

The Isle of Wight study, an approach to allergy prevention

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Pediatr Allergy Immunol 1994; 5 (Suppl 1): 61–64. © Munksgaard 1994.

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Those allergic disorders that are a manifestation of atopy occur in individuals who have inherited a genetic predisposition. Sensitisation to one or more allergens and the effect of other environmental factors play a part in the production of disease which is likely to reveal itself in one or more ways in 25% of the population.

For many years attempts have been made to influence the prevalence of atopic disorders by modifying the mode of feeding. A plethora of studies suggest that exclusive breastfeeding alone does not protect against the development of allergy (1). A small number of studies have demonstrated a benefit, but these have not revealed lower rates of sensitisation or lower levels of IgE or skin prick test positivity (2). It is possible that the small but measurable amounts of food antigen that pass into the breast milk of virtually all lactating women are sufficient to sensitise some infants (3).

At present, it remains uncertain whether sensitisation of the foetus occurs during intra-uterine life. There have been few studies and although Chandra et al. have demonstrated a benefit from restricting the diet of pregnant women in later pregnancy a study from Sweden of a cohort of high-risk infants did not confirm these results (4, 5). There was neither less atopy nor lower IgE levels in an intervention group than in the control group whose mothers continued on an unrestricted diet. It is uncommon to demonstrate specific IgE in cord blood but this could be because methods are not sufficiently sensitive to detect the very low levels that might be present. It would be premature to discount the possibility of some intra-uterine sensitisation for workers in Japan and the United Kingdom have reported finding T-lymphocytes in the cord blood which show a high proliferative response to food antigens such as beta-lactoglobulin and ovalbumin. (6, 7).

The evidence for sensitisation after birth is mounting. There are few longitudinal population studies which show the development of atopic disease but the reports from Tucson indicate how the exposure to environmental allergens is reflected in the development of IgE mediated allergy as childhood progresses (8). The precise nature of the sensitisation reflects the exposure and such exposure early in life appears particularly, although not exclusively, relevant. The correlation of birch pollen related respiratory tract allergy with births in February to April in Northern Europe is supported by British data associating asthma with summer birth and early autumn birth (9–11). In the latter grass pollen and house dust mite could contribute to the periods of increased prevalence. Exposure to house dust mite and to cat antigen in infancy recently has been related to significant increase in sensitisation to these antigens later in childhood (12). Interestingly these authors could not find significant relationships after the age of seven years. Another British study has been able to demonstrate a relationship between mite sensitive asthma at age eleven years and exposure to mite antigen Der p1 at birth (13).

The development of allergy is influenced by other factors, some of which are now recognised as playing a major triggering role. The effect of passive smoking and other environmental pollutants is becoming increasingly evident. Although the mechanism of such adjuvants is uncertain the consequences are not. Our own data has emphasised that maternal smoking substantially increases the risk of recurrent wheezing particularly in the formula fed infant (10). Many socio-economic factors may influence the development of atopy. Living in an overcrowded or damp environment may increase the rate of infection and also exposure to such allergens as moulds. The presence or absence of central heating

Table 1. Factors influencing the development of allergy

Allergenic	Non-allergenic
Foods	Genetic
Mites/insects	Infections
Pollens	Adjuvants e.g. tobacco smoke
Moulds	Pollutants
Animal danders	Socio-economic e.g. housing

and the age of carpets, bedding and furnishings may all be relevant to the development of allergy. The precise role of cats, dogs, birds and other domestic pets in atopic disease has yet to be clarified although many children are found to be sensitised to them (14). The factors influencing the development of allergy are enumerated in Table 1.

Any attempt to modify the development of atopic disease must identify the population at greatest risk. At the present time the family history offers the best indication. Although the cord IgE will indicate some infants who will develop atopy our experience up to age two years showed a sensitivity of only 12% with a specificity of 90% with a cut-off of 0.6 ml kU/L IgE (15).

Having identified a group at high-risk of atopy it is then necessary to decide on such prevention of exposure to potential allergens and adjuvants as is practicable. It might be considered that an ideal programme would consist of an intervention group exclusively breast fed, with mothers on a diet free from potential major antigens, with strict environmental control and no exposure to passive smoking or pets. Such a demanding programme is likely to be acceptable only to a small number of highly dedicated parents – at once confounding the study. Therefore intervention programmes at present have to be tested within the limitations of practicability.

The Isle of Wight Allergy Prevention Study elected to focus on avoidance of food antigens and to reduce exposure to house dust mite as the major aero-allergen identified in this population. An allergy history was taken from all mothers attending the hospital ante-natal clinic during one year. Sixty per cent of those with a history of atopy in themselves or first degree relatives agreed to take part in the study. Eventually 139 mothers fulfilled all criteria and entered the study. They had previously been allocated to intervention or control groups. Of these 120 have been followed at 12 and 24 months.

In the intervention group lactating mothers restricted their intake of dairy products, eggs, fish and nuts as long as they were breast feeding. They were closely supervised by a dietitian and given supplements of calcium and vitamins. If unable to breast feed or supplements were necessary a hydrolysed soy and collagen formula, Aptamil HA, was used.

Table 2. Effect of risk factors on prevalence of allergy at 12 months

Risk factor	odds ratio (95% CI)			
	Tot all	Asthma	Eczema	Food int
Control group	6.34 ³ (2.0–20.1)	4.13 ¹ (1.1–15.5)	3.59 ¹ (1.0–12.5)	3.29 (0.6–17.3)
Parental smoking				
Either	3.97 ¹ (1.2–13.6)	3.33 (0.8–14.6)	2.35 (0.7–7.9)	1.46 (0.2–9.7)
Both	4.72 ¹ (1.2–18.2)	11.0 ³ (2.5–48.2)	0.88 (0.2–5.6)	5.72 ¹ (1.1–29.5)
Sibling allergy	4.59 ¹ (1.3–15.8)	5.71 ¹ (1.3–24.5)	1.39 (0.4–4.5)	0.74 (0.2–3.7)
Maternal allergy	5.92 ² (1.5–23.0)	significant for total allergy		

Paternal allergy and presence of pets not significant for total allergy. Male sex, maternal or paternal allergy, presence of pets not significant for individual allergic disorders.

¹p < 0.05, ²p < 0.01, ³p < 0.005

Four applications of an acaricidal foam and powder were made to the carpets in the infant's bedroom and main living room and to upholstered furniture at three monthly intervals, beginning at birth. Dust was collected for Der pl assay before and during the course of such treatments. Infants in the control group were fed conventionally by breast or bottle. No specific anti-mite measures were taken.

At the end of the first year, when assessed by a paediatric allergist unaware of the group of the infant, 8 (13%) from the intervention group and 25 (40%) from the control group had developed one or more allergic disorders. Logistic regression analysis showed that specifically both asthma and eczema occurred more frequently in the control group (Table 2). Parental smoking was also identified as a significant risk factor (16).

The cohort are now all in the third year of life and they were seen close to their second birthday. At this age 17 (28%) of the children in the intervention group have some manifestation of atopy compared with 36 (58%) of the control group. The intervention group continues to manifest significantly less total

Table 3. Effect of allergen avoidance in infancy on allergic manifestations at age two years

Risk of developing allergic disorder
Control (62) vs prophylactic groups (58)

	Odds ratio	(95% CL)	
Asthma	2.46	(0.71–2.14)	p = 0.15
Eczema	9.52	(1.81–50.1)	p = 0.008
Food int.	1.25	(0.27–5.79)	n.s.
Pos. spt.	10.26	(1.58–66.7)	p = 0.007
Any allergy	9.70	(2.72–34.55)	p = 0.0005

atopy and eczema although the difference in asthma prevalence no longer achieves significance. Of particular interest is the highly significant difference in skin test positivity, both to food and to aero-allergens, between the two groups (Table 3). The regimen appears to have significantly reduced sensitisation, not only to foods and the house-dust mite, but also to other aero-allergens.

The conclusion so far is that a programme of intervention for infants judged at high-risk can reduce the manifestations of atopy in the first two years of life. A longer period of followup will reveal whether the protection is sustained but at the least there has been a real reduction in allergic disease in the first months and years of life.

It is not possible to determine whether the reduced contact with food antigen or the reduction in exposure to dust mite has been the more important. Studies in which a similar approach has been taken to foods have shown an initial reduction in allergy although prevalence rates in intervention and control groups have tended to converge and be similar by the age of four years. (17). The reduction in Der p1 levels after enthusiastic acaricidal application was generally disappointing. Although mean levels of Der p1 were reduced from 25.9 µgm/gm dust at the outset to 6 µgm/gm dust at nine months this still leaves a substantial residuum of antigen (18). Levels of 2 µgm/gm of dust have been suggested as amounts above which sensitisation might occur (19). Although numbers are small only one infant in the intervention group is sensitised to the house-dust mite at age two years and it transpires this child spent five days a week in an untreated home and only the week-ends in the environment that had received the acaricide.

Our belief is that the dual approach to allergen avoidance has in some way proved complementary and that both dietary and aeroallergens should be targeted when the genetic risk is considered high enough to warrant an intervention programme. It should be a condition of any such programme that the child will not be exposed to passive smoking.

It is naive to believe that other factors might not be as or even more important in the development of allergy. Many questions remain unanswered. Does sensitisation occur in utero? Do partially hydrolysed formulae have a role in the prevention of allergy? How long does the lactating mother need to restrict her own diet? How big is the window in infancy during which the child is particularly vulnerable to sensitisation? Should more be done to remove pets from homes into which an infant at high-risk of atopy is born? Knowledge of these matters is limited at present although the general public is keenly aware of research in this area. Environmental control can be costly. Hypoallergenic formulae are not en-

tirely free from the risk of major reactions even anaphylaxis. Dietetic supervision is essential to any mother restricting her diet. It would be unfortunate and potentially dangerous for mothers to embark on so demanding a regimen without appropriate medical support.

Efforts to influence the development of allergic disease are themselves in their infancy. There is now sufficient evidence that atopy can at least be limited in its expression to allow cautious optimism that this approach has validity. Nevertheless any physician embarking on an allergen avoidance regime should be sure that it is indicated by the family history, and that the consequences of such a programme are not themselves going to add to the problems of the family.

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