

House dust mite allergen (*Der p I*) and respiratory symptoms in children: a case-control study

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Summary

The association between house dust mite allergen in house dust and childhood respiratory symptoms was investigated in a case-control study of 259 children with reported chronic respiratory symptoms and 257 control children without reported respiratory symptoms. The *Der p I* concentration in floor dust of the living room and bedroom and in mattress dust was determined using an enzyme immunoassay. Venous blood samples were taken from all children for serum IgE determination against house dust mite (*Dermatophagoides pteronyssinus*) by radioallergosorbent assay (RAST). A questionnaire was administered to the parents of the children to elicit information about the home, about changes made to the home in the past in relation to respiratory symptoms, and about a number of risk factors for childhood respiratory disease. In 83% of the dwellings of cases and 89% of those of controls, *Der p I* concentrations higher than 2000 ng/g were found, and in 54% of the dwellings of cases and 57% of those of controls, the concentrations exceeded 10 000 ng/g dust. In a crude analysis, cases were generally exposed to lower *Der p I* concentrations than controls. Restriction of the analysis to cases sensitized to dust mites, and non-sensitized controls, taking the type of floor covering into account, showed not significantly higher *Der p I* concentrations in bedroom floor dust of cases. However, restriction of the analysis to cases sensitized to dust mites and cases not sensitized to house dust mites — adjusting for allergen avoidance measures taken in the past — revealed a positive association between the *Der p I* concentrations in bedroom floor dust and mattress dust and sensitization. This finding indicates that allergen avoidance measures modify current exposure to *Der p I*. This obscures the relationship between the exposure to mite allergens and sensitization, and hampers the estimation of the association between exposure to house dust mite allergens, sensitization and the development of respiratory symptoms.

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Introduction

About 30 years ago house dust mites were identified as the major cause of house dust allergy [1]. Since then the major allergens of house dust mites have been characterized and standardized, allowing the assessment

of the potential exposure to these allergens and the presence of specific IgE in serum, using immunochemical techniques [2,3]. It is now clear that house dust mites produce strong allergens. Exposure of genetically pre-disposed subjects to these allergens can lead to sensitization and subsequently to asthma [4,5]. A number of studies investigated the relationship between the exposure to house dust mite allergens and respiratory symptoms. Lau *et al.* [6] reported a dose-response relationship between the concentrations of *Der p I* and

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Der f I (the major allergens of *Dermatophagoides pteronyssinus* and *D. farinae* respectively) in house dust and the risk of sensitization to these allergens. In this study atopic children sensitized against house dust mites were compared with atopic children not sensitized. Price *et al.* [7] also reported a positive association between the level of house dust mite allergen in house dust and sensitization among asthmatic children. Wickman *et al.* [8] measured the levels of house dust mite allergens in house dust of 53 mite-sensitized children, 54 non-mite-sensitized children, 54 non-mite-sensitized atopic children and 53 non-allergic controls. Increased mite allergen levels were more often found in homes of children sensitized to house dust mite than in the homes of children not sensitized to house dust mite. The largest difference was found between the group of house dust mite sensitized children and the group of non-sensitized atopic children. Based on the results of studies on the relationship between the levels of *Der p* I in house dust and sensitization, provisional hygienic threshold limits have been proposed [4]. Concentrations of more than 2000 ng *Der p* I/g dust are regarded as representing a risk for the development of specific IgE to house dust mite allergen in genetically predisposed individuals, and levels higher than 10 000 ng *Der p* I/g are supposed to increase the risk for acute attacks of asthma. Based on the results of studies on the relation between exposure to house dust mite allergens and asthma, Sporik *et al.* [9] concluded that the primary cause of asthma in many areas of the world is exposure to house dust mite allergens, especially in children and young adults.

A case-control study was conducted to explore the relationship between a number of indoor risk factors and respiratory symptoms in children. This paper focuses on differences in mite allergen exposure between children with chronic respiratory symptoms, denoted as cases, and children without chronic respiratory symptoms, denoted as controls. The hypotheses tested were: (i) that there is no difference in the exposure to *Der p* I between cases and controls, irrespective of sensitization to *D. pteronyssinus*, (ii) that there is no difference in the exposure to *Der p* I between cases sensitized to house dust mites and controls not sensitized to house dust mites, and (iii) that there is no difference in the exposure to *Der p* I between cases sensitized to house dust mites and non-sensitized cases.

Materials and methods

Subjects

A case-control study on the relationship between chronic respiratory symptoms and a number of indoor risk

factors was conducted among children aged 6–12 years. Cases and controls were selected from a random sample of 7632 children from 18 schools in the province of Noord Holland, and from 20 schools in the province of Gelderland. The parents of the children completed a screening questionnaire regarding respiratory symptoms, based on existing, validated childhood respiratory symptom questionnaires [10]. The response to the screening questionnaire was 74.6% in Noord Holland, and 85.5% in Gelderland. Cases were selected from children reporting chronic wheeze in the past 12 months, cough on most days or nights for 3 consecutive months in the autumn/winter season, attacks of shortness of breath with wheezing in the past 12 months and/or doctor-diagnosed asthma (ever in life). Controls were selected from the group of children without reported respiratory symptoms. Of all cases randomly requested to participate, 78% agreed. For the controls, this percentage was 60%. The latter value was partly caused by a very low response among children of two schools in Gelderland with a high proportion of children with an orthodox religious background. Altogether, 259 cases and 257 controls participated in the study. As prevalent cases may have had symptoms for some time already, it is conceivable that changes in exposure to allergens have occurred, e.g. due to mattress renewals, etc. Therefore, we enquired about allergen reduction measures taken in the past in great detail.

Specific IgE determination

Venous blood samples (20 ml) were taken from all children by a skilled nurse. After centrifugation, sera were stored at -20°C . Specific IgE against house dust mite (*Dermatophagoides pteronyssinus*) was determined by radioallergosorbent assay (RAST). The analyses were performed by the Central Laboratory of the Blood Transfusion Service in Amsterdam. Specific IgE determinations were done to permit more stringent case definitions and more detailed case-control comparison.

Pulmonary function

Spirometry was performed according to the protocol of the European Community for Coal and Steel (ECCS) [11]. A detailed description of our protocol has been provided by Houthuijs *et al.* [12]. A rolling-seal dry spirometer (Vicat 5, Mynhardt, Bunnik, the Netherlands) coupled with automatic data acquisition software has been used. From a minimum of three valid expiratory manoeuvres the highest forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and peak flow (PEF) were selected. The highest maximal

mid-expiratory flow (MMEF) was selected from a manoeuvre with a FVC within 5% or 100 ml of the highest FVC. Thus, selected pulmonary function values could be obtained from different curves. All pulmonary function data fulfilling the general acceptability criteria of the ECCS (such as no hesitant start, no early termination of the manoeuvre) were used in the analysis, including tests for which the highest FVC or FVC₁ was more than 5% or 100 ml larger than the second highest. This is in agreement with the recommendations of the ATS [13].

Dust sampling and assay for Der p I

Dust was sampled from the floors of the living room and the bedroom of the child, and the mattress of the child. Dust samples were obtained using a vacuum cleaner (Philips Topomatic T518), equipped with a special nozzle (ALK, Horsholm, Denmark) to collect dust on a cellulose filter (Schleicher & Schuell, 589 black ribbon 70 mm). The power of the vacuum cleaner was set at 1000 W. From each living room and bedroom floor an area of 2 m² was sampled for 4 min. The entire upper mattress surface with an area of approximately 2 m², was vacuum cleaned for 2 min after the bedding had been removed. Between each sampling, the sampling nozzle was cleaned thoroughly with 70% ethanol. After sampling the filters were placed in Petri dishes and stored at -20°C until analysis. A representative part (approximately 200 mg) of the fine dust (the dust was not sieved) from each sample was extracted by shaking for 2 h in 2 ml ammoniumbicarbonate buffer. The amount of *Der p I* was measured with a monoclonal enzyme immunosorbent assay (EIA), manufactured by ALK, Horsholm, Denmark, according to Lind [3]. The detection limit of the assay was 20 ng *Der p I*/g dust. Coefficients of variation were determined on the basis of 169 floor dust samples of wall-to-wall carpets, each of the 2 m² were sampled separately, 23 floor dust samples of wall-to-wall carpets that were extracted in duplicate, and 130 floor and mattress dust extracts that were analysed in duplicate. For ln-transformed floor dust concentrations the mean coefficient of variation was 5.3%, which was mainly due to sampling (sampling 4.7%, dust extraction 1.7%, analysis 1.5%). The results were also expressed in ng *Der p I*/m². Sampling was performed from October to November 1990.

Questionnaire

A detailed questionnaire was administered to the parents/guardians, about a variety of home characteristics. These included allergen avoidance measures taken in the past, types of floor coverings, and a number of risk

factors for childhood respiratory disease (amongst others, the presence of an unvented gas fired water heater (a so-called 'geyser'), smoking in the home, the presence of pets and socio-economic status).

Statistical analyses

Statistical analysis was performed by means of the Statistical Analysis System (SAS, version 6.06, SAS Institute Inc., Cary, NC, USA). The distributions of the *Der p I* concentrations were right skewed and became by approximation normally distributed after ln-transformation. To evaluate the relationship between case-control status and *Der p I* exposure, *Der p I* concentrations were grouped into three categories: < 2000 ng/g dust, 2000–10 000 ng/g dust, and > 10 000 ng/g dust. These levels correspond with the provisional hygienic thresholds discussed earlier. In the analysis, the lowest exposure level was used as a reference category, and odds ratios were estimated for intermediate and high exposure. The 'odds ratio' is a common measure of statistical association between exposure and disease in case-control studies [14]. Using three instead of just two categories of exposure, has the advantage that a crude exposure-response relationship can be detected if there is one.

The following comparisons were made:

- 1 Cases to controls, as defined by the screening questionnaire;
- 2 Asthmatic cases and controls;
- 3 Children with chronic cough, without other symptoms of asthma, to controls;
- 4 Sensitized cases to non-sensitized controls. This analysis was based on the assumption that *Der p I* exposure leads to sensitization among genetically pre-disposed subjects, and continued exposure leads subsequently to symptoms. This analysis was done for all three case definitions in 1–3;
- 5 Sensitized cases to non-sensitized cases. This analysis was based on the findings reported by Lau *et al.* [6] and Wickman *et al.* [8], referred to in the introduction;
- 6 Cases to controls (as defined in 1–4), removing all subjects from the analysis in whose homes allergen measures had been taken;
- 7 Sensitized cases to non-sensitized cases, with the same restriction;
- 8 Finally, the analyses were repeated using *Der p I*/m² as exposure variable instead of *Der p I*/g dust. All comparisons were made with and without adjustment (by logistic regression [14]) for a number of potential confounders. As such, passive smoking, the presence of an unvented geyser, the presence of

feathered or furred pets, age, gender, and socioeconomic status were considered.

Some additional analyses were made to compare geometric mean *Der p* I levels between cases and controls. This was done to gain insight into the actual differences in exposure between the two groups. Analyses were also made using other cut-off points than 2000 and 10 000 ng/g dust. This was done to assess the sensitivity of the results to the level of the cut-off point. The results of the major analyses are reported in tabular form. The results of others are referred to in the text.

Results

Table 1 presents information on some characteristics of the study population. The case and control groups were found not to be different regarding mean age, the proportion of smokers and pets in the home, and the type of floor covering in the living room. However, there were more boys among the cases, and textile flooring in the bedroom was less common among cases. Among the cases, there were 76 children with doctor-diagnosed asthma, and 81 children for whom chronic cough was reported without other symptoms of asthma. For the

asthmatics, the proportions of girls, smokers and pets in the home, and textile floor coverings in the living and bedroom were lower compared with the entire group of cases. A higher proportion of cases was sensitized (RAST > 0) against house dust mite compared with the controls (37.9% vs 12.3%). The highest sensitization rate was found for asthmatic children. Allergen avoidance measures taken in the home because of respiratory symptoms of one or more of the occupants, were reported only for cases, more frequently for asthmatic children than for children with chronic cough.

A valid pulmonary function test was obtained for 93% ($n = 473$) of the children. The percentage difference of pulmonary function of cases, asthmatics and children with chronic cough, compared with the controls, was calculated by linear regression, adjusting for age, height, weight and gender. For all cases and the children with doctor-diagnosed asthma there was a significant ($P < 0.05$) difference of FEV₁, PEF, FEV₁/FVC and MMEF, compared with the control group. For children with chronic cough, the same pulmonary function parameters were also lower, compared with those of the controls, but these differences were not statistically significant (Table 1).

Table 1. Characteristics of the study population

	Controls ($n = 257$)	Cases ($n = 259$)	Asthma ($n = 76$)	Chronic cough ($n = 81$)
Girls (%)	58.8	47.9	38.0	53.5
Age, mean (years)	8.6	8.3	8.5	8.0
Smokers in the home (%)	58.1	58.0	46.2	65.1
Textile flooring in living room (%)	78.6	78.0	73.4	76.7
Textile flooring in bedroom (%)	77.8	66.0	46.8	77.9
Pets present in the home (%)	61.8	58.5	49.4	59.3
Never kept pets in the home (%)	16.3	17.8	29.1	11.6
Sensitized against dust mite (Rast ≥ 1 , %)	12.3	37.8	54.7	27.2
Percentage decline of pulmonary function				
FVC		-0.6	0.4	-1.8
FEV ₁		-2.7*	-5.1*	-1.8
FEV ₁ /FVC		-2.2*	-5.5*	0.0
PEF		-3.2*	-5.7*	-2.2
MMEF		-8.4*	-18.3*	-2.1
Reported allergen avoidance measures taken because of respiratory complaints:				
Change of living room floor cover	0.0	13.1	25.3	9.3
Change of bedroom floor cover	0.0	22.0	36.7	12.8
Change of mattress	0.0	7.3	15.2	6.9

* $P < 0.05$.

Table 2. Concentrations of *Der p I* (geometric mean [GM], geometric standard deviation [GSD], range) in house dust of cases, expressed in ng/g dust and ng/m²

Location	n	ng/g dust			ng/m ²		
		GM	GSD	Range	GM	GSD	Range
Living room	257	2035	6.4	85-150 519	500	10.3	7-391 993
Smooth floor covering	57	414	3.2	106-31 084	30	5.2	7-28 141
Textile floor covering	200	3207	5.8	85-150 519	1122	6.2	27-391 993
Bedroom	258	1959	4.8	86-67 092	320	10.2	4-44 567
Smooth floor covering	87	669	2.7	86-5247	31	3.1	4-1547
Textile floor covering	171	3381	4.6	98-67 092	1059	6.1	11-44 567
Mattress	258	4643	4.0	95-72 992	1431	5.7	6-43 436
In bedroom with smooth floor cover	88	4407	4.0	170-68 506	1342	5.9	30-26 969
In bedroom with textile floor cover	170	4770	4.0	95-72 992	1479	5.7	6-43 436

The *Der p I* concentrations per g dust and per m² varied widely (Tables 2 and 3). Due to sampling errors, data were missing for the living rooms of two cases and two controls, for the bedrooms of one case and one control, and for the mattresses of one case and three controls. The highest geometric mean *Der p I* concentrations were found for mattress dust. The geometric mean concentrations in dust from smooth floorings were significantly lower than those found in dust from textile floorings (*t*-test, *P* < 0.001). The *Der p I* concentrations expressed in ng/g dust were divided into three categories as described. In 83.4% of the homes of cases and 89.1% of the homes of controls, *Der p I* concentrations higher than 2000 ng/g dust were found. In 53.7% of the homes of cases and 56.6% of those of controls, the highest *Der p I* concentration found exceeded the proposed threshold limit value of 10 000 ng/g dust.

Table 4 shows the crude odds ratios for the comparison of cases and controls. The lowest category of the *Der p I* concentrations (< 2000 ng/g dust) was used as reference. The estimated odds ratios were mostly smaller than one. Only for bedrooms with textile floorings an odds ratio of 1.00 was found when the lowest and highest categories of *Der p I* were compared. For asthmatic children and children with chronic cough similar odds ratios were found. This suggests a negative association between the *Der p I* concentrations in house dust and reported respiratory symptoms. Using logistic regression analysis, the crude odds ratios were adjusted for passive smoking, the presence of an unvented geyser, the presence of feathered or furry pets, age, gender and socioeconomic status. The adjusted odds ratios were similar to the crude odds ratios. Odds ratios could not be calculated for smooth floorings separately, because there

Table 3. Concentrations of *Der p I* (geometric mean [GM], geometric standard deviation [GSD], range) in house dust of controls, expressed in ng/g dust and ng/m²

Location	n	ng/g dust			ng/m ²		
		GM	GSD	Range	GM	GSD	Range
Living room	255	2763	6.2	99-95 222	704	11.1	5-45 030
Smooth floor covering	55	331	2.3	99-2067	25	2.9	5-561
Textile floor covering	200	4949	4.8	101-95 222	1765	5.9	12-45 030
Bedroom	256	2475	5.0	93-103 559	593	9.4	4-57 354
Smooth floor covering	57	599	2.7	93-14 103	34	3.5	4-1469
Textile floor covering	199	3715	4.5	99-103 559	1345	5.6	20-57 354
Mattress	254	5558	3.9	112-280 880	1730	5.5	2-153 123
In bedroom with smooth floor cover	57	4675	3.5	230-38 874	1626	4.9	21-48 387
In bedroom with textile floor cover	197	5837	4.1	112-280 880	1762	5.8	2-153 123

Table 4. Crude odds ratios for elevated *Der p I* concentrations in house dust; comparison of cases and controls (95% confidence limits in parentheses)

Location	2000–10 000 ng/g vs < 2000 ng/g	> 10 000 ng/g vs < 2000 ng/g
Living room	0.76 (0.50–1.16)	0.72 (0.47–1.10)
Living room (textile flooring)	0.63 (0.39–1.03) [#]	0.59 (0.36–0.96)*
Bedroom	0.75 (0.50–1.12)	0.79 (0.47–1.10)
Bedroom (textile flooring)	0.80 (0.49–1.31)	1.00 (0.60–1.67)
Mattress	0.62 (0.40–0.98)*	0.69 (0.44–1.10)

[#] $P < 0.10$. * $P < 0.05$.

were very few dust samples with *Der p I* levels higher than 2000 ng/g. In the second analysis, a comparison was made between cases sensitized against house dust mites, and controls who were not sensitized against house dust mites. Again, most of the crude odds ratios were smaller than 1. Only for textile floorings in the bedroom the calculated odds ratios were greater than 1 and marginally significant ($P < 0.10$), when the lowest and highest categories of *Der p I* were compared (odds ratio 2.20). The comparison of sensitized asthmatics and non-sensitized controls gave similar odds ratios. For sensitized children with chronic cough most crude odds ratios were larger than one but not statistically significant. The adjusted odds ratios were comparable with the crude odds ratios.

The next step was a restriction of the analysis to cases who were sensitized against dust mites and cases who were not sensitized against dust mites (Table 5). Most of the crude odds ratios became greater than one after this

restriction. The highest odds ratios were found when comparing the lowest and highest categories of *Der p I* concentrations. However, the crude odds ratios were not statistically significant. Adjustment for confounding variables did not change the odds ratios substantially. When comparing sensitized asthmatics with non-sensitized asthmatics, and sensitized children with chronic cough with non-sensitized children with chronic cough, most odds ratios became also greater than 1. For both asthmatics and children with chronic cough the odds ratios were higher than for the entire group of cases. For example, the following odds ratios were found comparing the lowest and highest categories of *Der p I* concentrations for sensitized asthmatics vs non-sensitized asthmatics: 1.46 (95% confidence interval 0.47–4.49) for the living room, 1.92 (95% confidence interval 0.43–8.54) for the bedroom, and 2.75 (95% confidence interval 0.75–10.10) for mattresses. However, due to the smaller numbers of children

Table 5. Crude odds ratios for elevated *Der p I* concentrations in house dust; comparison of cases sensitized to dust mites and cases not sensitized to dust mites, (i) irrespective of allergen avoidance measures taken in the homes (I), and (ii) restricted to those living in homes where no allergen avoidance measures had been taken in the past (II) (95% confidence limits in parentheses)

Location	2000–10 000 ng/g vs < 2000 ng/g	> 10 000 ng/g vs < 2000 ng/g
I		
Living room	1.13 (0.60–2.12)	1.34 (0.71–2.53)
Bedroom	0.68 (0.36–1.26)	1.13 (0.58–2.21)
Mattress	1.04 (0.54–2.02)	1.49 (0.78–2.85)
II		
Living room	1.29 (0.62–2.67)	1.54 (0.74–3.19)
Bedroom	1.19 (0.50–2.83)	2.54 (1.11–5.83)*
Mattress	1.19 (0.58–2.46)	1.80 (0.90–3.62) [#]

[#] $P < 0.10$. * $P < 0.05$.

involved, the confidence intervals became wider. A comparison was also made between controls sensitized against dust mite and controls not sensitized against dust mites. The odds ratios were comparable with those found comparing sensitized cases with non-sensitized cases. As shown in Table 1, parents of children with respiratory symptoms reported to have taken allergen avoidance measures in the past more often than parents of control children. This may have caused lower *Der p 1* concentrations in dust of the homes of cases. The relationship between exposure to house dust mite allergen and sensitization might therefore be obscured when current *Der p 1* concentrations in house dust are compared between cases and controls. Therefore, the analysis was repeated by comparing cases sensitized against dust mites and cases not sensitized against house dust mites, both living in homes where no allergen avoidance measures had been taken in the past. This implied that the analysis was restricted to cases with textile floorings in living room and/or bedroom, and cases whose mattresses never had been changed because of respiratory symptoms. The results are presented in Table 5. All odds ratios increased after this restriction, and some now became statistically significant. The highest odds ratios were found by comparing the lowest and highest categories of *Der p 1* content in house dust. The same picture was obtained comparing sensitized asthmatics with non-sensitized asthmatics, and sensitized children with chronic cough with non-sensitized children with chronic cough, all living in homes where no allergen avoidance measures had been taken. Due to the smaller numbers of children involved the confidence intervals became wider. The adjusted odds ratios were generally higher than the crude odds ratios, and some became statistically significant.

Comparisons were also made between the geometric mean concentrations of *Der p 1* for the different groups of cases and controls. The results were essentially the same. For example, the geometric mean concentrations in dust of the living room with textile floorings were 3207 and 4949 ng/g dust for cases and controls respectively ($t = -2.61$, $P < 0.01$). The geometric mean concentration for cases sensitized against house dust mites was 4256 ng/g dust, compared with 2816 ng/g dust for non-sensitized cases ($t = 1.58$, $P = 0.11$).

For the sensitized and non-sensitized cases, both living in homes where no allergen avoidance measures had been taken, adjusted odds ratios were also calculated using *Der p 1* concentrations below 1000 ng/g dust as reference and concentrations equal to or higher than 1000 ng/g dust as exposed. The adjusted odds ratio for living rooms with textile floorings was 1.17 (95% confidence interval 0.54–2.54). For bedrooms with textile floorings the

adjusted odds ratio was 1.62 (95% confidence interval 0.62–4.20), and for mattresses 3.09 (95% confidence interval 1.13–8.39).

Using the amount of *Der p 1*/m² as exposure variable, comparisons were made between the geometric mean concentrations for the different groups of cases and controls. The results of these comparisons were not different from the results using the amount of *Der p 1*/g dust as exposure variable (data not shown).

Discussion

In this study, high concentrations of *Der p 1* were found in the dust of textile floorings and mattresses. In 86% of the houses included in the study, *Der p 1* concentrations exceeded the provisional threshold limit of 2000 ng/g dust. This limit is regarded as representing a risk for the development of specific IgE to house dust mite allergen in genetically predisposed individuals [4]. In 55% of the homes, concentrations of more than 10 000 ng *Der p 1*/g dust were found, representing an increased risk for acute attacks of asthma [4]. The concentrations found in dust from smooth floorings were 5–10 times lower than the concentrations found in dust from textile floorings. The *Der p 1* concentrations (in ng/g dust) found in this study were comparable with those reported by Price *et al.* [7] and Reiser *et al.* [15]. Lower concentrations were reported by Lau *et al.* [6] and Wickman *et al.* [8], whereas Sporik *et al.* [16] reported somewhat higher concentrations of *Der p 1*/g dust. We did not sieve the dust prior to analysis. However, this does not seem to be the explanation for the higher concentrations found in our study, as Reiser *et al.* [15] and Sporik *et al.* [16] sieved the dust prior to analysis, whereas Wickman *et al.* [8], Lau *et al.* [6] and Price *et al.* [7] analysed unsieved dust.

The prevalences of house dust mite sensitization among cases and controls were comparable with those reported in the literature. Reported prevalences range from 45 to 85% among asthmatics and from 5 to 50% among controls [4]. Pulmonary function was measured in all children. Most pulmonary parameter values of the cases were significantly lower than those of the controls. The largest differences were found for children with doctor-diagnosed asthma. These results are in agreement with an earlier Dutch study comparing children with chronic respiratory symptoms to controls [17].

In a crude analysis, without taking into account sensitization against house dust mite and allergen avoidance measures taken in the past, cases were generally exposed to lower *Der p 1* concentrations than controls. Similar results were found for asthmatic children and children with chronic cough. Restriction

of the analysis to cases with elevated serum IgE against dust mites, and to controls without elevated serum IgE levels, taking the type of floor covering into account, increased the odds ratios. However, only the estimated odds ratios for the *Der p* I content in dust of bedrooms with textile floorings became greater than 1.

When the analysis was restricted to cases sensitized to dust mites and cases not sensitized to dust mites, most odds ratios became greater than 1. The highest odds ratios were found comparing the lowest and highest categories of *Der p* I content in house dust, which is indicative of an exposure-response relationship. Similar results were obtained comparing sensitized asthmatics and sensitized children with chronic cough with non-sensitized asthmatics and non-sensitized children with chronic cough respectively. However, the odds ratios were not statistically significant. Odds ratios increased again when the analysis was restricted to homes where no allergen avoidance measures had been taken in the past. This indicates that parents of children with chronic respiratory symptoms take effective allergen reduction measures, and that they do so more often when their children are sensitized against house dust mites. These results are in agreement with those of other cross-sectional studies on the relation between the exposure to house dust mite allergens and sensitization among atopic children. Lau *et al.* [6] reported similar concentrations of house dust mite allergens for atopic and non-atopic children. However, higher concentrations were found for atopic children sensitized to house dust mites than for atopic children not sensitized to house dust mites. Price *et al.* [7] found a positive association between the *Der p* I concentrations in house dust and skin sensitivity, comparing atopic children sensitized to dust mites and atopic children not sensitized to dust mites. Wickman *et al.* [8] also reported higher *Der p* I concentrations in homes of children sensitized to dust mites compared with the concentrations found in the homes of non-sensitized atopic children. When we compared sensitized to non-sensitized cases, the estimated odds ratios at a cut-off point of 1000 ng *Der p* I/g dust, were also all greater than 1. These results suggest that the risk for sensitization might also be increased at *Der p* I concentrations below the proposed threshold limit of 2000 ng/g dust, above which the risk for genetically predisposed individuals for the development of specific IgE to house dust mites is supposed to be increased [4]. Our results are in agreement with those presented by Price *et al.* [7]. They found no association between skin sensitivity and the *Der p* I concentration in carpet dust at a cut-off point of 2000 ng/g dust. However, with cut-off points of 1000 ng *Der p* I/g dust and 500 ng/g dust, statistically significant differences between atopic

children sensitized to house dust mites and atopic children not-sensitized to house dust mites were found. Lau *et al.* [6] also reported a relationship between the concentrations of *Der p* I and *Der f* I in house dust below 2000 ng/g dust and the risk for sensitization. Using concentrations of *Der p* I plus *Der f* I below 400 ng/g dust as reference and concentrations equal to or higher than 2000 ng *Der p* I plus *Der f* I/g dust as exposed, they found an odds ratio of 7 (95% confidence interval 3–18).

Colloff *et al.* [18] recently suggested that the concentrations of *Der p* I expressed by m² might be a better estimation of the potential exposure. However, using the amount of *Der p* I/m² as exposure variable, we found the same associations between exposure to house dust mite allergen and sensitization to house dust mite among children with respiratory symptoms.

Sporik *et al.* [16] used the highest allergen level in the home as exposure variable, irrespective of the location of sampling. In our study, in 51% of the houses the highest *Der p* I levels were found in mattress dust. Therefore, the results using the highest *Der p* I concentrations found in the home as exposure variable were similar with those using the levels in mattress dust as exposure variable.

Parents of children with chronic respiratory symptoms were found to have taken allergen avoidance measures regularly in the home. Therefore, lower *Der p* I concentrations might be measured in the houses of children with respiratory symptoms. A comparison of the present concentrations in house dust of cases and controls therefore obscures the relationship between the exposure to house dust mite allergens and sensitization. This hampers the estimation of the association between exposure to house dust mite allergen, sensitization and the development of respiratory symptoms. Prospective studies, or case-control studies based on incident cases, are needed to further clarify the relationship between dust mite allergen exposure, sensitization and childhood respiratory symptoms.

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