

# The Role of Allergen Avoidance in Primary and Secondary Prevention

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The strong association between allergic sensitisation and childhood asthma raises the question of whether reducing exposure to allergens from before birth can reduce sensitisation and whether this has any effect on the development of allergic disease. The primary prevention studies are, by design, long term and will take many years to report the definitive findings. We here describe the studies in progress which have published results of clinical outcomes, focussing on studies of inhalant allergens (summarised in Table 1).

## ISLE OF WIGHT STUDY

This was the first study to implement an intervention designed to reduce exposure to inhalant allergens as part of a primary prevention programme in 120 in high-risk children (58 active and 62 control) [1–3]. The intervention comprised combined avoidance of food and dust mite allergens to age 9 months. Acaricides were applied to carpets and upholstered furniture, and infants in both groups slept on polyvinyl-covered mattresses with vented head area. Lactating mothers were asked to avoid dairy, eggs, wheat, fish, soya and nuts, and these foods were not introduced into the infant's diet until after 9 months of age. Infants who were not breast fed were given a soy-based hydrolysed formula. Levels of Der p 1 at 9 months were significantly lower levels in the active compared to the control group, but even after the intervention the levels were still higher than the baseline levels seen in most other studies [1].

Follow up of all 120 children was achieved at age 1, 2, 4 and 8 years. A reduction in sensitisation and in wheeze was reported at age 1 year, but at ages 2 and 4 years differences in respiratory symptoms failed to reach statistical significance. At age 8 years, sensitisation to mite was reduced by more than 50% in the active group, despite only modest reductions in mite allergen levels. In the multivariate analysis, the active group were significantly less likely to have current wheeze (aOR 0.26, 95%

CI 0.07–0.96,  $p = 0.04$ ), nocturnal cough (aOR 0.22, 95% CI 0.06–0.83,  $p = 0.02$ ), wheeze with bronchial hyper-responsiveness (aOR 0.11, 95%CI 0.01–1.02,  $p = 0.05$ ) and atopy (aOR 0.21 95% CI 0.07–0.62).

## CANADIAN PRIMARY PREVENTION STUDY (CAPPS)

Children at high risk of allergic disease were recruited antenatally, and 497 of the 545 randomised subjects were reviewed at age 1 year [4]. The multifaceted intervention included measures to reduce exposure to inhalant and food allergens. Mite allergens were significantly reduced in the parental bed throughout the study. For the child's mattress, levels were low in both groups after birth. Despite advice, there was no reduction in the use of carpets, with a similar reluctance to part with the family pet. At age 1 year, the authors assigned children as having possible or probable asthma based on an *a priori* standard of frequency and duration of episodes of symptoms and asthma medication usage. Another clinical outcome was rhinitis without colds. Using these descriptions, there was a significant reduction in probable asthma and in rhinitis in the active group.

## SPACE

The Study on the Prevention of Allergy in Children in Europe recruited new born children from Austria, Germany and the UK [5]. In total, 696 high-risk children were included in the 3 centres. The intervention was directed towards both inhalant and food allergens. Mite

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**Table 1. Clinical outcome measures in allergen avoidance studies, results quoted are for active group compared to control group**

|                                                | MAAS                                                                               | PIAMA                                                                             | CAPS                                                                            | SPACE                                      | CaPPS                                         | IOW                                                |
|------------------------------------------------|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------|-----------------------------------------------|----------------------------------------------------|
| Age                                            | 1 year                                                                             | 2 years                                                                           | 18 months                                                                       | 1 year                                     | 1 year                                        | 8 years                                            |
| Sensitisation to mite                          | 2% A vs. 1% C, NS                                                                  | 0.7% A vs. 0.8% C, NS                                                             | ~10% all groups                                                                 | 1.9% A vs. 5% C, $p < 0.03$                | % A vs. 0.4% C                                | 11% (A) vs. 31% (C); $p = 0.01$                    |
| Sensitisation to cats                          | 3% A vs. 0% C, NS                                                                  | Not specifically reported                                                         | 0-1% all groups                                                                 | NR                                         | 3.7% A vs. 1.6% C                             | 7.3% (A) vs. 16.1% (C) ( $p = 0.16$ )              |
| Sens to food allergens                         | 14% A vs. 11% C, NS (egg)                                                          | Not specifically reported                                                         | 11-12.5% all groups                                                             | 5% A vs. 5% C (egg)                        | No difference ( $p = 0.6$ )                   | 0% (A), 8.1% (C), $p = 0.06$                       |
| Atopy                                          | 17% A vs. 14% C, NS                                                                | 14.4% A vs. 14% C, NS                                                             | 18-21%, $p = 0.96$                                                              | 6% A vs. 10.7% C, $p < 0.03$               | 4.6% A vs. 4.4% C, $p = 0.4$                  | 20% (A), 46.8% (C), $p = 0.003$                    |
| Wheeze                                         | ↓ severe wheeze with SOB, or after exertion, ↓ medication for wheeze $p \leq 0.05$ | No difference                                                                     | ↓ In dietary intervention group only ( $p = 0.02$ )                             | Wheezy bronchitis 18.1% A, vs. 17.8% C, NS | NR                                            | 13.8% (A), 27.4% (C), $p = 0.08$                   |
| Cough                                          | No difference                                                                      | ↓ night cough without cold                                                        | No difference                                                                   | NR                                         | NR                                            | 13.8% (A), 32.3% (C) $p = 0.02$                    |
| Asthma (see text for definition in each study) | Too young NR,                                                                      | Too young, NR                                                                     | No difference, but less oral steroid use in mite avoidance group ( $p = 0.04$ ) | Too young                                  | 15.1% in A, 20.2% in C, ( $p = 0.04$ for aOR) | 9.6% (A), 15.5% in (C), $p = 0.4$ , (Wheeze + BHR) |
| eczema                                         | 40% A vs 37% C NS effect                                                           | ↑ if no mite allergen in cot mattress, but no difference between groups at 1 year | ↑ in Mite avoidance group ( $p = 0.03$ )                                        | 11.6% a vs. 13.5% C                        | NR                                            |                                                    |

allergen avoidance focused on the infants' bed (mattress encased).

No measurements of allergen levels in homes were undertaken. Mothers were advised to breast feed children (hypoallergenic formula was recommended as an alternative) and to delay the introduction of potentially allergenic foods. Compliance with the measures was reported to be good. Results reported at 1 year showed a reduction in sensitisation to dust mites and in atopy. There was no difference in the proportion of children who had ever wheezed (21% both groups).

### THE CHILDHOOD ASTHMA PREVENTION STUDY (CAPS)

CAPS is a multicentre, parallel group, randomized controlled trial which began in Sydney, Australia in 1997 [6]. Families at risk (without a cat in home) were randomised into one of 4 study groups:

- mite avoidance with placebo dietary intervention ( $n = 155$ )

- mite avoidance with active dietary intervention ( $n = 153$ )
- active dietary intervention alone, no mite avoidance ( $n = 159$ )
- placebo dietary intervention, no mite avoidance ( $n = 149$ ).

Although a significant reduction in mite levels was achieved in the mite intervention group, these levels were much higher than pre-intervention levels in other studies.

The dietary intervention consisted of omega 3 fatty acids supplementation.

Clinical outcomes at age 18 months were available on 554 children. There was no difference in rates of sensitisation between the groups (Table 1). Almost 50% of the children had wheezed at some time during the first 18 months of life, and a similar percentage had been prescribed bronchodilators. Children in the active dietary intervention group had significantly less wheeze than those on the placebo supplements (42.8% vs. 52.6%,  $p = 0.02$ ). Most other wheeze indicators were lower in this group, but this did not reach statistical significance.

Eczema (both reported and on inspection) was higher amongst those using the mite allergen avoidance measures.

## PIAMA

The Prevention and Incidence of Asthma and Mite Allergy Study is a cohort study of over 4000 children which began recruitment in 1996 in the Netherlands [7]. Within this cohort is an intervention study of 810 high-risk infants who were randomly allocated to receive active mite proof encasings or placebo encasings for the mattress and pillows of the parental and infants bed. Baseline levels mite allergens in the parental mattress, were low in both groups. One year after introduction of the intervention, levels were significantly lower in the active group compared to the control, but with little change in the absolute value of total allergen recovered. For the child's mattress, over the first year levels of mite allergen increased significantly more in the control compared to the active group.

In the regression analysis at 2 years, the only significant difference between groups was a small reduction in night time cough without a cold in the active group (adjusted odds ratio 0.65, 95% CI 0.4–1.0) [7]. There was no difference in levels of serum total IgE or atopy at 1 year.

## MANCHESTER ASTHMA AND ALLERGY STUDY (MAAS)

MAAS is a whole population birth cohort study ( $n \sim 1000$ ), with a nested intervention study in the high-risk group [8]. Subjects were recruited and allocated to risk group antenatally, and high risk families with no pets were randomised to either a stringent environmental control ( $n = 145$ ) or normal regime ( $n = 146$ ). The environmental control regime included the fitting of mite proof encasings to the parental mattress, duvet and pillows by 16 weeks of pregnancy, advice to hot wash bedding weekly at  $> 55^\circ\text{C}$ , supply of a high filtration vacuum cleaner and Acarosan to apply to dust reservoirs with high mite allergen levels. Before birth of the child, custom made cot and carry cot mattresses (made of allergen proof fabric) were supplied to the family and carpets were removed from nursery and a vinyl cushion floor was fitted. A hot washable toy was also supplied. No attempt was made to introduce placebo devices into the control homes. A significant and sustained reduction in exposure to mite, cat and dog allergens was achieved in the homes of the children in the active group [9]. Clinical outcome measures on the effect of the environmental control are only published at age 1 year [10]. There was slightly more atopy in the high risk active group (17% vs. 14%), but this did not reach statistical significance.

Asthma like symptoms were consistently lower in the active compared to control group, and this reached statistical significance for attacks of severe wheeze with shortness of breath, prescribed medication for wheezy attacks and wheeze after playing or exertion ( $p < 0.05$ ). No difference was seen for eczema between the groups.

## CONCLUSIONS

All studies have focussed on children from atopic families. Only one of the six studies included placebo measures which allowed the study to be double blind (PIAMA), but this study incorporated the least stringent measures of environmental control. More stringent regimes make blinding difficult. Encasing the cot mattress is the only measure common to all studies, with advice on washing the second most common. Four of the studies included a dietary intervention, but only one was of factorial design which will allow the investigators to determine which of the interventions was responsible for the difference in clinical outcomes (CAPS).

The largest reductions in allergen levels were seen in MAAS. These reductions reflect the fact that this was by far the most stringent set of environmental control measures, and that pet owners were excluded from this part of the study. However, all 5 studies in which allergen levels were measured achieved some reduction in allergen levels, at the very least introducing a difference in exposures between groups.

Except for the Isle of Wight study, clinical outcomes are reported so far at age 2 years or younger. Although the reported results are interesting, they are preliminary and are not as yet going to change clinical practice.

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