

WHAT'S NEW IN PAEDIATRIC FOOD ALLERGY?



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Over the last decade, a number of changes have been introduced to clinical practice guidelines and committee recommendations in the management of food allergy in children. Most recently, these changes have been in relation to the primary prevention of allergy.¹

There is now a large body of evidence to guide us on how vitamin and mineral supplementation and other dietary factors, such as pre- and probiotics, given during the pre- and postnatal period, can influence outcomes of allergic disease.² The addition of nutritional components to hypoallergenic formulas for both prevention of allergies and the induction of tolerance, have also been explored. This can often be a minefield for healthcare professionals and, as such, this article provides an update on the current recommendations and emerging research on nutrition and allergy in paediatrics to guide clinical practice.

ALLERGY PREVENTION: CURRENT GUIDELINES

Due to the significant impact that food allergy can have on quality of life, morbidity and the financial implications from consultations and treatments, there has been great interest in the primary prevention of food allergy. It is thought that cows' milk protein allergy (CMPA) alone has a cost of £25 billion to the NHS³ and is the leading cause of fatalities from food allergy in the UK.⁴

In 2014, following a systematic review, the European Academy of Allergy and Clinical Immunology (EAACI) published an evidence-based guideline to provide advice on

preventing food allergy, particularly for those at high risk of developing allergic disease.¹ The recommendations are summarised in Table 1. Exclusive breastfeeding is recommended for all infants aged four to six months. If breastfeeding is insufficient or not possible, it is recommended that infants at high risk are given a hypoallergenic formula.¹ These recommendations are supported by the Cochrane review on dietary prevention of allergic disease and food hypersensitivity in children.⁵ The EAACI guideline also states that there is no need to avoid introducing complementary foods beyond four months. With the exception of peanut (following the publication of the EAACI guidelines), there is insufficient evidence to provide recommendation about either withholding or encouraging exposure to potentially allergenic foods after four months once weaning has commenced, even if there is a family history of atopy.¹ The EAACI guidelines are also in accordance with the American Academy of Paediatrics recommendations on the effects of early nutritional interventions on the development of atopic disease.⁶

EATING HABITS AND THE DEVELOPMENT OF ALLERGY AND FEEDING BEHAVIOUR

Healthy eating has been shown to reduce food allergy in infancy. In ►

a recently published birth cohort study led by Grimshaw et al, it was shown that infants whose diets included high levels of fruits, vegetables and home-prepared foods, were less likely to have a food allergy by the age of two years compared to those with unhealthy diets.⁷ This study highlights the importance of giving healthy eating advice to all families during consultations, including those with children at high risk of developing food allergies.

Another study published last month by Maslin et al, showed that young children consuming an exclusion diet for CMPA had higher scores for feeding difficulties, fussy eating and were slower to eat at mealtimes than those consuming an unrestricted diet up to 10 years after outgrowing their CMA.⁸ It is, therefore, important for children with CMPA to see a dietitian following diagnosis, to provide targeted guidance on weaning, including advice on texture, increasing variety and feeding behaviour.⁹ Children with CMPA should also be challenged as early as possible to assess tolerance

Table 1: Summary of recommendations for primary prevention of food allergy from EACI food allergy primary prevention guideline¹

- Recommendations for all infants:**
- No special diet during pregnancy or the lactating mother
 - Exclusive breastfeeding for four to six months
 - Introduction of complementary foods after the age of four months according to normal standard weaning practices and nutrition recommendations, for all children irrespective of atopic heredity.
- Further recommendations for high-risk infants:**
- If supplemental feeding is needed during the first four months, an approved hypoallergenic formula is recommended.

and progression of outgrowing their allergy, in order to prevent feeding difficulties later on.

HYPOALLERGENIC FORMULAS

A Hydrolysed formulas for allergy prevention

Hypoallergenic formulas may also have a role in the prevention of allergy. The 10-year

Figure 1: MAP guideline flow chart¹³

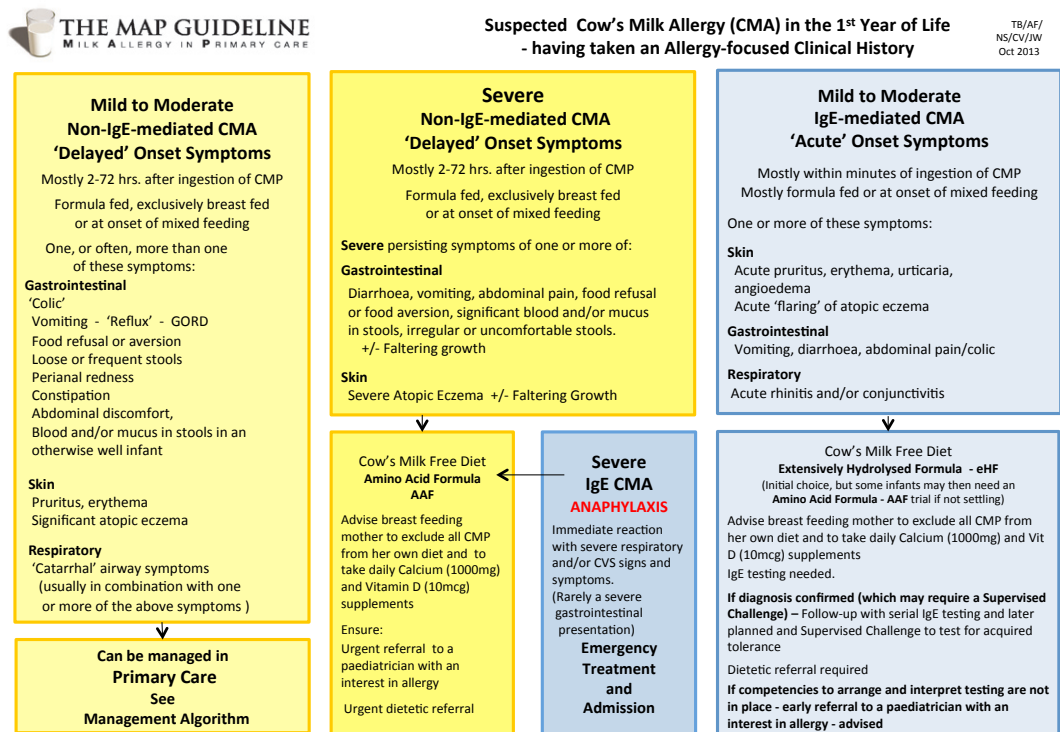


Table 2: Extensively hydrolysed and amino acid formulas available on prescription in the UK

Feed name	Manufacturer	Protein Source	Lactose content
Extensively hydrolysed formulas			
Althera	SMA	Hydrolysed whey	Contains lactose
Aptamil Pepti 1	Milupa	Hydrolysed whey	
Aptamil Pepti 2			
Cow and Gate Pepti-Junior	Cow and Gate		Contains residual lactose
Infatrini Peptisorb	Nutricia		
Nutramigen 1 Lipil	Mead Johnson	Hydrolysed casein	Lactose free
Nutramigen 2 Lipil			
Pregestimil Lipil			
Similac Alimentum	Abbott		
Amino Acid Formulas			
Alfamino	SMA	Amino acids	Lactose free
Neocate LCP	Nutricia		
Neocate Active			
Neocate Advance			
Nutramigen Puramino	Mead Johnson		

German Infant Nutritional Intervention (GINI) study showed that intervention with partially hydrolysed whey and extensively hydrolysed casein formula in non-breastfed infants with a family history of allergy, led to a reduction in allergy disease, particularly atopic eczema/dermatitis lasting up to 10 years of age.¹⁰ Two systematic reviews and three randomised control trials reviewed by EAACI in 2014, show evidence to suggest that extensively hydrolysed whey or extensively hydrolysed casein formula also have a protective effect in high risk formula fed infants.¹¹

B Hydrolysed formulas for management of CMPA

An important role for dietitians is to provide support and education to other health professionals and General Practitioner's on the hypoallergenic formula available and appropriate prescribing, particularly due to the economic burden that prescriptions of these formulas can present.² Guidelines, such as those from the British Society of Allergy and Clinical Immunology and Milk Allergy in Paediatrics (MAP) (see Figure 1), can prove very helpful in the decision making for managing CMPA in both the breastfed and formula-fed infant.^{12,13}

The range of hypoallergenic prescription formulas and commercially available cows' milk substitutes that are accessible in the UK continues to increase. The prescription milks available in the UK are detailed in Table 2. In the last few years we have had the addition of Extensively Hydrolysed Formulas (EHFs): Althera (Nestle) and Similac Alimentum (Abbott) and Alfamino, an amino acid formula (AAF) from Nestle. There was also a recent name change from Nutramigen AA to Nutramigen Puramino (Mead Johnson).

NUTS

Peanut allergy is an increasingly global health problem, which affects between 1.0 and 3.0% of children in westernised countries.¹⁴ There is now evidence to support early rather than delayed peanut introduction during the period of complementary food introduction in infants. In the Learning Early About Peanut Allergy (LEAP) study performed at the Evelina children's hospital, it was shown that consumption of peanut protein in high-risk infants (such as those with more severe eczema and egg allergy) can prevent peanut allergy.¹⁴ This study showed an 80% reduction in prevalence of peanut allergy in the

There is increasing evidence that disturbances in the gut microbial composition play a role in the pathophysiology of immune mediated disorders, such as food allergy.

peanut protein consumption group (3.2%) compared to the avoidance group (17.2%).¹⁴

Following the results of the LEAP study, a consensus document on early peanut introduction and the prevention of peanut allergy in high-risk infants, was published by the World Allergy Organisation (WAO).¹⁵ Based on existing guidelines and LEAP trial data, this document provides guidance to assist the clinical decision making of healthcare providers regarding early peanut introduction. The guidance from this document advises that infants with early-onset atopic disease, such as severe eczema, or egg allergy in the first four to six months of life, might benefit from evaluation by an allergist or a physician trained in the management of allergic diseases. It states that clinicians can perform hospital peanut challenges for those with evidence of positive peanut skin tests to determine whether they are clinically reactive before home introduction is initiated.¹⁵

Further studies are required to identify the optimal age for introduction of other allergenic foods into the diet of high-risk of allergy or already allergic children, to look for ways to improve practice and prevent food allergy. We eagerly await the results of the UK Enquiring About Tolerance study (EAT) (www.eatstudy.co.uk), which is designed to test the hypothesis that repeated exposure to potentially allergenic foods (specifically wheat, sesame, fish, eggs and nut) through consumption at an early age, helps prevent food allergies in childhood.

PRE-/PROBIOTIC DEBATE

There is increasing evidence that disturbances in the gut microbial composition play a role in the pathophysiology of immune mediated disorders, such as food allergy.¹⁶ The concept that increasing prevalence of allergic disease has resulted from a lack of microbial stimuli during infancy and early childhood, is known

as the hygiene hypothesis.¹⁶ As such, there is great interest in understanding the role that pre- and probiotics might play in the prevention and treatment of allergy.

Probiotics are live bacteria that colonise the gastrointestinal bacteria and provide a health benefit to the host.¹⁷ Many studies have been performed on a variety of different probiotic strains on diverse paediatric at risk populations. Conflicting results have been found, which has made it difficult for guidelines to be formulated on their routine use for both prevention and allergy disease modification. These different findings may be related to the overall composition and nutrient content of the diet. However, preliminary evidence shows that *Lactobacillus rhamnosus* GG (LGG) may accelerate development of oral tolerance in cows' milk allergic infants.¹⁸ Probiotics during pregnancy have also been associated with a reduced risk of eczema in high-risk infants.¹⁹ Despite this research, there is insufficient evidence at present to support a recommendation for the use of probiotics for the prevention or treatment of food allergy in routine practice and further research is required.

Prebiotics are non-digestible food components that selectively stimulate the growth or activity of 'healthy' bacteria in the colon.²⁰ There is some evidence that prebiotics (commonly oligosaccharides) added to infant feeds may prevent eczema and asthma in infants. However, a Cochrane review performed in 2013 indicated potential concern about the reliability of some of the prebiotic studies.²⁰ As with probiotics, it is also early days before routine use can be recommend for prebiotics for the prevention of allergy and further research is required before they are recommend in routine practice. It is also important to determine which of the prebiotic and probiotic strains are suitable and for which patient population.¹

Maternal intake of folate supplements during pregnancy may influence childhood immune phenotypes via epigenetic mechanisms.

VITAMINS AND MINERALS

Other nutritional components have been investigated to assess their effect on the immune system. These include vitamin D, vitamin E, zinc and folate. The potential link between allergic disease and vitamin D emerged when it was identified that higher rates of allergic disease were observed in higher latitudes, where vitamin D deficiency is more common.²¹ A number of recent studies have examined the link between vitamin D and eczema. In several observational studies, lower serum vitamin D levels were associated with increased risk of eczema and skin barrier dysfunction in children.^{22,23} An association has also been found between low serum vitamin D levels and the diagnosis of asthma in children.²⁴ The Department of Health (DoH) currently recommends vitamin D supplementation for: (a) all pregnant and breastfeeding women and (b) infants and young children aged six months to five years should have vitamin D supplementation.²⁵ The DoH states that the infants who are formula fed do not need supplementation until they are receiving less than 500mls of formula.²⁵

Several studies have examined dietary intake of vitamin E intake during pregnancy.²⁵ A reduction in childhood wheeze has been associated with both maternal vitamin E and zinc intake.^{26,27} There were no significant results found for asthma, eczema or food allergy with maternal vitamin E intake.²⁵ Maternal intake of folate supplements during pregnancy may influence childhood immune phenotypes via epigenetic mechanisms.²⁸ Folic acid supplementation is recommended for all pregnant women to reduce the risk of congenital malformation. Current National Institute of Clinical Excellence (NICE) guidance recommends that health professionals advise all women who may become pregnant to take 400 micrograms daily before pregnancy and

throughout the first 12 weeks, even if they are already eating foods fortified with folic acid or rich in folate.²⁹ There has been some conflicting evidence about folic acid in late pregnancy, with a possible increase in childhood asthma.³⁰ Further research is required and there is no change in recommendation for the supplementation of folic acid in pregnancy.

IN SUMMARY

A significant amount of interest and research surrounds the prevention and treatment of allergy. Guidelines now exist for the primary prevention of food allergy. Exclusive breastfeeding continues to be strongly recommended. If breastfeeding is insufficient or not possible, an approved hypoallergenic formula is recommended for high-risk infants. In terms of the management of CMA, the number of EHF and AA formulas available in the UK continues to increase and it is important that we follow existing guidelines and educate other health professionals on these in order to ensure appropriate prescribing.

Irrespective of atopic family history, normal standard weaning practice and nutrition recommendations remain unchanged for now for the introduction of complementary foods after the age of four months and delayed introduction of allergenic foods is not recommended. As we now know that there is an association between healthy eating and outcome of food allergy, it is important for health professionals to deliver healthy eating advice. In recent years, there have been great strides forward in the management of food allergy in paediatrics, making the role of the dietitian increasingly essential. The field of paediatric food allergy continues to grow in these exciting times.

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