Prevention of allergy / food intolerance

Introduction

An allergy is a specific IgE reaction to a normally harmless substance (allergen), one that does not bother most people. Common allergies include allergic rhinitis or hay fever, asthma, eczema or atopic dermatitis and food allergies. Food intolerance is defined as a reproducible adverse reaction to a specific food or food ingredient. It does not imply any specific type of mechanism. The risk of allergy and food intolerance in an infant increases if a first-degree relative is also allergic or has food intolerance. An increased duration of exclusive breast-feeding has been associated with a reduced incidence of allergy. The use of adapted cow’s milk formulas in the first month of life is associated with the development of cow’s milk protein intolerance / allergy (CMPI / CMA). However, many infants are not exclusively breastfed (UNICEF 1). As a result, infants may receive either short or long term supplementary or sole feeding with an infant formula (usually adapted cow's milk or soymilk), or are weaned early from the breast to formula.

This guideline reviews the evidence for specialised infant formulas for the prevention of allergy and food intolerance in infants. It does not address drug allergies, other allergy prevention measures or infants with an existing allergy.

Incidence and risk factors

Allergy:

- Common allergies, including asthma, hay fever, eczema and food allergies affect more than 1 in 5 people 2, 3, 4, 5, 6, 7, 8, 9. The prevalence of allergic diseases may be increasing 3, 8, 10, 11.
- > 50% of infants with allergy do not have a family history of allergy 9, 12, 13.
- Risk of allergy in an infant is increased to about 1 in 3 if one first-degree relative (parent or sibling) is allergic and to 7 in 10 if both parents are allergic 7, 9, 12, 13, 30.
- Increased duration of exclusive breast-feeding has been associated with a reduced incidence of atopy 13a, 14, 15, 16, although not all studies support this association 17.

Food intolerance:

- The term food intolerance does not imply any specific type of mechanism, and is defined as a reproducible adverse reaction to a specific food or food ingredient. Mechanisms for food intolerance comprise immunological reactions (i.e. food allergy), enzyme defects, pharmacological effects, irritant effects, and toxic reactions. 18, 19, 20.
- Food intolerance is diagnosed by resolution of typical symptoms with elimination from the diet, with confirmation by blinded challenge. 18, 19, 20.
- 2-3% of babies develop an intolerance to a particular food. About 90 percent of all food reactions are caused by eight foods: milk (including infant formula), egg, wheat, peanut, soy, tree nuts, fish and shellfish. 18, 19, 20.
- The principle symptoms in infants with proven CMPI are gastrointestinal (~50%), dermatological (~31%) and respiratory (~19%). 19, 20, 21.
- 2 in every 3 infants with cow’s milk protein intolerance (CMPI) have a family history of atopy. 21
- CMPI is strongly associated with feeding an adapted cow’s milk formula to infants in the first month of life. 22.

Consequences:
Many childhood allergies persist to adulthood with approximately 50% of childhood asthma sufferers \(^{23, 24, 25}\) and 80% of hay fever sufferers \(^{26}\) continuing to have symptoms. Persistent symptoms were reported in 25 - 50% of childhood eczema sufferers at 16 years \(^{27}\) and 45% of 10 year olds who had cow's milk allergy in infancy. \(^{28}\)

Many infants with CMPI become tolerant over time with approximately 30% at 1 year, 50% at 2 years and 70% at 3 years tolerant to cow's milk challenge. The risk of persisting intolerance is increased with evidence of allergic response (increased serum IgE, RAST test or skin prick test positive). \(^{20, 29}\)

---

**Investigations**

**Risk factors for allergy / food intolerance:**

Infants requiring supplemental or sole infant formula feeding should have a family history of allergy and food intolerance obtained. Only confirmed allergy (requiring treatment, confirmed by a clinician or by testing) in a first degree relative (parent or sibling) should be taken as significant. The evidence of benefit (see below) of allergen avoidance measures relates to trials that included infants at high risk of allergy \(^{7, 9, 12, 13, 30}\)

- Risk is greatest if both parents have asthma (risk of asthma increased 6 times) or hayfever (risk of asthma increased 4 times).
- The mother has asthma (risk of asthma increased 3 times) or a sibling (brother or sister) has an allergy (risk of allergy increased 2 times).
- Cow's milk protein intolerance is also more likely with a family history of allergy. \(^{21}\)
- It is least if only the father has an allergy.

The predictive value of family history is increased with the addition of cord blood IgE antibody testing, but its accuracy and cost is probably not adequate for population screening. \(^{9, 30, 31}\)

---

**Recommendations for prevention of allergy / food intolerance**

The parents of infants with a first degree relative with allergy (either a parent or sibling) should be offered information / education concerning the increased risks of their infant developing an allergy / food intolerance, and the potential benefits of avoiding cow's milk protein in the first months of life. **The primary intervention is to encourage and facilitate exclusive and prolonged breast-feeding.** Where this is not possible, the parents should receive information regarding the benefits and costs of using an extensively hydrolysed infant formula. If the parents elect to feed their baby with an extensively hydrolysed formula, then this should be made available to them in hospital for early supplemental / sole feeding. Provision of a hydrolysed formula after discharge is the responsibility of the parents as they are not currently government funded.

**Infants at high risk of atopy:**

If there is a family history of allergy / food intolerance then the following have been shown to be of benefit:

1. **Exclusive breast-feeding** for at least 6 months is the best and cheapest way to prevent allergy / food intolerance. This means giving the baby breast milk only to drink and no solids until they are at least 6 months old. After the introduction of solids, continuation of breast-feeding beyond 12 months (and avoiding cow's milk) may be of benefit in preventing allergy. \(^{13a, 14, 15, 16}\) When breast-feeding is not possible, then expressed breast milk has the same advantages. \(^{32}\)
2. If the baby is unable to establish exclusive breast-feeding and needs to be bottle fed at any time...
then feeding with an **extensively hydrolysed formula** for at least 6 months has been shown to prevent allergy / food intolerance. Meta-analysis of 4 randomised studies 33, 34, 35, 36, 43 comparing the prolonged use of a hydrolysed formula with an adapted cow's milk formula found the risk of any allergy was reduced by about 50% [RR 0.53, 95% CI 0.38-73; NNT = 5]. The benefit was demonstrated to 5 years of age 33. Meta-analysis of 2 studies 37, 38 found that extensively hydrolysed formula was better than partially hydrolysed formula at preventing CMPI / CMA.

3. If the baby just needs a supplementary feed with formula in the first days of life, it is not certain whether using an extensively hydrolysed formula is of any benefit but we would recommend using this formula for the following reasons:

   i. If the baby needs formula feeding later the parent will be familiar with what formula to use, and
   ii. The research to date from quasi-randomised studies 39, 40, 41 is only in babies at low risk of allergy / food intolerance. There is some evidence of a benefit in preventing CMPI from using an extensively hydrolysed formula compared to an adapted cow's milk formula, 40 although the evidence is conflicting. 39, 41

**Note**: using a soy milk formula has not been shown to prevent allergy in high-risk formula fed infants. 42, 43, 44

What is an extensively hydrolysed formula?

Most powdered milk for babies is either modified cow's milk or soymilk. The protein in these formulas is recognised as being foreign in some allergic infants. In infants with CMPI the protein may be toxic. By breaking up the very complex protein molecules up into smaller parts the protein is no longer recognised as being 'foreign', or is no longer 'toxic'. These milks are called "extensively modified formula" and still provide all the nutritional needs for the infant in the first months of life.

How much does an extensively hydrolysed formula cost?

Extensively hydrolysed formulas are not currently subsidised by the government to prevent allergy / food intolerance. The cost varies. A standard formula costs between $15-18 for a 900g tin. An extensively hydrolysed formula costs 2-3 times this from your chemist. Clearly, it is much better and cheaper to breast feed where this is possible. We use Pepti-Junior as it is the cheapest extensively hydrolysed formula available to us.

<table>
<thead>
<tr>
<th>Key Points</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infants who develop allergy do not have a first degree relative with an allergy</td>
<td>★★ 9, 12, 13</td>
</tr>
<tr>
<td>Infants with a first degree relative with allergy / food intolerance are more likely to develop an allergy or food intolerance</td>
<td>★★★ 7, 9, 12, 13, 30</td>
</tr>
<tr>
<td>Prolonged exclusive breast-feeding is associated with a reduced incidence of allergy / food intolerance</td>
<td>★★★★ 13a, 14, 15, 16</td>
</tr>
<tr>
<td>When prolonged supplementary / sole formula feeding is required for high risk infants, an extensively hydrolysed infant formulas reduces the incidence of allergy / food intolerance</td>
<td>★★★★★ 34, 35, 36, 43</td>
</tr>
</tbody>
</table>
When short-term supplementary / sole formula feeding is required in hospital for high risk infants, an extensively hydrolysed infant formula should be offered to facilitate education of parents of high risk infants

References


15. Saarinen UM, Kajosaari M. Breastfeeding as prophylaxis against atopic disease: prospective follow-up


33. Chandra RK. Five-year follow-up of high-risk infants with family history of allergy who were exclusively breast-fed or fed partial whey hydrolysate, soy, and conventional cow's milk formulas. *Journal of Pediatric Gastroenterology & Nutrition*. 1997; 24: 360-8.


35. Odelram H, Vanto T, Jacobsen L, Kjellman NI. Whey hydrolysate compared with cow's milk-based formula for weaning at about 6 months of age in high allergy-risk infants: effects on atopic disease and


