

# Food Protein-Induced Enterocolitis Syndrome

Highlighting the complexity and challenges of managing this frequently misdiagnosed, rare, form of gastrointestinal food allergy



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Food protein-induced enterocolitis syndrome (FPIES) is a serious form of non-IgE-mediated gastrointestinal food allergy that manifests in infancy as repetitive projectile vomiting, diarrhoea and a systemic inflammatory response. Symptoms typically present 2-4 hours after ingestion of the offending food protein.<sup>1</sup> In some children, it may progress to dehydration, and shock. In cases of delayed diagnosis, FPIES can present as failure to thrive.<sup>2</sup>

Despite increasing recognition of FPIES, this rare type of food allergy is difficult to initially diagnose. FPIES is a clinical diagnosis based on history and clinical features. Negative serum IgE and skin prick tests (SPT) are the usual finding in this condition, as it is not mediated by IgE antibodies. The following case study outlines some of the challenges associated with FPIES diagnosis and management, from both a clinical and dietetic perspective.

## Birth history

Baby M\* was a first born, normal vaginal, term delivery with no neonatal issues reported. His birth weight (3.2 kg) and length (50 cm) fell on the 25th centile. Atopic dermatitis (mild) developed at six weeks; his father has asthma, but his mother has no atopic history.

## Feeding and clinical history

Baby M was exclusively breastfed from birth to five weeks. His weight and length tracked well along the 25th-50th centiles during the first six weeks. The first supplementary formula feed was introduced at five weeks; 120 ml of regular cows' milk-based formula was ingested and well tolerated. Two further

supplementary formula feeds were given during the 6th week of life, with no issues reported.

## First allergic reaction

At seven weeks of age, the fourth supplementary bottle of formula milk was given. A total of 90 ml was ingested. Two hours later, Baby M began to vomit repeatedly, subsequently becoming lethargic and pale. He was admitted to hospital with a diagnosis of hypovolemic shock, secondary to suspected gastrointestinal infection. He was given antibiotic cover due to his poor condition at presentation. Twenty-four hours into his admission, he developed mucously diarrhoea. It was concluded that this was due to the antibiotics. He was discharged after a five-day admission.

\*The name of the patient has been changed to protect patient confidentiality.

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## Second allergic reaction

At 10 weeks of age, the fifth supplementary formula milk feed was given (100 ml ingested). Similar to the previous reaction, vomiting began after two hours, resulting once again in the infant becoming lethargic. However, the parents managed to rehydrate Baby M at home. Two days later he developed diarrhoea that lasted for 24 hours. Following a GP visit, Baby M was diagnosed with a second suspected gastrointestinal infection.

## Third allergic reaction

At 12 weeks of age, mum changed the formula type to a partially hydrolysed whey-based feed and gave Baby M his sixth supplementary formula milk feed (120 ml ingested). Over two hours later, he presented with the same symptoms, and was referred on to a paediatrician for further investigation.

## FPIES diagnosis and dietetic management

At 15 weeks, FPIES was diagnosed, based on Baby M's clinical presentation and history. Baby M was referred on to a paediatric allergist and dietitian. Avoidance of cows' milk protein until two years was recommended. Dietary management goals focused on ensuring sufficient nutritional adequacy for optimal growth and development. Supporting mum to continue breastfeeding was a key objective, as well as providing advice on avoidance of cows' milk protein in Baby M's diet, including understanding labels, how to avoid cross contamination (e.g. at crèche) and accidental exposures. In view of the fact that breast milk was well tolerated from an unrestricted maternal diet, mum was encouraged to consume her regular diet including cows' milk protein-based products, without the need for any dietary restrictions. Baby M's parents were provided with information on a suitable hypoallergenic supplementary formula milk, and timely weaning onto age and texture-appropriate spoon feeds.

In view of the severity of the FPIES reactions, an amino acid-based formula (AAF) was recommended as the supplementary feed of choice (Neocate LCP). At 17 weeks, the first bottle of AAF was offered, and refused by Baby M. A slow graded introduction of the formula was therefore suggested. On Day 1, 90 ml of expressed breast milk (EBM) was mixed with 30 ml of formula. On Day 2, 60 ml of EBM was mixed with 60 ml of formula; on Day 3, 30 ml of EBM was mixed with 90 ml of formula. A full Neocate LCP feed (at normal concentration: 13.8%) was successfully taken by Day 4.

## Weaning onto solids

At five and half months, Baby M was weaned onto cows' milk protein-free solids. Foods were introduced slowly, in cooked form and in small amounts initially, offering one vegetable or fruit type at a time, every 2-3 days. At eight months it was mum's choice to fully discontinue breastfeeding. Given that a high proportion of infants with FPIES react to both cows' milk and soy proteins, Baby M was slowly introduced to soya yoghurts, which were well tolerated. He continued on Neocate LCP, and at one year was changed over to an AAF for children over one year of age, which was taken from a beaker cup. There were no issues with his weight, and he was growing proportionately (weight at 11 months: 9.55 kg [50th centile]; length: 72.5 cm [25th centile]). Vitamin D and ferritin levels were checked intermittently during the first 22 months, and all levels were within normal limits.

## IgE and skin prick test results

Baby M was tested and found to have a raised serum IgE and a positive SPT to cows' milk (**Table One**); such positive allergy tests can occur in up to 30% of FPIES cases.<sup>3</sup> He was also sensitised to egg (positive serum IgE and SPT). His parents were advised to start introducing egg in baked form only. The introduction of peanut into the diet was also recommended as serum IgE and SPT values for peanut were both negative.

**Table One: Serum IgE and Skin Prick Test (SPT) Results at 11 Months of Age\***

|            | IgE (kU/l) | SPT (mm) |
|------------|------------|----------|
| Total IgE  | 25         |          |
| Cows' milk | 3.33       | 3        |
| Egg white  | 7.22       | 4        |
| Soya       | <0.35      | 0        |
| Peanut     | <0.35      | 0        |

\*IgE and SPT tests need to be interpreted together with the clinical history.

## Re-evaluation

At two years of age, an in-hospital oral milk challenge was performed; this was successful, and Baby M commenced on cows' milk and other dairy foods. Oral food challenges (OFC) for infants with FPIES should only be performed under the supervision of experienced paediatricians. The placement of a secure peripheral venous access before the OFC is recommended. The OFC usually takes place over a period of 24-48 hours.

## Discussion and learning points

This case study highlights the challenges associated with FPIES diagnosis and management - including the fact that symptoms can overlap with other gastrointestinal conditions. It is not uncommon for infants with FPIES to initially tolerate the offending food allergen several times before an allergic reaction occurs<sup>4</sup> - making early recognition of the allergy more difficult.

Although cows' milk, soy and rice proteins are the most common food allergens implicated in FPIES, other foods traditionally considered to be hypoallergenic, have also been reported (e.g. sweet potato, oats, chicken). Dietary management of FPIES involves removing the offending food from the diet and ensuring dietary adequacy. If breast milk is well tolerated from an unrestricted maternal diet, continued breastfeeding should be supported.

For infants requiring supplementary formula feeds, food allergy guidelines recommend either an extensively hydrolysed<sup>5, 6</sup> or an amino acid-based<sup>7</sup> formula for the management of FPIES. However, the choice of formula is a clinical decision based on several factors including severity of reactions, infant growth pattern and tolerance.

Infants, particularly those who are breast-fed, may initially refuse hypoallergenic formulas due to taste issues. A slow graded introduction of hypoallergenic formula volumes mixed with breast milk over a period of 4-5 days may help increase acceptance.

Nutritional and growth monitoring and advising parents on a suitable supplementary formula milk are all part of the dietetic role in FPIES management. Providing guidance on introducing timely age- and texture-appropriate spoon feeds and finger foods is also important. A practical weaning guide for infants with FPIES is summarised by Venter and Groetch (2014).<sup>8</sup>

Although the current case study involved one food implicated in FPIES, it is possible for these infants to react to more than one food (e.g. rice and chicken) which can complicate the weaning process. For this reason, a slow graded introduction of foods, one at a time, in cooked form initially, starting in very small amounts (e.g. one teaspoon) with incremental daily increases, is advised in this patient group.

To prevent fussy eating and aversive feeding behaviour, encourage parents to introduce new foods every 3-4 days, and continue to progress the infant through the stages of weaning, as appropriate. It is also worthwhile monitoring markers of nutritional status, such as vitamin D, haemoglobin and ferritin, especially in breastfed infants (not supplemented with formula milk), those who have a limited diet, and where poor compliance with vitamin/mineral supplementation is reported.

The OFC remains the gold standard for monitoring resolution of FPIES.<sup>3</sup> It should be pointed out to parents that the prognosis for FPIES is favourable, with the majority of patients having resolution of their reactions by five years of age.<sup>9, 10</sup>

**Disclaimers:** Neocate LCP is a Food for Special Medical Purposes for the dietary management of Cow's Milk Allergy, Multiple Food Allergies and other conditions requiring an Amino Acid-based Formula, and must be used under medical supervision. This case study has been commissioned by Nutricia and is intended for HCPs only.

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