

RISK OF WHEEZING ASSOCIATED WITH HOUSE-DUST MITE ALLERGENS AND INDOOR AIR QUALITY AMONG THREE-YEAR-OLD CHILDREN. KRAKÓW INNER CITY STUDY

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Abstract
Objectives: The aim of the study was to describe the distribution of house-dust mite (HDM) allergens in homes of three-year-old children and to test the hypothesis whether the content of HDM allergens exceeding 2 µg/g of dust may be regarded as a risk level possibly affecting respiratory health in early childhood. **Materials and Methods:** House-dust samples were collected in 275 dwellings from mattresses, children’s bedrooms and kitchen floors. In the laboratory, dust samples were analyzed for Der f 1 and Der p 1 using monoclonal antibody enzyme-linked immunosorbent assays (ELISA). At the time of the house-dust collection, mothers were interviewed on the household characteristics and their children’s respiratory health. Respiratory outcome variables included wheezing or whistling in the chest irrespective of respiratory infections. The number of the wheezing episodes and their duration in days over the last 6 months were recorded in the questionnaire. In the multivariate Poisson regression analysis on the association between the occurrence of wheezing and exposure, a set of potential confounders, such as child’s gender, maternal education, maternal allergy, older siblings, presence of moulds, house dampness, and environmental tobacco smoke (ETS) was taken into account. **Results:** The adjusted incidence rate ratios (IRR) of wheezing ascribed to a higher HDM level (> 2.0 µg/g dust) were 1.84 (95% CI: 1.45–2.34) for duration of wheezing and 1.56 (95% CI: 0.88–2.75) for episodes. Of the confounders taken into consideration, the presence of moulds had the strongest impact on the risk of wheezing (IRR = 4.24; 95% CI: 3.08–5.84). **Conclusion:** The data support the view that exposure to a higher level of HDM allergens increases the burden of respiratory diseases in the early childhood and the effect is independent of maternal atopy, ETS, and moulds in homes.

Key words:
Wheezing symptoms, Children, House dust-mite allergens, Moulds, Environmental tobacco smoke, Maternal atopy

Received: February 19, 2007. Accepted: April 11, 2007.
The study was supported by the grant from the Center for Research and Studies in Biomedicine, Luxembourg. The project is the part of the collaborative study on the vulnerability of fetus and child to environmental factors carried out by the Chair of Epidemiology and Preventive Medicine, College of Medicine, Jagiellonian University, Kraków, Poland, and the Columbia Center for Children’s Environmental Health, Mailman School of Public Health, Columbia University, New York, NY, USA. Address reprint requests to Prof. W. Jedrychowski, MD, PhD, Chair of Epidemiology and Preventive Medicine, College of Medicine, Jagiellonian University, Kopernika 7A, 31-034 Kraków, Poland (e-mail: myjedryc@cyf-kr.edu.pl).

INTRODUCTION

Over the recent few decades many epidemiological studies have shown a remarkable increase in the prevalence of both asthma and other allergic symptoms in children and young adults [1–3]. Since genetic traits probably do not contribute to this rising trend, it seems that environmental factors might play a considerable role in the development of childhood asthma. The observed increase in indoor allergen exposure, particularly house-dust mites (HDM), is one of the candidate risk factors that is potentially involved. HDM exposure during early childhood may lead to allergic sensitivity, airway inflammation and asthma in children [4–10]. Some authors hypothesize that the content of HDM allergen exceeding 2.0 µg/g dust may be regarded as a risk level of sensitization [4,6].

There are mentioned several factors, which may affect the variation and the level of house-dust mites within the households. The primary determinants of these variations are indoor humidity and temperature [11]. Household pets, which shed skin scales, a food source for HDM, are also contributing to the level of dust mite and frequency of allergy in children [12–15]. In addition, some indoor conditions may favor HDM growth and proliferation; carpets and beds provide a reservoir of moisture and nutrients. House gas equipment for cooking or heating may allegedly alter indoor conditions and increase humidity.

Despite data published earlier [16], Poland has a high level of morbidity associated with asthma and a high prevalence of allergy to HDM. The recently published analysis of trends in hospitalization rates of asthma among children in Poland [17] showed their sharp increase over the last two decades, which doubled for both genders in the years 1984–1996. Among boys the rates were 1.6 times higher than in girls. On average, the rates increased annually by 12% among boys and by 11% in girls, but the most rapid increase has been noted in the youngest children aged less than 4 years. The prospective epidemiological study carried out in schoolchildren from the Kraków inner city area over the period of three years (1995–1997) has shown that 4.8% of boys and 4.0% of girls had ever experienced persistent wheezing and 3.9% of boys and 1.8% of girls reported

attacks of breathlessness with wheezing independent of respiratory infections [18]. Allergy to HDM has been confirmed in 42% of schoolboys and 13.4% of schoolgirls [19]. Up till now very little information on the concentrations of HDM allergens in Polish houses is available.

The aim of this study was to describe the distribution of HDM allergens in houses of the three-year-old children. Furthermore, the hypothesis was tested whether the content of HDM allergen exceeding 2.0 µg/g dust may be regarded as a risk threshold level possibly increasing the burden of respiratory symptoms in early childhood. The study may help in defining the risk groups for subsequent prospective analysis of the association between respiratory morbidity in children and indoor-dust mite allergen exposure during early childhood.

MATERIALS AND METHODS

This study used data from an earlier established Kraków birth cohort of children, being the part of the collaborative study with the Columbia University in New York, on the vulnerability of fetus and child to environmental factors [20]. The enrollment (November 2000 – August 2003) included only non-smoking women, aged 18–35 years, with singleton pregnancies without illicit drug use and HIV infection, free from chronic diseases, such as diabetes or hypertension, and residing in Kraków for at least one year prior to pregnancy. The enrolled women gave birth to 505 children. In 2005, a total of 275 children were 3 years of age and all of them were eligible for the present HDM study. The study was approved by the Ethical Committee of the Jagiellonian University.

House-dust samples were collected from the mattresses, children's bedrooms and kitchen floors. Floors were sampled over a 2-min period from a 2 m x 2 m frame; in bedrooms this was adjacent to the bed, and in kitchen where the child used to spend time. The children's parents were requested not to clean the mattresses, sweep or vacuum these floors for 48 h before sampling. The same vacuum cleaner was used to collect dust samples from all household sites, and the trained staff performed the dust collection. To avoid cross-contamination between samples

from different sites, vacuum cleaner parts were cleaned with wet cloths and dried after each sampling. All dust samples were sealed in plastic bags and sent to the laboratory of the Department of Clinical Immunology, the Polish-American Institute of Pediatrics (College of medicine, Jagiellonian University), where they were stored at 4°C, under desiccant, until they were extracted. Extracted dust samples were assayed for Der f 1 and Der p 1 by ELISA (Indoor Biotechnologies, Chester, U K).

At the time of house dust collection, trained interviewers held a standardized interview with mothers on the children's health over the last 6 months. Respiratory outcomes included wheezing or whistling in the chest irrespective of respiratory infection. The number of wheezing episodes and their duration in days over last 6 months were recorded in the questionnaire. An episode of respiratory symptom was defined as the occurrence of a specific symptom over at least one full day. Data on the number of cigarettes smoked daily by all household members were used to assess environmental tobacco smoke (ETS) at home. Maternal allergy was recognized if the mother reported allergic disorders confirmed by the medical diagnosis. The definition of home with mould problem was based on the responses to questions concerning visible patches of mould growth on the internal walls of the household.

Statistical analysis

The concentrations of mite allergens (micrograms per gram of dust) were compared between the household sites, where the dust collection was done. To dust samples, where concentration of dust mite was undetectable, we assigned a value of 0.005 µg/g of dust (which was half the minimum detectable concentration) and included in the analysis. Dust mite exposure was categorized as Der f 1 or Der p 1 at the following levels: 1) 10 µg/g dust or higher (including concentrations exceeding detectable limits); 2) 2 to less than 10 µg/g dust; and 3) less than 2 µg/g dust (including samples below the limits of detection). Subsequently, the HDM mean exposure was calculated for each dwelling taking into account all the measurements of both allergens.

Bivariate and multivariate Poisson regression models were used to analyze the association between house-dust mites and the occurrence of wheezing symptoms over the last 6 months. Dependent variables were observed counts of episodes and observed total number of days the wheezing symptom was present as recorded in the interview with the mother. As mentioned earlier, the analysis was restricted to infants of non-smoking mothers (never smoking status during pregnancy). For the multivariate analyses, potential predictors, such as child's gender, season of dust collection, maternal education, maternal allergy, presence of older siblings, ETS, presence of moulds and house dampness, were introduced in the regression models as dummy variables. In all statistical analyses, the significance level was assumed as $p < 0.05$. Statistical analyses were performed with STATA 9 software for Windows [21].

RESULTS

Table 1 presents the characteristics of children included in the study, while Figures 1–4 show the prevalence of exposure to Der f 1 and Der p 1 allergens at various house sites, where the measurements were done. It turns out that both allergens were more prevalent in children's beds than elsewhere in the house. About half (47.8%) of children's beds showed the mean HDM allergen level exceeding 2 µg/g of dust; this allergen level was found on the bedroom floors in 34% of houses, and only in 6.9% of kitchen floors. In 101 (36.6 %) households, the HDM mean level exceeding 2 µg/g dust was found in one of the three collection sites, in 66 (23.9%) households in two, and in 4 (1.4%) households in three house sites.

Correlation between concentrations of a given allergen in various sites at home were assessed with the Spearman correlation coefficient. We found a significant correlation between Der p 1 allergen in children's beds and on the floor beside the beds ($r = 0.51$; $p = 0.000$), but lower for Der f 1 ($r = 0.36$; $p = 0.000$). There was a weaker correlation between HDM concentrations found in the bedrooms and kitchens ($r = 0.21$).

In the total group of children, wheezing symptoms occurring over the last 6 months prior to the study were

Table 1. Characteristics of the study sample

	Total (n = 275)	HDM level		P
		< 2 µg/g	≥ 2 µg/g	
Gender (n, %):				
Boys	137 (49.8)	57 (54.3)	80 (46.8)	0.2982
Girls	138 (50.2)	48 (45.7)	90 (53.2)	
Birth length (cm):				
Mean	54.5	54.4	54.5	0.9195
SD	3.1	3.1	3.0	
Birth weight (g)				
Mean	3399.5	3399.2	3399.6	0.9948
SD	506.8	514.7	503.5	
Length at the age of 3 years (cm):				
Mean	99.3	99.5	99.2	0.5665
SD	4.0	3.7	4.2	
Missing data	36	15	21	
Weight at the age of 3 years (kg):				
Mean	15.2	15.0	15.3	0.3171
SD	1.9	1.8	2.0	
Missing data	36	15	21	
Maternal atopy confirmed by physician (n, %)	68 (24.6)	27 (25.7)	41 (24.0)	0.8561
Environmental tobacco smoke (ETS) (n, %)	31 (11.3)	11 (10.5)	20 (11.8)	0.8950

P — significance level.

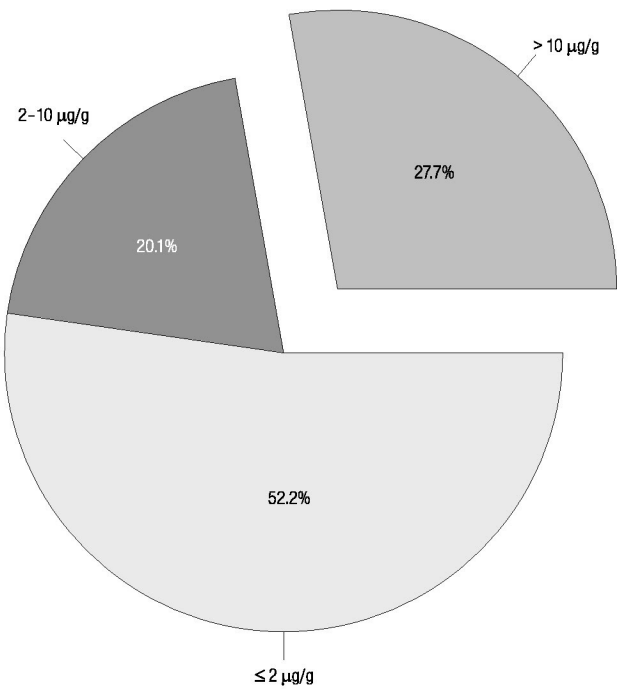


Fig. 1. Concentration of total dust mites (Der f 1 + Der p 1) in children's beds.

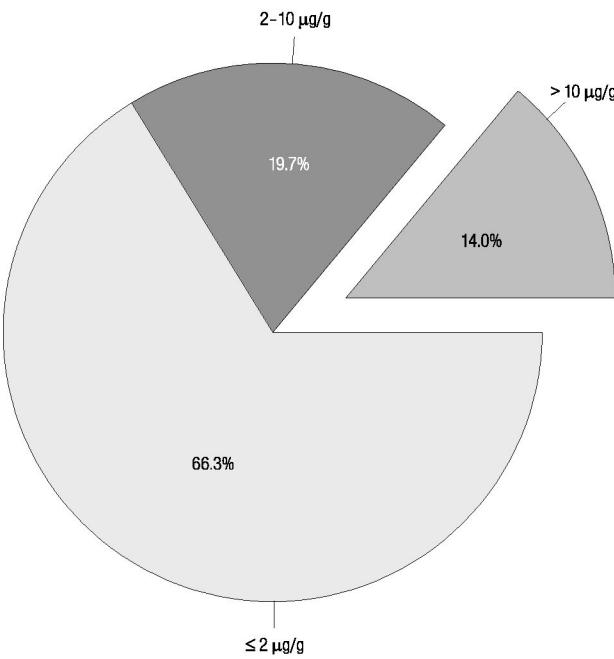


Fig. 2. Concentration of total dust mites (Der f 1 + Der p 1) on bedroom floors.

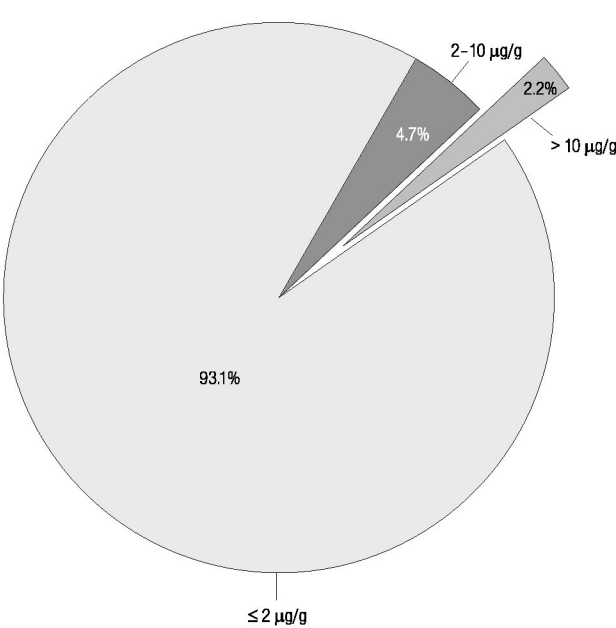


Fig. 3. Concentration of total dust mites (Der f 1 + Der p 1) on kitchen floors.

reported by 10.5% of children. A great majority of cases reported wheezing, which lasted longer than two days (Fig. 5). Average duration of wheezing was longer (11.8 days) in children exposed to a higher HDM level (> 2 µg/g dust) and shorter (9.1 days) in those with lower exposure.

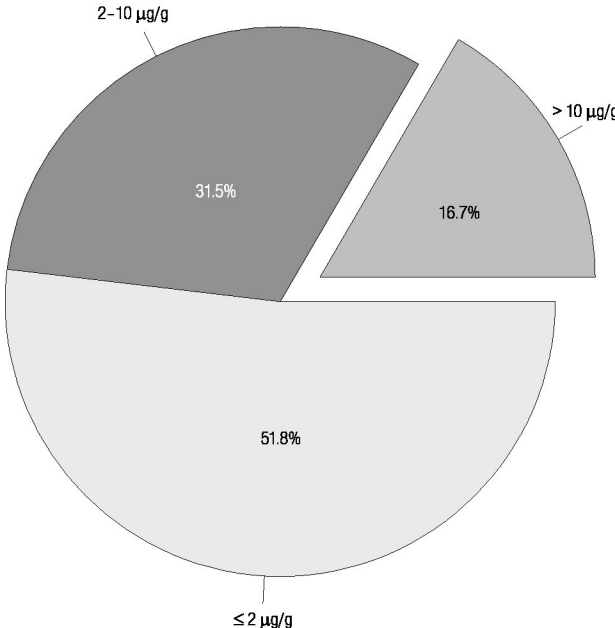


Fig. 4. Concentration of total dust mites (Der f 1 + Der p 1) in the household.

The multivariate Poisson regression analysis showed that the incidence rate ratio (IRR) of wheezing was positively associated with the exposure to the HDM exposure level (Tables 2 and 3). The adjusted IRR for wheezing (days) was 1.84 (95% CI: 1.45–2.34) and that for wheezing

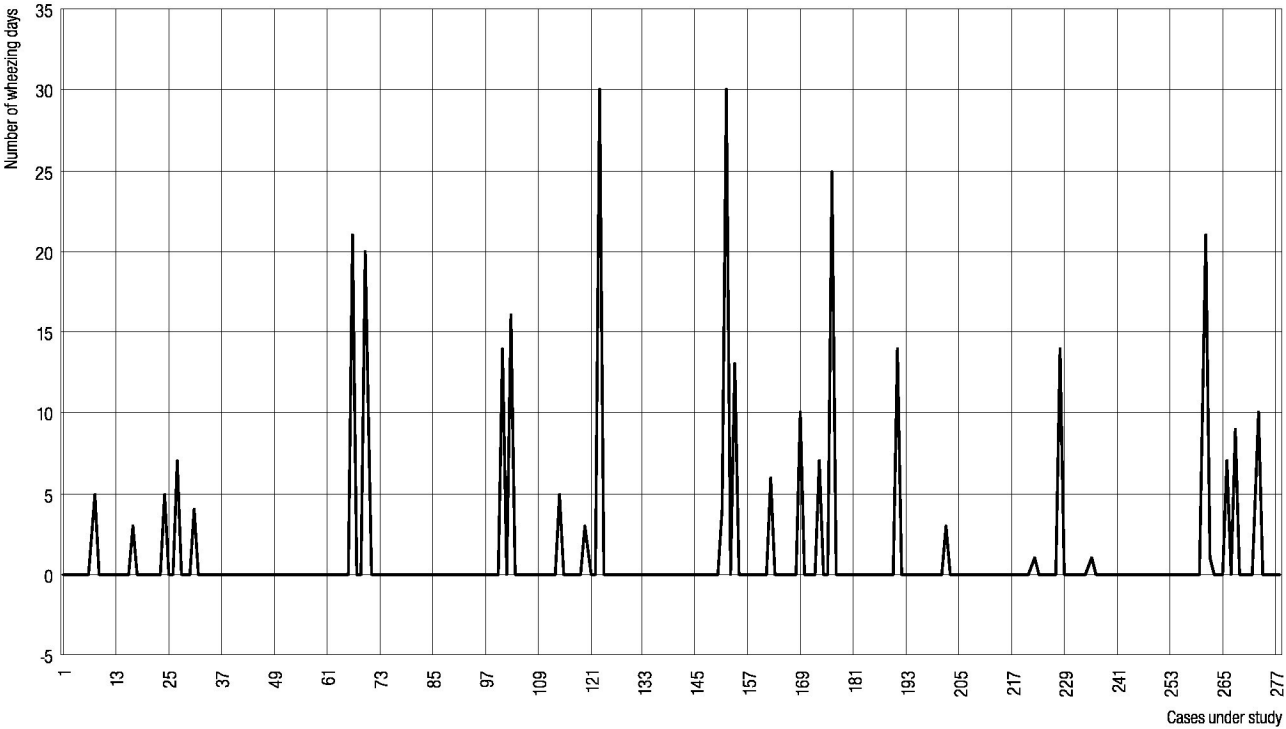


Fig. 5. Sequential stacked plot of wheezing days over a 6-month period preceding the measurements of house-dust mites (HDM).

Table 2. Incidence risk ratio (IRR) for the reported wheezing days over the last 6 months preceding the HDM measurement related to the house-dust mites level and potential confounders. Estimated from the multivariate Poisson regression model

Predictors	IRR	SE	Z	P	95% CI	
HDM level*	1.84	0.23	4.94	0.000	1.45	2.34
House dampness**	1.38	0.27	1.65	0.099	0.94	2.01
Indoor Moulds**	4.24	0.69	8.86	0.000	3.08	5.84
Maternal allergy**	1.30	0.17	2.05	0.041	1.01	1.67
Maternal education***	1.25	0.06	4.70	0.000	1.14	1.38
Older siblings**	1.76	0.12	8.51	0.000	1.55	2.01
ETS**	1.08	0.01	6.45	0.000	1.05	1.10
Child's gender****	0.70	0.08	-2.98	0.003	0.56	0.89
Season of the study*****	1.00	0.12	0.03	0.972	0.80	1.26

SE — standard error; Z — value of significance test; P — significance level; 95% CI — 95% confidence interval.
* Mean HDM dichotomized (2 µg/g dust);
** All dummy variables: 0 = absence of the factor, 1 = presence of the factor;
*** Years of schooling;
**** Gender: 0 = boys, 1 = girls;
***** Season: 0 = spring-summer, 1 = autumn-winter.

Table 3. Incidence risk ratio (IRR) for the reported wheezing episodes over the last 6 months preceding the HDM measurement related to the house-dust mites level and potential confounders. Estimated from the multivariate Poisson regression model

Predictors	IRR	SE.	Z	P	95% CI	
HDM level*	1.56	0.45	1.53	0.125	0.88	2.75
House dampness**	1.49	0.69	0.84	0.399	0.60	3.66
Indoor Moulds**	3.22	1.40	2.69	0.007	1.37	7.54
Maternal allergy**	1.01	0.33	0.04	0.965	0.54	1.92
Maternal education***	1.45	0.18	2.98	0.003	1.14	1.85
Older siblings**	1.60	0.27	2.76	0.006	1.15	2.23
ETS**	1.11	0.03	4.16	0.000	1.06	1.16
Child's gender****	0.86	0.24	-0.53	0.595	0.49	1.51
Season of the study*****	1.21	0.34	0.65	0.513	0.69	2.11

SE — standard error; Z — value of significance test; P — significance level; 95% CI — 95% confidence interval.
* Mean HDM dichotomized (2 µg/g dust);
** All dummy variables: 0 = absence of the factor, 1 = presence of the factor;
*** Years of schooling;
**** Gender: 0 = boys, 1 = girls;
***** Season: 0 = spring-summer, 1 = autumn-winter.

episodes was 1.56 (95% CI: 0.88–2.75). Of the confounders taken into consideration, the presence of moulds had the strongest impact (IRR = 4.24; 95% CI: 3.08–5.84) on the risk of wheezing (days). The interaction term (HDM level * moulds in household) appeared to be insignificant. Other confounders, such as maternal allergy, maternal education, older siblings, and ETS, were also positively

associated with the estimated risk of wheezing, however, to a lesser degree (Table 2). The risk of wheezing was significantly lower in girls (IRR = 0.70; 95% CI: 0.56–0.89) and the effect of season, in which the field study has been carried out, was insignificant. The estimates of the effect of confounders on the number of wheezing episodes were found to be very similar (Table 3).

DISCUSSION

The results of our study showed that about half (48.8%) of the dwellings present a potential risk for early sensitization of children due to a higher mean concentration ($> 2 \mu\text{g/g}$ dust) of HDM allergens. As expected, the most frequent site with high HDM concentrations was found to be the child's bed and floor around it. The lowest concentrations of HDM allergens were measured in the dust collected from kitchen floors. Our findings that HDM allergen concentration was higher in the bed than on the floor close to the bed may result from a greater shedding of skin scales in the bedroom, and the transfer of mites from the bed to the floor. The lower level of HDM on the kitchen floor may partly result from the dilution of allergen by the presence of non-allergen-containing dust collected from the kitchen floor.

We showed that a higher mean HDM exposure was positively associated with the number of episodes and duration of wheezing (in days). We also confirmed that in children who were at a higher HDM exposure ($> 2 \mu\text{g/g}$ dust), the excess risk of wheezing (days) was 1.84 (95% CI: 1.45–2.34) and that of wheezing episodes was 1.56 (95% CI: 0.88–2.75). Of the confounders taken into consideration, the presence of moulds had the strongest impact (IRR = 4.24; 95% CI: 3.08–5.84) on the risk of wheezing days. Since the interaction term (HDM level * moulds in household) was insignificant, the effects of both indoor factors were independent from each other.

The increased risk of wheezing associated with the higher exposure to mite allergens may result from their sensitization effect on the bronchial tree and the subsequently increased susceptibility to respiratory infections. Nevertheless it is possible that the presence of mites is only an indicator of the indoor air quality related to some other potential respiratory hazards. The long-term consequences of these findings remain to be determined in the planned follow-up study. In the present study we could not confirm the HDM sensitization of children by independent testing, however, it has been found in other studies that the risk of sensitization to HDM increased even at low levels of exposure to mites, which were comparable with the levels in our study [22].

Our study results are in agreement with the evidence that postnatal early exposure to HDM allergen affects the respiratory system of young children and that exposure to dust mites during infancy may lead to the development of childhood asthma [23–25]. Important potential modifying or confounding variables, such as moulds and postnatal ETS exposure in the house, were taken into consideration in the statistical models. In our study, we also considered the effect of older siblings who play an important role in the transmission of respiratory infections within the household environment. The latter issue is of importance since the role of respiratory infections as being protective or as a risk factor for asthma or allergy is not clearly explained. As compared with other similar studies, the fact that infants exposed to maternal smoking in pregnancy have been excluded at the enrolment of study subjects is a very strong point of our study. Since it might be argued that the measurement of allergen levels in one house reservoir like the bed does not accurately reflect the total allergen exposure of the child, our study considered the combined HDM mean index exposure based on measurements of both HDM allergens taken from the different house sites. Studies investigating the association between mite allergen exposure and asthma in children have produced conflicting results. For example, in children with at least one atopic parent, Sporik et al. [4] showed an increased risk of asthma at 11 years of age with exposure to high concentrations of mite allergens ($> 10 \mu\text{g/g}$ dust), however, these results were not confirmed by later studies [26–28]. The prospective study following a large birth cohort that included both low-risk and high-risk children has been reported by the Multicenter Allergy Study Group [28]. Adjusting for parental history of atopy, the authors of the latter study found no relation between very early indoor allergen exposure in infancy and the prevalence of asthma, wheeze, and bronchial hyperresponsiveness at the age 7 years. The fact that the study dealt with very low levels of dust-mite allergen, could explain the failure to assess properly the anticipated association. However, the authors revised this finding with their most recent publication [29] and found that children sensitized at the age of 3 years were more likely to have lower lung function at 7 years of age and

even more likely if they were also exposed to allergens in the early years of life.

While HDM sensitization thresholds are used in the literature, we have to keep in mind that these thresholds are not supported by solid evidence in respect of the health effects. First of all, the suggested thresholds were based on a small cohort and subsequent studies have observed sensitization with lower levels of exposure [30,31]. Among others, the issue is complicated by the fact that selective avoidance of HDM allergens in persons with asthma or allergy may produce an apparent lack of significant relationship between the allergen level and asthma. Moreover, the allergic sensitization thresholds are likely to depend on other co-exposures (e.g., endotoxin) and genetic predisposition [32]. In addition, the debate in the literature on the sensitization thresholds is based on studies carried out in persons at various ages, but allergic sensitization thresholds in early childhood may be quite different from those observed in older children or adults. Pearce et al. [33] even challenged the hypothesis that dust mites or other allergen exposure may be causally related to the childhood asthma. The authors questioned the validity of ecologic, longitudinal, and cross-sectional studies in supporting an etiologic relationship. In fact, we have to agree with the authors that the careful longitudinal studies at large and unselected populations with a variety of potential indoor hazards are required before a clear primary or secondary causation link may be established between mite allergens and childhood asthma.

In conclusion, the results of our study indicate that about 50% of three-year-old children in the Kraków inner city area are at risk of HDM sensitization (allergens > 2 µg/g of dust) that may be manifested in the early life by the increased occurrence of wheezing. The significant association found in the present study between the increased HDM allergen level and the occurrence of wheezing symptoms in three-year-olds is an argument supporting the view about an impact of early postnatal HDM exposure on children's health. The results of these initial observations need to be followed further to assess the long-term health consequences of early-life exposure to HDM allergens.

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