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ORIGINAL ARTICLES

Effect of allergen avoidance on development of allergic disorders in infancy

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There is much evidence that the development of allergic disorders may be related to early exposure of allergens, including those in breastmilk. We have tried to find out whether avoidance of food and inhaled allergens in infancy protects against the development of allergic disorders in high-risk infants.

In a prenatally randomised, controlled study 120 infants with family history of atopy and high (>0·5 kU/l) cord-blood concentrations of total IgE were allocated randomly to prophylactic and control groups. In the prophylactic group (n=58), lactating mothers avoided allergenic foods (milk, egg, fish, and nuts) and avoided feeding their infants these foods and soya, wheat, and orange up to the age of 12 months; the infants' bedrooms and living rooms were treated with an acaricidal powder and foam every 3 months, and concentrations of *Dermatophagoides pteronyssinus* antigen (*Der p* I) in dust samples were measured by enzyme-linked immunosorbent assay. In the control group (n=62), the diet of mothers and infants was unrestricted; no acaricidal treatment was done and *Der p* I concentrations were measured at birth and at 9 months. A paediatric allergy specialist unaware of group assignment examined the infants for allergic disorders at 10–12 months. Odds ratios were calculated by logistic regression analysis for various factors with control for other confounding variables. At 12 months, allergic disorders had developed in 25 (40%) control infants and in 8 (13%) of the prophylactic group (odds ratio 6·34, 95% confidence intervals 2·0–20·1). The prevalences at 12 months of asthma (4·13, 1·1–15·5) and eczema (3·6, 1·0–12·5) were also significantly greater in the control group. Parental smoking was a significant risk factor for total allergy at 12 months whether only one parent smoked (3·97, 1·2–13·6) or both parents smoked (4·72, 1·2–18·2).

Reduced exposure of infants to allergens in food and in housedust lowered the frequency of allergic disorders in the first years of life. Passive smoking is an important risk factor that should be addressed in any prophylactic programme.

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Introduction

In infancy, a family history of atopy is the most important predictor of risk of allergic disorders such as allergic asthma and atopic eczema. A high cord-blood concentration of IgE may also be useful in predicting atopy.[1] There is evidence that immediate hypersensitivity in later life depends on allergenic factors encountered in infancy.[2–5] Sporik and colleagues' study[6] suggests that the development of sensitivity to housedust-mite antigen and the symptoms and severity of asthma in later childhood are directly related to exposure to the antigen in infancy, and infants exposed to cats from birth show increased sensitisation to cat dander.[7] Parental smoking and household overcrowding may be contributing factors.[8,9] Among infants who first receive egg yolk at the age of 3 months intolerance of this food is common, whereas intolerance is rare when egg yolk is introduced at 9 months or later.[10] In 1936, Grulee and Sanford[11] showed a seven-fold increase in eczema in babies fed cows' milk. However, the subject remains controversial.[12]

Small amounts of protein ingested by the mother are secreted unchanged into breastmilk.[13,14] In this way potentially allergenic food eaten by the mother can be transferred to the infant and can cause sensitisation. Thus, maternal dietary restriction during lactation seems to be important.[15–17] We have tried to find out whether avoidance of food and housedust-mite allergens in early life protects against the development of allergic disorders in at-risk infants.

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cigarettes a day. Birthweight was recorded and infants were weighed at each visit. Information was also obtained on social class (classified by father's occupation except when the mother was single or the father unemployed and the mother employed) and whether the infant shared a bedroom with parents or other children. The social classes were defined according to the Registrar-General's classification. Analysis was done with classes 1, 2, and 3 grouped together as the higher socioeconomic group and classes 4 and 5 as the lower socioeconomic group.

We sought a 50% reduction in allergic disorder in the prophylactic group. This large reduction combined with the likely high incidence of allergy in this population meant that at least 60 infants were required in each group to give 80% power of detecting a difference at 5% significance. For *Der p* I, comparison of group means was done by the unpaired *t* test and means within groups were compared by the paired *t* test. Logistic regression analysis was used to assess the independent contribution of factors to the risk of allergic disorders. The presence of any allergic disorder at 3, 6, and 12 months' follow-up and individual allergic disorders at 12 months was used as the dependent variable. All risk factors of interest were included in the model and significance was tested for each one, with control for all other factors, by means of the Wald statistics. Adjusted odds ratios with 95% confidence intervals (CI) were calculated. Statistical analysis was done with SPSS/PC+ V4 (SPSS, Chicago, Illinois, USA).

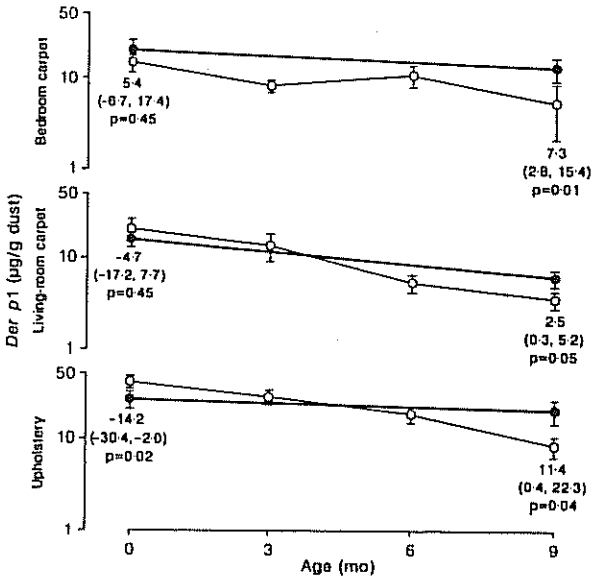
Results

The two groups had similar heredity characteristics, cord-blood IgE distribution, and home environments (table I). Rates of breastfeeding, formula feeding, and introduction of solid foods were similar in the two groups (table II). All infants gained weight satisfactorily; for example, at 3 months the mean (SD) weight was 5·62 (0·84) kg in the prophylactic group compared with 5·73 (0·84) kg in the control group, and at 12 months the groups' respective mean weights were 9·18 (1·15) kg and 9·56 (1·34) kg. The growth pattern of infants fed Aptamil HA from birth was similar to that of the rest of the group (data not shown).

The measures to reduce concentrations of *Der p* I in the homes of the prophylactic group were successful in that the concentrations were significantly lower than those of the control group at 9 months (see figure). In the prophylactic group, the mean *Der p* I concentration for upholstery and living-room and bedroom carpets was 25·9 μg/g dust at birth and 6·0 μg/g dust at 9 months.

By the age of 12 months one or more allergic disorders had developed in 25 (40%) control children and 8 (14%) prophylactic-group children. Although the doctor who made follow-up assessments at 3 and 6 months was aware of group allocation, the pattern was similar (3 months control 18% *vs* prophylactic 5%; 6 months 32% *vs* 12%). Signs of asthma were present at 12 months in 12 (19%) infants in the control group and 4 (7%) of the prophylactic group. The corresponding numbers for eczema were also 12 (19%) and 4 (7%). 7 (11%) control-group infants were classified as having food intolerance, in most to cows' milk or egg, at 12 months. Only 2 (3%) infants in the prophylactic group had food intolerance: in 1 a rash developed when egg was introduced at the age of 7 months; and the other infant had asthma and wheezed after drinking cows' milk when Aptamil HA was stopped at 9 months. 6 (10%) infants in the control group had positive skinprick tests to a range of allergens including housedust mite, cows' milk, egg, wheat, cat, and grass pollen. 2 (3%) infants in the prophylactic group showed positive skinprick tests—1 to egg and 1 to cat dander.

To control for possible effects, despite randomisation, of genetic and environmental factors and to assess the influence



Mean (SEM) *Der p* I concentrations in prophylactic (○) and control (●) groups.

Boxes show mean and (95% CI) difference between groups.

of other risk factors on the development of allergic disorders, we carried out multivariate logistic regression analysis to obtain the adjusted odds ratios for each factor. Logistic regression was done with the presence of any allergic disorder at 3, 6, or 12 months as the dependent variable and all risk factors of interest as independent variables (table III). The process was repeated with individual allergic disorders (at 12 months) as the dependent variables (table IV). After adjustment for other confounding variables, the control group was at significantly greater risk than the prophylactic group for all allergy at each follow-up examination and for asthma and eczema at 12 months. Parental smoking was the other important risk factor irrespective of whether only one or both parents smoked in the house. Maternal smoking was not used as a separate variable, since only 5 mothers smoked and had partners who did not. As expected, maternal allergy, sibling allergy, and male sex were other significant risk factors for total allergy. The prevalence of all allergy at

TABLE III—EFFECT OF RISK FACTORS ON PREVALENCE OF TOTAL ALLERGY

Risk factor	Reference group	Odds ratio (95% CI) 3 mo	6 mo	12 mo
Control group	Prophylactic group	5·64 (1·3–24·2)*	3·98 (1·4–11·5)†	6·34 (2·0–20·1)‡
Parental smoking				
Either	Neither	1·25 (0·2–6·4)	3·36 (1·1–10·7)*	3·97 (1·2–13·6)*
Both	Neither	5·12 (1·2–22·5)*	1·81 (0·5–6·9)	4·72 (1·2–18·2)*
Allergy in				
Mother	No such allergy	2·38 (0·5–11·8)	3·18 (0·9–11·9)	5·92 (1·5–23·0)†
Sibling	No such allergy	1·69 (0·4–6·9)	1·36 (0·5–4·0)	4·59 (1·3–15·8)*
Male	Female	4·17 (1·0–18·3)*	1·93 (0·7–5·5)	1·44 (0·5–4·2)
Low socio-economic group	High socio-economic group	1·43 (0·4–5·4)	1·41 (0·5–4·0)	3·30 (1·1–10·2)*

*p < 0·05, †p < 0·01, ‡p < 0·005, for comparison with reference group.

allergic disorders during infancy and should be avoided, especially in genetically predisposed families. It is possible that allergen avoidance merely delays rather than prevents the development of allergic disorders.[25] In our study foods were introduced at age 9–12 months in the prophylactic group and only 1 infant reacted to cows' milk. Longer follow-up is required, at least into later childhood, to find out whether the reduction in allergic manifestations will be maintained. Because of their high prevalence, allergic disorders are a huge burden to personal and family life and a substantial health-care cost. If the benefit shown in this study is maintained, it is likely to outweigh the costs of dietary supervision, hypoallergenic formulae, and antidust-mite measures.

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Effects of topical nasal anaesthesia on shift of breathing route in adults

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The position of the soft palate is known to determine the breathing route, but the physiological mechanisms that bring about a shift from nasal to oral breathing are unclear. To test the hypothesis that activation of receptors in the nasal passage may be involved in reflex initiation of oral breathing after nasal obstruction, we investigated respiratory responses to nasal occlusion before and after topical lignocaine anaesthesia of the nasal passages.

Eleven volunteers were fitted with custom-made partitioned face masks, which separated nasal and oral passages. Air flow through each passage was detected by changes in airway pressure and carbon dioxide concentration. Nine subjects were habitual nasal breathers both before and after topical anaesthesia with 4% lignocaine. Among these subjects, the time to initiate oral breathing in response to nasal occlusion was significantly shorter before anaesthesia than afterwards (mean 4·4 [SD 2·5] *vs* 10·8 [7·4] s, $p<0·01$). Similarly, the time to resume nasal breathing after release of nasal occlusion was significantly shorter before topical anaesthesia than afterwards (6·9 [4·9] *vs* 12·1 [7·8] s, $p<0·01$). Topical anaesthesia did not affect respiration rate, end-tidal carbon dioxide concentration, or arterial oxygen saturation.

These findings suggest that in human beings sensory information from receptors in the nasal passage has an important role in controlling the shift of breathing route.

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