

Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study

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Summary

Background In a prospective birth-cohort study, we assessed the relevance of mite and cat allergen exposure for the development of childhood asthma up to age 7 years.

Methods Of 1314 newborn infants enrolled in five German cities in 1990, follow-up data at age 7 years were available for 939 children. Assessments included repeated measurement of specific IgE to food and inhalant allergens, measurement of indoor allergen exposure at 6 months, 18 months, and 3 years of age, and yearly interviews by a paediatrician. At age 7 years, pulmonary function was tested and bronchial hyper-responsiveness was measured in 645 children.

Findings At age 7, the prevalence of wheezing in the past 12 months was 10·0% (94 of 938), and 6·1% (57 of 939) parents reported a doctor's diagnosis of asthma in their children. Sensitisation to indoor allergens was associated with asthma, wheeze, and increased bronchial responsiveness. However, no relation between early indoor allergen exposure and the prevalence of asthma, wheeze, and bronchial hyper-responsiveness was seen.

Interpretation Our data do not support the hypothesis that exposure to environmental allergens causes asthma in childhood, but rather that the induction of specific IgE responses and the development of childhood asthma are determined by independent factors.

Lancet 2000; **356**: 1392–97

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Introduction

Epidemiological surveys indicate that there has been a notable increase in the prevalence of both asthma and other allergic symptoms in children and young adults.^{1,2} Since it seems unlikely that genetic factors contribute to this rising trend, environmental factors might play a major part in the development of childhood asthma. Several potential determinants have been proposed, such as lack of severe or repeated infections,^{3,4} obesity and lack of physical exercise,⁵ decreased family size,⁶ changing dietary habits,^{7,8} and increase of indoor allergen exposure.⁹

There is some evidence that the level of indoor allergen exposure is related to an individual's capacity to mount specific IgE responses towards these allergens.^{10–12} Some recently published cross-sectional studies assessing cat exposure retrospectively failed to detect a positive association.^{13,14} However, the extent to which the inception of childhood asthma is also determined by the level of indoor allergen exposure remains unclear.^{15,16} Epidemiological surveys of children raised in environments with very low exposure to dust-mite allergen indicate that the prevalence of asthma is not decreased compared with children in mite-infested areas.^{17,18}

We prospectively investigated the relation between indoor allergen exposure and the development of asthma in a large cohort of German children up to age 7 years.

Methods

Study design

In the German Multicentre Allergy Study, 7609 newborn infants were recruited in five German cities (Berlin, Düsseldorf, Freiburg, Mainz, and Munich) during 1990. Of these 7609 children, 1314 were selected for the prospective study. 499 infants (38%) were included as being at high risk of developing asthma (having at least two atopic first-degree family members or raised cord-blood IgE >0·9 kU/L). 815 infants (62%) were chosen at random from the remaining newborn infants (one or no atopic family members and cord-blood IgE values <0·9 kU/L). A detailed description of study participants and methods is given elsewhere.¹⁹

The study was approved by the local ethics committee. The children were followed up at 1 month, 3 months, 6 months, 12 months, and 18 months, and then every year until age 7 years. At each follow-up visit, parents completed a questionnaire and responded to structured questions about atopic symptoms and diseases of their children. The outcomes at ages 4, 5, 6, and 7 years were assessed by use of the International Study of Asthma and Allergies in Childhood (ISAAC) questions on wheeze.²⁰ Study participation rate at age 7 years was 71·5%. If parents agreed, blood samples of the children and carpet dust samples were collected.

Parents were invited into the clinic at the 7th birthday of their child (±6 weeks). In a structured interview with the study doctor, parents were asked whether the child had ever had "a wheezing or whistling noise in the chest

while breathing”, and whether the child had “wheezed in the past 12 months” before the interview. Current wheeze was defined as at least one episode of wheezing during the 12 months before the interview. Parents were also asked whether a doctor had ever diagnosed asthma, hay fever, or eczema. Furthermore, several questions about environmental exposures were asked, such as exposure to cigarette smoke and pet ownership. Parental history of atopy (asthma, hay fever, or eczema), number of older siblings (defined as the number of previous deliveries), social status according to the highest school education of the parents (low, medium, high) were assessed at time of birth. Parents were defined as atopic if they reported at least one of the following atopic disorders or relevant symptoms: atopic eczema, allergic rhinitis or asthma, or sensitisation to food, pollen, house dust mites, pets, or moulds.

Serum samples were obtained from the children at birth, and every year until 7 years of age. As described previously,¹⁹ cord-blood IgE, total serum IgE, and specific serum IgE antibodies to hen's egg, cow's milk, soy, and wheat, and to four inhalant allergens (house-dust mite, cat dander, mixed grasses, and birch pollen) were measured with a radioallergosorbent fluorescence immunoassay (CAP-RAST-FEIA; Pharmacia, Freiburg, Germany). 679 of 939 children provided blood samples at 7 years. Since blood samples were not available for all participants, measurements of the previous 2 years were also used in the definition of atopic sensitisation to obtain the maximum number of children with non-missing measurements of specific IgE. Sensitisation to a specific allergen was defined as a concentration of at least 0.7 kU/L ($\geq$ CAP class 2).

Carpet dust was obtained when children were aged 6 months, 18 months, and 3 years. Dust samples were collected near to the birthday of the child (± 1 month). Parents collected dust samples according to detailed written instructions that asked them to vacuum 1 m² areas of the carpet in the living room, parents' bedroom, and child's bedroom for 3 min with their own vacuum cleaner and a new dust bag. The dust bag was put into a plastic bag, mailed to the central laboratory in Berlin, and kept at 4°C until extraction and analysis.

Extraction and analysis of Der p 1, Der f 1, and Fel d 1 allergens in carpet-dust samples was done as previously described¹⁰ by sandwich ELISA (ALK, Copenhagen, Denmark). Assay sensitivity was 0.002 µg/g dust. Previous experiments showed an interassay coefficient of variation of 17–25% and an intra-assay coefficient of variation of 5–10%.¹⁸ In a pilot phase, we furthermore assessed the variability introduced by different field workers. The coefficient of variation was 15–35% if a site was vacuumed by three different persons at different days and 5–25% if the same person vacuumed the same site on different days (n=10).

Baseline lung function tests were done according to the criteria of the American Thoracic Society with the same type of full body plethysmograph in all study centres (Master-Lab, E Jaeger, Würzburg, Germany). β_2 -agonists were withdrawn for at least 12 h. Bronchial histamine challenge was done in 645 children by the reservoir method (Pari Provo Test II, Pari, Starnberg, Germany).²⁷ Briefly, the provocation device consisted of a high-quality nebuliser system combined with a 10 L storage bag that allowed standardised pulmonary aerosol deposition at saturated ambient temperature and pressure conditions. Provocation tests were done in a titrated manner starting with 0.125 g/L histamine dihydrochloride (Merck, Darmstadt, Germany). After

	Number of children
Children in birth cohort in 1990	1314
Parental questionnaire at age 7 years	939 (71.5%)
Questionnaire and dust sampling at age 6 months, 18 months, or 3 years	885 (94.2%)
Plus lung function at 7 years	760 (80.9%)
Plus histamine challenge at 7 years	610 (65.0%)
Plus blood sampling at 7 years	648 (69.0%)

Table 1: Study population and response rates

measuring forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC), increasing provocation doses were applied (0.5 g/L, 2.0 g/L, and 8.0 g/L). Challenge was stopped if the highest concentration was tolerated or if FEV₁ fell by more than 20%. The concentration of histamine that would produce a 20% decrease of FEV₁ was estimated by linear interpolation between the last two measurements. If a decline of 20% was not reached by 8 g/L, the value above 8 g/L was defined as giving a 20% decline in FEV₁. Since 5% of the children had a fall in FEV₁ of 20% or greater after the first concentration administered, baseline FEV₁ and 0 g/L histamine was used as the first datapoint for interpolation in these cases.

The dose-response slope was defined as the gradient of the line connecting the last datapoint of the dose-response curve with the origin of the curve (ie, calculated as the percentage fall in FEV₁ at the last concentration divided by the last concentration). This slope expresses the percentage change in FEV₁ per g/L histamine. For multivariate regression analysis, the dose-response slope was log-transformed to satisfy normality.

Statistical analyses

Statistical analysis was done with SPSS for PC (version 8.0) and SAS (version 6.12). All analyses used the maximum number of children available (ie, prevalences of disease at age 7 years were calculated for all participating children at that age and not only for those with complete data on early indoor allergen exposure). For bivariate analysis, Pearson's χ^2 test was used for the association of categorical data, and non-parametric Mann-Whitney *U* test or Kruskal-Wallis test were used for the association of categorical and continuous data, respectively. To assess the role of early indoor allergen exposure as a risk factor for asthma at the age of 7 years, multivariate regression models were calculated. Logistic regression models, adjusted for social status and family history of atopy, were calculated for the binary outcome variables “doctor's diagnosis of asthma”, “wheeze ever”,

	Number of samples	Median (IQR) allergen concentration (µg/g dust)
Mite allergen (Der p 1 + Der f 1)		
Carpet		
6 months	965	0.184 (0.033–0.985)
18 months	794	0.223 (0.058–1.306)
3 years	639	0.480 (0.073–2.27)
Mattress		
5 years	565	5.6 (0.54–28.33)
Cat allergen (Fel d 1)		
Carpet		
6 months	948	0.055 (0.015–0.217)
18 months	768	0.060 (0.027–0.190)
3 years	636	0.030 (<0.002–0.1)
Mattress		
5 years	536	0.1 (0.03–0.42)

Table 2: Concentrations of major mite and cat allergens in carpet and mattress dust samples at different times

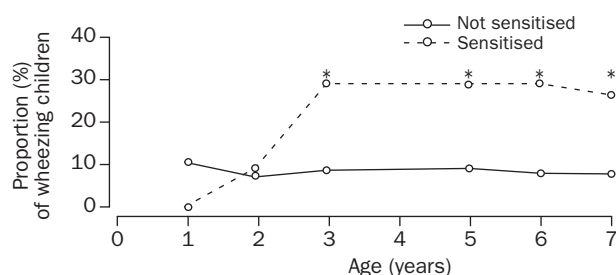


Figure 1: **Proportion of wheezing in children with and without sensitisation to mite allergen, by age**

* $p < 0.001$.

and “current wheeze”. Indoor allergen exposure levels were grouped according to exposure quartiles with the lowest quartile as reference group. Linear regression models, adjusted for study centre and season of testing, were calculated for the log-transformed dose-response slope as outcome variable. Indoor allergen exposure levels were log-transformed for this analysis. Wilcoxon test for matched pairs and Spearman rank test were used to estimate the differences of allergen exposure in the same household at different times.

Results

At age 7 years, 939 children presented for check-up. Complete data from questionnaires, indoor allergen exposure, and specific sensitisation were available for 648 children (table 1). To assess potential participation bias, participating children were compared with all other children in the Multicentre Allergy Study birth cohort, on the basis of data collected at birth (for pet ownership and indoor allergen exposure data based on the first 3 years of life). The study population (648 children) was also compared with the 291 other children with incomplete data who were participating at age 7 years, on the basis of follow-up data.

Participating children were more likely to have parents who did not smoke at the time of birth (45.3 *vs* 55.4%, $p < 0.001$) and to have parents who had a higher education (completed high school 39% *vs* 32.3%, $p < 0.004$, Mantel-Haenszel test for trend). However, participating children did not differ significantly from the other children with respect to sex, family history of atopy at birth, cord-blood IgE concentration, number of older siblings, pet ownership in the first 3 years of life, and allergen exposure at age 6 months and 18 months. Median concentrations of house-dust-mite allergens at age 6 months between participating children with complete information on sensitisation ($n=648$) were 0.2 $\mu\text{g/g}$ compared with 0.16 $\mu\text{g/g}$ among children lost to follow-up ($p=0.31$). The respective figures for cat allergen exposure were 0.055 $\mu\text{g/g}$ and 0.05 $\mu\text{g/g}$ ($p=0.59$). Furthermore, at time of follow-up they did

not differ significantly with respect to atopic sensitisation, total serum IgE, doctor's diagnosis of asthma, wheeze (ever and current), lung function, bronchial reactivity, passive smoking, or pet ownership (data not shown). Similar results were seen when we compared participating children with complete data on exposure, sensitisation, and histamine challenge at age 7 years ($n=610$) with non-participating children.

At age 7 years, the prevalence of “wheezing ever” was 17.4% (163 of 938), of “ever asthma, diagnosed by a doctor” 6.1% (57 of 939), while the period prevalence of “current wheeze” was 10.0% (94 of 938). 47 (50%) children with “current wheeze” reported wheezing episodes during the first 3 years of life and 66 (70%) showed specific sensitisation to inhalant or food allergens at age 7 years.

Mite and cat allergen concentrations measured in carpet dust samples remained low over time (table 2). There was a significant increase of mite allergen concentrations between 6 months and 18 months and 3 years, which was not the case for cat-allergen exposure. Allergen contents of samples collected in the same household at age 6 months, 18 months, and 3 years were significantly correlated (6 months *vs* 18 months, $r=0.7$ for mite allergen exposure, $r=0.6$ for cat allergen exposure, $p=0.01$; 6 months *vs* 3 years, $r=0.55$ for mite allergen exposure, $r=0.44$ for cat allergen exposure, $p=0.01$). Mattress-dust exposure measured by age 5 years (table 2) showed a median concentration of 5.6 $\mu\text{g/g}$, whereby 331 (61.8%) of children had levels higher than 2 $\mu\text{g/g}$ dust in their mattress.

There was no difference in mite and cat allergen concentrations at 6 months and 18 months between families with and without family history for asthma or atopy (Der p 1 and Der f 1 exposure at 6 months, 0.2 $\mu\text{g/g}$ in families with negative family history *vs* 0.2 $\mu\text{g/g}$ in families with asthma or atopy; Fel d 1 exposure, 0.05 $\mu\text{g/g}$ in families with negative history *vs* 0.06 $\mu\text{g/g}$ in families with positive family history for asthma or atopy, not significant). At 6 months, families that owned a cat showed significantly higher exposure than families without a cat (Fel d 1 exposure, 20 $\mu\text{g/g}$ *vs* 0.046 $\mu\text{g/g}$, $p < 0.0001$). However, there was no difference in the prevalence of wheeze in the past 12 months and bronchial hyper-responsiveness due to cat ownership.

There was a strong association between sensitisation to mite or cat allergens and wheezing (figure 1), which became significant at 3 years of age. Furthermore, children with sensitisation to indoor allergens showed higher bronchial responsiveness (ie, a steeper dose-response slope) at age 7 years than those without sensitisation (median dose-response slope 15.3 [IQR 7.7–47.8] *vs* 9.2 [4.9–16.5], $p < 0.0001$). Indoor allergen exposure was strongly related to specific sensitisation at age 3–7 years (figure 2); however, at 7 years, this effect

	Odds ratio (95% CI) by exposure quartile*			
	First	Second	Third	Fourth
Cat allergen exposure (Fel d 1)				
Risk of current wheeze ($n=732$)	1.0	0.946 (0.445–2.884)	1.420 (0.700–2.988)	1.473 (0.726–2.688)
Risk of wheeze ever ($n=732$)	1.0	0.947 (0.543–1.680)	1.152 (0.656–2.021)	1.405 (0.812–2.433)
Risk of asthma diagnosed by a doctor ($n=732$)	1.0	1.154 (0.464–2.866)	0.930 (0.357–2.423)	1.523 (0.640–3.622)
Mite allergen exposure (Der p 1 + Der f 1)				
Risk of current wheeze ($n=790$)	1.0	1.407 (0.728–2.717)	1.111 (0.569–2.169)	1.039 (0.528–2.042)
Risk of wheeze ever ($n=741$)	1.0	1.115 (0.650–1.912)	0.927 (0.542–1.584)	0.880 (0.512–1.515)
Risk of asthma diagnosed by a doctor ($n=741$)	1.0	1.358 (0.544–3.391)	2.041 (0.886–4.700)	0.725 (0.263–2.000)

*Cat allergen exposure quartiles: first <0.002 – 0.014 $\mu\text{g/g}$ carpet dust, second 0.015–0.055 $\mu\text{g/g}$, third 0.056–0.215 $\mu\text{g/g}$, fourth 0.216–47 $\mu\text{g/g}$. Mite allergen exposure quartiles: first <0.002 – 0.032 $\mu\text{g/g}$ carpet dust, second 0.033–0.184 $\mu\text{g/g}$, third 0.185–0.980 $\mu\text{g/g}$, fourth 0.981–240 $\mu\text{g/g}$.

Table 3: **Odds ratios for exposure to indoor allergens at age 6 months and asthma at age 7 years**

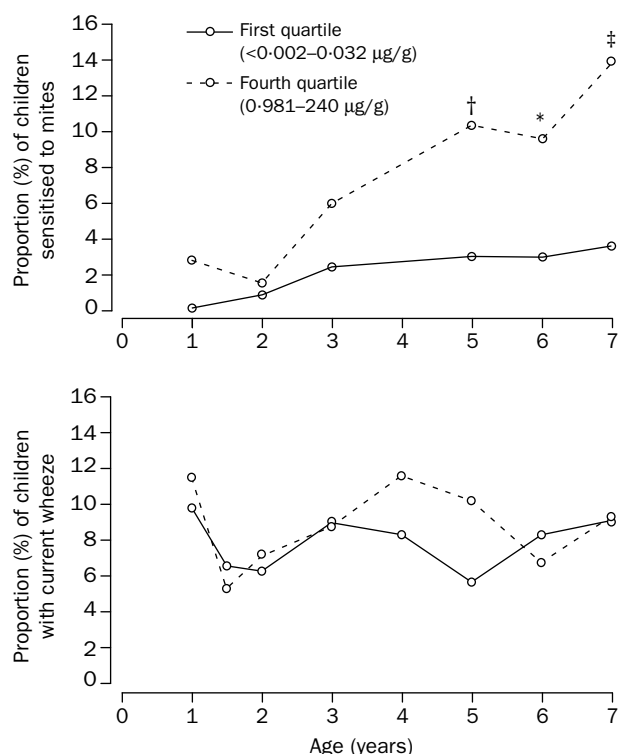


Figure 2: Prevalence of sensitisation to house dust and wheeze stratified by highest and lowest quartiles of house-dust-mite exposure at age 6 months

* $p < 0.01$; † $p < 0.001$; ‡ $p < 0.0001$.

was more pronounced for mite allergens than for cat allergens.

We were unable to detect a consistent dose-response relation for early indoor allergen exposure and “doctor’s diagnosed asthma”, “wheezing within the last 12 months” or “wheezing ever” (table 3, figure 2). Similar results were seen for indoor allergen exposure on carpets at 4 years and 5 years and on mattresses at 5 years (data not shown). When we adjusted for potential confounding factors in multiple regression analysis, the results remained almost unchanged. The results also remained unchanged when we restricted the analysis further to the subset of children with complete data on bronchial hyper-responsiveness, sensitisation at age 7 years, and dust sampling.

When we stratified the analysis for atopy (sensitisation to house dust mites and atopic dermatitis with sensitisation to food allergens), no association between indoor allergen exposure to house dust mites or cat dander and wheezing was seen (data not shown). Furthermore, exposure to indoor allergens was not related to the age of onset of wheezing, or to the severity of disease defined as the frequency of wheezing episodes in the past 12 months at age 7 years (data not shown). Similar results were obtained by use of an objective trait associated with asthma (ie, bronchial responsiveness, defined as log-transformed dose-response slope) as outcome. In a linear regression, after adjustment for study centre and season of testing, mite allergen exposure at age 6 months was not related to bronchial responsiveness at 7 years (β -coefficient 0.0177, SE 0.0204; $p = 0.38$) and 18 months (0.0091, 0.0277; $p = 0.69$), nor was cat allergen exposure at 6 months (0.0155, 0.0192; $p = 0.42$) and 18 months (0.0232, 0.0207; $p = 0.26$). Similar results were obtained when we

used 20% decline in FEV_1 as the definition of bronchial hyper-responsiveness.

There was no relation between baseline lung function (forced expiratory volume in 1 s [FEV_1], forced vital capacity [FVC], FEV_1/FVC ratio, and maximum expiratory flow at 24, 50, and 75% of FVC) and indoor allergen exposure (data not shown).

Discussion

In this large prospective study, the development of childhood asthma was not related to cat and mite allergen exposure in the first years of life or to cat ownership, although sensitisation to mite and cat allergens was associated with indoor allergen exposure, as reported previously.^{10–12} The association between allergic sensitisation to indoor allergens and the prevalence of bronchial hyper-responsiveness and asthma, which has been shown in cross-sectional studies,^{22–24} was confirmed in our cohort.

The fact that we could not find a consistent dose-response relation between exposure to cat and mite allergens and asthma was probably not attributable to participation bias, because participating and non-participating children did not differ with respect to allergen exposure and asthma rates. The generalisability of our findings may, however, be somewhat limited since non-smoking parents of high socioeconomic status were more likely to participate in these measurements.

There is no general definition of “asthma”, but use of various definitions of diagnosis and symptoms such as “wheezing” in the evaluation did not change the results. Moreover, the objective measure of bronchial hyper-responsiveness did not show an association with indoor allergen exposure. At age 7 years, the diagnosis of asthma is presumably not confounded by early wheezing illnesses due to viral infections.

The prevalence of measure in the past 12 months of our study of 10% at age 7 years is similar to 9% reported in Munich (west Germany) and 6.9% in Dresden (east Germany) according to the findings of the German ISAAC study in 5–7-year-old children in these areas 5 years after reunification.²⁵ The slightly higher prevalence of wheeze in the past 12 months in the Multicentre Allergy Study is probably attributable to its study design enriching the cohort with children at risk of atopy and asthma. According to the ISAAC data the prevalence of asthma is lower in children aged 6–7 years than in children aged 13–14 years. We cannot exclude with certainty that the young age of assessment in the Multicentre Allergy Study cohort might have contributed to the negative results. However, over 80% of asthma cases in adolescence are already manifest at 5 years of age,²⁶ suggesting that increasing prevalence over childhood years does not explain the lack of association.

Indoor allergen concentrations in carpet dust were low in this study relative to those in reports from other parts of the world where mite infestation is stronger and asthma prevalences are highest.⁹ This finding might be due to avoidance measures by parents. However, no intervention and allergen avoidance strategies were intended in this study and the levels probably reflect exposure encountered in families with usual counselling by their doctors. No relation between respiratory symptoms and allergen exposure at age 3–5 years was seen, suggesting that allergen avoidance strategies before age 7 years in children with increased allergen concentrations and symptoms do not explain the negative findings at age 7 years. If avoidance procedures had been applied in families at risk of asthma and atopy,

the prevalence of asthma, specific sensitisation to cat or mite and family history for asthma and atopy should have been higher in the low-exposure quartiles, which was not the case. Furthermore, encasing devices had only been introduced in Germany in 1993, and reimbursement of costs by insurance companies did not start until 1995. Other avoidance strategies have been shown to reduce indoor allergen levels to only a small extent. The variability of results within homes was only slightly higher in the Multicentre Allergy Study than in a pilot phase with instructed field workers or reports from investigations with standardised sampling schemes.²⁷

One might argue that mattress-dust sampling is a better marker of indoor allergen exposure than carpet-dust sampling. However, during the first years of life, parents of infants and young children tend to change their children's beds and mattresses several times, thereby decreasing exposure. Allergen levels in carpet dust may thus be a better surrogate marker for assessment of a child's early overall allergen exposure in the home, which also reflects exposure to additional allergen sources such as furniture and toys. Indoor allergen exposure on mattresses at age 5 years was ten-fold higher than on carpets, as shown in previous exposure studies in Germany,²⁸ but was not related to asthma and the association with sensitisation was weaker than early exposure in carpet dust (data not shown). Moreover, in this cohort, specific sensitisation to house-dust-mite and cat allergens was strongly related to allergen levels in carpet dust (odds ratio for upper quartile of mite allergen exposure and specific sensitisation at age 3 years 8.8, $p < 0.0001$; for upper quartile of cat allergen exposure and specific sensitisation 2.1, $p = 0.008$).¹⁰ Although we cannot exclude with certainty that the use of carpet dust for exposure assessment may have biased our results towards null, the effects, if any, would be small and their relevance for the inception of childhood asthma doubtful.

Our findings differ from one previous study on a small number of children by Sporik and co-workers.²⁹ Using similar criteria to those applied in that study (onset of wheezing related to very high $\geq 10 \mu\text{g/g}$ exposure in a high-risk group), we were unable to reproduce Sporik and colleagues' findings. One reason might be the low number of cases in the British cohort, the higher exposure in the UK, and the arbitrary cut-off level of $10 \mu\text{g/g}$ exposure used. We cannot exclude from our findings that higher exposure might in fact relate to the incidence of asthma. However, a recent review points to the lack of epidemiological evidence of a causal link between allergen exposure at higher concentrations, such as in Australia and the UK, and asthma development.³⁰ In turn, the results of our study are in accordance with those from Los Alamos (NM, USA),¹⁸ Briançon (France),¹⁷ and other high-altitude or desert areas,³¹ which did not show a reduced prevalence of asthma in children raised in areas with very low mite-allergen exposure.

Growing evidence suggests that factors determining the development of atopy are at least in part different from those inciting childhood asthma and wheezing illnesses. The strong relation between sensitisation to house-dust mites and asthma as seen in this and previous studies may reflect the susceptibility of an individual with asthma to become sensitised to perennial allergens that are most prevalent in the environment rather than an increased risk of asthma when exposed to these allergens. The results of our study support this notion.

This change in paradigm might have strong public-health implications, since it questions the role of indoor allergen avoidance for the prevention of childhood asthma. Several primary prevention studies are continuing, such as the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study in the Netherlands, the Study on Prevention of Allergy in Children in Europe (SPACE) in Europe, the Children's Allergy Prevention Study (CHAPS) in Southampton, UK, and other cohort studies in Canada, Australia, and Manchester, UK.³² So far, results indicate only that long-term indoor allergen reduction is possible and that specific sensitisation to house-dust mites may be at least postponed in atopic children.³³ Data from another British prevention study from the Isle of Wight suggest that even when lower sensitisation rates are achieved, the prevalence of asthma up to age 4 years is not affected.³⁴

Whereas indoor allergen exposure has a clear influence on atopy, the link to asthma is less pronounced in an area with moderate exposure. Our findings suggest that factors independent of allergen exposure, such as genetic and other environmental factors, are of importance for the development of the different phenotypes of asthma, influencing structural abnormalities regarding growth and elasticity of airways and lung parenchyma.

Once sensitisation has occurred and asthma is expressed, persistent allergen exposure is undoubtedly associated with an increase of symptoms and use of medication.³⁵ Thus, indoor allergen avoidance as part of secondary and tertiary prevention strategies can still be recommended in the management of patients with asthma, but conclusions should be drawn with caution about the possible effect of primary prevention measures.

Contributors

Ulrich Wahn is the coordinator of the German Multicentre Allergy Study. Bodo Niggemann supervised the lung function testing and bronchial challenge tests. Renate Bergmann developed the questionnaires and supervised the physical examination of the children. Christine Sommerfeld, Sabina Illi, and Erika von Mutius analysed the statistical data. Susanne Lau measured the major indoor allergens in dust samples and specific IgE in serum samples, analysed the data, and wrote the paper.

Acknowledgments

We thank the collaborators of the Multicentre Allergy Study group: Volker Wahn, Marketa Groeger (Düsseldorf); Fred Zepp, Imke Bieber (Mainz); Johannes Forster, Uta Tacke (Freiburg); Carl-Peter Bauer (Geisach); Karl-E Bergmann (Berlin); the nurses Petra Wagner (Berlin), Gabriele Leskosek (Düsseldorf), Roswitha Mayerl (München), Brigitte Hampel (Mainz); and the statistician Günter Edenharter.

This study was supported by the German Ministry of Research and Education grant numbers 07 ALE 27 and 01EE9405/5.

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