

Knowledge of food protein–induced enterocolitis syndrome among general pediatricians



Food protein–induced enterocolitis syndrome (FPIES) is a potentially severe, non–IgE-mediated food hypersensitivity. Typically, FPIES presents in infancy, either acutely with profuse emesis, dehydration, and lethargy 1 to 4 hours after intermittent ingestions; or insidiously with frequent, watery diarrhea, intermittent emesis, and failure to thrive with chronic ingestions.¹ Common eliciting foods include cow's milk and soy proteins; solids (rice, oat, fish, poultry, fish, and shellfish) are also culprits.^{2–6} Management often requires intravenous hydration in an inpatient setting.¹ Diagnosis is made clinically and may be confirmed with an oral food challenge.¹ Despite this condition being more prevalent than previously thought,⁴ diagnostic delays, multiple severe reactions, and extensive (often unnecessary) testing are common.⁶ As an initial effort toward improving recognition of FPIES, this study was designed to identify relevant knowledge gaps and to motivate educational efforts directed at primary care physicians.

Investigators created a 32-question survey, collecting information regarding participants' experience with FPIES and knowledge of FPIES diagnosis and management (eTable 1). Respondents could choose one or more answers to each question. A preliminary version of the survey was administered to a small sample of general pediatricians for assessment of readability and face validity. The institutional review board at the Icahn School of Medicine at Mount Sinai, New York, New York, approved the study. The final version of the survey was presented to physicians who participated in a continuing medical education activity on FPIES, which was posted to the Medscape Pediatrics website on April 13, 2013, and e-mailed to Medscape account holders who had indicated interest in pediatrics. Survey questions were embedded in the online platform, with knowledge-based questions preceding relevant material. Only Medscape account holders, who indicated profession and specialty on registration, could participate. Participation was voluntary; all responses were anonymous. Survey participants' responses with profession and specialty were collected by Medscape through July 14, 2013, and delivered to investigators. Only responses from those who indicated specialization in general pediatrics were included. Analyses (conducted with Rstudio, version 0.99.896, RStudio Inc, Boston, Massachusetts) included general descriptive frequencies, odds ratios (ORs) with mid-*P* calculation, and multivariable-adjusted logistic regression.

Of 4,024 general pediatricians who read the article, 90.9% responded to at least 1 survey question. The median response rate was 66.2% (interquartile range [IQR], 48.7%–85.8%) for knowledge questions and 21.8% (IQR, 21.6%–22%) for questions regarding physician characteristics. Among pediatricians who reported having patients with FPIES (*n* = 1,222), the median response rate to patient-related questions was 84.8% (IQR, 82.7%–100%). A complete list of questions (with number responding) and answers (with percentage selecting each) are included in eTable 1. Selected ORs and logistic regression model for variables of special interest are provided in Table 1 and eTable 2.

Regarding pediatrician experience, 35.9% reported caring for patients with FPIES, with odds increased among physicians practicing 5 years or fewer (OR 3.60; 95% confidence interval [CI], 2.78–4.66; *P* < .001). Pediatrician responses to patient-related

questions, including inciting foods, diets, timing of food reintroduction, and diagnosing and managing physician, are detailed in eTable 1.

In questions assessing physician knowledge (eTable 1), 67% reported having some understanding of FPIES, with odds increased among pediatricians caring for patients with FPIES (OR 13.7; 95% CI, 10.0–18.7; *P* < .001) and among those practicing 5 years or fewer (OR 2.11; 95% CI, 1.39–3.18; *P* < .001). In response to a case identification question describing acute and chronic FPIES, colic, and food protein–induced proctocolitis, 73% correctly identified acute or chronic FPIES, and 18% identified both, whereas 21.8% and 6% misdiagnosed proctocolitis and colic as FPIES, respectively. In a multivariable-adjusted logistic regression model (eTable 2), pediatricians caring for patients with FPIES were more likely to identify acute FPIES (*P* = .03) than those without FPIES patients. Practicing in the United States, self-reported knowledge, and years in practice were not significantly associated with better odds of FPIES identification.

Most respondents identified severe vomiting (83.5%) and failure to thrive (70.3%) as manifestations of FPIES (eTable 1). Fewer recognized severe manifestations (hypotension and cyanosis), with odds increased among those with patients with FPIES and those reporting knowledge of FPIES (OR 1.36; 95% CI 1.13–1.63; *P* = .001; and OR 1.77; 95% CI 1.44–2.19; *P* < .001, respectively). Regarding management of acute FPIES (eTable 1), most correctly recommended immediate emergency care (65.1%) and provision of written emergency treatment plan (62.1%), with odds increased among those who correctly identified acute FPIES (OR 1.47; 95% CI 1.20–1.81; *P* < .001; and OR 1.34; 95% CI 1.08–1.66; *P* = .007, respectively). Fewer pediatricians advised inappropriate first-line care with administration of epinephrine (16.3%) or antihistamines (5.0%).

Our survey responses suggest that many pediatricians have a basic but incomplete understanding of FPIES diagnosis and initial management. Almost three-quarters identified acute or chronic FPIES in a case question; less than 20% identified both. With more than half responding that they were unsure of presenting symptoms or had never heard of FPIES, many respondents may not recognize FPIES in their own patients and may have incorrectly stated they had never cared for patients with FPIES. Although the majority identified the most common presenting features (emesis, diarrhea, elevated white blood cell count),^{1,6} the majority also did not recognize hypotension and cyanosis as manifestations of FPIES. Physicians must recognize that FPIES reactions are commonly accompanied by dehydration, pallor, lethargy, and hemodynamic instability; other well-documented manifestations include methemoglobinemia, hypothermia, and acidosis.^{1–3,7–9} Regarding management, most respondents recognized the need for rehydration and provision of an emergency plan; however, a significant portion recommended inappropriate first-line therapies, including epinephrine and antihistamine.^{1,10} Guidelines state that, although mild reactions may be managed initially with oral rehydration at home, repetitive emesis or lethargy requires transfer to a medical facility for intravenous hydration and supplemental therapies (ondansetron, methylprednisolone, and supportive measures).¹

Our study design has several limitations. The selection pool was limited to a convenience sample that consisted of those with a Medscape account, among whom there could be a self-selection bias in those responding. The survey did not require a response to every question, resulting in variable response rates. Consistency in respondents' answers was not assessed. Survey questions were

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Table 1

Selected Odds Ratios from Analysis of Pediatrician Responses to an Online Survey Assessing Participant Knowledge of FPIES

Outcome	Odds ratio (95% CI)	P value
US pediatricians (n = 2,050) compared with non-US pediatricians (n = 1,511)		
Identified chronic and acute FPIES	0.99 (0.84–1.18)	.95
Identified acute FPIES	0.99 (0.86–1.13)	.83
Identified chronic FPIES	1 (0.87–1.14)	.97
Pediatricians with FPIES patients (n = 1,222) compared with those without (n = 2,127)		
Identified acute FPIES	0.96 (0.83–1.10)	.55
Identified chronic FPIES	0.75 (0.65–0.87)	<.001
Pediatricians in practice ≤5 years (n = 647) compared with those in practice >5 years (n = 475)		
Reported having FPIES patients	3.60 (2.78–4.66)	<.001
Pediatricians who identified acute FPIES (n = 892) compared with those who did not (n = 707)		
Emergency treatment plan	1.47 (1.20–1.81)	<.001
Emergent care for any reaction ^a	1.34 (1.08–1.66)	.007
Antihistamines prescription ^b	1.07 (0.68–1.67)	.77
Oral rehydration at home first ^a	0.89 (0.72–1.08)	.24
Pediatricians who identified chronic (n = 946) compared with those who did not (n = 652)		
Emergency treatment plan	1.00 (0.81–1.23)	.98
Emergent care for any reaction ^a	1.08 (0.87–1.33)	.49
Antihistamines prescription ^b	1.45 (0.91–2.32)	.12
Oral rehydration at home first ^a	1.18 (0.97–1.44)	.11

Abbreviations: CI, confidence interval; FPIES, food protein–induced enterocolitis syndrome.

^aAccording to guidelines, mild reactions may be managed with oral rehydration at home; repetitive emesis and lethargy warrant emergency medical care.¹

^bNot recommended by consensus guidelines.¹

not formally validated to determine statistical correlation with knowledge of FPIES. It is possible some readers navigated backward to questions after reviewing continuing medical education material. Despite these limitations, this survey is the first to assess knowledge of FPIES among pediatricians and was thus intended as exploratory.

In conclusion, this study provides an evaluation of general pediatricians' understanding of FPIES and has identified knowledge gaps in initial diagnosis and management. Pediatricians need to be aware of FPIES as a cause for potentially severe symptoms, including profuse emesis, dehydration, lethargy, and hypotension. As first contacts for patients with FPIES, pediatricians should be familiar with basic management, including avoidance of offending foods and treatment of acute reactions. Educational initiatives directed at primary care physicians are needed to improve initial identification and management of patients with FPIES.

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Hypogammaglobulinemia E in 216 adults with IgG subclass deficiency and respiratory tract infections

Hypogammaglobulinemia E has been reported in 0.8% to 3.0% of adults unselected for disease associations.^{1,2} In persons with subnormal serum immunoglobulin (Ig) E, the prevalence of frequent or severe respiratory tract infections,^{3,4} other subnormal

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Supplementary Data

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immunoglobulin isotypes,^{3,5} and autoimmune conditions^{3,4} was significantly greater than that in control subjects.^{3–5} To learn more, we performed a retrospective study to determine clinical and laboratory associations of hypogammaglobulinemia E (serum IgE <1 IU/L [$<2.4 \mu\text{g/L}$]) and IgE levels at diagnosis in 216 index adult patients with IgG subclass deficiency (IgGSD).⁶

We studied the records of non-Hispanic white adults (≥ 18 years of age) referred to a single practice in a large suburban medical

eTable 1Questions With Answer Options to an Online Survey Assessing General Pediatrician Knowledge of FPIES^a

Question (Total No. of Respondents)	Answers	Responses, %
1. How would you describe your knowledge of FPIES? (n = 3,524)	a. I have never heard of FPIES b. I have heard of FPIES but I am unsure of its presenting symptoms c. I understand the presenting symptoms but I am not familiar with diagnostic criteria or appropriate management d. I have a full understanding of FPIES presentation, diagnostic criteria, and management	33.1 19.9 37.3 9.8
2. Do you have any patients with a diagnosis of FPIES in your practice? (n = 3,401)	a. Yes b. No	35.9 64.1
3. For which of the following cases would you strongly consider FPIES as the diagnosis? (n = 3,561)	a. A 2-month-old infant exclusively breastfed who developed mucus and blood in the stool but who is otherwise well b. A 5-month-old infant with 2 episodes of severe, repetitive emesis starting within 2 hours after ingesting rice cereal who becomes listless and pale but appears well in between the episodes c. A 6-week-old thriving infant with frequent inconsolable episodes of crying and gas who spits up frequently d. A 2-month-old infant with failure to thrive, chronic diarrhea with blood and mucus, and elevated WBC count who has been fed a CM-based formula since birth	21.8 51.3 6.0 57
4. Which signs/symptoms are suggestive of FPIES? (n = 2,697)	a. Mild vomiting b. Severe vomiting c. Mild diarrhea d. Severe diarrhea e. Hypotension f. Cyanosis g. Failure to thrive h. Elevated WBC count i. Other	8.4 83.5 19.6 57.7 33.4 3.5 70.3 55.9 1.0 71.0
5. How many of your patients had FPIES in the past year? (n = 1,960)	a. None b. 1 child c. 2–5 children d. >5 children	23.3 16.6 4.4 42.6
6. How many patients with FPIES have you cared for in your career? (n = 1,958)	a. None b. 1 child c. 2–5 children d. >5 children	16.4 22.7 13.2 39.2
7. Who made the diagnosis of FPIES for your patients? (n = 1,256)	a. I made the diagnosis myself b. General pediatrician c. Family medicine physician d. Allergist e. Gastroenterologist f. Emergency physician g. Other	7.3 0.2 13.8 27.5 0.3 19.6 34.1
8. If you have patients with FPIES in your practice, do you manage them yourself or refer to another clinician? (n = 1,357)	a. I manage FPIES myself b. I refer to an allergist c. I refer to a gastroenterologist d. I refer to a specialist not listed above	27.7 37.0 1.3 62.9
9. Emma is diagnosed with FPIES. How would you manage her at this time? (n = 1,583)	a. I would provide a written emergency treatment plan for acute reactions. b. I would prescribe epinephrine autoinjectors for acute reactions c. I would prescribe oral steroids to use in acute reactions d. I would prescribe oral antihistamines to use in acute reactions e. I would prescribe antiemetics to use in acute reactions f. I would recommend oral rehydration at home first, followed IV hydration in ED if oral rehydration fails g. I would recommend calling 911 or going straight to ED with any FPIES acute reactions h. Other	16.4 3.7 5.1 10.8 44.8 65.7 11.7
10. When do you usually recommend reintroducing the offending food following the most recent FPIES reaction? (n = 1,037)	a. Within 6 to 11 months b. Between 12 and 17 months c. Between 18 and 24 months d. I do not recommend reintroducing the food but rather refer to a specialist to make that decision e. Other	23.6 15.8 45.4 3.4
11. In what setting do you recommend reintroducing the food that caused FPIES? (n = 1,025)	a. At home b. At a food challenge in an outpatient setting c. At a food challenge in a hospital or emergency department d. I do not recommend reintroducing the offending food but rather refer to a specialist to make that decision e. Other	9.4 13.2 39 32.0 1.2
12. What is the location of your practice? (n = 883)	a. Rural b. Suburban c. Urban	10.4 36.9 52.7

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eTable 1 (continued)

Question (Total No. of Respondents)	Answers	Responses, %
13. Which of the following best defines your practice setting? (n = 886)	a. Hospital based b. Private solo c. Private single specialty d. Private multispecialty e. Academic f. Other	35.3 10.5 28.7 14.2 6.3 5.0
14. How many outpatients do you see in a typical week? (n = 871)	a. 0–10 patients b. 11–25 patients c. 26–50 patients d. 51–75 patients e. >75 patients	11.1 14.4 23.1 20.6 30.9
15. How many years have you been in practice since completing your training? (n = 871)	a. <5 years b. 6–10 years c. 11–15 years d. >15 years	24 15.4 15.5 45.1
Among your patients with active/ongoing FPIES, how many react to the following food? For food(s) listed at left, respondents were prompted to select among answer choices at right.		
16. Soy only (n = 1,448)	a. None b. 1 child c. 2–5 children d. >5 children	74.8 14.8 8.3 31.0
17. CM only (n = 1,492)	a. None b. 1 child c. 2–5 children d. >5 children	41.9 21.4 23.8 12.9
18. Oats only (n = 1,338)	a. None b. 1 child c. 2–5 children d. >5 children	89 7.1 3.1 0.7
19. Rice only (n = 1,368)	a. None b. 1 child c. 2–5 children d. >5 children	78.9 15.7 4.5 1.0
20. Chicken and turkey only (n = 1,320)	a. None b. 1 child c. 2–5 children d. >5 children	91.4 6.1 2.1 0.38
21. Both CM and soy; no solid foods (n = 1,330)	a. None b. 1 child c. 2–5 children d. >5 children	62.3 17.0 14.7 6.0
22. Both CM and soy; at least one solid food (n = 1,331)	a. None b. 1 child c. 2–5 children d. >5 children	70.5 17.5 9.2 2.9
23. Only solid foods; no CM or soy (n = 1,320)	a. None b. 1 child c. 2–5 children d. >5 children	78.6 14.1 6.0 1.3
How many of your patients with FPIES are on the following diets? For each diet listed at left, respondents prompted to choose one of answer choices at right.		
24. Exclusive breastfeeding (n = 1,000)	a. None b. 1 child c. 2–5 children d. >5 children e. Do not recall	48.6 21.8 11.8 5.6 12.2
25. CM formula (n = 942)	a. None b. 1 child c. 2–5 children d. >5 children e. Do not recall	72.9 7.5 5.6 2.5 11.4
26. Soy-based formula (n = 911)	a. None b. 1 child c. 2–5 children d. >5 children e. Do not recall	73.7 8.2 5.4 1.2 11.4
27. Casein-based hypoallergenic formula (n = 957)	a. None b. 1 child c. 2–5 children d. >5 children e. Do not recall	45.8 17.4 20.1 7.3 9.4
28. Amino acid-based formula (n = 936)	a. None b. 1 child c. 2–5 children d. >5 children e. Do not recall	49.1 24.3 13.1 4.7 8.8

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eTable 1 (continued)

Question (Total No. of Respondents)	Answers	Responses, %
How many of your patients currently have active (unresolved) FPIES? For each age group listed at left, respondents were prompted to select between the answer choices listed at right.		
29. Infants <1 year of age (n = 916)	a. None	60.6
	b. 1 child	20.0
	c. 2–5 children	10.0
	d. >5 children	2.7
	e. Do not recall	6.7
30. 1- to 3-year-olds (n = 902)	a. None	68.0
	b. 1 child	17.5
	c. 2–5 children	7.1
	d. >5 children	0.55
	e. Do not recall	6.9
31. 4- to 10-year-olds (n = 870)	a. None	85.4
	b. 1 child	5.9
	c. 2–5 children	2.5
	d. >5 children	0.5
	e. Do not recall	5.7
32. Children >10 years of age (n = 869)	a. None	89.0
	b. 1 child	2.5
	c. 2–5 children	0.8
	d. >5 children	0.5
	e. Do not recall	7.0

Abbreviations: CM, cow's milk; ED, emergency department; FPIES, food protein–induced enterocolitis syndrome; IV, intravenous; WBC, white blood cell.

^aRespondents could choose more than one answer to most questions.

eTable 2

Logistic Regression Models to Identify Factors Associated With Correct Identification of Acute and Chronic Presentations of FPIES

	Odds ratio (SE)	z	P (> z)
Identification of acute FPIES			
In practice >5 years	−0.0147 (0.184)	−0.080	.94
Self-reported knowledge of FPIES	−0.241 (0.246)	−0.978	.33
Identification of chronic FPIES	−2.20 (0.176)	−12.5	<.001
Experience with FPIES patients	0.365 (0.167)	2.19	.03
US physician	0.269 (0.159)	1.69	.09
Identification of chronic FPIES			
In practice >5 years	0.0714 (0.187)	0.382	.70
Self-reported knowledge of FPIES	−0.226 (0.245)	−0.921	.36
Identifying chronic/acute FPIES	−2.19 (0.176)	−12.5	<.001
Experience with FPIES patients	−0.133 (0.168)	−0.792	.43
US physician	0.0967 (0.162)	0.597	.55

Abbreviation: FPIES, food protein–induced enterocolitis syndrome.