

Food Protein-induced Enterocolitis Syndrome: Insights from Review of a Large Referral Population

Melanie A. Ruffner, MD, PhD^{a,*}, Kathryn Ruymann, BA^{b,*}, Simona Barni, MD^{b,c}, Antonella Cianferoni, MD, PhD^{a,b}, Terri Brown-Whitehorn, MD^{a,b}, and Jonathan M. Spergel, MD, PhD^{a,b} Philadelphia, Pa; and Florence, Italy

What is already known about this topic? Food protein–induced Enterocolitis (FPIES) is a nonspecific syndrome with symptoms of vomiting and diarrhea that can be severe and accompanied by pallor, lethargy, and hypotension, which occurs 2-6 hours after ingestion of trigger foods such as milk, soy, grains, etc.

What does this article add to our knowledge? This retrospective chart series of 462 patients demonstrates milk, soy, rice, oat, and egg as the most frequent FPIES trigger foods, and we see a high proportion of patients with more than one FPIES trigger food.

How does this study impact current management guidelines? A total of 43% of patients with FPIES to milk also react to soy, and 41.6% of the patients with a grain trigger reacted to two or more grains. Introduction of foods must be guided by risk of additional FPIES reaction for these patients.

BACKGROUND: Food protein–induced enterocolitis (FPIES) is a rare non-IgE mediated disease. Most studies have been limited in nature, with the largest cohort being 66 patients. The most common foods that have been reported are milk and soy. **OBJECTIVE:** A retrospective chart review of patients seen in the Allergy Section at The Children’s Hospital of Philadelphia with International Classification of Diseases Ninth Revision code of 558.3 (Allergic Gastroenteritis and Colitis) between 2007 and 2012 was conducted to identify patients with suspected FPIES. **Diagnosis of FPIES was confirmed based on meeting clinical criteria of delayed reaction with pronounced vomiting and/or**

diarrhea. Data regarding patient characteristics and features of their reactions were collected for analysis and comparison with existing studies.

RESULTS: A total of 462 cases were identified in our chart review. Patients had a similar demographic profile to the normal allergy patients seen in our clinic. The most common foods identified were milk (67%), soy (41%), rice (19%), oat (16%), and egg (11%). Patients had onset of FPIES to milk and soy around 7 months of age compared with 12 months of age for solid foods. FPIES reactions were identified to meats, tree nuts, peanuts, fruits, and vegetables; 70% of the patients reacted to one or two foods. Skin prick testing and atopy patch testing were not helpful in identifying the foods.

CONCLUSION: FPIES reactions were seen more frequently than previously described. However, the presentation and clinical features were similar to previous reports. Milk- and soy-triggered FPIES were common, and 43.5% of patients who had a milk trigger reacted to soy. There is no laboratory test to identify foods that cause FPIES, and clinician-supervised oral food challenge is the only definitive test available. © 2013 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol: In Practice 2013;1:343-9)

Key words: Food Allergy; Food protein–induced enterocolitis syndrome; FPIES; Vomiting; Diarrhea

Food protein–induced enterocolitis syndrome (FPIES) is a non-IgE-mediated food allergy that typically occurs within the first 6 months of life.¹ It differs from classic IgE-mediated allergies because children with FPIES show symptoms of profuse vomiting, pallor, lethargy, and diarrhea² at 2-6 hours after ingesting a trigger food compared with the immediate reactions seen in IgE-mediated reactions.³ The features of FPIES are nonspecific and are often treated as sepsis due to the age of the child and severity of presentation.⁴

^aDepartment of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pa

^bDivision of Allergy and Immunology, The Children’s Hospital of Philadelphia, Philadelphia, Pa

^cAllergy and Clinical Immunology Unit, Pediatric, A. Meyer Children’s Hospital, Florence, Italy

*These authors contributed equally to this work.

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Corresponding author: Jonathan M. Spergel, MD, PhD, The Children’s Hospital of Philadelphia, University of Pennsylvania School of Medicine, 3550 Market Street, Philadelphia, PA 19104-4399. E-mail: spergel@email.chop.edu.

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Abbreviations used

ANOVA- Analysis of variance

APT- Atopy patch testing

FPIES- Food protein–induced enterocolitis

Ig- Immunoglobulin

OFC- Oral food challenge

SD- Standard deviation

SPT- Skin prick testing

TGF- Transforming growth factor

TNF- Tumor necrosis factor

FPIES is thought to be a rare disease, but some data suggest that its incidence may be increasing. In a large birth cohort study of more than 13,000 patients born in 2004 to 2006 in Israel, Katz et al identified 44 patients, for an incidence of 0.34%.⁵ In a retrospective study of 16 years in Sydney, Australia, Mehr et al found an increase in prevalence, from 6 cases in 1992 to 1995, to 14 cases in 2004 to 2007.⁶ Recently, Sopo et al⁷ published their experience in a multicenter study in Italy and found a rise from 4 cases in 2004 to 13 cases in 2010. It is unclear if this rise is due solely to an increased awareness of the disease or to a true rise in incidence. Milk and soy are the most commonly reported trigger foods in FPIES, but other foods, including fish, rice, poultry, egg, grains, vegetables, fruit, and peanuts have been described.^{7,8} Nevertheless, fewer than 400 cases have been reported in the literature, with the biggest series being 44 children⁵ and 66 children.⁷

The exact mechanism of FPIES is unclear, but it is assumed to be a cell-mediated food hypersensitivity because most patients are skin-test negative and it has a delayed onset.^{2,9,10} Results of studies indicate that TNF- is involved, which would account for the symptoms of hypotension and fever.⁸ A relative lack of expression of TGF- may also be implicated in the pathogenesis of disease.¹¹

The current study, from The Children's Hospital of Philadelphia, is the largest study to date, with approximately sevenfold more patients than previous studies. We described the clinical symptoms, demographics, and allergy testing in our cohort of 462 patients. Overall, we found similar trigger foods to previous studies with milk and soy predominating.

METHODS**Patient identification**

Patients were identified by retrospective chart review of electronic medical records (Epic Medical System, Madison, WI) from 2007 to 2012 at The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania. All charts of patients with "allergic gastroenteritis and colitis" were identified by International Classification of Diseases Ninth Revision coding of 558.3. Patients were identified based on physician diagnosis of food protein–induced enterocolitis (FPIES). Patient histories were reviewed to assess if their documented presentations met the standard definition of FPIES.¹² Data regarding implicated food, age of onset, self-identified sex and race, allergy skin testing, maternal diet, and symptoms on presentation regarding the first and subsequent FPIES episodes were collected via chart review.

Disease definition

We used the following inclusion criteria from the documented history to determine if patients had FPIES: subjects had

reproducible, delayed episodes (2–6 hours after exposure to the food) of pronounced gastrointestinal symptoms of prolonged vomiting with or without diarrhea. If patients had hypotension, needed intravenous fluids, or had significant pallor, they were identified as having severe reactions. Patients with IgE-mediated food allergy and chronic symptoms, including gastroesophageal reflux, failure to thrive, constipation, isolated bloody and/or mucousy stools, and chronic diarrhea, were excluded from this study. Skin testing was performed as previously described by using standardized techniques with commercial prepared extracts (Greer Labs, Lenoir, NC) with a bifurcated needle.¹³ Atopy patch testing (APT) was performed as previously described.¹⁴

Atopic comorbidity was based on physician diagnosis of the subjects at the time of diagnosis of FPIES. Children diagnosed with eczema and started on topical steroids were considered to have atopic dermatitis, and children with recurrent wheezing responsive to albuterol were designated as "wheezing." Children being followed up for FPIES were considered to have IgE-mediated food allergy if they developed immediate, classic symptoms with ingestion of food described in history and provider-prescribed epinephrine autoinjector.

Food challenge and age of resolution

Age of resolution for the purpose of this study was determined by meeting one of two criteria: passing a supervised food challenge or tolerating a full serving dose of the food at home. In our division, selected patients are challenged at least 1 year after their last clinical reaction based on clinician judgment and parental preferences. Challenges are done with two doses by following standard protocol.¹⁵ Patients were then observed for 4 hours in our Day Medicine Unit at The Children's Hospital of Philadelphia. Telephone follow-up was done the following week to check for any late-phase reactions. Patients are considered to have outgrown their FPIES reaction if they tolerated the full dose and had no reactions during the challenge or while continuing to eat the food over the subsequent 7 days.

Statistical analysis

Statistical analysis was done by using Graph Pad Version 6.0 (Prism Software, San Diego, CA). All statistical tests were two-tailed by using .05 level of significance with ANOVA or unpaired t-tests as needed. Data were expressed as means \pm SD, unless otherwise stated. The Children's Hospital of Philadelphia's Institutional Review Board approved the study.

RESULTS

The Children's Hospital of Philadelphia is a large referral hospital with patient populations primarily from Pennsylvania, New Jersey, and Delaware. We also see patients referred from across the nation, including those with FPIES. Our initial review of electronic medical records identified 992 patients with allergic gastroenteritis and colitis based on the International Classification of Diseases Ninth Revision coding of 558.3 seen in the Allergy Section at The Children's Hospital of Philadelphia from our electronic medical records. We have approximately 15,000 patient-visits a year in the Allergy Section, with 7000 individual patients seen a year. We identified 543 patients with physician's diagnosis of FPIES. Of those, 462 patients met the classic definition of FPIES with reproducible episodes of prolonged vomiting or diarrhea 2 to 6 hours after exposure to the inciting allergen. There was an even distribution of patients across all

years reviewed, with no clear increase in number of patient cases over time. The remaining 81 patients had symptoms of colitis with chronic diarrhea, mucousy diarrhea, or bloody diarrhea that resolved with food elimination and were excluded from analysis.

The patient population was primarily male patients (60%) and white (65%) (summarized in Table I). This is nearly identical to the patient population seen in the Division of Allergy and Immunology with 60% male patients and 65% white.¹⁶ In contrast, patients with eosinophilic esophagitis have significantly more male patients (75%) and whites (84%) than what we observe in our FPIES population. The rate of breast-feeding of 47% was similar to the national rate of breast feeding at 47.2% at 6 months.¹⁷ The patient cohort has a higher rate of atopic dermatitis (30%) than generally seen in population-based studies of US preschool children,¹⁸ but an equivalent rate of wheezing (17%) as seen in the study by Martinez et al¹⁹ of infant and toddler respiratory disease.

The clinical presentation was by definition, primarily vomiting and diarrhea (Table II). We saw an approximately equal distribution between patients who presented with primarily vomiting and those who presented with both vomiting and diarrhea. Five percent of the patients presented with a more-severe phenotype in which hypotension, pallor, and/or cyanosis were present in addition to the gastrointestinal symptoms.

Foods inducing FPIES reactions

Milk represents the most common trigger food, with reactions observed in 67% of patients (Figure 1). The next most common food was soy, which was seen as a trigger in 41% of patients. Similar to other patient cohorts, we found grains to be the next most common group of causative foods (rice in 19%, oats in 16%, wheat in 10%, and corn in 8%). (Figure 1, A and B). Overall, FPIES induced by grains was seen in 25.3% of the reactions and in 34.6% of total patients. We also found that egg was a fairly common cause in our cohort and affected 11% of patients.

FPIES reactions to other foods did occur, albeit less commonly. Meats (chicken, turkey, pork, and beef) and fish represented 6.3% of all FPIES reactions. Of those, chicken and turkey were the most common and were observed in 4.5% and 4.1% of patients, respectively (Figure 1, C). FPIES reactions to peanut and tree nuts were uncommon. Peanut was the most common in this group, which affected 1.9% of patients. Reactions to fruits and vegetables were seen in 7.8% and 11.6% of the patients, respectively (Figure 1, D and E). Overall, they accounted for fewer than 15% of FPIES reactions. Reactions to bananas were the most common among the fruits and seen in 3.5% of the patients. Among vegetables, sweet potato and peas were the two common triggers, with reactions seen in 4.1% and 3.2% of patients, respectively.

Reactions to multiple foods

The majority of patients with FPIES have reactions to a limited number of foods (Figure 2); 70% of patients reacted to one or two foods. Many of patients with multiple FPIES reactions reacted to milk, soy, or grains; 29.2% of patients reacted to both milk and soy, 38% reacted to milk alone, and 11.6% to soy alone. For the grain-triggered FPIES reactions, 41.6% of the patients with grain sensitivity reacted to two or more grains, and 20% of the patients reacted to soy or milk and a grain.

TABLE I. Demographics of patients with physician-identified FPIES

Population characteristics	
No. of patients	462
No. of episodes	1031
Male patients, no. (%)	279 (60.4)
Breastfed, no. (%)	161 (46.9)
Patient self-reported race, no. (%)	
White	302 (65.4)
Hispanic	12 (2.6)
African American	24 (5.4)
Asian	12 (2.6)
Other	111 (24)
Initial atopic history, no. (%)	
Wheezing	62 (17)
Atopic dermatitis	125 (34.3)

FPIES, Food protein–induced enterocolitis.

TABLE II. Clinical characteristics of FPIES population

Clinical characteristics: symptoms	Percentage
Vomiting predominant	45.3
Both vomiting and diarrhea	54.7
Severe symptoms (ie, lethargy, pallor/cyanosis, dehydration, or hypotension)	5.1

FPIES, Food protein–induced enterocolitis.

A small but not insignificant percentage (5%) reacted to more than six foods. Many of these patients reacted to milk, soy, or grain but also reacted to multiple fruits and vegetables, with FPIES symptoms. IgE-mediated sensitivity to foods based on positive skin tests was seen in 19.6% of the patients. These reactions were to the most-common IgE-mediated foods (milk, egg, peanut, and tree nuts).

Allergy testing in FPIES

Skin prick testing (SPT) was performed in 84% of the patients and was negative in 96% of patients regardless of the food tested (Table III). This is consistent with previous results.⁷ In a small pilot study, we had previously seen that positive APT was correlated with FPIES symptoms during oral food challenge (OFC).¹⁴ However, in our current cohort of patients, APT was only negative 45% of the time over all foods. This was not significantly improved for any individual food because corn had the highest positive rate at 75%.

Age of onset

Overall, children have first FPIES reactions to milk and soy at a significantly younger age of onset at 7.0 ± 0.7 months compared with 12.1 ± 1.1 months for the solid foods ($P < .007$) such as grains, vegetables, fruits, and meats. In the United States, these solid foods are typically introduced to children at later ages. Milk- and soy-based FPIES occurred at an earlier age compared with other foods (at mean of 6.3 and 7.7 months, respectively [Table III]). First FPIES reactions to solid foods, in particular, wheat, corn, and chicken, tended to occur at a later age ($P < .05$; mean, 11.7–14.5 months of age). Rice (7.3 ± 5.1 months) and

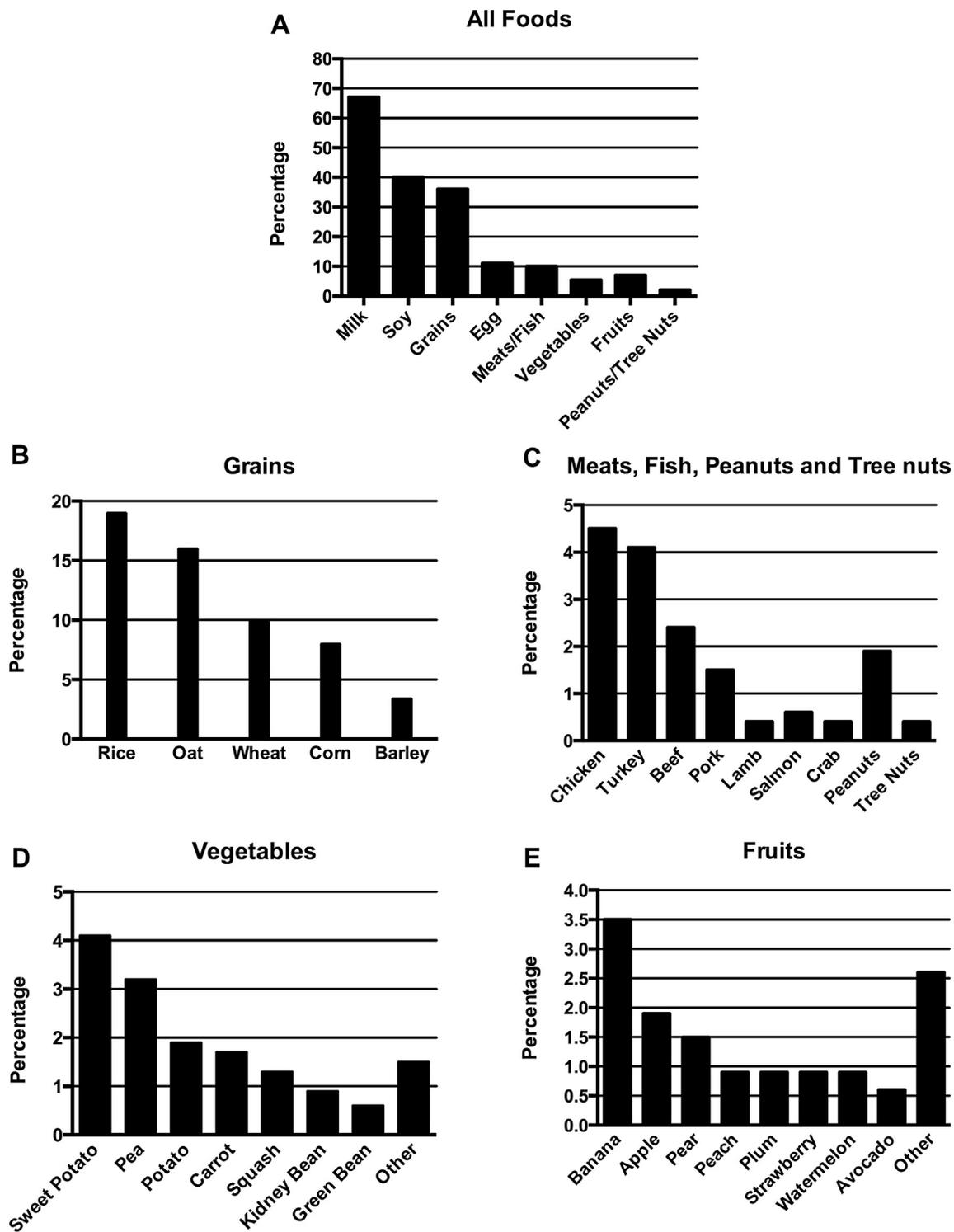


FIGURE 1. Foods that cause food protein–induced enterocolitis (FPIES) reaction. Foods were identified as causing symptoms 2-4 hours after exposure. **A**, Foods are expressed as a percentage of patients with FPIES reaction to the given food. Meats, fruits, vegetables, and grains are grouped together. **B-E**, FPIES reactions to individual foods expressed as percentage of patients for individual foods: **B**, grains; **C**, meats, fish, peanuts, and tree nuts; **D**, vegetables: those with fewer than 0.5% of patients were grouped into the other category and included tomato, spinach, cauliflower, cucumber, lentil, and legume; **E**, fruits: those with fewer than 0.5% of patients were grouped into the other category and included blueberry, apricot, grape, cherry, coconut, orange, kiwi, and raspberry.

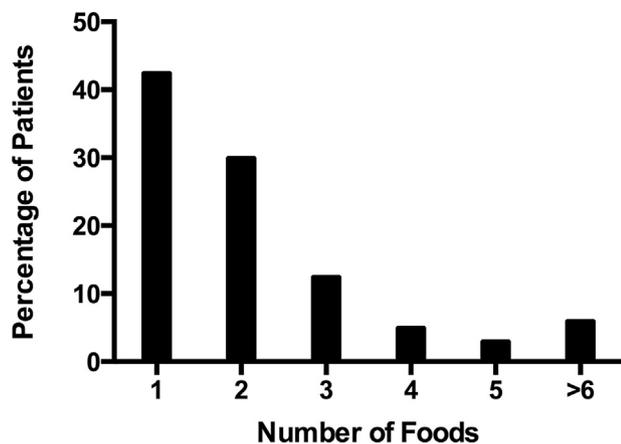


FIGURE 2. The number of foods that cause food protein–induced enterocolitis (FPIES) reaction per individual. Each fruit, grain, meat, and vegetable counted as a single food.

oat (9.3 ± 6.2 months) are some of the earliest solids introduced and also some of the most frequent triggers (Figure 1, B).

We also examined the onset of FPIES based on whether the children were breastfed or bottle fed. There were no significant differences in the groups. For milk-based FPIES, the children who primarily breastfed had an average age onset of 4.33 ± 4.08 months ($n = 102$) compared with children who were primarily on milk-based formula: average age onset: 5.07 ± 5.10 months ($n = 46$) or on soy-based formula: average age onset: 5.83 ± 5.08 months ($n = 19$). For soy-based FPIES, the children who primarily breastfed had an average age onset of 5.25 ± 4.77 months ($n = 68$) compared with children who were primarily on milk-based formula: average age onset: 6.0 ± 7.86 months ($n = 29$) or on soy-based formula: average age onset: 8.0 ± 11.86 months ($n = 6$).

Age of resolution

More than 85% of the patients had outgrown their FPIES reactions by school age (5 years of age) based on tolerating the foods at home or a negative food challenge. Overall, we found 35% of the patients outgrew their FPIES by 2 years of age, 70% by 3 years, 80% by 4 years of age. There was no significant difference for the age of resolution of liquid versus solid FPIES reaction (32.9 ± 0.95 months and 42.1 ± 3.8 months, respectively). Interestingly, we have two patients with persistent FPIES reactions as teenagers. One patient reacted to soy protein at 16 years of age that was confirmed by food challenge.

DISCUSSION

In our retrospective chart review of patients with FPIES, we found 462 patients with classic reactions of prolonged vomiting and diarrhea that occurred 2–6 hours after ingestion of the food. We chose this as our inclusion criteria because it is the described time frame and presentation of FPIES in the literature. However, there remains some debate on what constitutes a positive FPIES diagnosis.

Nowak-Węgrzyn and Muraro⁸ suggested that positive FPIES reactions after an OFC needs at least three of the following criteria: vomiting, diarrhea, and one laboratory criteria of increased neutrophils or eosinophils in the stool, increased neutrophils in the blood, and/or increased leukocytes in the

gastric juices. However, in our series as well as others, diarrhea occurred in 50% or fewer patients during FPIES reactions.^{5–7} Katz et al⁵ and Sopo et al⁷ suggest that clinical observation of repeated vomiting accompanied by pallor and lethargy are adequate for an FPIES diagnosis after OFC. These researchers and our department primarily rely on clinical history of repeated episodes of pronounced vomiting (with or without diarrhea, pallor, and lethargy) 2–6 hours after the ingestion of a trigger food in the diagnosis of FPIES instead of laboratory findings because there are no diagnostic laboratory tests. However, there is not a clear consensus at this time on what exact clinical criteria should be to make a diagnosis of FPIES.

Similar to previous studies,^{5–8} which has been based on clinical presentation of prolonged vomiting 2–6 hours after food exposure, the majority of patients had a milder phenotype, presenting without hypotension or cyanosis. Only 5% of patients (23 patients) developed a more-severe phenotype presenting with hypotension, pallor, and cyanosis.

This cohort of patients is approximately seven times larger than previous studies. There are several possible explanations for this larger cohort. The true incidence of FPIES is unknown in the US population, but our large cohort may simply reflect the size of our referral base. We can estimate that the greater Philadelphia area has approximately 1.5 million children and that 462 patients are perhaps less than what one would expect to observe based on the 0.34% incidence found in Israel by Katz et al.⁵ Another potential reason for a larger number of patients is that we included patients with milder symptoms. We did not restrict our cohort to only patients with cyanosis and severe hypotension. We included all patients with the classic symptoms of vomiting and diarrhea 2–6 hours after exposure to the food trigger. It remains unclear at this time why some children seem to have more severe FPIES reactions than others, and more work is needed to understand why there seems to be a difference in the severity of the reactions.

Common FPIES trigger foods observed in previous studies were also seen in our retrospective study.^{9,10,15} Milk and soy were the predominant foods that triggered FPIES reactions. Eighty percent of patients reacted to either milk or soy. Forty-three percent of patients with milk allergies also reacted to soy, similar to findings by Burks et al,²⁰ Sicherer et al,¹⁰ and Nowak-Węgrzyn and Muraro.⁸ This was in contrast to Sopo et al⁷ and Katz et al,⁵ who found that most patients with milk allergies tolerated soy. The dramatic difference in cross reactivity between the US studies (Nowak-Węgrzyn et al,² Sicherer⁹ and ours) compared with the studies in Italy⁵ and Israel⁷ may be due to the order of food introduction and potential microbiome differences.

The second most common FPIES trigger food group that we observed in our cohort was grains, with rice being most prevalent, at 18.6%. Our results are very similar to those of Nowak-Węgrzyn and Muraro⁸ which were also found in a US population. In Italy, Sopo et al⁷ found fish to be the second most common trigger food after cow's milk. These differences are probably cultural. Rice and grains are typically early foods in the United States, whereas fish are introduced at an early stage in the Italian diet.

Although the majority of patients react to only one or two foods, approximately 30% of patients react to 3 or more foods. We found that 42% of patients who react to one type of grain also reacted to another type (compared with 50% in Nowak-Węgrzyn et al²). In addition, 24% of the patients with milk- and

TABLE III. Allergy testing in FPIES: characteristics of FPIES trigger foods

Allergen	Negative SPT, no. (%)	Negative APT, no. (%)	Age at onset (mo), mean (SD)	Age outgrown (mo), mean (SD)
Milk	245 (93.1)	60 (49.6)	6.3 ± 7.2	32 ± 24.1
Soy	158 (99.4)	37 (43.5)	7.7 ± 8.9	33.9 ± 23.4
Wheat	35 (97.2)	10 (35.7)	11.9 ± 9.5	31.1 ± 14.5
Oat	47 (100)	15 (37.5)	9.3 ± 6.2	37.4 ± 25.6
Rice	54 (100)	24 (54.54)	7.3 ± 5.1	43.3 ± 24
Barley	11 (100)	5 (50)	11.7 ± 9.1	55.3 ± 51.9
Corn	27 (100)	7 (25)	14.5 ± 13.5	60.4 ± 33.7
Chicken	11 (100)	7 (53.8)	17.6 ± 12.3	33.8 ± 7.8
Turkey	12 (100)	4 (40)	13.3 ± 7.3	33 ± 13.1
Egg	40 (88.9)	13 (40.6)	11.3 ± 9.6	41.8 ± 39.2
Overall	721 (96.4)	220 (45.7)	9.7 ± 10.2	37.8 ± 25.5

APT, Atopy patch test; FPIES, food protein–induced enterocolitis; SD, standard deviation; SPT, skin prick test.

soy-triggered FPIES react to one or more of the grains. Rarely, some patients reacted to both chicken and turkey. Approximately 5% of our patients reacted to more than 6 foods. The majority of patients who reacted to multiple foods reacted to milk, soy or both. In patients who reacted to multiple foods, there was a significant overlap with milk, soy, and the grains, as we have described above. There is a small minority of patients within our cohort who had reactions to numerous fruits or vegetables. Although the majority of patients with FPIES (70%) react to one or two foods, knowledge of potential cross reactivity should be considered and reviewed with the family.

We would not recommend introducing soy at home to a child with milk-triggered FPIES because 43.5% of patients with milk-triggered FPIES also react to soy. However, other foods can be introduced at home because fewer than 25% of patients with milk-triggered FPIES react to other foods besides soy. Therefore, in patients with milk- and soy-triggered FPIES, food introduction should continue by normal standard practices for fruits and vegetables. However, we recommend having a careful conversation with parents of patients with FPIES to both milk and soy before rice and grains are tried to discuss the risk of a potential FPIES reaction to grain. In some cases, OFC may be the safest method for introduction of foods if the child has very pronounced symptoms. Similarly, if a patient reacts to two or more grain types, then we would recommend OFC as the method to determine if a new grain could be introduced into the diet, given that 41% of patients who react to grains react to multiple grain types.

The age of onset of FPIES is similar in most studies and occurs between 6 and 9 months with the first introduction of foods. Sopo et al⁷ and Katz et al⁵ both found that the age of first FPIES reaction to be before 6 months compared with 9.7 months for the age of initial FPIES reactions in our study. However, if you look at our milk subgroup, the major allergen in the studies by Sopo et al⁷ and Katz et al,⁵ we observed an age of onset of 6.3 months, which is similar to their overall reported age of onset. Similar to the study by Nowak-Węgrzyn et al,² we found that solid food-induced FPIES occurred at a significantly older age (12 months).

Despite the fact that these infants developed severe reactions to foods, the majority will outgrow them before early childhood. Sopo et al⁷ found that milk- and soy-triggered FPIES was typically outgrown by 18 months of age and fish- and egg-triggered

FPIES were outgrown at 53 months. In our practice, we typically wait approximately 18 months after the last reaction to rechallenge the food. Therefore, it is not surprising that we find our patients' age of resolution for food-induced FPIES (whether it was liquid or solids) to be around 3 years of age. This difference is in part due to parents' willingness to rechallenge foods (which would make our earliest dates around 2 years of age older than the study by Sopo et al⁷). Although most patients have outgrown their FPIES reaction in the school-age years, we have 2 teenagers with persistent FPIES, which is consistent with a recent report of FPIES in adults.²¹

Similar to previous studies, allergy testing by SPT to foods was not informative, which indicated that this is a non-IgE reaction.^{1,2,5-10,12,15,20} We had previously found that APT had a predictive value for the diagnosis of FPIES reaction in a pilot study of 10 patients. APT is designed to identify allergens that cause cell-mediated hypersensitivity. This non-IgE mechanism is the presumed mechanism in FPIES. However, recent work by the Jarvinen et al²² found that APT was not helpful in diagnosing patients with FPIES. In the current retrospective review, APT was not helpful, because we found a 45% false-negative rate (Table III). This high rate of false negatives indicates that this test is far from ideal in the diagnosis of FPIES. The lack of predictive testing (SPT or APT) indicates an important need for future research. Sicherer⁹ found that patients with FPIES and with positive skin tests did not outgrow their food sensitivity as quickly. Due to the retrospective nature of this study, we do not have follow-up data at this time to parse characteristics that determine which patients are more prone to developing chronic symptoms of FPIES.

In summary, we found 462 cases of FPIES in our retrospective chart review of electronic medical records. Our data confirm previous findings that a majority of FPIES reactions are due to milk and soy. We saw FPIES triggered by solid foods in 50% of the population. The majority of patients react to one or two foods (with milk and soy being the most common combination, 43.5% of patients with milk-triggered FPIES also reacted to soy). Similarly, approximately 42% of patients with grain-triggered FPIES reacted to other grains. It is important to consider these facts when introducing new foods to patients with FPIES. Fortunately, most patients FPIES reactions had resolved by 3 years of age. However, there are some rare patients who have persistent FPIES until adolescence and beyond.

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