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PAEDIATRIC FOOD ALLERGY

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Food allergy is an adverse immune response to food allergens. It can be classified into IgE-mediated, non-IgE-mediated and mixed IgE mediated allergy. IgE-mediated reactions are acute and frequently have rapid onset. Non-IgE-mediated food allergy is frequently delayed in onset and may need the expert opinion of a paediatrician or paediatric dietitian to enable a diagnosis to be made (see Table 1 for symptoms associated with both types).

Adverse reactions to food cause a lot of confusion for professionals and the public alike. Food hypersensitivity is the term that has been recommended by the World Allergy Organisation (2) to refer to all reactions to food that are not psychologically based. They define food hypersensitivity as any objectively reproducible symptoms or signs that could be reproduced even if disguised (blind). If immunological symptoms can be demonstrated, then the reaction is defined as food allergy, again subdivided in to IgE mediated if the reaction can be attributed to IgE (this is what was previously known as food allergy), or non-IgE mediated if other immunological mechanisms are involved (previously known as food intolerance). All other reactions should be known as non-allergic food hypersensitivity.

Food allergy is amongst the most common of the allergic disorders and has been recognised as a major paediatric health problem in western countries. This is because of the potential severity of reactions and a dramatic increase in diagnosed prevalence over recent decades. The prevalence of food allergy in Europe and North America has been reported to range from six to eight percent in children up to the age of three years (1). Correct diagnosis of food allergy is important because it will help to distinguish true adverse reactions and avoid unnecessary dietary exclusion of foods that are safe and which should be eaten as part of a normal, healthy diet. The common food allergens in the UK are listed in Table 2. This article will focus on cows' milk allergy as it is by far the most common food allergy in the UK.

In North Wales, at a meeting of paediatric dietitians in 2011, concerns were expressed that cows' milk allergy was being diagnosed and treated poorly

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Table 1: Signs and symptoms of possible food allergy (1)

IgE mediated	Non IgE mediated
Pruritus	Pruritus
Erythema	Erythema
Cute urticaria	Atopic eczema
Angioedema	Gastro-oesophageal disease
Nausea	Loose or frequent stools
Colicky abdominal pain	Blood and/or mucous in stools
Vomiting	Abdominal pain
Diarrhoea	Infantile colic
Upper respiratory tract symptoms (nasal itching, sneezing, rhinorrhoea or congestion [with or without conjunctivitis])	Food refusal/aversion
Lower respiratory symptoms (cough, chest tightness, wheezing, shortness of breath)	Constipation
Signs or symptoms of anaphylaxis or other systemic allergic reactions	Perianal redness
	Pallor and tiredness
	Faltering growth (in conjunction with at least one or more GI symptom above (with or without atopic eczema)

Table 2: Common food allergens in the UK

Milk
Egg
Soya
Wheat/gluten
Fish
Shellfish
Peanut
Other Nuts

and that there were poor prescribing practices of the associated formulas. Following discussion among ourselves and with our paediatricians and health visitors, we developed a pathway which consisted of a flow diagram and text detailing the evidence base behind it (see Table 3 for flow diagram). This was discussed with Medicines Management and further modified as a result of their input. It also became clear that there was a significant financial cost associated with the prescription of these formulas and that improved prescribing practices had the potential to reduce costs.

We also developed patient information leaflets on reflux, colic, lactose intolerance and cows' milk allergy to support the pathway, at the suggestion of Medicines Management, for use mainly by GPs and health visitors. As part of a service improvement project, the health visitor teams in North Wales all received training on the pathway, which led to further modifications as a result of their input. The most controversial of these related to lactose-free formulas. There was clear evidence of a large degree of social prescribing of these formulas and prescribing that continued long after there was likely to be a continued clinical need for their use. These formulas were already not available on prescription in one area of North Wales, so the decision was made that parents would be expected to buy the lactose-free formulas in the whole of North Wales. There were problems with identifying all the stakeholders - at least all those who believed themselves to be stakeholders and felt that they should be consulted - and in ensuring that all stakeholders remained informed as the pathway evolved. It was finally approved and launched at the end of 2013. Although it is early days and no reduction in costs is yet being realised, there is evidence to show that those formulas not on the pathway are already being used less, which is very encouraging.

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IMPORTANT NOTICE: Breast milk is the best nutrition for babies. *The decision to discontinue breastfeeding may be difficult to reverse and the introduction of partial bottle-feeding may reduce breast milk supply. Failure to follow preparation instructions carefully may be harmful to your 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. EU 11.564.*

Typically an infant will suffer from gastroenteritis causing diarrhoea, which recurs whenever milk is included in the diet . . .

INFANT MILK ALLERGIES

NICE (1) have recently published guidance for the diagnosis and assessment of allergy in children and young people in primary and community settings. This is to aid community practitioners (primarily GPs) in the assessment, diagnosis and care of children and young people with allergic reactions. However, a key confusion among GPs and health visitors alike, is the difference between lactose intolerance and cows' milk allergy in infants.

- Lactose intolerance is the inability to digest lactose (milk sugar), due to the relative or absolute absence of the enzyme lactase in the small bowel.
- Cows' milk allergy is caused by an allergic response to one of more of the milk proteins.

LACTOSE INTOLERANCE

Lactose intolerance, as described above, is caused by varying degrees of deficiency of the enzyme lactase in the brush border of the small intestine. Lactose that remains undigested in the bowel causes osmotic diarrhoea and is also fermented by colonic bacteria. This results in symptoms such as abdominal distension, flatulence and explosive watery diarrhoea which is often acidic, causing irritation to the perianal area, seen as severe nappy rash in babies. More controversially, colic may also be caused by lactose intolerance in some cases.

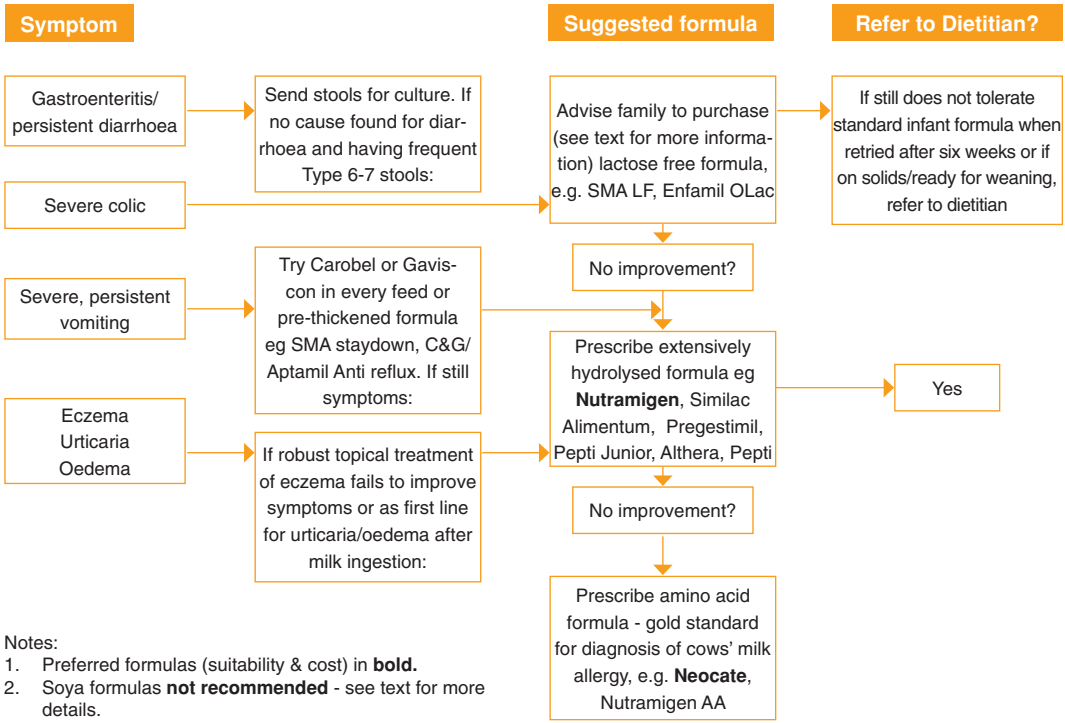
Secondary lactase deficiency is the most commonly seen in clinical practice. Typically an infant will suffer from gastroenteritis causing diarrhoea, which recurs whenever milk is included in the diet; which is obviously constantly for a young infant. Gastroenteritis can cause damage to the villi and, since the lactase enzyme sits at the end of gut villi, it is very vulnerable to damage. Treatment is six to 12 weeks of a lactose-free formula (and diet if the infant is weaned), after which time the baby can usually go back onto a normal diet. If this occurs post weaning, dietetic advice will be needed to ensure that the infant avoids sources of lactose, while consuming an otherwise adequate diet.

COWS' MILK ALLERGY

Parents perceive cows' milk allergy in their children far more often than can be proven by oral food challenge; however, true CMPA does seem to peak in the first year of life, with a prevalence of approximately two to three percent in the infant population (3). Since the majority of these infants are likely to have non IgE mediated cows' milk protein allergy, no clinical tests are available; clinical resolution of symptoms when cows' milk is removed from the diet and renewed symptoms when it is restarted, remains the gold standard. In practice, although challenge remains an important part of treatment, this is usually delayed until the infant is older (typically one year of age). Most breastfed infants will be able to tolerate the small amounts of cows' milk protein in their mother's milk. However, for a minority, the mother will need to follow a cows' milk-free diet herself. For the formula fed infant, there are several potential options:

Table 3: Pathway for use of specialist milk formulas for cows' milk allergy/lactose intolerance in formula fed infants

- This pathway is only intended for use if symptoms are severe and ongoing in formula fed infants.
- Where breastfeeding babies present with feeding problems they should be referred for assessment by a skilled breastfeeding practitioner as the instigation of breastfeeding/lactation management strategies may be helpful.



Notes:
1. Preferred formulas (suitability & cost) in **bold.**
2. Soya formulas **not recommended** - see text for more details.

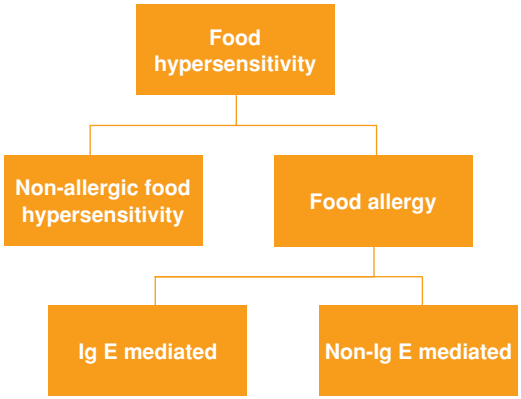
1. Other mammalian milks

Use of goats' milk and other mammalian milk as a substitute for cows' milk is a popular practice in some sectors of society. However, there is 90 percent cross reactivity between cows' milk and the milk of other mammals, making it unsuitable for use in those with cows' milk allergy; similar levels of lactose also make it unsuitable for use in lactose intolerance. Historically, there has been one infant formula on the market based on goats' milk protein. However, in 2006 this was withdrawn from the market after the European Food Safety Authority (EFSA) concluded that there was insufficient evidence to establish the suitability of goats' milk as a protein source in infant and follow-on formula. It was also of the view that there was no convincing data to support the belief that the incidence of allergic reaction is lower when feeding goats' milk based formula compared to cows' milk based formula. However, earlier this year, following positive assessment by the EFSA, goats' milk protein is now permitted to be used to make infant formula milks (4) which will for the first time allow goats' milk based formulas onto the UK market. Nevertheless, it was recently reiterated by the Government that goats' milk is not suitable for the treatment of cows' milk allergy.

2. Soya

Historically, cows' milk allergy and lactose intolerance in infancy were treated with a soya infant formula, but these have not be recommended in the last 10 years (5,6) - particularly in infants under six months - because of the theoretical risks to future fertility (particularly in boys). However, a recent meta-analysis did not

Table 4: Food hypersensitivity



find strong negative effects on reproductive and endocrine function (7) and a study is planned to look into the safety of soya infant formulas in cows' milk allergy in an additional publication. This is relevant because of the significant previously reported risk of cross reactivity with cow's milk protein, particularly infants with non-IgE mediated cow's milk allergy (up to 50 percent) (8). The advice at present remains that soya should not be used as an alternative protein source in the treatment of cows' milk allergy - particularly in the first six months of life to avoid sensitisation to soy protein and exposure to phyto-oestrogens. However, small amounts of soya containing foods can be introduced as part of the weaning diet in the second six months of life. After a year, supermarket soya drinks may be used if cows' milk is still not tolerated and the dietitian considers that the child is receiving adequate nutrition from other foods.

3. Extensively hydrolysed formulas

These are formulas in which (as the names suggests) the cows' milk protein has been extensively hydrolysed into small peptide fragments that will not provoke an allergic reaction in most infants with cows' milk allergy. These formulas can be based on whey or casein protein. Whey hydrolysates are said to be more palatable; however, casein hydrolysates have smaller protein fragments and are, therefore, said to be less allergenic. Some whey hydrolysates contain lactose which may make them unsuitable for some infants with gastrointestinal symptoms, as the damage caused by cows' milk allergy may lead to a temporary lactose intolerance. Versions of these formulas are also available with a proportion of the fat as medium chain triglycerides (MCT), making them also suitable for infants with malabsorption syndromes.

4. Amino acid formulas

These are totally artificial formulas made from amino acid mixes and can, therefore, not cause an allergic reaction. If produced in a totally milk-free environment, these formulas are the gold standard for diagnosis of cows' milk allergy as they cannot cause an allergic reaction; if the infant continues to have symptoms, they cannot be caused by cows' milk allergy. There is a significant excess cost associated with using an amino acid based formula, so most Trusts and Health Boards will want to minimise its use. One company makes a weaning food version of their formula which can be useful in babies with multiple intolerances, have faltering growth, or take only very limited amounts of formula (which is particularly common in infants with gastro-oesophageal reflux [GOR] who not infrequently become aversive to the bottle, associating it with pain).

CHALLENGE

As previously mentioned, challenge is an important part of the care of children with food allergy. For the minority with IgE mediated allergy, this will be under the supervision of the allergy team; for the rest this will usually be done at home under the supervision of a dietitian. Most infants with cows' milk allergy will be challenged with cows' milk after their first birthday; 50 percent of infants with cows' milk allergy can expect to have grown out of their allergy at a year, while over 90 percent are likely to have outgrown it by around the time of school entry (3). Milk ladders are becoming increasingly popular as a method of carrying out a food challenge (9). If the challenge is successful, the child can go back to a normal cows' milk containing diet. For those who fail the challenge, alternative supermarket products are available. One soya drink (Alpro soya 1+) is specifically designed for this age group.

If it is suspected that a child is having adverse symptoms after wheat, then it is important that coeliac disease is excluded before a wheat-free diet is commenced.

For children over two years of age, all other soya drinks with added calcium can be used. If soya is not tolerated, the dietitian may suggest an alternative based on coconut or oats fortified with calcium, giving advice to ensure that calorie and protein requirements are met from other sources. Rice drinks are not suitable for under four and half-year olds due to the presence of trace amounts of arsenic (10).

OTHER FOOD ALLERGIES

Nut allergies and peanut allergies are the most common IgE mediated food allergies, followed by cows' milk. Children with IgE mediated food allergy can have their diagnosis confirmed by skin prick testing and/or specific IgE levels. They need careful dietetic advice to ensure that they avoid all sources of the food allergen. Parents should be advised to read food labels carefully and avoid unwrapped foods. They even need to avoid foods labelled 'may contain' in case they have been contaminated with the food allergen.

The vast majority of children with IgE mediated food allergy will carry an adrenaline auto-injector in case of accidental ingestion of the offending food. If any child develops any type of respiratory compromise because of an allergic reaction, or if adrenaline has had to be used, the emergency services should be called immediately.

For children with other non-IgE mediated food allergies, similar principles will apply; i.e. avoiding the offending food, finding substitutes for the food and challenging at a suitable interval after resolution of symptoms has been noted. If it is suspected that a child is having adverse symptoms after wheat, then it is important that coeliac disease is excluded before a wheat-free diet is commenced.

IN CONCLUSION

Excluding any major food from the diet of an infant or young child has the potential to cause nutritional compromise. It is, therefore, important for the family to have access to a dietitian who can advise comprehensively on excluding the food allergen from the child's diet and on ensuring the remaining diet is nutritionally adequate. Obtaining this support can minimise the anxiety that a family will inevitably experience in dealing with the stress of a food allergy.

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Questions relating to: *Paediatric food allergy*
Type your answers below and then **print for your records** or print and complete answers by hand.

Q.1	Explain the classifications of food allergy.
A	
Q.2	What is the WHO definition of food hypersensitivity?
A	
Q.3	Describe the difference between lactose intolerance and cows' milk allergy (CMA).
A	
Q.4	What can be the symptoms and effects of lactose intolerance in children?
A	
Q.5	What is secondary lactase deficiency?
A	
Q.6	Explain why other mammalian milks may not be suitable substitutes for cows' milk.
A	
Q.7	Why is soya infant formula not recommended as a substitute for cows' milk?
A	
Q.8	What are extensively hydrolysed formulas?
A	
Q.9	Explain how 'challenge' works in the treatment of infant CMA.
A	
Q.10	Describe some of the other major paediatric food allergies and how they can be tested and treated.

Please type additional notes here . . .