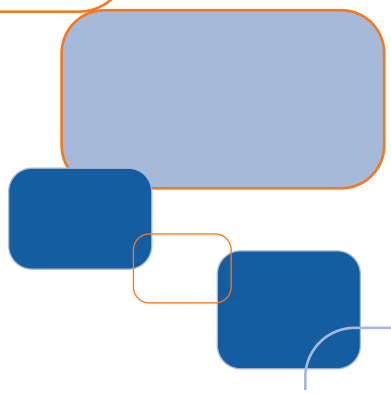
Reducing food allergy risk

Understanding the increased risk



Strategies for prevention

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Reducing food allergy risk

The prevalence of food allergy has increased at an alarming rate over the past decade. It is vital to identify key issues and implement strategies that might help prevent the development of food allergies in infants. This guide discusses such issues and proposes key prevention strategies.

Food allergy is a food hypersensitivity reaction where the mechanism involved is immunologic. It is subdivided into IgE mediated and non IgE mediated (Fig 1). Anywhere between 11-26 million adult Europeans are estimated to suffer from food allergy (specifically the IgE-mediated form). Along with other types of allergic disease, the prevalence of food allergies is perceived to be increasing, particularly in the last 10 years. It is now thought 5-8% of toddlers suffer from food allergy (often life threatening).

In the UK, allergic disease currently accounts for 6% of general practice consultations and 10% of the prescribing budget. Add to this the impact allergic disease has on quality of life of both sufferers and carers and that there is currently no cure, it is natural that attention is turning to possible prevention strategies.

Allergic diseases manifest differently with increasing age (the Atopic March; see Fig 2). Food allergy and eczema are most common in infancy but as the child gets older these conditions are usually replaced by asthma and allergic rhinitis. Consequently prevention of the first stage of the allergic march seems the obvious course of action when trying to reduce the prevalence of allergic disease. This is called primary prevention and its main aim is to prevent allergic sensitisation (ie the production of IgE antibodies). Such strategies are likely to focus on pregnancy and the neonatal period. Secondary prevention strategies are those which prevent the progression from allergic sensitisation to allergic manifestation and are usually most effective if employed in the first years of life. Halting the progression from one disease manifestation to another (i.e. the Atopic March) is a tertiary prevention strategy and mostly involves the use of pharmaceuticals.

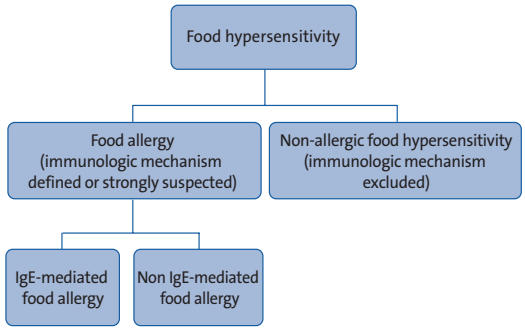

FIGURE 1. Food hypersensitivity, from Muraro et al. Immunol 2004; 15: 202.

DEVELOPMENT OF ALLERGIC DISEASE

The development of allergic disease is a result of complex interactions between genetic and environmental influences. It has been shown that newborns with either one or two atopic parents are at increased risk of developing an allergic condition compared to infants with no family history of atopy. However, many children who develop allergic symptoms have parents without atopic heredity, suggesting that genetic factors are not in themselves the whole story. Environmental influences interact with the genetic constitution to either increase or decrease the probability of allergic sensitisation and subsequent allergic disease. Most research into the prevention of allergic disease has focussed on high risk infants. As a result recommendations are applicable only to high risk infants as they are the population that has been studied.

ALLERGY PREVENTION STRATEGIES

Allergen avoidance

Since it has been recognised that the fetus can mount an allergic response to allergens from the

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middle of the second trimester of pregnancy it has been suggested that allergen avoidance during pregnancy may prevent allergic sensitisation. Several studies have investigated this theory looking at avoidance during pregnancy and lactation. The avoidance measures have been dietary and/or environmental, but the results are inconclusive and until more work is done it is inappropriate to make any recommendations on allergen avoidance during pregnancy and lactation as a primary or secondary prevention strategy[1].

Maternal diet

It is known that a mother's nutritional status can have a significant impact on the developing fetus's immune responses. Due to the important role of Ω-3 polyunsaturated fatty acids on the production of immune active factors (such as prostaglandins and leukotrienes) recent work has looked at the effect of fatty acid supplementation during pregnancy and subsequent allergic sensitisation. Although supplementation appeared to reduce allergic sensitisation, further work needs to be done before firm recommendations can be made.

Another maternal dietary factor that may be important is dietary antioxidant intake (from fruit and vegetables) as an inverse relationship between fruit and vegetable intake and allergic sensitisation has been demonstrated[2]. Therefore mothers should be advised to ensure their diet is nutritionally balanced with a good intake of oily fish, fresh fruit and vegetables.

Infant feeding

There have been an enormous number of articles published on the relationship between breastfeeding and the development of allergic disease with widely discrepant results. This may be due to differences in study design but also differences in breast milk constituents which in turn are affected by ethnicity, maternal diet and atopic status. Despite this, a recent systematic review of the literature has come to the conclusion that breast-feeding does have protective influences, particularly on reducing food allergy and eczema in the early life years and that the effect is stronger in children with atopic heredity[3]. Mothers should therefore be encouraged to exclusively breastfeed for 6 months if possible, but it should be emphasised that exclusive breastfeeding should continue for at least 4 months[4].

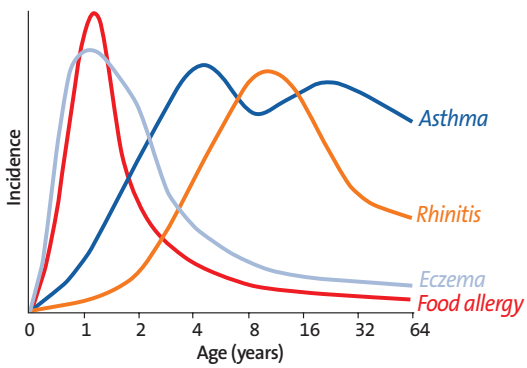

FIGURE 2. The Atopic March. Adapted from Durham S.R., Church M.K. Allergy. 2nd Edition 2001 Mosby.

If a mother is unable or chooses not to breastfeed there are some actions she can take which can reduce allergy risk. Van Odijk et al in their review stated that hydrolysed formula reduces the early manifestations of allergic disease when compared to standard infant formula[3]. However the extent of hydrolysis of the milk and the form of the predominant milk protein appears to be important. A recent study on high risk infants showed that both extensively hydrolysed casein and partially hydrolysed formula led to less allergic disease in the offspring compared to infants receiving a standard infant formula. However, further analysis revealed that only the extensively hydrolysed casein formula led to less allergic disease when the mother herself had atopic dermatitis. Interestingly the extensively hydrolysed whey formula had no effect[5].

Soy based formulae have in the past been used widely as an alternative to cow's milk formula in those infants who already are milk-allergic. The use of soya formulae as a primary prevention has not been shown to have any impact and it is now advised that soya formula should not be given as an alternative to cow's milk formula for the prevention of allergy in infants under 6 months of age, as it is considered that soy formulae are as allergenic as cow's milk based formulae[6]. There is debate about this fact and a recent publication summarises studies investigating how many cow's milk protein allergic infants develop soy milk allergy and puts the figure at less than 15%[7]. However, with the Chief Medical Officer advising against the use of soy formula in infants unless there is a specific medical indication[8], the debate about the use of soy formula in allergy prevention has become academic.

Introduction of solids

Until early 2004 the only published studies on the relationship between the introduction of solids and the development of allergic disease were observational, looking at solid food introduction before 6 months of age and the later development of eczema[9]. Despite this, delaying the introduction of solids into the diet to prevent the development of allergic disease has been advocated for a number of years. It has been incorporated into many allergy prevention studies and is commonly advised by specialist texts for professionals working in the field. More recently investigators have started to question the validity of advising

delaying the introduction of solids into an infant's diet. An observational study, showed that delayed introduction of egg and milk was associated with a statistically significant increased risk of eczema and a non-significant increased risk of preschool wheezing[10]. Our own food allergy study group have also observed a positive association between delaying the introduction of egg into the diet until after six months of age and sensitisation to egg at one year. In light of these findings, the recommendation to delay the introduction of allergenic foods beyond six months should not be advocated.

Hygiene hypothesis

The hygiene hypothesis dictates that if our early life experiences do not include exposure to infections and endotoxins, we are more likely to become atopic. There are many epidemiological studies to support this hypothesis including the observed inverse relationship between infectious diseases and the prevalence of allergic disease, the lower rate of allergic sensitisation and allergic disease in children growing up on livestock farms and the observation that first-born children have a higher allergy risk than subsequent children who will have earlier exposure to infection. As an allergy reducing strategy, promoting active infection is unlikely to ever be acceptable, but a possible way of using microbial action is the use of pre- and probiotics that alter the gut microflora. One study has shown a reduced accumulative prevalence of atopic eczema in infants who had probiotic administered both prenatally (via mothers) and postnatally, when compared to control infants[11]. However, no effect on allergic sensitisation was observed and consequently it is difficult to explain these findings. Clearly more research is needed before any recommendations that address the hygiene hypothesis can be made and this was recommended in a recent position paper from a task force from the European Academy of Allergy and Clinical Immunology[12].

CONCLUSION

Recommendations given to reduce allergy risk must be based on the best evidence available. Although great advances have been made in our understanding of allergic disease over the last 20 years, further research is still required before we can make definitive recommendations to reduce allergy risk. However, we are able to make a number of recommendations from the current evidence base. The recommendations[4] are listed below, but for reasons explained earlier, are applicable only to infants at a high risk of developing allergy.

- No pregnancy or lactation allergen avoidance (except mothers with allergy in her or her partner's family, who may wish to avoid peanuts and tree nuts during pregnancy and lactation, according to COT advice)
- A healthy balanced maternal diet with sufficient portions of fruit, vegetable and Ω-3 fatty acids
- Exclusive breastfeeding for at least four months, preferably six
- Use of a hydrolysed formula with proven efficacy until the age of six months, if breastfeeding is not possible
- Delay of the introduction of all solid foods until at least four months, preferably six, with allergenic foods not being introduced before six months of age.
- Avoidance of exposure of infants to cigarette smoke during pregnancy (*in utero*) as well as after birth.

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