FPIES
reaction:
recovered at
home**

- Food that caused past mild reaction was definitely ingested OR shows signs of FPIES reaction:
- Monitor for symptoms. If symptoms appear:
 - If available, administer ondansetron orally for patients older than 6 months, 0.15 mg /kg, max dose 8 mg; may repeat once if patient vomited within 10 minutes after the first dose
 - Attempt oral rehydration with clear liquids or breast milk, small amount, e.g., ice chips or 1 teaspoon 20 min after vomiting episode, advance as tolerated; monitor for dehydration (tears, saliva, wet diapers)
 - If symptoms continue, go the ED by private car and wait outside, enter ED only if symptoms worsen, e.g., continued forceful emesis, lethargy, signs of dehydration
 - If initial symptoms are severe (lethargy, unresponsiveness, floppy, dusky appearance) activate EMS or go to the ED by private car if prolonged waiting time for ambulance

Figure 1. Modified management algorithm for acute food protein–induced enterocolitis syndrome during the coronavirus disease 2019 pandemic stratified by the severity of the past reactions. The contact number to activate emergency medical services is 911 in the United States and Canada; 999 in the United Kingdom; 112 in the countries of the European Union; and 119 in Japan and South Korea.

Treatment- ED letter

To Whom It May Concern:

*** has an adverse reaction to foods, called **food-protein induced enterocolitis syndrome or FPIES**.

[He is **avoiding *****, with a history of FPIES reactions to these foods.]

FPIES is a non-IgE-mediated, adverse reaction to food that is characterized by delayed onset of symptoms (~1-4h after eating), as opposed to immediate, IgE-mediated symptoms occurring within minutes to <2h after eating an allergen. FPIES does not result in “typical/classical allergy symptoms” (e.g., hives or wheezing), but rather results in profuse and protracted vomiting in all patients, and many will also be lethargic, have pale color, and be cool and clammy. Diarrhea can occur, but is more variable, and may not develop until much later into the reaction. More severe reactions can include hypotension, acidemia, and/or methemoglobinemia. Symptoms will typically resolve within 2-6h, and to date, there is no report of an acute FPIES reaction leading to fatality.

The **treatment of FPIES reactions** is symptomatic and supportive. It can include:

- **Zofran** (ondansetron IM, IV or ODT) is very effective at decreasing the amount/severity of emesis and shortening the duration of the reaction. It should be given at the first sign of an FPIES reaction.
- Intravenous **fluids** (e.g., normal saline bolus and/or maintenance fluid) and/or oral rehydration
- Systemic corticosteroids (e.g., Solumedrol 1-2 mg/kg IV) have been used in the past (pathophysiology is believed to be T-cell mediated), but given the efficacy of Zofran, steroids are rarely needed.

Epinephrine is NOT a treatment for an FPIES reaction (it will not treat the symptoms, nor will it stop the progression of a reaction, as FPIES does not result in anaphylaxis). Laboratory evaluation is no longer recommended.

Treatment- ED letter

To Whom It May Concern:

*** has an adverse reaction to foods, called **food-protein induced enterocolitis syndrome or FPIES** to ***. Additionally, they have IgE-mediated food allergies to ***.

FPIES is a non-IgE-mediated, adverse reaction to food that is characterized by delayed onset of symptoms (~1-4h after eating), as opposed to immediate, IgE-mediated symptoms occurring within minutes to <2h after eating an allergen. FPIES does not result in “typical/classical allergy symptoms” (e.g., hives or wheezing), but rather with profuse and protracted vomiting in all patients, and many will also be lethargic, have pale color, and be cool and clammy. Diarrhea can occur, but is more variable, and may not develop until much later into the reaction. More severe reactions can include hypotension, acidemia, and/or methemoglobinemia. Symptoms will typically resolve within 2-6h, and to date, there is no report of an acute FPIES reaction leading to fatality.

The **treatment of FPIES reactions** is symptomatic and supportive. It can include:

- **Zofran** (ondansetron IM, IV or ODT) is very effective at decreasing the amount/severity of emesis and shortening the duration of the reaction. It should be given at the first sign of an FPIES reaction.
- Intravenous **fluids** (e.g., normal saline bolus and/or maintenance fluid) and/or oral rehydration
- Systemic corticosteroids (e.g., Solumedrol 1-2 mg/kg IV) have been used in the past (pathophysiology is believed to be T-cell mediated), but given the efficacy of Zofran, steroids are rarely needed.

Epinephrine is NOT a treatment for an FPIES reaction (it will not treat the symptoms, nor will it stop the progression of a reaction). However, given that *** has both FPIES and IgE-mediated food allergy, it is possible that they could have a combined or mixed reaction, but the time course of each reaction should be different (as above). Laboratory evaluation is no longer recommended to confirm an FPIES reaction. If believed to be having an IgE-mediated reaction alone or in combination with an FPIES reaction, the immediate hypersensitivity reaction should be treated promptly following standard protocols or guidelines. The FPIES reaction should be treated concurrently, but following the evaluation and management of the airways and breathing, as part of the primary assessment.



QUESTIONS