

The Practical Dietary Management of Food Protein-Induced Enterocolitis Syndrome

Marion Groetch RDN , Mary Grace Baker MD ,
Raquel Durban RDN , Rosan Meyer PhD, RD ,
Carina Venter PhD, RD , Antonella Muraro MD

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Title: The Practical Dietary Management of Food Protein-Induced Enterocolitis Syndrome

Authors: Marion Groetch, RDN¹, Mary Grace Baker, MD¹, Raquel Durban, RDN², Rosan Meyer, PhD, RD,³ Carina Venter, PhD, RD,⁴ Antonella Muraro, MD⁵

Author affiliations:

¹ Division of Pediatric Allergy & Immunology, Icahn School of Medicine at Mount Sinai, New York, New York, USA

² Asthma & Allergy Specialists, Charlotte, North Carolina, USA

³ Department Paediatrics, Imperial College London, UK

⁴ Section of Pediatric Allergy and Clinical Immunology, Children's Hospital Colorado, University of Colorado, USA

⁵ Food Allergy Referral Centre, Department of Woman and Child Health, Padua University Hospital, Padua, Italy

Corresponding author information:

Marion Groetch, MS, RDN

Division of Pediatric Allergy & Immunology

Icahn School of Medicine at Mount Sinai

1 Gustave L. Levy Place, Box 1198

New York, New York 10029

P 212-241-8925

F 212-426-1902

Marion.groetch@mssm.edu

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Objective: Food protein-induced enterocolitis syndrome (FPIES) is a non IgE-mediated food allergy with potential risk of malnutrition related to the early onset of disease, frequent avoidance of cow's milk, and the possibility of multiple food triggers. This publication is aimed at providing an evidence-based, practical approach to the dietary management of FPIES.

Data sources: This is a narrative review summarizing information from National/International guidelines, retrospective studies, population studies, review articles, case reports and case series to assess for nutritional risk and develop guidance for risk reduction in children with FPIES.

Study Selections: We have included retrospective clinical cohort studies, population based studies, case reports and case studies. We did not exclude any studies identified due to the small number of studies addressing the nutritional management of individuals with FPIES.

Results: Children with FPIES are at risk of malnutrition due to suboptimal oral intake, limited food choices and knowledge deficits related to feeding. In particular, children with three or more FPIES triggers appear to be at increased risk for poor weight gain and developing food aversion. Caregivers of children with FPIES also report a high degree of psychosocial burden.

Conclusion: Appropriate dietary management entails three essential components: supporting normal growth and development, avoidance of allergens, and advancement of complementary foods. Education to avoid the trigger food and assisting caregivers in creating an individualized, well-designed complementary feeding plan to meet the infant's nutritional needs for optimal growth and development are essential.

Key words:

FPIES, food protein-induced enterocolitis syndrome, food allergy, complementary feeding, nutrition

Abbreviations:

Food protein induced enterocolitis syndrome (FPIES)

Complementary feeding (CF)

International Consensus Guidelines for the Diagnosis and Management of Food Protein Induced Enterocolitis Syndrome (ICG)

Oral food challenge (OFC)

Amino acid-based formula (AAF)

Extensively hydrolyzed milk protein-based formula (EHF)

Dietary Guidelines Advisory Committee Report (DGAC)

Responsive feeding (RF)

Key Messages:

- Suboptimal oral intake, limited food choices, and knowledge deficits related to feeding have contributed to overt malnutrition and malnutrition risk for children with FPIES.
- Children with FPIES to three or more foods are at increased risk of developing food aversion and having poor body weight gain.
- Caregivers of children with FPIES report a high degree of psychosocial burden.
- Dietary management of FPIES entails avoidance of allergens, supporting normal growth and development, and advancement of complementary foods.
- Providing a detailed individualized feeding plan may help prevent feeding aversions and nutritional deficiencies and ease the burden on caregivers.

Introduction

Food allergies present nutritional challenges and risks in the pediatric population. The term food allergy covers a wide spectrum of clinical diseases, each with its own nutritional implications. Children with cow's milk allergy, early onset food allergy, and those with non-immunoglobulin (IgE)-mediated disease and mixed IgE-/non-IgE-mediated disease are at greatest nutritional risk^{1,2}. Food protein-induced enterocolitis syndrome (FPIES) meets criteria for increased nutritional risk, as it is a non-IgE-mediated food allergic disorder with early onset of disease, frequently triggered by cow's milk, possible involvement of multiple food triggers, and may result in persistent gut inflammation when the food trigger(s) remains in the diet^{1,3}. A recent retrospective study of 203 patients with FPIES found that compared with FPIES cases with 2 or fewer triggers, patients with multiple triggers were more likely to develop food aversion (43.2% vs 16.9%; $P < .001$) and to have poor weight gain (21.6% vs 6.6%; $P = .005$)⁴. To compound the risk, a 2017 survey found that approximately 1/3 of pediatricians surveyed had

never heard of FPIES and another 1/3 were not familiar with diagnostic criteria or appropriate management⁵.

Appropriate dietary management entails three essential components: supporting normal growth and development, avoidance of allergens, and advancement of complementary foods. Education to avoid the trigger food and assisting caregivers in creating an individualized, well-designed complementary feeding (CF) plan to meet the infant's nutritional needs for optimal growth and development are essential management strategies. This publication is aimed at providing an evidence-based, practical approach for healthcare professionals working with patients with FPIES.

Overview of FPIES

FPIES is characterized by delayed, often dramatic, gastrointestinal symptoms⁶. FPIES classically presents in infancy or early childhood, with most children developing tolerance by school age, although reports of adults with suspected FPIES are increasing^{7,8}. While much remains to be learned about the pathophysiology of FPIES, it is thought to be cell-mediated with cytokine release contributing to increased intestinal permeability and inflammation⁶. Two phenotypes of FPIES have been described, acute and chronic. Some patients with FPIES also become sensitized to the FPIES trigger, and this is termed atypical FPIES⁹.

Phenotypes

Chronic FPIES occurs when the culprit food is ingested regularly, resulting in chronic symptoms not temporally related to feedings⁶. This condition has been described exclusively in early infancy, and most cases are triggered by cow's milk- or soy-based formula, with symptom

onset within 1-4 weeks of introducing formula¹⁰⁻¹². Symptoms include intermittent but progressive vomiting and watery diarrhea that may contain blood and/or mucus^{9,13}. As feedings with the culprit formula continue, infants become ill with lethargy/irritability, failure to thrive, weight loss, abdominal distention, and/or dehydration, which may be severe and cause hypotension or shock. Upon evaluation, infants often demonstrate significant laboratory abnormalities including leukocytosis with a neutrophilic predominance, anemia, thrombocytosis, methemoglobinemia, hypoalbuminemia, metabolic acidosis, and/or electrolyte disturbances; these findings may initially be mistaken for sepsis¹³⁻¹⁷. Imaging may reveal dilated loops of bowel, sometimes with air-fluid levels and intramural gas. Treatment is supportive, with intravenous fluids, electrolyte repletion, and avoidance of the food trigger. With elimination of the culprit food, recovery is expected in days to weeks¹¹. If the culprit food is briefly avoided then re-introduced, patients may experience an acute FPIES reaction, confirming the diagnosis^{6,11}.

Acute FPIES is typically diagnosed in older infants or young children, often around the time of solid food introduction. With acute FPIES, children experience repetitive, profuse vomiting 1-4 hours after ingestion of the culprit food. The vomiting may be accompanied by pallor and lethargy, with diarrhea that may contain blood and/or mucus occurring 5-10 hours after ingestion¹². Due to the profuse vomiting, children with a severe presentation are at risk for dehydration and even shock. Laboratory evaluation often reveals a leukocytosis with a neutrophilic predominance, mimicking infectious etiologies and potentially delaying the FPIES diagnosis^{9,12}. Treatment is supportive with intravenous fluids, anti-emetics, and steroids, related to the theory that FPIES is cell-mediated. Symptoms often resolve completely within hours, although diarrhea may be a delayed symptom that is more persistent.

Atypical FPIES describes patients with a compelling history of FPIES who also have evidence of IgE sensitization to the trigger food⁹. It is estimated that atypical FPIES may occur in 5-25% of cases, and it is thought to be more common for cow's milk and egg^{13,14,18-24}. Atypical FPIES has been associated with a more prolonged course, with possible persistence of FPIES reactivity even into adulthood^{9,25}. In addition to sensitization to their FPIES triggers, children with FPIES may be more likely to develop IgE-mediated allergy to other foods as well^{13,19,26}.

Diagnosis and oral food challenge

The diagnosis of FPIES is established based on a compelling clinical history⁶. There are currently no laboratory or imaging tests to confirm the diagnosis. A positive oral food challenge (OFC) to the suspected FPIES trigger is confirmatory, but often not necessary for diagnostic purposes in the setting of a suggestive history. Therefore, more commonly, OFCs are used to assess tolerance development⁶.

FPIES OFC protocols have not been studied systematically. Guidance from the International Consensus Guidelines for the Diagnosis and Management of Food Protein-Induced Enterocolitis Syndrome (ICG) recommends OFCs in patients with suspected FPIES to a specific trigger food in a medically supervised setting where prolonged observation and fluid resuscitation are available.⁶ The consensus dosing recommends 3 equal doses over a 30-minute period, with a cumulative dose between 0.06-0.6 g food protein/kg body weight (usually 0.3 g food protein/kg body weight), not to exceed 3 grams of total food protein, 10 g total food or 100mL liquid for the initial feeding. Recommended observation is 4-6 hours. The OFC protocol is at the discretion of the physician, and lower starting doses or longer observation periods may

be reasonable depending on the individual clinical presentation. If a very low starting dose is utilized and tolerated, then a second full-dose may be offered 2-3 hours after the initial feeding, followed by an observation of 4 hours.

Atypical FPIES requires a hybrid OFC approach, beginning with a small dose and offering gradually increasing doses every 15-30 minutes as is typical with IgE-mediated food allergy, followed by a prolonged observation period common with FPIES²⁷.

Decisions on timing of OFC to determine tolerance may depend on a number of factors including the clinical history, food trigger, time lapse since the last reaction to the food, and even the patient's country or region as geographical disparities in FPIES presentation and resolution are reported. The ICG recommend offering an OFC 12-18 months after the last reaction to the food, although this has not been critically evaluated and is based on expert opinion. Looking at the natural history of FPIES to specific foods, Wang *et al.*²⁸ reported the mean age of tolerance development to milk, soy and grain was earlier than that to other solid foods in a US population (35 months-of-age at the time of passed challenge for milk, 38 months for soy, and 36 months for grains). Other solid foods included egg, corn, beef, poultry, sweet potato, butternut squash, carrot, white potato, peanut, coconut, and peach, with 12% outgrowing FPIES by 2 years, 31% by 3 years, 60% by 4 years, and 70% by 5 years. The mean age of passing a challenge to these foods was 44.9 months (n =19, SD = 23.6).

Food Triggers

Common chronic and acute FPIES triggers are summarized in Table 1. Given that chronic FPIES appears to occur only in early infancy with regular ingestion of the culprit food, almost all cases are linked to cow's milk- and soy-based formulas, with only case reports

suggesting a role for traces of these and other food triggers in breastmilk^{9,11,12,14,22,29}. Co-reactivity to cow's milk and soy is reported in 20-40% of infants in the United States but does not appear to be as common in other parts of the world^{13,21,22,24-26,30-32}.

Acute FPIES reactions occur upon ingestion of solid foods that are eaten intermittently or after a period of avoidance of chronic FPIES triggers. The most common acute FPIES triggers include grains (particularly oat and rice), cow's milk, soy, egg, seafood, poultry, and select fruits/vegetables^{13,18-21,23,26,30,33-35}. Reports of acute FPIES to peanut appear to be increasing, possibly related to early introduction³⁶. Geographical variation in the prevalence of individual FPIES triggers has been noted, and this is speculated to be related to differences in feeding practices.

Most children (65-80%) have FPIES to only a single food trigger^{6,13,19-22,30,37}. However, it has been observed that children with FPIES to cow's milk or soy early in life are at risk for FPIES to solid foods. Additionally, children with FPIES to one solid food appear more likely to react to other food triggers, with especially high co-reactivity among grains^{13,22,25}. Some case series report up to 30% of patients with multiple FPIES triggers^{24,44}. In a recent cohort, 69.4% of caregivers reported that their children avoided at least two food groups because of FPIES³³. Although multiple food FPIES is not the norm, prophylactic multiple food avoidance may be more common.

Nutrition and Feeding

Dietary avoidance education

ICG summary statement on avoidance states: "Do not routinely recommend avoidance of products with precautionary allergen labeling in patients with FPIES," though the guidelines

group acknowledges the limited dataset on which this recommendation is based⁶. Currently, no studies have been performed to set reliable thresholds in children or adults with FPIES. Katz *et al.*²⁴ reported 82% of children tolerated 50 ml of milk before a reaction developed. Sopo *et al.*³⁸ reported 78% of their patients reacted only after consuming a full portion of the trigger food. Finally, Fogg *et al.* reported reactions to 0.15g of protein/kg body weight³⁹. This relates to 30 mL of milk, 45 mL or soy milk or ¼ large egg in a 6-month-old infant ($7.8 \text{ kg} \times 0.15 \text{ g} = 1.15 \text{ g}$ of protein), which is still much higher than amounts of protein detected in products with or without precautionary advisory labelling. Ford *et al.* reported detectable levels of 0.084 to 0.26 mg egg per serving, 0.13 to 7.3 mg milk per serving, and 0.17 to 5.8 mg peanut per serving in products with precautionary labels for these allergens⁴⁰.

Caregivers should be educated about how to read a label to identify the food trigger as an intentional ingredient. The key to successful culprit food elimination is sufficient avoidance to prevent reactions without excessive avoidance that may hinder food choices and nutritional intake.

Breastfeeding

Human milk is the best source of nutrition for infants, and breastfeeding should be supported by healthcare professionals⁴¹. Limited data exist on the occurrence of FPIES in exclusively breastfed infants. Meyer *et al.*⁴² summarized data from one population study,²² six retrospective studies,^{9,13,20,38,43,44} four review publications,⁴⁵⁻⁴⁸ one international guideline publication⁶ and four case studies/case series^{29,49-51} in a recent European Academy of Asthma, Allergy and Clinical Immunology position statement (Table 2). The position statement concludes

that it is uncommon to see FPIES in exclusively breastfed infants. This is in agreement with the ICG, which do not recommend routine maternal allergen avoidance unless a child presents with symptoms whilst breastfeeding, in which case maternal allergen avoidance may be considered.⁶

Formula choices

High rates of co-reactivity to cow's milk and soy have been reported for infants in the United States, so avoidance of both food triggers is recommended for affected infants^{6,9,12,13,25,31,32}. Breastfeeding or hypoallergenic formulas are preferred sources of nutrition and are recommended by the National Institute of Allergy and Infectious Diseases (NIAID)⁵² and the ICG in the presence of milk- or soy-triggered FPIES⁶. There are no specific recommendations from these US groups regarding which hypoallergenic formula should be offered, amino acid based formula (AAF) or extensively hydrolyzed formula (EHF), although the ICG reports 10-20% will not tolerate EHF and AAF will be required. There is a lack of research directly comparing different hypoallergenic formulas. International guidelines for the management of cow's milk allergy provide different formula recommendations for FPIES. The European^{53,54} and World Allergy Organization guidelines⁵⁵ recommend the use of an EHF. The British Society of Allergy and Clinical Immunology⁵⁶ recommends the use of an AAF. The choice of formula may be clearer by focusing on other factors and not just the clinical diagnosis. EHF may be suitable for many infants and children with FPIES, but according to guidance by Meyer *et al.*,⁵⁷ the use of AAF should be considered in children with FPIES who also present with growth faltering and multiple food allergies. AAF may also be considered, on an individual basis, when a supplemental formula or transition to complete formula feeding is desired for

infants who have had a severe FPIES presentation to cow's milk protein formula or who have reacted to the small amount of milk protein present in breast milk.⁵⁸

Impact on growth and nutrition

The impact of food allergy on growth has been well described in both IgE- and non-IgE-mediated food allergy⁵⁹. Whilst underweight, defined by weight-for-age z-score of < -2 is described in just above 5% in an international survey, stunting, defined by a height-for-age < -2 z-score is much more prevalent, affecting approximately 10% of pediatric food-allergic patients¹. Although several studies have assessed growth in children with non-IgE-mediated allergy^{1,60,61} and failure to thrive (FTT) is part of the diagnostic definition for chronic FPIES, there are limited data regarding the prevalence of malnutrition specifically in FPIES. In 2019, Blackman *et al.* in a retrospective case series of 76 FPIES patients from a US allergy center, reported failure to thrive in 16 (22%) children³⁵. Ten of the 16 children with FTT were evaluated by the dietitian, six of whom were given the nutrition diagnosis of malnutrition with associated etiologies of suboptimal oral intake and limited food choices related to FPIES, while the remaining four were identified as at increased risk of malnutrition related to FPIES knowledge deficits. It is therefore crucial as part of the diagnosis and ongoing monitoring of FPIES patients to assess weight, stature, and where appropriate, head circumference to inform both diagnosis and dietary management and provide feeding guidance that addresses avoidance and nutritional needs.

Other factors may influence growth, including ongoing inflammation due to other atopic co-morbidities, persistent unnoticed inflammation and feeding difficulties as hypothesized by Meyer *et al.*⁶², but these have been poorly studied in FPIES. In 2002, a study highlighted the increased expression of TNF- α on both epithelial and lamina propria cells, which was

significantly greater in the patients who had villous atrophy with FPIES soon after diagnosis³.

This cytokine, in addition to IL-6 and IL1- β , has been shown to have a significant impact on the longitudinal growth plates through decreased chondrocyte proliferation and hypertrophy as well as increased apoptosis⁶³. However, there are no data on these cytokines in asymptomatic children with appropriately treated FPIES

In addition, children with FPIES may also have other atopic disorders including eczema and asthma,¹³ that may further impact longitudinal growth. This implies there are factors outside of dietary elimination and vitamin/mineral deficiencies that may contribute to poor growth.

A recent study has highlighted the psychosocial impact on parents of children with FPIES, with increased anxiety, stress and worry, which can have a negative impact on the introduction and expansion of nutritious solid foods in growing infants⁶⁴. This delay may also lead to missing oral-motor and behavioral milestones essential in developing normal eating skills, thereby increasing the risk of feeding difficulties that may also negatively impact growth^{65,66}. Several micronutrients are critical for ongoing growth, including sodium, chloride, zinc, vitamin D and iron⁶⁷. Children with FPIES may have impaired absorption, reduced intake and excessive losses as part of their clinical presentation⁶. All of these may negatively impact micronutrient status (Figure 1).

Preventing and correcting vitamin and mineral deficiencies

Vitamin and mineral deficiencies, in particular vitamin D, vitamin A, calcium, iron and zinc have been well described in food-allergic patients^{61,68-70}. Whilst there are limited data on specific vitamin and mineral deficiencies in FPIES, it is assumed that this population has the same risk as other food-allergic children. Health care providers should, as a baseline, follow

country-specific guidelines for vitamin/mineral supplementation for all children (i.e. iron, vitamin D)⁷¹. In addition, dietary assessment, ideally performed by a dietitian, may be useful in gauging necessity of further specific vitamin and mineral supplementation advice⁶. It is important to understand that particularly in inadequately managed food allergies, vitamin and mineral deficiencies are difficult to predict through dietary intake alone, as this does not account for poor absorption and/or excessive losses⁷². Therefore, targeted nutritional laboratory biomarkers may be useful in some patients, but knowledge of the accuracy of measures and influencing factors is crucial in the interpretation of the markers⁷³.

Any identified micronutrient deficiency should be corrected with supplementation but also the cause should be identified and addressed, which may be dietary or related to reduced absorption/excessive losses. Identification of the nutrition problem and the etiology is part of the nutrition care process and highlights the importance of the dietitian in the management of FPIES. Table 3 provides practical tips on prevention and treatment of vitamin and mineral deficiencies.

Guidance for early complementary feeding to minimize nutritional risk

In 2014, Venter and Groetch⁴⁸ already recognized the importance of providing clear feeding advice to parents with FPIES to minimize the nutritional risk and ensure optimal and timely exposure to new tastes and textures. The recent ICG have expanded this further, based on new research, with a suggested CF plan for patients with FPIES⁶. Figure 2 provides guidance for CF; it includes foods that are nutritionally dense (meat, fish, poultry, eggs, nuts, seeds, legumes, fruits, vegetables, grains), follows current infant feeding guidelines⁷⁴, and stratifies foods by their risk for triggering FPIES based on case series⁶. It is, however, important that clinicians individualize these CF recommendations based on the foods that are current triggers for that

patient, the cluster patterns associated with those foods, the patient's nutritional needs, and locally acceptable/available foods.

A common question among caregivers is how quickly to introduce new foods. Mehr and colleagues reported in their cohort of 350 infants, just over half (51%) reacted on the first exposure to the food, 14% on the second exposure, 11% after 2 tolerated exposures, and 24% after 3 or more tolerated exposures¹⁵. It is commonly recommended that caregivers introduce higher risk foods as a single ingredient and continue feeding for at least 4 days before introducing any other new food to observe for the development of a reaction⁶. As the infant tolerates a greater number of foods, the amount of time between food introductions should be reduced to prevent delays in feeding a diverse and balanced diet. In the event of an FPIES reaction to the food, waiting until the symptoms have fully resolved before introducing a new food is a practical approach.

During the CF period, beginning around 6 months of age, micronutrient intake must increasingly be met by complementary food. A systematic review by Obbagi *et al.* found strong evidence that high-iron complementary foods helped maintain iron stores and prevent iron deficiency anemia (IDA) in the first year of life for breastfed infants⁷⁵. Recent published draft guidance by the US Dietary Guidelines Advisory Committee Report (DGAC) suggests including 0.5 ounce of fortified infant cereal in the early complementary diet for the breastfed infant to help meet iron and zinc needs- nutrients with critical gaps⁷⁴.

For infants with FPIES, however, adding grains in the early CF period may be challenging due to the risk of multiple food FPIES reported in case series in 15.8% - 69.4%^{6,13,19,22,28,35}, with grains being the most commonly avoided food group in some recent reports^{4,22,35}. The risk of co-reactivity is higher between rice and oat^{13,76,77} than between these

two grains and wheat or corn. Wang *et al.* reported no patient (n=13) challenged to wheat due to oat or rice triggered FPIES had a positive challenge, with a mean challenge age of 27 months (range, 9-50 months)²⁸. Blackman *et al.*³⁵ also reported low cross reactivity with wheat (5%) in those with rice FPIES (n=39), as did Mehr *et al.*²² with a cross reactivity of 5% for wheat and 1% for corn. These reports should be reassuring when introducing grains, especially fortified grains for the breastfed infant, as wheat and corn are more commonly fortified. Whole grain wheat plus other ancient and pseudo grains such as millet, quinoa, buckwheat, and amaranth are all excellent grain options, especially for bottle-fed infants receiving sufficient iron-fortified formula who do not benefit from fortified grains⁷⁴.

The AAP recommends supplemental iron (1mg/kg/day) for infants with no dietary source of iron after 6 months of age to prevent iron deficiency⁷¹. The DGAC suggests screening those at risk of iron deficiency prior to supplementation⁷⁴. Country specific dietary supplement guidance should always be considered as nutritional intake and needs can be affected by the distinctive regional and culturally relevant infant foods.

Feeding skill development

FPIES is associated with oral feeding aversion and delay in achieving feeding milestones⁶⁵. In a retrospective review by Su *et al.*⁴ the risk of developing food aversion in a cohort of children with FPIES increased in cases triggered by 3 or more foods compared to just 1 or 2 foods (adjusted odds ratio, 3.07; 95% CI, 1.38-6.82; P = .006). Early food avoidance imposes limitations, not only on food choices, but also on mealtime structure, feeding skill development, and frequency of feeding interaction with the caregiver, making the consequences of FPIES in the CF period multifaceted⁶⁵.

Although an infant's age provides a goal timeline for acquired infant feeding skills to begin CF, each child will develop skills within a range of suggested months. In the three phases of CF, stage one initiates introduction of solids to infants around 6 months of age beginning with smooth purees. In stage two, between 6 to 9 months of age, the infant will have acquired skills needed to consume soft lumpy, mashed food, and soft finger foods. By stage three, the infant is 9 to 12 months of age and has typically developed the ability to eat chopped, minced foods as well as firm finger foods⁴⁸ (Figure 2).

However, all feeding skills in this time-period are learned through the presentation of foods, so CF of diverse flavors and textures is important to skill development. To achieve diet diversity, it is recommended that nutritionally valuable, low-risk, complementary foods be introduced beginning by 6 months of age to meet growing nutritional demands while progressively advancing the variety and textures of foods to support feeding skill development^{6,48}. The selection of low-risk complementary foods should be valued during the initial CF stages for its versatility to provide an assortment of textures to support timely feeding skill acquisition. The range of flavors and textures a food offers directly correlates with prevention of feeding aversion^{78,79}. If an infant's diet is limited in variety, texture advancement can still be achieved, even with just one food, by changing methods of preparation from smooth puree, mashed food, foods with lumps and bumps and finally soft finger foods.

While food selection and its creative preparation can lend to nutrition and achieving feeding skill goals, the dynamic between caregiver and infant should also be assessed to ensure successful implementation of recommendations in the event of parental worry to proceed with feeding⁴⁸. Building a repertoire of safe food fosters a positive relationship with food, facilitates

oral motor skill development, and nurtures the relationship between infant and caregiver as it relates to feeding⁸⁰.

Additionally, responsive feeding (RF) should be encouraged. RF involves reciprocity between the child and caregiver during the feeding process and is characterized by caregiver recognition of and response to the child's cues of hunger and satiety⁸¹. RF guides caregivers on how to feed their infants and young children, which complements existing global guidance on what to feed young children and also emerging US guidance on what to feed children 0-2 years of age⁷⁴. RF fosters healthy eating habits and has the potential to optimize child growth and development outcomes, especially where malnutrition is a risk.

Should appropriate food selection, diverse preparation, and secure caregiver bond and responsiveness not result in successful progression of feeding, feeding therapy may be considered. Early recognition of feeding difficulties can initiate an appropriate referral for collaborative care with a speech language pathologist or occupational therapist or comprehensive feeding clinic. Techniques to support feeding skill development can be facilitated by these therapists to lessen the burden of impact from feeding aversion⁶⁵.

Conclusion

Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated food allergy with onset in early infancy and risk of multiple food triggers, which presents nutritional challenges that are best addressed preemptively by the health care provider. Dietary and nutritional management of FPIES entails appropriate avoidance of the trigger food(s) without excessive avoidance, guidance on early introduction of safe and nutritious complementary foods, and progressive advancement of skill-appropriate food textures that will provide the backdrop for

feeding skill development. Close growth monitoring of children with FPIES is warranted to identify and address poor growth, which is a risk factor in this population. Lastly, an awareness of the psychosocial impact of the disease will help clinicians work closely and collaboratively with families to address their feeding concerns. This highlights once more the need for a comprehensive management plan for FPIES as well as for other clinical phenotypes of food allergy⁸². The implementation of an integrated multidisciplinary approach should include a dedicated dietitian with expertise in food allergy in the regular assessment of these patients. Providing a well-managed and detailed individualized feeding plan will help prevent feeding aversions, nutritional deficiencies, and overt malnutrition in the child and ease the burden of disease on caretakers.

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Figure 1: Potential contributing factors to growth faltering in FPIES

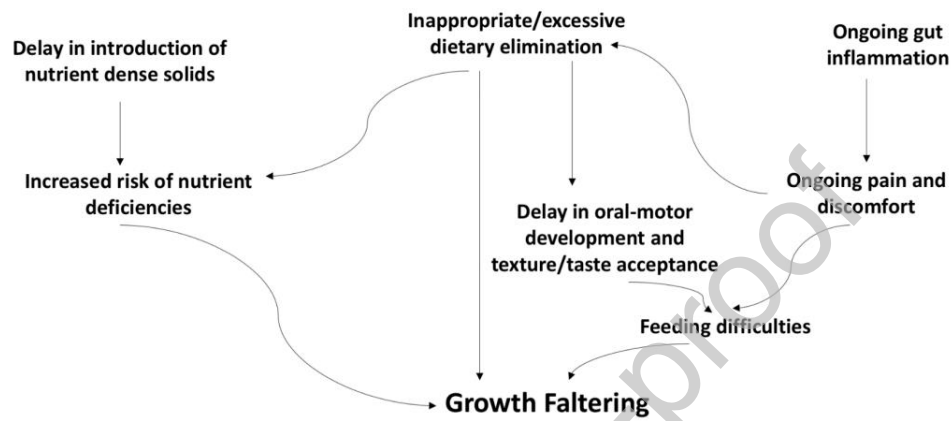


Figure 2 Guidelines for Early Feeding

^a The limited variety of foods in this table provides a starting point for feeding based on available data. Categories listed are no guarantee of tolerance or adverse effect. Additionally, there are many foods not listed that should be added to the infant diet as age and tolerance dictates.

WHAT to feed your baby (as tolerated and advised by your baby's doctor) ⁽⁸⁵⁾		FOODS BASED ON RISK AS FPIES TRIGGER ^{a (6)}			
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 ½- 1 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 Other protein foods	Lamb, beef, pork, bison Tree nuts, seeds	Peanut	Fish, poultry Soy, egg
Meats & proteins	3/4 - 3 ounces Serve a variety of meat, poultry, eggs, fish, nuts and seeds.	Grains	Quinoa, millet, amaranth	Wheat, corn	Rice, oat
Fruits and vegetables	1/8-1/2 cup each Serve a variety of dark green, red, orange and other vegetables and fruits.	Vegetables	Broccoli, cauliflower, parsnip, turnip, beet	Squash	Pea, sweet potato
The amounts listed in this table are approximate amounts to serve so caregivers know how to provide nutrition in a balanced, diverse, and proportional manner. These amounts are NOT a prescription on how much your baby should eat as each baby is unique.		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 ⁽⁸⁶⁾ 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

Table 1. Major food triggers for chronic and acute FPIES. Chronic FPIES triggers are consistent worldwide. Major acute FPIES triggers listed by region based on presently available data.

Condition	FPIES Triggers
Chronic FPIES	>99% of cases [9,11,12,14,15,29] Cow's milk-based formula Soy-based formula <1% of cases Food triggers in breast milk
Acute FPIES	United States [13,26,30,33,35] Cow's milk Soy Grains Egg Fruits & vegetables Europe [18-21, 23] Cow's milk Fish Egg Grains Soy Australia [22] Rice Cow's milk Egg Oat Poultry

Table 2 Presentation of FPIES during exclusive breastfeeding

Country	Study characteristics	Number	Findings
Australia [22]	population-based survey	240 infant and children	5% (n=11) acute FPIES while exclusively breastfed (milk, grains, chicken)
Japan [14]	Clinical cohort	46 children	6.5% reacted during exclusive breastfeeding (rice and soy)
Israel [43]	Birth cohort	64 children	9.3% presented with first FPIES reaction whilst breastfed
USA [9]	Clinical cohort	16 children	50% presented with first FPIES reaction whilst breastfed
Italy [38]	Clinical cohort	66 children	95% of children with FPIES were breastfed, but it is unclear if exclusively breastfed
Australia [51]	Case	1 infant	Infant; exclusively breastfed developed acute FPIES from maternal ingestion of a large amount of soy. This group reported that 21 breastfed infants with acute FPIES presented during breastfeeding, but not clear if they were exclusively breastfed.
USA [50]	Case study	1 infant	Infant exposure to rice and sweet potato while exclusively breastfeeding
Italy [49]	Case studies	2 children	Chronic FPIES caused by maternal cow's milk ingestion
USA [13]	Retrospective study	160 children and adults	3 children presented with chronic FPIES by while exclusively breastfed (milk)

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 (i.e. cereals) when appropriate • Avoid over-supplementation in a child where no deficiency is suspected • Monitor patient frequently to ensure that CF 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 side effects of supplements (i.e. iron) • Understand interaction between supplemented micronutrients (i.e. copper and zinc) • Monitor supplementation to ensure supplements are stopped when required • Assess and address causes of deficiency