

Modifying the infant's diet to prevent food allergy

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Received 14 September 2015

Revised 2 July 2016

Accepted 24 July 2016

ABSTRACT

Recommendations and guidelines on the prevention of food allergy have changed in recent decades. The aim of this review of the current evidence and ongoing studies is to provide a comprehensive and up to date picture of prevention of food allergy for healthcare professionals. The review was undertaken as part of the European Union funded Integrated Approaches to Food Allergy and Allergen Management (iFAAM) study. This is a wide ranging project bringing together expertise across the breadth of food allergy research. Specifically, the review discusses dietary manipulation in food allergy prevention, and covers the possible preventive strategies of allergen avoidance, early allergen introduction, general nutrition and supplements, as well as other strategies, such as prebiotics and probiotics. The review concludes that despite agreement that allergen avoidance strategies should not be undertaken for allergy prevention, there is currently no consensus regarding what actions should be recommended beyond exclusive breastfeeding for the first 4–6 months of life. Recent and upcoming trial results, which are detailed in this review, should help inform the debate and add clarity to the topic.

INTRODUCTION

Food allergy affects all ages and has serious health consequences.¹ There has been much speculation regarding its pathophysiology, with research focusing on prevention. Additionally, there have been numerous recommendations on how to prevent food allergy from groups as diverse as national health bodies to mothers' blogs. This advice has changed over time, causing confusion among healthcare professionals and for the general public.

A further complication is the different terminology used to define food reactions.^{2–3} This leads to conditions with differing immunological mechanisms being considered together under an umbrella term of 'food allergy', thus hindering identification of causative factors because of the heterogeneity of the cases studied.

Here we present an up to date review of the current understanding of primary and secondary IgE mediated food allergy prevention in relation to infant feeding (figure 1). The recent publication of important randomised controlled trials (RCTs) makes this a timely review, delivering a critical and independent overview of current evidence.

ALLERGENIC FOOD AVOIDANCE

In 1906, the principle that an allergic reaction occurred on the second and subsequent exposures

to the allergen following initial allergen priming was first proposed. This led to the concept that exposure to the food allergen early in an infant's immunological development was important in food allergy initiation.⁴ As knowledge in the field of immunology progressed, with the concept of immunological sensitisation and the discovery of IgE, it became clear that the first exposure could be in utero or during breastfeeding. Consequently, allergen avoidance became the primary strategy for allergy prevention, with an idealised strategy for allergy prevention being published in 1983.⁵ It aimed to avoid intrauterine and postnatal sensitisation by minimising exposure to sensitising proteins during the third trimester of pregnancy and during lactation by recommending exclusive breastfeeding of the infant (or fed an extensively hydrolysed infant formula) until 6 months of age. It then advocated the introduction of 'relatively non-allergenic foods', with the introduction of milk, corn, citrus, legumes, egg, peanuts and fish being delayed until 1–3 years of age. RCTs using this strategy initially had encouraging results,^{6–9} and hence the concept of allergen avoidance for food allergy prevention continued into the late 1990s, with national and regional guidelines supporting these recommendations.^{10–11}

Early this century, research on allergy prevention focused on pregnancy,^{12–13} environmental factors^{14–15} and infant feeding strategies.¹⁶ Related research suggested acquiring tolerance to foreign (food) proteins was an active rather than a passive process.^{17–18} Consequently, early introduction of allergenic foods into the diet should not lead to sensitisation or allergic disease.^{19–21} This meant avoidance as an allergy prevention strategy was questioned. In addition, newer publications from observational birth cohort studies^{22–25} and a subsequent systematic review¹ suggested that evidence for recommending avoidance strategies in pregnancy and lactation was lacking, and delaying solid introduction did not appear to protect against food allergy. The latest recommendation for allergy prevention by the European Academy of Allergy and Clinical Immunology (EAACI) does not support avoidance as an allergy prevention strategy during pregnancy, lactation or complementary feeding.²⁶ The American Academy of Pediatrics (AAP),²⁷ the Australasian Society of Clinical Immunology and Allergy (ASCIA)²⁸ and other national bodies^{29–30} have similar views. EAACI does however state that "current evidence does not justify any recommendations about either withholding or encouraging exposure to potentially allergenic foods after 4 months once weaning has commenced".²⁶

To cite: Grimshaw K, Logan K, O'Donovan S, et al. *Arch Dis Child* Published Online First: [please include Day Month Year] doi:10.1136/archdischild-2015-309770

INTRODUCTION OF ALLERGENIC FOODS

The WHO recommendation for exclusive breastfeeding for the first 6 months with complementary feeding thereafter alongside breastfeeding to 2 years of age remains the basis for infant feeding recommendations in the UK and around much of the world. However, it should be remembered that the primary aim of the WHO was to reduce gastrointestinal infections, and allergy prevention was not considered.³¹ The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) committee recommends exclusive or full breastfeeding for about 6 months as a desirable goal. It also adds that complementary feeding should not start before 17 weeks but should have started by 26 weeks.³² Meanwhile, advice from the USA and Australia is that solid food introduction, including allergenic foods, may begin between 4 and 6 months.^{27–28} Feeding recommendations relating to allergenic foods also differ.³³ Reported feeding practices vary—for example, 4% of infants are first introduced to solids before 4 months of age in Australia and Greece, compared with 43% of infants in the UK (table 1).

Several observational studies have examined the association between age of complementary feeding and allergy development.^{24–34–42–44} Unfortunately, interpretation of these studies is

limited by their heterogeneity, particularly regarding duration of breastfeeding. This may prove to be more important than the duration of exclusive breastfeeding as there are emerging data of a possible protective effect on the development of allergy after the introduction of solids with concurrent breastfeeding.^{23–44} This supports the WHO recommendation that introduction of solids should ideally take place alongside continued breastfeeding.³¹ Additionally, there is initial evidence that introducing allergens as complementary foods and as part of a healthy diet is also protective.^{45–46} However, even well designed observational birth cohort studies cannot determine causality, only associations. Nevertheless, anecdotal or observational evidence points to lower allergy rates in countries where consumption of dietary allergens as complementary foods starts at an earlier age.^{42–44–47} Evidence from large scale RCTs is required to assess whether there is a causal relationship between early consumption and reduced risk of food allergy, and a number of RCTs have been established with the aim of addressing this issue.

Three of these RCTs have reported fully: Solids Timing for Allergy Research (STAR), Learning Early About Peanut (LEAP) and Enquiring About Tolerance (EAT). The STAR study enrolled 86 high risk infants aged 4–6 months with moderate/severe eczema.⁴⁸ Of the infants randomised to receive egg powder, 31% had an allergic reaction to the egg powder, leading to the study being stopped prematurely. At 12 months of age, there was a trend in this small study towards fewer infants randomised to the egg ingestion group being diagnosed with IgE mediated food allergy (33% vs 51%; $p=0.11$).

Initial findings from the LEAP study, which enrolled 530 high risk infants with moderate/severe eczema and/or egg allergy aged 4–11 months, have been reported.⁴⁹ Among infants randomised to open label peanut consumption, 1.9% had peanut allergy determined by double blind, placebo controlled challenge at age 5 years compared with 13.7% in the control group who avoided peanuts ($p<0.001$). In a second group of 98 high risk infants from the LEAP study with a 1–4 mm skin prick test wheal to peanuts, 10.6% of the early consumption group developed peanut allergy compared with 35.3% in the avoidance group ($p=0.004$). The findings from this study led to a consensus communication, providing interim guidance on early peanut introduction and the prevention of peanut allergy in high risk infants.⁵⁰

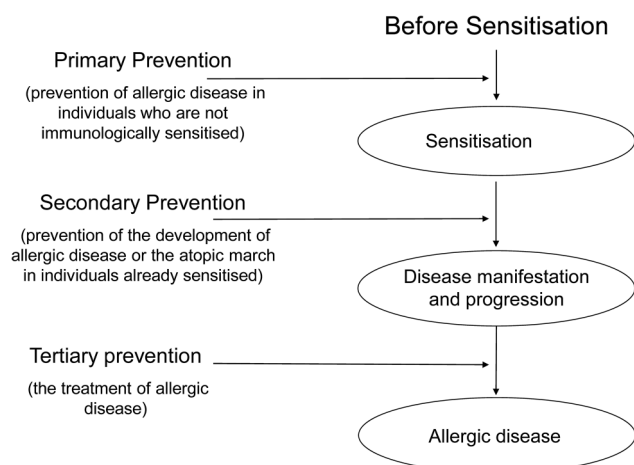


Figure 1 Algorithm of the three stages of allergy prevention.

Table 1 International reported practices of food introduction in infants

Country	Year data collected	Reference	Proportion of infants introduced to solids before 4 months	Proportion of infants introduced to solids after 6 months	Proportion of infants introduced to allergenic foods before 6 months	Proportion of infants introduced to allergenic foods by 8–10 months
Australia	2008–2010	Koplin <i>et al</i> ³⁴	4%	5%		
France	2003–2006	de Lauzon-Guillain <i>et al</i> ³⁵	~30%	~30%		
Germany	2002–2006	Tromp <i>et al</i> ³⁶		55%	69% cow's milk; 21% hen's egg; 15% peanuts; 13% tree nuts; 29% soy	
Greece	2005–2007	de Lauzon-Guillain <i>et al</i> ³⁵	~4%	~10%		
Ireland	2008–2012	O'Donovan <i>et al</i> ³⁷	18% (<17 weeks)	3% (>26 weeks)	57% cow's milk; 57% gluten (wheat (39%), barley (13%), rye (16%)); 40% soy; 8% egg; 6% fish; 6% kiwi	n/a
Portugal	2005–2006	de Lauzon-Guillain <i>et al</i> ³⁵	~5%	~20%		
UK	2010* 2006–2008†	Lennox <i>et al</i> , ³⁸ †McAndrew <i>et al</i> , ³⁹ Grimshaw and Roberts ⁴⁰	43% 36.6%‡	1.7%	54% cow's milk; 42% wheat; 10% hen's egg; 19% fish; 6% kiwi; 0.5% peanuts‡	8% (peanuts)
USA	2005–2007	Luccioli <i>et al</i> ⁴¹	34%		70% cow's milk; 0.9% hen's egg; 0.5% peanuts; 0.7% soy; 0.2% fish	

Recently, a follow-up to the LEAP study (LEAP-ON study) has been published.⁵¹ The participants were reassessed for peanut allergy after being on a peanut avoidance diet for 1 year. Peanut allergy at 6 years continued to be much more prevalent in the LEAP avoiders than in consumers (18.6% vs 4.8%; $p<0.001$) and there was no increase in peanut allergy in the LEAP consumption arm. These results suggest that early introduction of peanuts into the diet may induce long term tolerance.

The EAT study focused on the early introduction of six common food allergens into the diet of 1303 breastfed 3 month old infants recruited from a general (not high risk) population.⁵² In an intention to treat analysis, 7.1% of the standard introduction group and 5.6% of the early introduction group developed food allergy to one or more of the six intervention foods (peanuts, egg, cow's milk, sesame, white fish and wheat) up to 3 years of age ($p=0.32$). However, when the analysis was adjusted for adherence to early introduction, there was a statistically significant reduction in food allergy in the early introduction group (6.4% vs 2.4%; $p=0.03$), suggesting introduction of sufficient amounts of allergenic foods into the infant diet at 3–6 months alongside continued breastfeeding may be effective in the prevention of food allergy. However, poor adherence to the study protocol highlights the challenges around introducing solids into the diets of infants less than 6 months of age.

Four of the six ongoing studies have been completed but their findings have not yet been published. The final two will be completed over the next few years (table 2). The four completed studies looked at early introduction of egg in the general population (Hen's Egg Allergy Prevention (HEAP)) and in children at moderate risk of developing an allergy (Beating Egg Allergy (BEAT), Prevention of egg allergy in infants with atopic dermatitis (PETIT) and Starting Time for Egg Protein (STEP)). The studies have similar study designs and large enrolment numbers. HEAP has reported limited results in a conference abstract⁵³ and symposium presentation, with a conclusion that early consumption of hen's egg was not effective in preventing hen's egg allergy. However, the full results are awaited.

BEAT and PETIT have also published preliminary reports in abstract form. PETIT reported a scheduled interim analysis which showed a significant difference in the prevalence of egg allergy in the intention to treat analysis (37.7% in the placebo group and 8.3% in the egg group; $p=0.0013$) with no significant difference in adverse events between the groups.⁵⁴ The findings from the BEAT study showed a significant reduction in egg skin test sensitisation rates and higher egg specific IgG4/IgE in infants who had egg introduced at 4–6 months compared with those introduced after 8 months. They reported no difference in clinical egg allergy and a significant rate of egg allergic reactions on initial exposure in infants randomised to receive egg, suggesting many at risk infants may already be allergic and may not be amenable to early introduction of egg by 4–5 months of age.⁵⁵

The Preventing Peanut Allergy in Atopic Dermatitis (PEAAD) study will look at early peanut consumption in infants with eczema and at a high risk of developing a peanut allergy. Children in this study are not randomly assigned to intervention/control groups; instead, the carer chooses whether their child will consume or avoid peanuts. The age when children begin peanut consumption is wider than in the LEAP study, thus providing data on the impact of peanut introduction beyond the first year of life.

Finally, the Preventing Atopic Dermatitis and Allergies in Children (PreventADALL) study will assess the impact of the introduction of four allergenic foods by 4 months, and/or

emollient use to 9 months of age on development of food allergy. All of these studies address slightly different populations in terms of allergy risk, resulting in a broad picture across the atopic risk spectrum. Data from all of these trials will be brought together in the EU funded Integrated Food Allergy and Allergen Management (iFAAM) project to provide advice on allergy prevention strategies for clinicians and families.

MICRONUTRIENTS AND ALLERGY PREVENTION

As most food allergens are proteins, these have usually been the focus of research into prevention of food allergy. However, with greater knowledge of the role of macronutrients and micronutrients in immunological processes, there is increasing interest in the relationship between dietary nutrients and the development of allergic conditions. Observational data linking delayed allergen introduction and increased allergy rates may also be explained by the reduced intake of immunologically active nutrients.^{19 34 56 57} Polyunsaturated fatty acids (PUFAs), antioxidants (selenium, and vitamins A, C, E and β carotene), vitamin D, iron, zinc and folate are of particular interest for allergy prevention.^{58–66}

To date, PUFAs have been the most extensively studied immunomodulatory nutrient. Observational studies have related increased intake of omega-3 rich foods during pregnancy, lactation and infancy with decreased risk of allergic disease.^{57 66} However, findings from interventional studies have been inconsistent, possibly due to small sample sizes and heterogeneous allergy outcomes. A recent Cochrane review looked at eight RCTs of omega-3 PUFA supplementation during pregnancy (five trials), lactation (two trials) or both (one trial). Supplementation showed a clear reduction in any IgE mediated allergy in children aged 12–36 months but not beyond 36 months. For specific allergies there was no clear difference in food allergies at 12–36 months, but a clear reduction was seen for children up to 12 months of age. The author concluded that “there is limited evidence to support maternal n-3 long chain PUFA supplementation during pregnancy and/or lactation for reducing allergic disease in children”.⁶⁷ Large intervention trials (completed or ongoing, table 3) may further clarify the association between PUFAs and development of food allergy.^{68–71}

Vitamin D has received considerable attention in recent years, with a suggestion that vitamin D supplementation and/or food fortification is the cause of the increasing prevalence of allergic disease.⁷² Associations between high maternal and infant vitamin D status and allergic disease^{73 74} support this theory. Conversely, latitudinal differences in auto-injector prescriptions for food induced anaphylaxis⁷⁵ and hypoallergenic infant formula use⁷⁶ have suggested a causal link with low vitamin D status. Associations between vitamin D intake and status and allergic disease risk are from a diverse literature, including cross sectional, case control and cohort studies, with variable outcome definitions, analytical procedures and study quality.^{73 74 77–80} However, the HealthNuts study, which used a validated food allergy outcome measure, showed that low vitamin D status may be a risk factor for infant food allergy.⁸¹ The VITALITY trial (NCT02112734) is currently looking at the impact of infant vitamin D supplementation on the prevalence of food allergy at 1 year.

Lower intakes of antioxidants are suggested to reduce antioxidant defences and increase the risk of atopic disease.^{82–86} In particular, vitamins A, E and C and zinc may confer some protection. However, appropriately designed controlled studies are required to establish if there is a causal relationship.⁶²

Differing reports of observed associations between immune modulatory nutrients and allergic disease may be explained by

Review

Table 2 Summary of current studies investigating the hypothesis that the early introduction of allergenic foods can induce oral tolerance

Name of trial	Country (institution)	Allergen(s) of interest	Population	Study details	Study status
Enquiring About Tolerance (EAT)	UK (Kings' College, London)	Cow's milk, hen's egg, peanuts, cod, sesame, wheat	General population	▶ Open label RCT ▶ n=1106 ▶ Enrolled at 3 months of age then consumption of 6 allergenic foods until 6 months or exclusive breastfeeding until 6 months of age ▶ Outcome: prevalence of IgE mediated food allergy to any of the 6 allergenic foods between 1 and 3 years of age	Reported
Learning Early About Peanut allergy (LEAP)	UK (Kings' College, London)	Peanuts	High risk (infants with moderate/severe eczema and/or egg allergy)	▶ Open label RCT ▶ n=640 ▶ Enrolled at 4–11 months then peanut consumption or avoidance until age 5 ▶ Outcome: prevalence of DBPCFC confirmed peanut allergy at 5 years of age	Reported
Hen's Egg Allergy Prevention (HEAP)	Germany (Charite Hospital, Berlin)	Hen's egg	General population	▶ RCT, placebo controlled ▶ n~800 ▶ Enrolled at 4–6 months then consumption of egg powder or placebo until 12 months of age ▶ Outcome: prevalence of IgE mediated egg allergy at 12 months of age	Completed. Abstract presented ⁵³
Preventing Peanut Allergy in Atopic Dermatitis (PEAAD)	Germany (Charite Hospital, Berlin)	Peanut	High risk (infants with atopic dermatitis)	▶ Non-randomised, self selected ▶ n~460 ▶ Enrolled at 5–30 months of age then peanut consumption or avoidance for 1 year ▶ Outcome: prevalence of IgE mediated peanut allergy after 1 year of enrolment	Ongoing
Prevention of egg allergy in infants with atopic dermatitis (PETIT)	Japan (National Centre for Child Health and Development, Japan)	Hen's egg	High risk (infants with atopic dermatitis)	▶ RCT, placebo controlled ▶ n~200 ▶ Enrolled at 4–6 months then consumption of egg powder or placebo until 12 months of age ▶ Outcome: prevalence of IgE mediated egg allergy at 12 months of age	Completed. Abstract presented
Solids Timing for Allergy Research (STAR)	Australia (University of Western Australia)	Hen's egg	High risk (infants with moderate/severe eczema)	▶ RCT, placebo controlled ▶ n=86 ▶ Enrolled at 4–6 months of age then consumption of egg powder or placebo until 8 months of age ▶ Outcome: prevalence of IgE mediated egg allergy at 12 months of age	Reported
Starting Time for Egg Protein (STEP)	Australia (University of Western Australia)	Hen's egg	Moderate risk (infants without eczema but atopic mothers)	▶ RCT, placebo controlled ▶ n~1500 ▶ Enrolled at 4–6 months of age then consumption of egg powder or placebo until 12 months of age ▶ Outcome: prevalence of IgE mediated egg allergy at 12 months of age	Completed
Beating Egg Allergy (BEAT)	Australia (Sydney University Children's Hospital)	Hen's egg	Moderate risk (sibling/parent with allergy)	▶ RCT, placebo controlled ▶ n~290 ▶ Enrolled at 4 months of age then consumption of egg powder or placebo until 8 months of age ▶ Outcome: primary egg white sensitisation. Secondary: prevalence of IgE mediated egg allergy at 12 months of age	Completed
Preventing Atopic Dermatitis and Allergies in Children (PreventADALL)	Norway (Oslo University Hospital)	Hen's egg, milk, wheat, peanut	General population	▶ Open label RCT with four arms: observation, early introduction by 4 months, skin care, both early introduction and skin care ▶ n=5200 ▶ Outcome: food allergy, atopic dermatitis	Ongoing

DBPCFC, double blind, placebo controlled food challenge; RCT, randomised controlled trial.

the fact that the whole diet rather than one particular nutrient modifies immunological function. This hypothesis is supported by a number of studies that have found an association between

the whole diet (including diversity) and allergic disease.^{45 46 87 88} In addition, recent research demonstrated that an infant diet consisting of high levels of fruits, vegetables and

Table 3 Intervention trials with food allergy as a primary or secondary outcome

Nutrient	Study name	Location	Recruitment status	Identifier
Vitamin D	The VITALITY trial	Australia	Recruiting	NCT02112734
Vitamin A	Vitamin A supplementation at birth and atopy in childhood	Guinea Bissau	Active	NCT01779180
PUFAs	DHA to Optimise Mother Infant Outcomes (DOMInO) trial	Australia	Completed	ACTRN12605000569606
PUFAs	The Infant Fish Oil Supplementation (IFOS) trial	Australia	Active	ACTRN12606000281594
PUFAs	Can supplementation with <i>Lactobacillus reuteri</i> and omega-3 fatty acids during pregnancy and lactation reduce the risk of allergic disease in infancy? (PROOM-3)*	Sweden	Recruiting	NCT01542970
Probiotics	Primary prevention of atopic disease by perinatal administration of probiotics	The Netherlands	Completed	NCT00200954
Probiotics	Influence of probiotics on atopy, immunological responses and gut microflora, follow-up to 5 years	Singapore	Completed	NCT00365469
Probiotics	Microbiota as a potential target for food allergy	Italy	Recruiting	NCT02087930
Probiotics	Effect of lactobacillus GG on atopic march	Italy	Recruiting	NCT01891916
Prebiotic	Prebiotics in the Prevention of Atopy (PIPA)	Italy	Completed	NCT02116452

†Atopic sensitisation.

PUFA, polyunsaturated fatty acid.

home prepared foods was associated with less food allergy by the age of 2 years.⁴⁵ This inverse association with processed foods has been observed elsewhere⁸⁷ and may be due to the higher microbial load of home processed foods compared with commercially prepared foods.⁸⁹ It may also be due to the fact that home processed fruits and vegetables are good sources of naturally occurring prebiotics. Both are thought to modify immune function.⁹⁰

OTHER STRATEGIES FOR PREVENTING FOOD ALLERGY

Hypoallergenic infant formula

In newborns, the mucosal barrier is immature and large quantities of macromolecules cross the epithelium into the systemic circulation. Intestinal permeability reduces with age but in the first few months of life, when combined with the immature status of the immune system, it is considered a risk factor for the development of food allergy. This is also the period in which standard infant formula is given if breastfeeding is not possible. If breastfeeding is not possible, it is recommended that high risk children (parent or sibling with a history of allergy) use a hypoallergenic (HA) cow's milk protein formula to avoid early exposure to intact milk allergens.^{27 28}

HA formulas are processed to reduce the allergenicity of milk proteins by 'snipping' them into smaller pieces (peptides). They are differentiated into extensively and partially hydrolysed formulas (eHFs and pHFs, respectively). eHFs contain predominantly small milk derived peptides with almost no allergenicity, whereas pHFs also contain larger milk derived peptides. eHFs were originally produced to treat milk allergic infants but are now also used for prevention of allergy^{91 92} whereas pHFs are produced only for allergy prevention.

Studies indicate that some pHFs and eHFs can reduce the risk of development of food allergy but other studies failed to demonstrate a protective effect.²⁶ Consequently, there is debate as to which is the best formula for prevention of allergy, as reflected in the different national and professional body recommendations,^{25–29} and individual clinicians' opinions.^{93 94}

However, a recent systematic review and meta-analysis, using a rigorous approach, failed to find a beneficial effect of HA infant formulas on food allergy.⁹⁵ The authors highlighted that many studies had an uncertain or high risk of bias, and they also found evidence of publication bias. They argued that earlier reviews were influenced by the more positive results from lower

quality design studies. As it appears that preventive efficacy is highly dependent on the specific formula studied, the EAACI guidelines group recommended the use of HA formulas with a *documented* preventive effect for high risk children in the first 4 months of life only.²⁶ No study showed a preventive effect in low risk children.

Prebiotics and probiotics

The microbiota of infants with atopic disease is both quantitatively and qualitatively different⁹⁶ from their non-atopic counterparts, with decreased populations of beneficial bacteria (bifidobacteria, bacteroides and lactobacilli) and higher numbers of coliforms and *Staphylococcus aureus*.⁹⁷ This has promoted research into the role of intestinal microbiota in the development of immune tolerance. Lower consumption of prebiotics (fibre/indigestible dietary components) is suggested to lead to less favourable colonisation patterns which may be implicated in the loss or inability to develop oral tolerance. Neonatal prebiotic supplementation trials have failed to show any effect of prebiotics on the development of food allergy but have shown favourable results for other allergic outcomes, such as eczema.⁹⁸ Findings from RCTs assessing the effects of probiotics in the prevention of eczema and/or food allergy have differed.^{99–103}

The most up to date Cochrane review states that further research is needed before probiotic use can be recommended for the prevention of allergy.¹⁰⁴ However, a recent World Allergy Organisation (WAO) systematic review has suggested using probiotics in infants at high risk of allergy due to the 'likely net benefit' from the prevention of eczema seen with the use of probiotics.¹⁰⁵ The guideline panel did however acknowledge that their recommendation was supported by very low quality evidence, highlighting the need for high quality intervention trials. There are a number of these ongoing (table 3), which may provide further insight in the future. These studies will also provide information on which strains are the most effective for allergy prevention and what dose is required, as these are important factors to consider and very little information currently exists.

SUMMARY AND CONCLUSIONS

This review described a number of approaches to prevent the development of food allergy. These approaches are likely to interact. Figure 2 summarises how factors (including prenatal

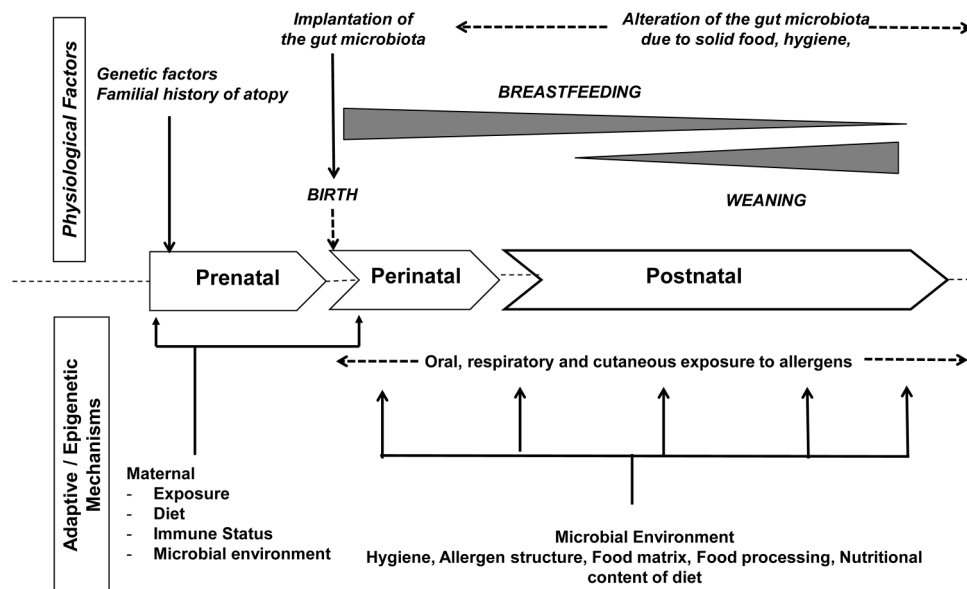


Figure 2 Early factors and mechanisms that interact to prevent or favour the development of an allergic response to a food protein.

factors which have not been considered in this review) may interact to prevent or promote the development of food allergy. Unlike in previous decades, national recommendations for strategies to prevent food allergy now largely agree, particularly concerning hypoallergenic formula use and not delaying the introduction of allergenic foods.^{26–29} However, while there is consensus that avoidance strategies are ineffective, guidelines do not provide any alternative strategies. There is a call for more high quality data from robust RCTs. Some have already been provided and appear to support the concept that ‘early’ consumption of allergenic food promotes the development of immune tolerance, and a recent consensus statement supports this too.⁴⁶ However, before the recommendations are updated, it is important to understand how best to introduce preventive interventions in a community context, particularly as there may be significant numbers of children already sensitised by the time they are weaned. Given their different intervention strategies and populations investigated, combining the new RCT data into meta-analyses or pooled analyses will broaden their scope in terms of providing information, and this is planned as part of the iFAAM study. However, even pooled, they may not tell us what dose of allergenic food should be given and for how long.

Data from ongoing studies on the introduction of solid food and nutritional supplementation may also provide a broader understanding of prevention of food allergy. As studies have generally focused solely on IgE mediated food allergy, their findings may not be applicable to the prevention of non-IgE mediated food allergy conditions, such as eosinophilic oesophagitis and food protein induced enterocolitis syndrome. Aetiology data for these conditions are lacking, and RCTs similar to those carried out for IgE mediated disease should be a future research priority in the field of food allergy.

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Acknowledgements We would like to acknowledge the support of our iFAAM colleagues. Also, we thank the European Academy of Allergy and Clinical Immunology (EAACI) for supporting and endorsing this paper as part of their facilitation of the activities of iFAAM Work Package 10 to improve the management of food allergy.

Contributors GR, KG and KL planned the manuscript. All authors contributed to drafting the manuscript and reviewing the final version.

Funding This work was supported by the European Union within the Seventh Framework Programme for research, technological development and demonstration under grant agreement No 312147 (iFAAM).

Competing interests MK, KB, GL, CM and GR received funding from the European Union within the Seventh Framework Programme for research, technological development and demonstration under grant agreement No 312147 (iFAAM). KG provided educational material for Danone. GR provided scientific advice to Danone, ALK-Abello and ThermoFisher. CM has board memberships with Novartis and the UK Food Safety Agency, and is a consultant for PepsiCo International. KB has received funding for research activities from Danone, ThermoFisher and DST Diagnostics. MK has received a grant from Danone Nutricia.

Provenance and peer review Not commissioned; externally peer reviewed.

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Modifying the infant's diet to prevent food allergy

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Arch Dis Child published online August 16, 2016

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