



Cow's milk allergy

Case studies

Rectal bleeding caused by cow's milk allergy
Severe eczema associated with cow's milk allergy

Yvonne Polydorou

Senior Paediatric Dietitian, Homerton University Hospital NHS Foundation Trust



Box 1. Summary of UK and international guidelines on management of CMA.

- Children with symptoms of mild to moderate CMA may be managed in primary care.¹
- European guidelines recommend that children with symptoms of severe CMA should be referred to a paediatric specialist, and cow's milk protein should be eliminated from their diet.¹ Many centres prefer that elimination diets start only after consultation with a specialist.
- In exclusively breast-fed children, a strict elimination of the causal protein from the diet of the lactating mother should be tried.^{1,2}
- Children with CMA who are not exclusively breast fed should receive a hypoallergenic* formula based on extensively hydrolysed protein as first line.^{1,3}
- In cases where extensively hydrolysed formula is ineffective, or if multiple or severe allergy is present, an amino acid-based formula should be used.^{1,3}
- Bottle-fed children aged under 6 months with moderate or severe atopic eczema should be offered a 6–8 week trial of an extensively hydrolysed protein formula or amino acid formula.⁴
- Formulas based on unmodified proteins of other species' milk (for example, goat's or sheep's milk), or partially hydrolysed protein, are not hypoallergenic* and should not be used for the management of CMA.²
- Soya-based formulas contain high phytate, aluminium, and phytoestrogen concentrations, the long-term effects of which are unknown. These formulas should not be used as the first choice for the management of children with proven cow's milk sensitivity.^{5,6}

* Hypoallergenic formulas are defined as formulas that are tolerated by at least 90% of children with documented CMA.⁷

1. Vandenplas Y *et al.* *Arch Dis Child* 2007;**92**:902–8
2. Host A *et al.* *Arch Dis Child* 1999;**81**:80–4
3. Kneepkens CM *et al.* *Eur J Pediatr* 2009;**168**:891–6
4. National Institute for Clinical Excellence. *CG57: Atopic eczema in children* 2007
5. Agostoni C *et al.* *J Pediatr Gastroenterol Nutr* 2006;**42**:352–61
6. Department of Health. *CMO's Update* 37, 2004;2
7. American Academy of Pediatrics. *Pediatrics* 2000;**106**:346–9

ISAAC

Rectal bleeding caused by cow's milk allergy

Six-week old Isaac presented with rectal bleeding and irritability. His symptoms resolved after careful removal of milk protein from his diet, which involved switching his bottle-feed to an extensively hydrolysed formula. The long-term prognosis for infants with CMA is good, and by age 1 year, Isaac was able to return to a full normal diet.

Presentation

Isaac presented in paediatric A&E at age 6 weeks with rectal bleeding, which his mother had first noticed 3 days prior. Isaac was born at full term, with a normal delivery and at birth, his weight was on the 75th centile; however, by the time of presentation it had fallen to the 25th centile. Isaac's mother had noticed that since introduction of infant formula to his diet, as a top-up to breast feeding, Isaac's stools had changed to a chalky colour, and often contained mucus. He had also become more irritable and unsettled.

Since introduction of infant formula to his diet, Isaac's stools had changed to a chalky colour and often contained mucus

Isaac was urgently referred to our clinic for consultations with a gastroenterologist and a paediatric dietitian. On examination, Isaac was found to be otherwise well and thriving, with a soft abdomen and a normal rectal examination. Full blood count, clotting profile and liver function were all within the normal range.

Management

We discussed removal of cow's milk protein from Isaac's diet by recommending a dairy-free diet for his mother. However, she indicated that she was keen to give up breast feeding. Therefore, it was decided that Isaac would be transferred from breast milk onto a hypoallergenic formula, his mother undertaking a dairy-free diet until this process was complete.

Isaac was prescribed Nutramigen* 1, to start immediately. We provided written information, which explained how to use the formula, that the formula could be expected to taste and smell different from other formulas, and that the change in diet may alter stool colour and consistency. Isaac's condition during the following month was monitored through follow-up telephone calls.

Isaac was prescribed Nutramigen 1, to start immediately

Three days after visiting the clinic, Isaac's mother was adhering well to the dairy-free diet. Although Isaac initially refused Nutramigen 1, it was successfully introduced in a 1:1 mix with breast milk, and the proportion was gradually increased until, after a few days, Isaac was feeding on Nutramigen 1 on its own. One week later, breast milk had been eliminated from Isaac's diet and he was feeding solely on Nutramigen 1.

At age 10 weeks, Isaac returned to the clinic for review. There was no blood in the stools and the quantity of mucus was reduced. Furthermore, Isaac's weight had improved and his mother reported that he was more settled and "back to his old self". We judged the improvement in symptoms to be sufficient to make a diagnosis of cow's milk allergy (CMA), and that referral to an allergy clinic was not necessary. We recommended that Isaac should continue receiving Nutramigen 1.

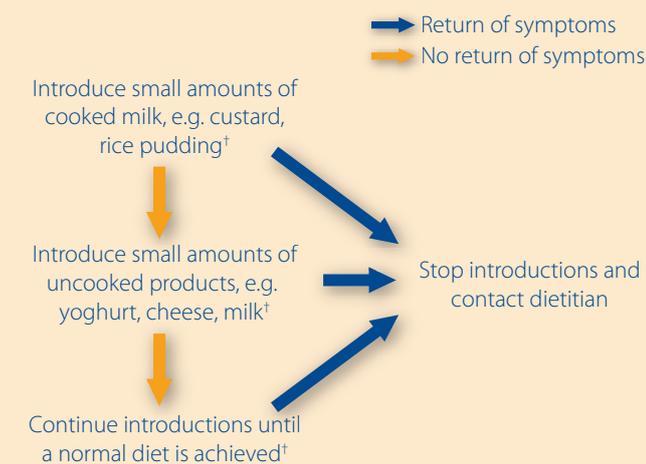
The improvement in symptoms was sufficient to make a diagnosis of cow's milk allergy



A further review at age 4 months indicated that Isaac was feeding well, with normal stools and normal weight gain. At 6 months he switched to Nutramigen 2, which contains more calcium and is therefore suited to older babies. We also gave Isaac's mother advice on dairy-free weaning and recipes. After discussion with a consultant paediatrician, we recommended that Isaac continue on a dairy-free diet until age 1 year.

At age 9 months Isaac was growing well (75th centile) and had a balanced diet of Nutramigen 2 and dairy-free foods. At 12 months, we recommended that dairy should be reintroduced, using a careful step-wise approach (Box 2). Gradual home introduction of milk may be appropriate for patients where an immediate-onset reaction (IgE-mediated CMA) is unlikely, as indicated by a negative skin test, undetectable serum milk-specific IgE level, and no history of convincing symptoms of immediate CMA. Otherwise, first introduction of dairy should be conducted under medical supervision.¹

Box 2. Algorithm for reintroducing dairy to the diet.



[†]Allow at least 3 days between each introduction

By age 13 months, Isaac was feeding on small amounts of dairy, with no return of symptoms. At age 17 months he was taking a normal diet, no longer supplemented by Nutramigen 2, and was growing well and symptom-free.

At age 17 months Isaac was taking a normal diet

Box 3. Key learning outcomes from Isaac's case.

1. Recognising triggers can be a crucial first step towards diagnosing CMA.

Isaac's symptoms appeared after cow's milk-based formula was introduced to his diet. Recognition of this trigger provided cause to suspect CMA.

2. Elimination diets are not easy and require dietetic support.

Dietetic support helped ensure that both Isaac and his mother received a diet that completely excluded cow's milk protein, while meeting their nutritional needs – a vital step in confirming CMA. Detailed practical advice, including milk-free weaning and recipes, was provided to help the family adhere to the diet. It is also helpful to offer advice on what to expect from a hypoallergenic formula. For example, all hypoallergenic formulas taste different from routine formula, due to the extensive break-down of the protein, and they may lead to frequent loose stools of a greenish colour. This is normal.

3. Diagnosis can be confirmed through careful monitoring of symptoms.

Careful monitoring revealed rapid improvement in Isaac's symptoms, including improved stool consistency, after starting Nutramigen 1. This

Box 3. Continued

permitted a diagnosis of CMA, and indicated that Isaac would benefit from maintaining an elimination diet.

4. Diets should change in line with the nutritional needs of the growing infant.

As infants grow and develop, it is essential to make sure their diet continues to match their changing needs. However, as they are weaned onto solid food their milk intake can start to decrease, and combined with a restricted diet, this can lead to a risk of nutritional deficiency. Hypoallergenic formulas for infants aged over 6 months provide higher levels of key nutrients such as calcium and iron, than formulas for younger babies. This provides older infants with the nutrients they

need from smaller quantities of formula. Isaac's switch at age 6 months from Nutramigen 1 to Nutramigen 2 provided him with a formula that has been optimised to meet the needs of older babies.

5. Regular follow-up can help achieve a good long-term outcome.

Regular follow-up permitted assessment of Isaac's progress and close monitoring of the reintroduction of dairy to his diet. This meant that Isaac was able to successfully restart feeding on dairy, without return of symptoms. Prognostic studies show that CMA is a usually temporary condition,^{2,3} and like Isaac, as many as half of infants diagnosed with CMA may be able to return to a normal diet by age 1 year.⁴

1. Fiocchi A et al. *World Allergy Organization Journal* 2010;**3**:57–161
2. Saarinen KM et al. *J Allergy Clin Immunol* 2005;**116**:869–75
3. Vanto T et al. *J Pediatr* 2004;**144**:218–22
4. Host A et al. *Allergy* 1990;**45**:587–96



EMILY

Severe eczema associated with cow's milk allergy

Emily first presented at age 2 weeks, with extensive eczema combined with nappy rash, persistent crying and faltering growth. After a comprehensive evaluation, she was diagnosed with cow's milk allergy. Although initial replacement of standard cow's milk-based formula with an extensively hydrolysed hypoallergenic formula showed only some success, switching to an amino acid-based formula gave rapid improvements. This methodical and stepwise approach enabled a timely diagnosis and successful management of Emily's allergy, with a very good long-term prognosis.

Presentation

Emily first presented to primary care at age 2 weeks with eczema covering her entire body and persistent nappy rash. Her weight had dropped from the 50th to the 25th centile, and she was not feeding well, was crying persistently, and was irritable and unsettled. Initially, she was exclusively breast fed, but infant formula top-up feeds were introduced at age 1 month.

At her appointment with the paediatric consultant, at age 6 weeks, Emily's eczema had been brought under control using topical steroids and an emollient, but her nappy rash was persisting. Emily's parents were anxious that feeding remained difficult, and Emily was crying persistently and appeared to be in pain. Gastro-oesophageal reflux (GOR) was diagnosed, and Gaviscon Infant⁵ and ranitidine were introduced. Emily was referred to the allergy clinic and a dietitian for further investigation.

Emily was crying persistently and appeared to be in pain

Management

Emily was first seen at the allergy clinic at age 9 weeks, at which point her weight had dropped below the 25th centile. She was still being breast fed, with infant formula

top-up feeds. Taking a detailed history revealed that symptoms had worsened after the introduction of top-up feeds. Therefore a skin prick test for cow's milk protein was conducted. A weal of 3x11 mm developed, confirming an allergy. As a result, the dietitian recommended that Nutramigen* 1 was used for the top-up feeds. When Emily showed only a very slight improvement within 2 weeks despite continuing with medication, Emily's mother was advised to follow a dairy-free diet for the next 2 weeks. This approach also gave a slight improvement, but Emily's weight continued to drop and her nappy rash was persisting. The dietitian switched Emily to Nutramigen AA for her top-up feeds.

Taking a detailed history revealed that symptoms had worsened after the introduction of top-up feeds

Two weeks later, there was a marked improvement in symptoms, and Emily's weight had increased to above the 9th centile. At age 20 weeks, Emily was much happier and more settled, and her nappy rash had cleared up. She was still being breast fed, with Nutramigen AA top-ups, and was feeding well. Gaviscon Infant and ranitidine were stopped, as Emily's symptoms were thought to be due to CMA. Emily's mother had tried to eat some dairy, but even taking milk in tea led to a recurrence of symptoms in Emily within 24 hours. Emily's mother was advised to delay weaning until Emily was 6 months old. The dietitian

⁵ Gaviscon Infant is registered trademark of Reckitt Benckiser Healthcare, Hull, UK.

discussed weaning onto a dairy-free diet and provided written information, including recipes using Nutramigen AA in cooking.

The dietitian switched Emily to Nutramigen AA for her top-up feeds. Two weeks later, there was a marked improvement in symptoms

At age 28 weeks, Emily was symptom free and thriving, with almost no eczema, and was no longer using steroids. She was no longer breast fed, but was still using Nutramigen AA to complement a dairy-free weaning diet. The dietitian advised on a milk- and dairy-free toddler diet, taking care to confirm that Emily was receiving sufficient calcium.

By the time Emily was 1 year old, her weight was once again on the 50th centile, and she remained symptom free. She was eating a dairy-free diet, with Nutramigen AA to drink. Skin prick tests for cows' milk at age 12 and 18 months resulted in 3x6 mm and 3x3 mm weals. She also developed weals to nuts, and was advised on a nut free diet. After Emily was inadvertently given biscuits containing milk with no ill effects, her parents were advised to try introducing small amounts of cooked dairy, but to keep a symptom and food diary, and to stop if any symptoms developed. However, ideally, the first introduction of dairy should be conducted under medical supervision.¹ Emily's symptoms did not return, and when she was next seen at the allergy clinic at age 2 years, Emily no longer gave a positive skin prick test result for cow's milk. Therefore, the dietitian advised that the Nutramigen AA in Emily's diet could be gradually replaced with cow's milk (while continuing the symptom and food diary). By age 2½ years, Emily was successfully eating dairy, but continued on a nut free diet, with follow-up recommended in 5 years' time.

By age 2½ years, Emily was successfully eating dairy

Box 4. Key learning outcomes from Emily's case.

1. Severe eczema in young babies may be accompanied by food allergy.

The prevalence of food allergy is high among infants with eczema, and it increases with the severity of eczema. Indeed, the prevalence of IgE-mediated food allergy is almost 70% among infants with severe eczema.² Studies have also shown that the earlier the onset of eczema, and the more severe it is, the more likely it is that the infant will also have food allergies.³ Therefore Emily's severe eczema, which became evident soon after birth, was an indicator for allergy. In accordance with NICE guidance on atopic eczema, Emily was offered a trial of an extensively hydrolysed formula (Nutramigen 1; see Box 1).⁴

2. Recognising patterns of symptoms can be key to identifying cases of CMA.

Presentation of any one of Emily's symptoms in isolation would not be cause to suspect CMA. However, Emily's presentation of GOR with persistent crying and faltering growth is considered a classic pattern of symptoms, which is associated with CMA. Combined with her history of eczema, there was strong cause to suspect CMA.

3. Infants with CMA who are not exclusively breast fed should receive a hypoallergenic formula.

In line with European guidelines,^{1,5} Emily was initially given a hypoallergenic formula based on extensively hydrolysed protein for her top-up feeds (Nutramigen 1). A small proportion of infants display sensitivity even to the broken-down proteins in extensively hydrolysed formula, as in Emily's case. Therefore, an amino acid-based formula was introduced (Nutramigen AA), which resulted in significant improvements in her symptoms.

Box 4. Continued

4. Careful monitoring of symptoms can help guide management of CMA.

Emily's initial treatments for GOR and eczema failed to fully control her symptoms, and this indicated that there was an underlying pathology. The slight improvements in Emily's symptoms that occurred with introduction of Nutramigen 1, combined with her mother's elimination diet, indicated that cow's milk protein might be causative. Consequently, switching to Nutramigen AA was recommended to help manage her severe CMA. This led to rapid improvement in Emily's symptoms.

5. Skin prick tests can help identify and monitor IgE-mediated CMA.

An initial positive skin prick test indicated that Emily had IgE-mediated CMA. Retests at 6-monthly intervals confirmed her ongoing hypersensitivity, until age 2 years, when the test was negative. This prompted the recommendation that milk could be fully reintroduced to Emily's diet. Prognostic studies show that CMA is usually a temporary condition,^{6,7} and like Emily, as many as three-quarters of infants with CMA may become tolerant to cow's milk protein by age 2 years.⁸

1. Vandenplas Y *et al. Arch Dis Child* 2007;**92**:902–8
2. Hill DJ *et al. Pediatr Allergy Immunol* 2004;**15**:421–7
3. Hill DJ *et al. Clin Exp Allergy* 2008;**38**:161–8
4. National Institute for Clinical Excellence. *CG57: Atopic eczema in children* 2007

5. Host A *et al. Arch Dis Child* 1999;**81**:80–4
6. Saarinen KM *et al. J Allergy Clin Immunol* 2005;**116**:869–75
7. Vanto T *et al. J Pediatr* 2004;**144**:218–22
8. Host A *et al. Allergy* 1990;**45**:587–96

IMPORTANT NOTICE: Breastfeeding is best for babies. The decision to discontinue breastfeeding may be difficult to reverse and the introduction of partial bottle-feeding may reduce breast milk supply. The financial benefits of breastfeeding should be considered before bottle-feeding is initiated. Failure to follow preparation instructions carefully may be harmful to a baby's health. Parents should always be advised by an independent healthcare professional regarding infant feeding. Products of Mead Johnson must be used under medical supervision. NUT/CASESTUDY1/7-10