

Early Life Environmental Control

Effect on Symptoms, Sensitization, and Lung Function at Age 3 Years

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We investigated whether environmental control during pregnancy and early life affects sensitization and lung function at the age of 3 years. High-risk children ($n = 251$) were prenatally randomized to stringent environmental control (active) or no intervention (control). Questionnaires, skin testing, IgE, and specific airway resistance (sRaw) measurement were completed at the age of 3 years. Children in the active group were significantly more frequently sensitized compared with control subjects (at least one allergen by skin tests: risk ratio, 1.61; 95% confidence interval [CI], 1.02–2.55; $p = 0.04$; mite by IgE: risk ratio, 2.85; 95% CI, 1.02–7.97; $p = 0.05$). However, sRaw was significantly better in the active group (kiloPascal/second, geometric mean [95% CI]: 1.05 [1.01–1.10] vs. 1.19 [1.13–1.25], $p < 0.0001$, active vs. control). Maximal flow at functional residual capacity was measured using rapid thoracic compression at the age of 4 weeks in a subgroup. Prospective lung function data (at infancy and 3 years) were obtained in 32 children (14 active and 18 control). There was no difference in infant lung function between the groups, but at 3 years, sRaw was significantly lower in the active compared with control children ($p = 0.003$). Stringent environmental control was associated with increased risk of mite sensitization but better results for some measurements of lung function in high-risk children at the age of 3 years.

Keywords: asthma; atopy; environmental control; lung function; primary prevention

There are strong associations between allergic sensitization and asthma and early life allergen exposure and sensitization. These raise the questions of whether reducing exposure to allergens in early life can reduce sensitization and whether this has any effect on the development of allergic disease. The National Asthma Campaign Manchester Asthma and Allergy Study is a birth cohort study investigating risk factors for the development of asthma and allergic diseases (1–3). Nested within the cohort is a randomized trial of the effect of stringent environmental control in high-risk children with no pets at birth (2, 3). We have previously reported that compliance with this regime is excellent (it achieved a low-allergen environment during pregnancy and in early life [2] and low mite (*Dermatophagoides pteronyssinus*), cat (*Felis domesticus*), and dog (*Canis familiaris*) allergen levels were maintained until age 3 years [4]). Clinical data at the age of 1 year suggested that environmental manipulation can reduce respiratory symptoms (3), but these early symptoms may not relate to the development of asthma.

In this type of study it is impossible to blind the parents to which study arm they are in. The consequent possibility of responder bias

in subjectively reported symptoms, which is inevitable in an intensive environmental intervention, emphasizes the need for objective outcomes (e.g., lung function). Preschool children cannot always reliably perform lung function requiring forced maneuvers. Specific airway resistance (sRaw) can be measured during normal tidal breathing using a single-step procedure without the measurement of thoracic gas volume, which obviates the need for panting maneuvers against a closed shutter (5). This measurement is potentially useful in young children, as a parent can accompany the child inside the plethysmograph cabinet if necessary (6). sRaw is a measure of airway caliber independent of lung size, and airway narrowing results in elevated values. We have previously reported on predictors of lung function at the age of 3 years in the observational arm of the cohort (7). We now report on symptoms, sensitization, and lung function in randomized high-risk children to investigate the effect of environmental control during pregnancy and early life on these outcomes.

METHODS

Subjects were recruited prenatally by screening parents using skin testing and questionnaires regarding allergic diseases (1). High-risk couples living in homes without pets (both parents atopic, mother sensitized to indoor allergen) were randomized to stringent environmental control (active) or normal regime (control) (1, 2). Of 1,499 couples meeting the inclusion criteria, 511 were identified as high risk, and 251 were prenatally randomized (Figure 1). The study had the approval of the local research ethics committee.

Interventions

Environmental control measures introduced prenatally are described in detail elsewhere (1). The intervention comprised allergen-impermeable covers for the maternal and child's bed, an allergen-impermeable cot/carrycot mattress, a high-filtration vacuum cleaner, vinyl flooring in the child's bedroom, bed linen that was hot washed weekly, and a washable soft toy.

Allergen Levels

We visited homes immediately after birth and at the age of 3 years. Dust samples from the child's bed, the child's bedroom floor, the parental bed, and the lounge floor were collected on each occasion. Mite (Der p 1), cat (Fel d 1), and dog (Can f 1) allergens were assayed using monoclonal antibody-based enzyme-linked immunoassays (2, 4). We estimated cumulative allergen exposure over the first 3 years of life as a sum of allergen levels in four sites at two time points.

Outcomes

During the first 3 years of life, parents kept diary cards regarding their child's health capturing symptoms, physician-diagnosed illnesses, and medication. Children attended a review at the age of 3 years (± 4 weeks). A standard respiratory questionnaire (2) was interviewer administered. Sensitization status was ascertained by skin prick testing (mite, cat, dog, mixed grasses, milk, egg [Bayer, Elkhart, IN]; sensitization defined as a wheal diameter 3 mm greater than negative control) and measurement of specific serum IgE (mite, cat, dog, milk, egg; UniCAP assay [Pharmacia, Uppsala, Sweden]; sensitization defined as a concentration of allergen-specific IgE > 0.35 kU/L).

sRaw was measured using a constant-volume whole-body plethysmograph (Jaeger, Würzburg, Germany) as previously described (7), by

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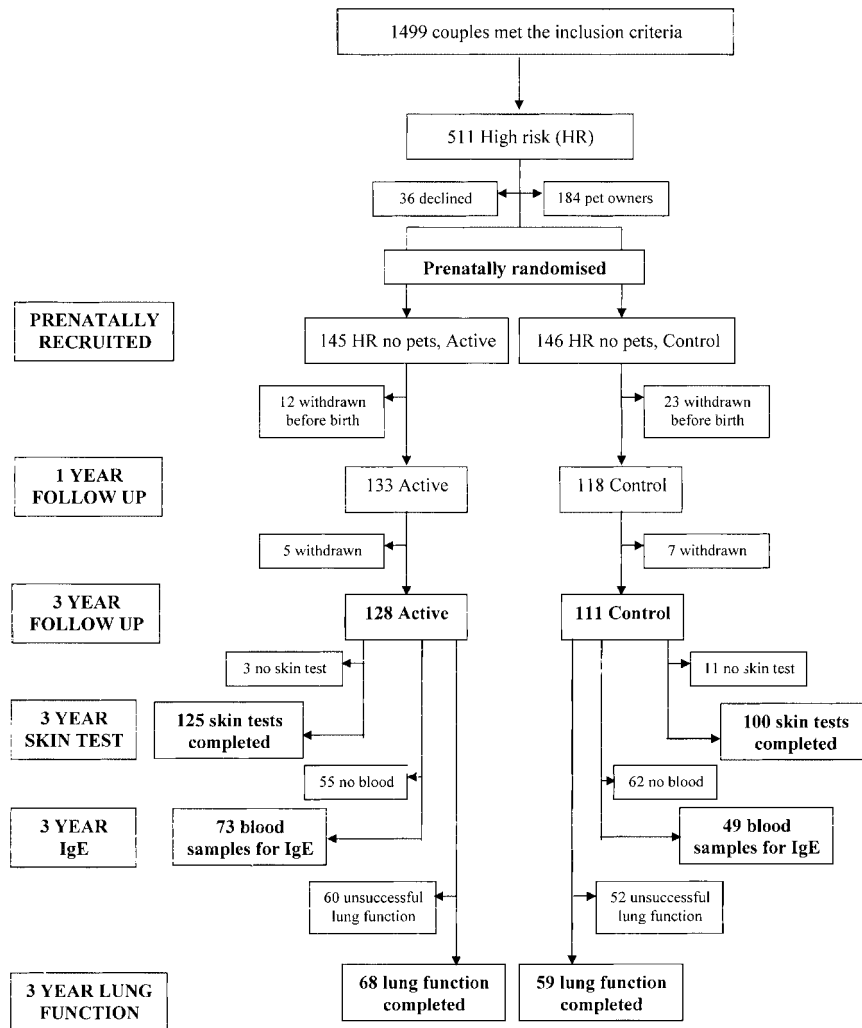


Figure 1. Schematic representation of trial profile. HR = high risk.

a single-step procedure from the simultaneously measured changes of respiratory flow and plethysmographic pressure, omitting the measurement of total gas volume. sRaw was calculated from the medians of five technically acceptable loops (7). Three measurements of effective sRaw were performed, and the mean of these was used in the analysis (i.e., each child performed at least 15 loops). Children were asymptomatic at the time of lung function assessment.

A subgroup of 69 infants was randomly recruited for lung function tests at the age of 1 month (8). $\dot{V}_{max}FRC$ was measured using rapid thoracic compression technique (8).

Statistical Analysis

We aimed to determine the magnitude of effect of environmental control on symptoms, sensitization, and lung function. Outcome data are presented as relative risks and 95% confidence intervals (CIs) (9). We estimated the outcome probabilities for active in relationship to the control group. To assess the independent effect of being in the active group on sensitization, adjustment for potential confounding factors (parental asthma, maternal smoking, child's sex, presence of older siblings, pet ownership at the age of 3 years) was modeled using multivariate logistic regression. Analysis of the factors affecting lung function was performed using general analysis of variance models. Results are presented as adjusted geometric means, 95% CI, F values, and p values.

RESULTS

Participant Flow

Figure 1 shows the trial profile; 239 participants attended the follow-up at the age of 3 years (128 active and 111 control). The

groups were well matched for sex, breast-feeding, number of siblings, socioeconomic status, parental history of asthma, and maternal smoking (3). Five participating families in the active (3.8%) and seven in the control group (5.9%) withdrew between follow-ups at 1 and 3 years. By the age of 3 years, 9 families (three active and six control) acquired a dog, and 11 families (four active and seven control) acquired a cat.

Allergen Levels

A full set of eight dust samples at birth and at the age of 3 years was collected from 219 participants (91.6%; 117 active and 102 control). Allergen levels are expressed both as micrograms of allergen per gram of dust and total allergen recovered (Table 1). Der p 1 and Fel d 1 allergen levels were substantially and significantly lower in the active group compared with control group (both concentration and total allergen), whereas for Can f 1, there was a significant difference between the groups in the total allergen recovered but not in allergen concentration.

Symptoms

Table 2 shows the frequency of signs and symptoms suggestive of atopic diseases in the two groups. The estimate of relative risks for most of the respiratory symptoms and eczema appeared lower in active compared with the control group, but this did not reach statistical significance.

TABLE 1. HOUSE DUST MITE, CAT, AND DOG ALLERGEN LEVELS IN TWO GROUPS

	Active (n = 117)	Control (n = 102)	p Value
Der p 1, µg/g	18.9, 14.7–24.8	30.3, 23.8–40.9	0.01
Total Der p 1, ng	3,951.3, 2,932.5–5,431.6	9,551.9, 6,861.6–13,297.1	< 0.0001
Fel d 1, µg/g	5.1, 4.2–6.2	8.9, 6.5–11.5	0.001
Total Fel d 1, ng	878.7, 710.7–1,096.9	2,147.7, 1,572.6–2,897.8	< 0.0001
Can f 1, µg/g	8.7, 7.2–10.6	10.1, 8.0–13.1	0.31
Total in Can f 1, ng	1,569.2, 1,264.5–1,977.9	2,571.1, 1,960.0–3,370.8	0.005
Total quantity of dust, mg	1,149.5, 1,052.6–1,255.1	2,077.4, 1,962.5–2,259.2	< 0.0001

Definition of abbreviations: Can f = *Canis familiaris*; Der p = *Dermatophagoides pteronyssinus*; Fel d = *Felis domesticus*.

Data expressed as µg/g dust and total allergen recovered in ng, geometric means, and 95% confidence intervals.

Number represents the sum of allergen levels in lounge floor, parental mattress, child's mattress, and child's bedroom floor at birth and at the age of 3 years.

Atopic Sensitization

Skin prick tests. A total of 225 children (94.1%) were successfully skin tested (except for egg, which was not performed in a further 21). The results are presented in Table 3. A significant proportion of children developed positive skin test to inhalant allergens, and dust mite was the most common sensitizer. The estimate of relative risk of being sensitized (skin test positive to at least one allergen) was significantly higher in the active group compared with the control group (relative risk, 1.61; 95% CI, 1.02–2.55). In the multivariate logistic regression analysis, controlling for the effect of sex, socioeconomic status, maternal smoking, breastfeeding, and position in sibship, atopic sensitization was significantly and independently associated with active group (odds ratio, 2.00; 95% CI, 1.04–3.86; $p = 0.04$), male sex (odds ratio, 2.49; 95% CI, 1.30–4.75; $p = 0.006$), and being a first-born child (odds ratio, 1.90; 95% CI, 1.00–3.62; $p = 0.05$). Inclusion of cumulative exposures to Der p 1, Fel d 1, and Can f 1 (or levels in any sampling site at any time point) did not affect the results.

Repeat of the analysis using a 2-mm cut-off point for wheal diameter to define sensitization did not materially change the result.

IgE levels. A total of 122 children (51%) provided a blood sample for measurement of total and specific serum IgE. There was no difference in the level of total serum IgE between the two groups (kU/L, geometric means and 95% CI: 21, 14–32 versus 26, 18–39, active and control group, respectively, $p = 0.41$). However, the proportion of children sensitized to dust mite was significantly higher in the active compared with control group (relative

risk, 2.85; 95% CI, 1.02–7.97; $p = 0.05$; Table 3). Among children sensitized to dust mite (i.e., specific IgE > 0.35 kUa/L), there was no difference in the levels of mite-specific IgE antibodies between the active and control groups (kUa/L, median, range, 1.7; 0.4–100.0 vs. 2.8, 0.7–4.7, active vs. control, respectively, $p = 0.86$, Mann-Whitney U test).

In the multivariate logistic regression analysis, controlling for the effect of sex, maternal smoking, socioeconomic status, position in sibship, Der p 1 exposure, and total serum IgE, sensitization to dust mite was significantly and independently associated with the active group (odds ratio, 4.00; 95% CI, 1.10–14.52; $p = 0.03$) and the total serum IgE level (odds ratio, 2.03; 95% CI, 1.39–2.96; $p < 0.001$). There was no interaction between the risk group and allergen exposure ($p = 0.53$).

There was no association between cat and/or dog ownership at the age of 3 years and either specific sensitization to cat and dog or sensitization to any allergen.

Lung Function

Of 239 reviewed children, an acceptable sRaw measurement was obtained in 127 subjects (53.1%; Figure 1); 30 (15 active and 15 control) were accompanied by a parent during the measurements. There was no difference between children who successfully completed lung function testing compared with those who did not in the prevalence of sensitization, reported symptoms, maternal smoking, and maternal asthma. Similar to our finding in the observational part of the cohort (7), children with a history of current wheeze had significantly poorer lung function compared

TABLE 2. SYMPTOMS SUGGESTIVE OF ALLERGIC DISORDERS IN TWO GROUPS OF CHILDREN

	Active (n = 128)		Control (n = 111)		Relative Risk and p Value (95% Confidence Interval)
	n	%	n	%	
Wheeze ever	43	33.6	46	41.4	0.81 (0.58–1.13), $p = 0.23$
Current wheeze (last 3 mo)	21	16.4	23	20.7	0.79 (0.46–1.35), $p = 0.4$
Wheeze age 1 to 3 yr	36	28.1	42	37.8	0.74 (0.52–1.07), $p = 0.13$
Wheezy attacks requiring medication	31	24.2	33	29.7	0.82 (0.54–1.24), $p = 0.38$
≥ 3 episodes of severe wheeze	6	4.7	7	6.3	0.74 (0.26–2.15), $p = 0.78$
Wheeze after exertion	7	5.5	7	6.3	0.87 (0.31–2.4), $p = 0.79$
Night-time cough	40	31.3	38	34.2	0.91 (0.63–1.31), $p = 0.68$
Cough apart from colds	12	9.4	16	14.4	0.65 (0.32–1.32), $p = 0.31$
Cough after exertion	11	8.7	11	9.9	0.87 (0.39–1.92), $p = 0.82$
Cough with excitement	4	3.1	10	9.0	0.35 (0.11–1.08), $p = 0.09$
Physician-diagnosed asthma	15	11.7	13	11.7	1.00 (0.50–2.01), $p = 1.0$
Current asthma medication	13	10.2	14	12.6	0.81 (0.40–1.64), $p = 0.68$
Rhinitis	3	2.3	5	4.5	0.52 (0.13–2.13), $p = 0.48$
Current eczema	27	21.1	32	28.8	0.73 (0.47–1.14), $p = 0.18$

TABLE 3. ATOPIC SENSITIZATION ASSESSED BY SKIN PRICK TESTING AND SPECIFIC SERUM IGE

	Active (n = 125)		Control (n = 100)		Relative Risk and p Value (95% confidence interval)
	n	%	n	%	
Skin prick tests					
<i>D. pteronyssinus</i>	25	20	12	12	1.67 (0.88–3.15), p = 0.15
Fel d 1	13	10.4	7	7	1.49 (0.62–3.58), p = 0.48
Can f 1	14	11.2	6	6	1.87 (0.74–4.68), p = 0.24
Mixed grasses	20	16	12	12	1.33 (0.69–2.59), p = 0.45
Milk	1	0.8	0	0	NA
Egg	12/121	9.9	4/93	4.3	2.31 (0.77–6.92), p = 0.19
Sensitized	42/121	34.7	20/93	21.5	1.61 (1.02–2.55), p = 0.04
IgE					
	Active, n = 73		Control, n = 49		
<i>D. pteronyssinus</i>	17	23.3	4	8.2	2.85 (1.02–7.97), p = 0.05
Fel d 1	9	12.3	6	12.2	1.01 (0.38–2.65), p = 1.0
Can f 1	7	9.6	5	10.2	0.94 (0.32–2.79), p = 1.0
Milk	8/70	11.4	2	4.1	2.72 (0.60–12.3), p = 0.19
Egg	8/71	11.3	4	8.2	1.35 (0.43–4.24), p = 0.76
Sensitized	26	35.6	13	26.5	1.34 (0.77–2.35), p = 0.33

Definition of abbreviation: NA = not applicable.

with those without (sRaw, kPa/s, geometric means, and 95% CI, 1.22, 1.10–1.38 vs. 1.10, 1.06–1.14, wheezers vs. nonwheezers, respectively, p = 0.03). There was no effect of allergen exposure on lung function.

sRaw in the two groups of children is presented in Table 4. A comparison between two groups was performed using *t* test. In contrast to atopy, lung function was markedly and significantly better in the active group compared with the control group (Table 4). Active children had better sRaw than control subjects, even when subdivided according to personal sensitization and parentally reported symptoms (i.e., skin test positive active children had significantly better lung function than skin test positive control children; skin test negative active children had significantly better lung function compared with skin test negative control children; for children with a history of wheeze there was a trend for active children to have better sRaw than control children; Table 4).

Regression analysis was performed including risk group (active or control) and variables for which a significant association with sRaw was found in the observational part of the cohort (7) (sex, child's sensitization status, child's history of wheeze and eczema, maternal and paternal history of asthma, maternal smoking during pregnancy). Effects of individual factors and

interactions between factors were investigated. Independent significant associations with sRaw were seen for risk group (F = 9.0, p = 0.003) and child's sensitization status (F = 8.5, p = 0.004). There were no significant interactions between the different risk factors (e.g., risk group and sensitization status, F = 0.07, p = 0.79). The estimated marginal means (means adjusted for other factors) for sRaw in a multiple model in relationship to the group allocation were as follows: active, 1.11, 95% CI, 1.03–1.20, and control 1.25, 95% CI 1.16–1.35. For sensitization status, they were as follows: not sensitized 1.12, 95% CI 1.04–1.20, and sensitized 1.25, 95% CI 1.15–1.35.

Lung Function in Infancy and at 3 Years of Age

Prospective data on lung function in infancy and at the age of 3 years were available in a subgroup of 32 children (14 active and 18 control). At the age of 4 weeks there was no difference in $\dot{V}_{maxFRC}$ between active and control children (p = 0.49; Figure 2). However, in the same subgroup of children at the age of 3 years, lung function (sRaw) was significantly better in the active compared with control group (p = 0.003; Figure 2).

DISCUSSION

Our results suggest that stringent environmental control during pregnancy and early life is associated with increased risk of sensitization to dust mite, but better results for some measurements of lung function in children at high risk of allergic disease at the age of 3 years. There were no significant differences in respiratory symptoms between the groups.

Limitations of the Study

The main limitation of the study is the length of the follow-up, which is not sufficient to disentangle different wheezing phenotypes (10). We therefore emphasize the objective measures of secondary phenotypes, which may or may not be associated with subsequent asthma (i.e., atopic sensitization and lung function). Another potential limitation is the fact that lung function is available in only a subset of subjects. However, this is unlikely to have influenced the results, as we found no difference between children who completed lung function measurement compared with those who did not in the prevalence of sensitization, reported symptoms, maternal smoking, and maternal asthma.

TABLE 4. SPECIFIC AIRWAY RESISTANCE IN THE ACTIVE AND CONTROL GROUP AT 3 YEARS OF AGE (WHOLE GROUP AND SUBDIVIDED ACCORDING TO PERSONAL SENSITIZATION AND PARENTALLY REPORTED SYMPTOMS)

	Active	Control	p Value
All children	1.05	1.19	< 0.0001
68 Active, 59 control	1.01–1.10	1.13–1.25	
Nonsensitized	1.02	1.15	0.003
48 Active, 44 control	0.97–1.07	1.08–1.22	
Sensitized*	1.13	1.31	0.02
20 Active, 14 control	1.03–1.24	1.20–1.44	
Never wheezed	1.04	1.17	0.002
51 Active, 40 control	0.99–1.09	1.10–1.24	
History of wheeze	1.10	1.23	0.09
17 Active, 19 control	0.91–1.22	1.12–1.35	

Values are geometric means and 95% Confidence intervals in kPa/s.

* One child who successfully completed lung function measurement was not skin tested.

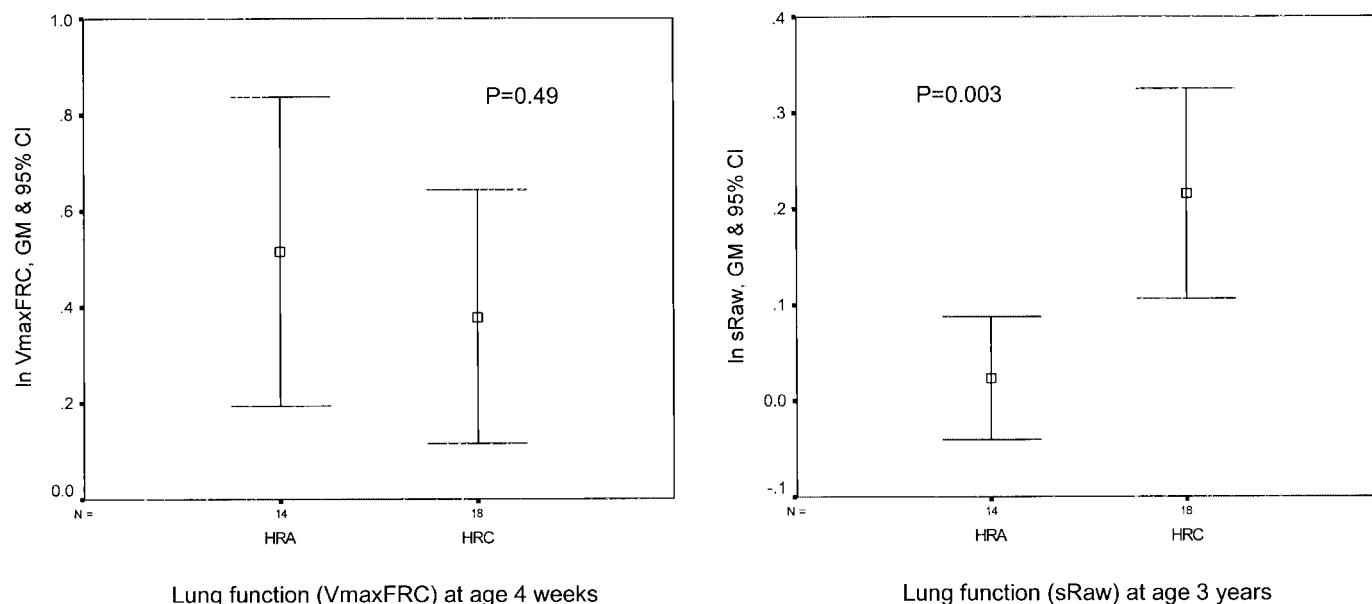


Figure 2. Prospective data on lung function in the high-risk active (HRA; $n = 14$) and high-risk control (HRC; $n = 18$) children in infancy and at 3 years of age. Geometric means (GM) and 95% confidence interval (CI) are shown. sRaw = specific airway resistance.

Comparison with Other Intervention Studies

In the Isle of Wight study, dietary intervention combined with modest mite avoidance significantly reduced allergy, asthma, and eczema by the age of 1 year (11). Although at the age of 4 years the difference for asthma was no longer significant (12), a recent report from the 8-year follow-up suggested that allergen avoidance in infancy may prevent some cases of childhood asthma (13). A Canadian cohort study combined dietary restrictions and dust mite avoidance with advice on avoidance of tobacco smoke and rehoming the pets and reported a significantly reduced risk for probable asthma but no difference in allergic sensitization at the age of 18 months (14). In the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study, mite-impermeable covers for the infant and parent's mattress resulted in a small reduction in night-time cough, with no effect on wheezing, eczema, and sensitization at the age of 2 years (15). Similarly, in the Australian Childhood Asthma Prevention Study, house dust mite avoidance intervention did not affect wheeze and sensitization but surprisingly resulted in a significantly higher prevalence of eczema (16).

Why Did Children Who Have Environmental Control Become Sensitized to Dust Mites?

In the National Asthma Campaign Manchester Asthma and Allergy Study, we employed much more stringent environmental control compared with any of the previously mentioned studies, resulting in significantly lower allergen levels in the active group both in early life (2) and at the age of 3 years (4). Follow-up at the age of 1 year suggested a significant reduction of severe wheeze and prescription of medication for wheeze but no difference in allergic sensitization (3). By 3 years of age, although the relative risks for respiratory symptoms tended to be generally lower in the active group, the differences did not reach statistical significance. However, we observed the counterintuitive finding of a higher prevalence of mite sensitization in the intervention group, despite considerably lower allergen exposure.

How did the children become sensitized to mite allergens if they had controlled exposure at home? Our intervention was very successful in reducing mite allergen levels, and it is unlikely

that more stringent environmental control in the home is feasible. The avoidance measures focused primarily on the sleeping areas in the house, and this is where the largest reduction in allergen levels was achieved (2, 4). We used a composite index of exposure comprising the sum of allergen levels in all living areas of the house and at two different time points to give us a better estimate of child's actual exposure during early life. It is clear from our data that even with this complex multifaceted intervention, there remains a residual mite allergen exposure within the home. This, coupled with a possible exposure in the homes of relatives or outside the home, may lead to intermittent exposure to mite allergen. It is possible that transient and intermittent exposure may favor sensitization in comparison to continuous exposure. Alternatively, it is possible that environmental control removes a protective factor (e.g., endotoxin), exposure to which could decrease the likelihood of sensitization (17), or that the lack of exposure in early life resulted in a missed chance for development of tolerance. However, increased sensitization with lower allergen exposure in the active group does not have an adverse effect on either the symptoms of allergic disease or lung function at the age of 3 years.

Effect of Intervention on Lung Function

It is important to emphasize that the absence of allergen exposure in sensitized individuals cannot explain the observed effect of intervention on lung function because lung function was significantly and considerably better in the active group both among sensitized and nonsensitized children. We have observed an important disconnect between sensitization and lung function consequent to intervention. We have previously reported that among 3-year-olds, sRaw is worse in sensitized compared with nonsensitized children and in high-risk children compared with medium risk or low risk (7). However, in the active group, sRaw was significantly better compared with control, despite a higher proportion of children being sensitized.

Modifiable environmental factors may underlie both abnormalities in airway function and the immunologic component of asthma. The environmental control clearly reduced exposure not just to

allergens. The total quantity of dust collected from homes was much lower in the active group, likely resulting in lower exposure to different microbial and fungal products. These may have differential effects on the developing lung and on sensitization.

Longitudinal data provide evidence for the important relationship between deficits in lung function and the clinical expression of asthma, suggesting that the majority of asthma originates in childhood in association with disordered lung function that tracks to subsequent persistent disease (18, 19). The Melbourne Asthma Study assessed lung function from the age of 7 to 42 years (18). Subjects with asthma and severe asthma were found to have persistent airflow obstruction throughout childhood and into adult life. The magnitude of the difference in lung function did not increase over time, suggesting that the deficits had occurred in early childhood and did not progress. Further evidence of the relationship between childhood events and respiratory health in adult life comes from a New Zealand study that followed 1,037 individuals from the ages of 9 to 26 years (19). Subjects with a low postbronchodilator FEV₁/VC ratio at 26 years of age already had a disordered lung function at the age of 9 years, with a slow progressive loss of reversibility, suggesting that airway remodeling begins in early childhood. Furthermore, increased airway responsiveness at the age of 1 month is associated with abnormal lung function and the development of asthma by the age of 6 years (20), and flow limitation in infancy predicts increased airway responsiveness at the age of 11 years (21). Extrapolating these results to our study, we hypothesize that the improvement in lung function in early life may affect the subsequent onset and severity of asthma symptoms, although we cannot discount the possibility that the variation in lung function may be the basis for the different responses to the intervention.

Effect of Intervention on Lung Function: *In Utero* or Postnatal?

Are children born with the deficit in lung function, or does a loss occur in early life (10)? Data from Tucson suggest that a deficit in lung function in "persistent wheezers" is not present early after birth but is acquired during the first years of life (22, 23). In contrast, the recent data from Australia suggest that reduced lung function in infancy is associated with persistent wheeze at 11 years of age independently of increased airway responsiveness and atopic sensitization in childhood (24). In our study, the differences in lung function between groups could be explained by chance imbalance in the trial allocation or the effect of environmental control on lung development *in utero*. Either of these seems unlikely. In children with longitudinal data, we observed no difference in lung function between the active and control groups in infancy, but there was a marked difference at the age of 3 years. However, we have to be cautious when interpreting the lung function data in infancy and at 3 years, as we used two different measurements, which may reflect different pathologies, and direct comparisons are difficult. Nevertheless, we believe that both methods reflect similar mechanical properties of the lung. Thus, the difference between the groups is likely to have arisen after 4 weeks but before 3 years of age because of some factor(s) affected by environmental control.

Conclusions

Childhood lung function is associated with respiratory disease in later life (18, 19). Environmental control may improve lung function in early life and reduce subsequent asthma morbidity and severity. However, further measures of lung function, such as forced expiratory measures, are needed at ages 5 to 8 years to explore further these interesting observations. Furthermore, the increase in sensitization in the intervention group is of concern, and only further follow-up will determine the long-term effects of the intervention.

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