

Mite allergen exposure is a risk for the incidence of specific sensitization

Joachim KuehrMD^a [\[MEDLINE LOOKUP\]](#)

Thomas FrischerMD^a [\[MEDLINE LOOKUP\]](#)

Rolf MeinertMSc^a [\[MEDLINE LOOKUP\]](#)

Regina BarthMD^a [\[MEDLINE LOOKUP\]](#)

Johannes ForsterMD^a [\[MEDLINE LOOKUP\]](#)

Sabine Schraub^a [\[MEDLINE LOOKUP\]](#)

Radvan UrbanekMD^b [\[MEDLINE LOOKUP\]](#)

Wilfried KarmausMD, MPH^c [\[MEDLINE LOOKUP\]](#)

• Freiburg, Germany, Vienna, Austria, and Hamburg, Germany

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Abstract

Background: Mite allergen exposure is essential for the process of specific allergic sensitization. However, it is not clear whether incidence of specific sensitization at school age depends on the level of mite antigen exposure. Therefore the relationship between mite allergen exposure and incidence of specific sensitization was investigated.

Methods: Eighteen hundred twelve primary school children were enrolled in a population-based 2-year follow-up study. In three consecutive skin prick tests (SPTs), each 12 months apart, sensitization to *Dermatophagoides pteronyssinus* (Dpt) and six non-Dpt allergens was ascertained. To assess exposure to Der p I between the first and second SPTs (period I) and the second and third SPTs (period II), the amount of antigen per gram of dust (taken from the children's mattresses) was measured. By using the SPT reactions to Dpt as a basis, conversions after "no wheal" were classified as doubtful incidence (average yearly incidence = 6.7%) or definite incidence (average yearly incidence = 3.2%). Then, with the use of multiple logistic regression, the risk of exposure to Der p I (medians: 1.4 µg/gm in period I, 1.6 µg/gm in period II) was analyzed with adjustment being made for gender, low gestational age, parental atopy, and initial sensitization to non-Dpt allergens.

Results: Regarding doubtful incidence, the analysis failed to identify a reliable cutoff point of exposure. For definite incidence, the Der p I exposure represents a significant risk in the total population, starting from a concentration of 9 µg/gm. This effect is modified by an initial sensitization to non-Dpt allergens: for these children exposure to concentrations above 2 µg/gm poses a significant risk, whereas for the population without other initial sensitizations, only an extremely high cutoff limit (>80 µg/gm) gains significance.

Conclusion: Our data suggest that a concentration limit of 2 µg Der p I antigen per gram of dust should be

regarded as minimal avoidance level for primary prevention in children with sensitization to other inhalant allergens. (J ALLERGY CLIN IMMUNOL 1994;94:44-52.)

CI	Confidence interval
Df	<i>Dermatophagoides farinae</i>
Dpt	<i>Dermatophagoides pteronyssinus</i>
logOR	Natural logarithm of the odds ratio
OR	Odds ratio
SPT	Skin prick test

Key words: [Dust mite](#), [exposure](#), [sensitization](#), [incidence](#), [childhood](#), [risk factor](#), [population-based study](#)

Inhalant allergy poses a worldwide health problem to large segments of the population and is relevant from early childhood to adulthood.¹ The clinical outcome, mainly represented by bronchial asthma and chronic rhinitis, has been shown to be preceded by sensitization to common inhalant allergens.^{2,3} Numerous studies have focused on the clinical relevance of sensitization to inhalant allergens (e.g., allergens originating from house dust mites).⁴ Intervention studies with patients experiencing allergic symptoms have shown that mite allergen avoidance is effective as a measure of tertiary prevention.⁵ However, primary prevention would require intervention before sensitization to the allergen has taken place. Very few data that are predictive for sensitization have been published on limits of mite allergen exposure.⁶ So far there is no information about the effect of exposure at different levels in groups with a higher or lower genetic risk for allergic responsiveness. For this purpose, studies with unselected populations are required. Thus a population-based 2-year follow-up study involving 1812 primary school children was initiated to investigate the risk of mite allergen exposure for incidence of sensitization to *Dermatophagoides pteronyssinus* (Dpt).

Methods

Data were collected in a longitudinal study designed to assess risk factors for allergy and asthma in children. To obtain a population-based sample of elementary school children, all parents whose children started school in 1989 were invited to participate. Questionnaires were distributed to 2604 families and were returned by 1812 families (70%). Data from the first cross section are presented in detail elsewhere.⁷ Three consecutive skin prick tests (SPTs), each 12 months apart, were carried out in spring 1990 ($n = 1470$), 1991 ($n = 1416$), and 1992 ($n = 1305$). The first and second exposure assessments refer to household visits between December and March of the respective winter in which dust samples from the children's mattresses were taken. The study was approved by the local ethical committee and also by local school authorities.

Questionnaire

A standardized questionnaire was filled out by the parents in 1990 before the first SPT. Questions of interest for this article were: bronchial asthma and hay fever (doctor's diagnoses); parental atopy (maternal or paternal history of asthma, hay fever, or eczema); low gestational age (child born at least 3 weeks before term); educational level (highest level achieved at school by father or mother); gender of the child.

Dust sampling and *Der p I* measurement

The dust was collected from the total area of the upper side of each mattress in a standardized manner with the same device (collector and filter; ALK, Horsholm, Denmark) and the same type of vacuum cleaner (Miele & CIE., GmbH & Co., Guetersloh, Germany) with an air flow of 56 L/sec (specified by the manufacturer) for 5

minutes. Each sample was transported to the laboratory immediately and stored at -20°C until it was extracted. Extraction and quantification by ELISA was performed with species-specific antibodies to *Der p I* (ALK) according to the method described by Lau et al.⁶ The antigen concentration in the sample was calculated by using the absorption of the sample and the shape of a standard curve with a range from 1.6 to 400 ng/ml (ALK) (internal standards for *Der p I* related to National Institute of Biological Standards and Control 82/518⁸). The monoclonal antibody to *Der p I* used (Nhp5) was shown to be highly specific.⁹ The intraassay ($n = 15$; interassay: $n = 23$) coefficient of variation ranged from 2.5% to 12% (3% to 12%) in our laboratory. Assay sensitivity was 0.004 μg antigen per gram of dust. Assays were carried out with three dilutions of each extracted sample (1:10, 1:50, 1:100); each dilution was assayed routinely in double control manner. The *Der p I* concentration used for exposure assessment is the arithmetic mean of values in the linear section of the standard curve.

SPT

On each of the three occasions, the SPT was carried out by trained members of staff under the supervision of a physician who used the same equipment and technique each time.⁷ Seven purified and immunochemically characterized inhalant allergens (ALK) were applied to the child's forearm with the aid of an uncoated Phazet needle (Pharmacia, Uppsala, Sweden). Extracts from grass pollens (mixture of the six most common species), birch and hazel pollens, *Dpt* and *D. farinae* (*Df*), and cat and dog dander were used (concentration: 10 Histamine Equivalents in prick testing). Histamine hydrochloride (10 mg/ml) and sodium chloride (9 gm/L) were applied as control solutions. The reactions were recorded after 15 minutes. The largest and perpendicular diameters of a wheal were measured, and the arithmetic mean was calculated. A reaction to the negative control was subtracted from the allergen value.

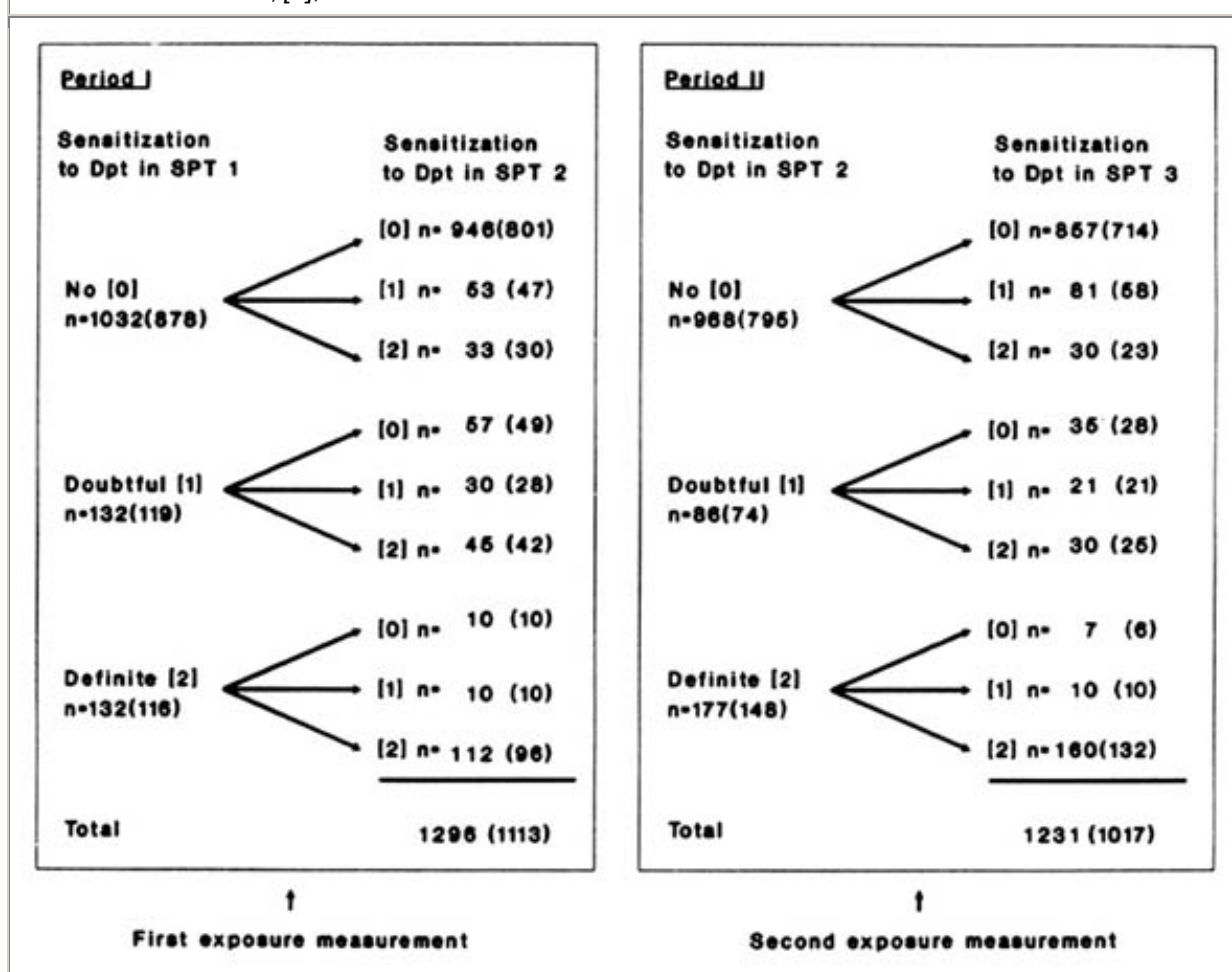
Classification of the SPT reaction

Results of SPTs were classified as "definite sensitization," "doubtful sensitization," or "no sensitization." Definite sensitization requires a wheal reaction to the allergen of 2 mm or larger in diameter and a ratio [wheal to allergen/wheal to histamine] of 0.5 or greater. Doubtful sensitization is defined by a wheal reaction to the allergen, which does not fulfill the criteria for definite sensitization. No sensitization is defined by no wheal reaction to the allergen.

Statistical analysis

Sensitization to *Dpt* is classified into three states: no sensitization (state 0), doubtful sensitization (state 1), and definite sensitization (state 2). A transition is defined as a change between two states within a period of 1 year (period I = between 1990 and 1991, period II = between 1991 and 1992) (■Fig. 1). A definite incidence, for example, is described by a transition from state 0 to state 2, and the yearly rate of definite incidences corresponds to the transition probability (TP_{02}), which can be estimated as the number of changes from state 0 to state 2 within the two periods *divided by* the total number of person-years accrued in state 0 within the two periods. We analyzed the transitions (changes in states) 0 to 1, 0 to 2, and 1 to 2, which correspond to doubtful incidences, definite incidences, and increases in the degree of sensitization to *Dpt*, respectively. Analyses were carried out in multistate logistic regression models, which are a simplification of the multistate model for Markov processes in continuous time¹⁰ and an extension of the generalized person-years approach.¹¹ Based on these approaches, the observations from 2 yearly periods are pooled and evaluated in one analysis. Three separate logistic regression analyses were performed for the state transitions 0 to 1, 0 to 2, and 1 to 2, whereby subjects with a change are considered cases, and subjects remaining in the initial state are considered references. The approach used enables the analysis of time-dependent covariates. When analyzing the transitions in period I, the *Der p I* concentration measured in winter 1990/91 is considered a risk factor; when analyzing the transitions in period II, the concentration of winter 1991/92 is used. In addition to *Der p I*, gender, low gestational age, parental atopy, initial definite sensitization to non-mite allergens and initial at least doubtful sensitization to *Df* are specified as potentially confounding variables in the regression models. In order to assess the cutoff point at which exposure to *Der p I* starts to be a significant risk factor for an incidence, the models are constructed with 30 different cutoff points, ranging from *Der p I* concentrations of 0.1 to 100 $\mu\text{g}/\text{gm}$. The odds ratios (ORs) calculated from logistic regressions with the statistical analysis system¹² are estimates of relative risks. The log odds ratios (logORs) and the corresponding 95% confidence intervals (CIs) were plotted against the allergen concentration.

FIG. 1. Numbers of transitions regarding status of sensitization to *Dpt* from first to second SPT (period I) and from second to third SPT (period II), respectively. Numbers in parentheses are numbers of participants with a respective *Der p I* exposure measurement. [0], No sensitization (no wheal); [1], doubtful sensitization; [2], definite sensitization.



Results

In the course of the 2-year follow-up study, the number of participants decreased from 1812 (initial age: mean, 7.3 years; standard deviation, 0.4 years) to 1392 (data with regard to the incidence of sensitization). However, the distribution of relevant variables did not change (Table I).

TABLE I. Distribution of relevant variables in total initial and total final samples

Variable	Total initial sample	Total final sample
	(n= 1812) (%)	(n= 1392) (%)
Asthma	3.5	3.6
Hay fever	5.9	6.0
Parental atopy	37.4	39.4
Low gestational age	7.6	7.6
Female gender	51.3	52.0

Educational level

High	37.3	37.9
Medium	28.3	29.2
Initial definite sensitization to 1 of 5 non-mite allergens	14.8 (of $n = 1470$)	15.0
Initial at least doubtful sensitization to <i>Df</i>	15.8 (of $n = 1470$)	15.2

The changes (transitions) regarding sensitization to *Dpt* between SPT 1 and SPT 2 (period I) and between SPT 2 and SPT 3 (period II) are presented in Fig. 1. During period I, among 1034 individuals with initially *Dpt*-negative results, in 5.1% a doubtful incidence (transition 0 to 1: $n = 53$) and in 3.2% a definite incidence (transition 0 to 2: $n = 33$) occurred. During period II, doubtful and definite incidences are obvious in 8.4% ($n = 81$) and in 3.1% ($n = 30$), respectively. The overall transition probability is 6.7% for doubtful incidence and 3.2% for definite incidence. In addition to these incidences, in the case of those children starting with doubtful sensitization, a change to definite sensitization (transition 1 to 2) occurred in 34.1% (period I) and 34.9% (period II).

Regarding the two exposure assessments, access was possible to 1113 households in period I and 1017 in period II. The *Der p I* concentration derived from the first measurement (median: 1.39 $\mu\text{g/gm}$; 5th to 95th percentile: 0.04 to 41.76 $\mu\text{g/gm}$) is highly correlated (Spearman: $r_s = 0.81$, $n = 879$, $p = 0.0001$) with the second measurement (median: 1.6 $\mu\text{g/gm}$; 5th to 95th percentile: 0.08 to 62.57 $\mu\text{g/gm}$).

Multivariate analysis

In Table II logistic regression analyses of doubtful incidence and definite incidence and of change from doubtful to definite sensitization to *Dpt* are compared with an arbitrary cutoff point of 10 $\mu\text{g/gm}$ *Der p I*. When doubtful and definite incidences are compared, similar risk estimations for each of the six independent variables can be seen. The effects are more strongly pronounced for definite incidence than for doubtful incidence. A prior non-mite sensitization and a wheal reaction to *Df* are significantly associated with both a doubtful and a definite incidence. A *Der p I* concentration above 10 $\mu\text{g/gm}$ is significantly associated with a definite incidence (OR = 2.2, $p = 0.013$). In the case of doubtful incidence, only a tendency ($p = 0.21$) toward a risk of exposure on the basis of this limit (OR = 1.4) can be seen. With regard to a change from doubtful to definite sensitization, all associations, with the exception of parental atopy, are less pronounced, and only an "initial at least doubtful sensitization to *Df*" gains statistical significance (OR = 2.7, $p = 0.016$).

TABLE II. Odds ratios (OR and 95% CI) and p values derived from multiple logistic regression analyses

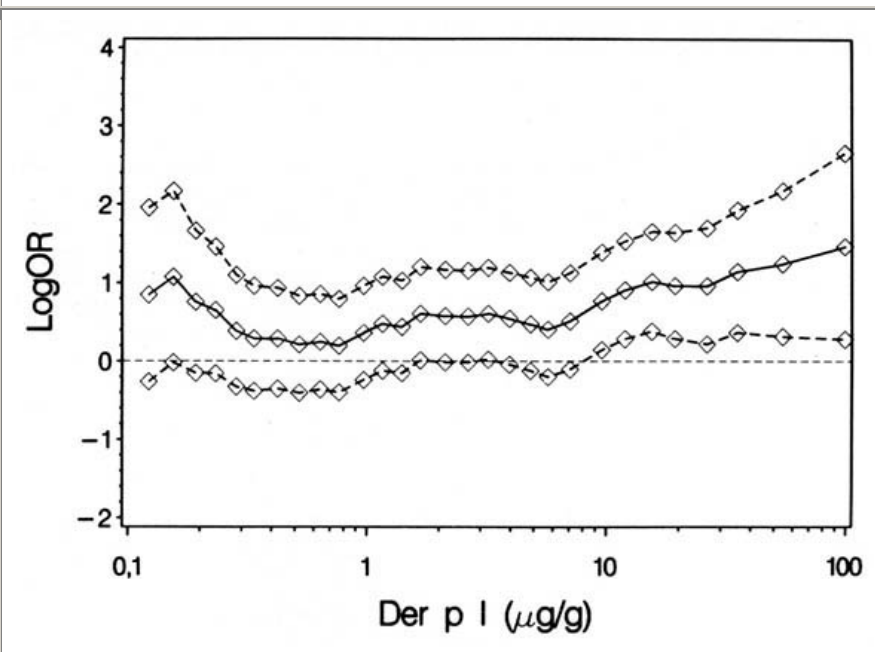
Independent variables	Doubtful incidence transitions; ($n = 105$ $n = 1501$ references)			Definite incidence ($n = 53$ transitions; $n = 1501$ references)			Change from doubtful to definite sensitization ($n = 67$ transitions; $n = 49$ references)		
	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
<i>Der p I</i> concentration > 10 $\mu\text{g/gm}$	1.4	0.8-2.2	0.21	2.2	1.2-4.1	0.013	0.6	0.2-1.7	0.34
Initial definite sensitization to 1 of 5 non-mite allergens	4.4	2.7-7.2	0.0001	6.6	3.5-12.5	0.0001	1.5	0.7-3.3	0.33
Initial at least doubtful sensitization to <i>Df</i>	4.6	2.4-8.5	0.0001	6.9	3.2-14.6	0.0001	2.7	1.2-6.2	0.016

Parental atopy	1.3	0.8-2.0	0.26	1.7	0.9-3.0	0.09	2.1	0.95-4.6	0.07
Female gender	0.8	0.5-1.2	0.25	0.7	0.4-1.2	0.18	0.9	0.4-2.0	0.75
Low gestational age	1.0	0.4-2.2	0.94	1.0	0.3-3.2	0.97	0.6	0.1-3.2	0.56

Dependent variables are doubtful incidence (transition 0 to 1), definite incidence (transition 0 to 2), and change from doubtful to definite sensitization (transition 1 to 2) to *Dpt*, respectively.

The risk of allergen exposure was investigated by using a spectrum of 30 dichotomous cutoff points, each as independent variable in the logistic regression models for doubtful and definite incidence. For doubtful incidence, no increase in the logORs can be seen for concentrations ranging from 0.1 to 10 µg/gm, and no statistical significance is yielded (data not displayed). Analysis of definite incidence shows that from a concentration of 9 µg/gm, exposure starts to represent a significant risk (95% CI of logOR does not include 0) (■Fig. 2). At this cutoff point the logOR is approximately 0.7, corresponding to an OR of 2.

FIG. 2. LogORs for relationship between *Der p I* exposure and risk for a definite incidence of sensitization to *Dpt* in the total population. LogORs (solid line) and 95% CIs (dashed lines) are based on logistic regressions with a spectrum of 30 dichotomous cutoff points for the *Der p I* concentration. Analyses are controlled for initial at least doubtful sensitization to *Df*, initial definite sensitization to one of five non-mite allergens, gender, parental atopy, and low gestational age.



The effect shown in ■Fig. 2 is modified by the presence of initial reactivity to a non-*Dpt* allergen. If both cases and references are restricted to children initially showing either a definite sensitization to non-mite allergens or at least a doubtful sensitization to *Df*, the relative risk of exposure starts to be statistically significant from a

cutoff point of 2 µg/gm (logOR 0.8 OR 2.2) (■Fig. 3). For the complementary population with no other sensitization initially, the relative risk gains statistical significance only for an extremely high cutoff point (■Fig. 4). The effect modification regarding definite incidence is clarified in ■Table III, showing the risk of exposure based on a cutoff point of 10 µg/gm in the total and the stratified population. For the total population, both non-*Dpt* sensitizations initially present show comparable ORs (OR for definite sensitization to a non-mite allergen = 6.6; OR for at least doubtful sensitization to *Df* = 6.9), both exceeding the OR for the *Der p I* exposure (OR = 2.2). In the stratification the exposure is a significant risk only in the case of subjects presensitized to non-*Dpt* allergens. In none of the three logistic regressions are any of the remaining three independent variables statistically significant.

FIG. 3. LogORs for relationship between *Der p I* exposure and risk for a definite incidence of sensitization to *Dpt* for the subpopulation with an initial non-*Dpt* sensitization (i.e., at least doubtful sensitization to *Df* or definite sensitization to one of five non-mite allergens). LogORs (solid line) and 95% CIs (dashed lines) are based on logistic regressions with a spectrum of 30 dichotomous cutoff points for the *Der p I* concentration. Analyses are controlled for gender, parental atopy, and low gestational age.

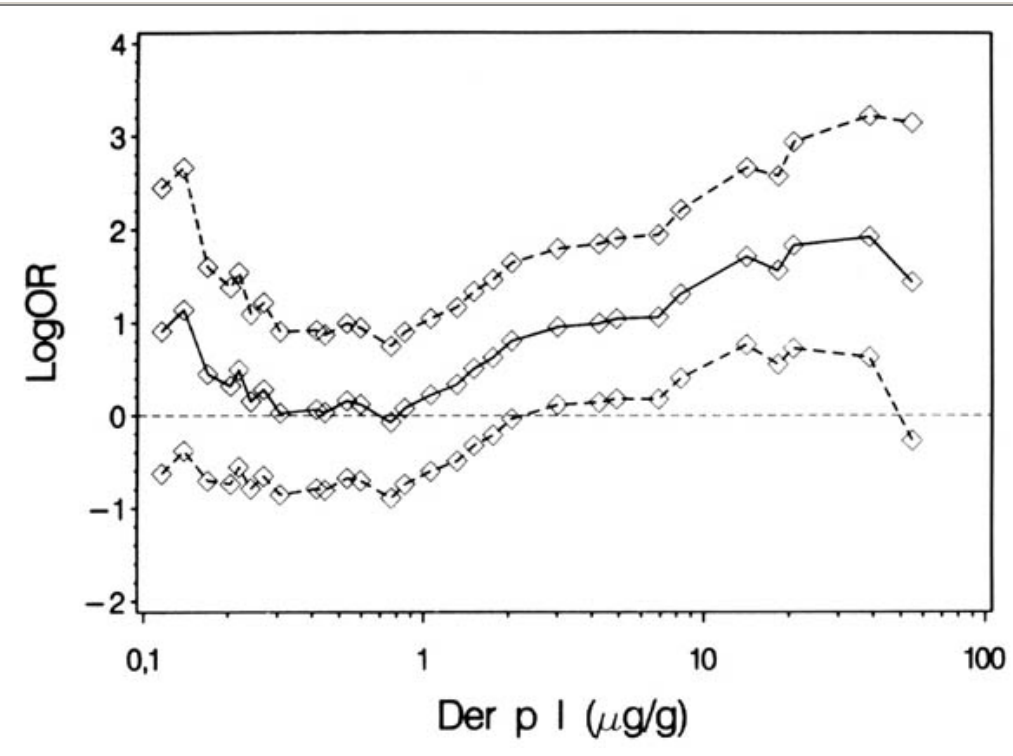


FIG. 4. LogORs for relationship between *Der p I* exposure and risk for a definite incidence of sensitization to *Dpt* for the subpopulation without an initial non-*Dpt* sensitization (i.e., at least doubtful sensitization to *Df* or definite sensitization to one of five non-mite allergens). LogORs (solid line) and 95% CIs (dashed lines) are based on logistic regressions with a spectrum of 30 dichotomous cutoff points for the *Der p I* concentration. Analyses are controlled for gender, parental atopy, and low gestational age.

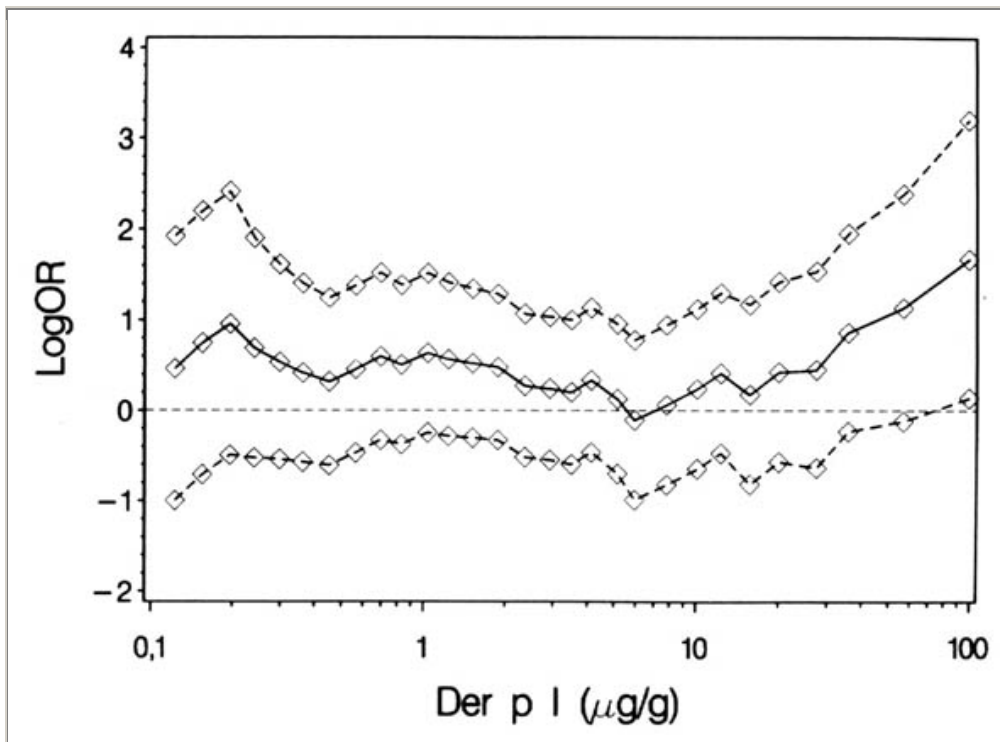


TABLE III. Odds ratios (ORs and 95% CI) and *p* values derived from multiple logistic regression analyses

Independent variables	Definite incidence in total population (<i>n</i> = 53 transitions; <i>n</i> = 1501 references)			Subpopulation with initial sensitization to a non- <i>Dpt</i> allergen (<i>n</i> = 28 transitions; <i>n</i> = 144 references)			Subpopulation without initial sensitization to a non- <i>Dpt</i> allergen (<i>n</i> = 25 transitions; <i>n</i> = 1357 references)		
	OR	95% CI	<i>p</i> Value	OR	95% CI	<i>p</i> Value	OR	95% CI	<i>p</i> Value
<i>Der p</i> I concentration > 10 μg/gm	2.2	1.2-4.1	0.013	4.2	1.7-10.4	0.002	1.2	0.5-3.0	0.64
Initial definite sensitization to 1 of 5 non-mite allergens	6.6	3.5-12.5	0.0001	-	-	-	-	-	-
Initial at least doubtful sensitization to <i>Df</i>	6.9	3.2-14.6	0.0001	-	-	-	-	-	-
Parental atopy	1.7	0.9-3.0	0.09	2.1	0.9-5.1	0.086	1.5	0.7-3.4	0.30
Female gender	0.7	0.4-1.2	0.18	0.8	0.3-1.8	0.55	0.7	0.3-1.5	0.34
Low gestational age	1.0	0.3-3.2	0.97	1.3	0.2-7.1	0.74	1.2	0.3-5.3	0.79

Dependent variable is definite incidence of sensitization to *Dpt* (transition 0 to 2). Analyses are performed for the total population and stratified for an initial sensitization to non-*Dpt* allergens (at least doubtful sensitization to *Df* or definite sensitization to < 1 of 5 non-mite allergens).

Discussion

The objective of this study was to investigate the effect of dust mite allergen exposure on the incidence of sensitization to *Dpt*. For this purpose, the *Der p* I concentration in a dust sample from each child's mattress, which has been shown to be the best indicator of mite infestation, was measured.¹³ Dust sampling was carried out in the same season, providing similar distribution patterns for the months in which the samples were taken. This aspect is of importance because natural variation and measurement errors could result in misclassification. However, when our first and second assessments are compared, the *Der p* I concentrations turn out to be stable to a great degree (correlation coefficient: $r_s = 0.81$). This is in accordance with other findings in Germany on seasonal variation of mite allergen concentrations in house dust samples.¹⁴

Because a general dichotomization of sensitization did not seem to be appropriate we decided to classify positive skin reactions into doubtful and definite sensitizations. Regarding the stability of sensitization to *Dpt*, it has been shown that the classification of definite sensitization remains stable in 85% to 90% of cases (■Fig. 1). The classification of doubtful sensitization is combined with similar transition probabilities for changes to no sensitization (41% to 43%) and to definite sensitization (34% to 35%) (■Fig. 1). Doubtful sensitization could therefore be a measurement error, as well as a real process. Hence, a dichotomization of SPT reactions would result in misclassification, whereas exclusion of doubtful sensitization would lead to incomplete biologic understanding. The differentiation between doubtful and definite sensitization has three major consequences for the analyses. First, it allows the total population to be taken into consideration without excluding participants. Second, the population of interest with no initial sensitization to *Dpt* is open to two different risks, to become sensitized either definitely or doubtfully. Third, it is also possible to determine whether a change from doubtful to definite sensitization is driven by other factors. For the population of interest with no initial wheal reaction to *Dpt*, an overall yearly transition probability of 6.7% for doubtful incidence and of 3.2% for definite incidence is estimated. These yearly incidences of sensitization to a single allergen are at the expected level.^{15, 16}

The hypothetical influence of exposure to *Der p* I was investigated by applying a wide spectrum of dichotomous cutoff points. Statistical relevance of *Der p* I exposure for doubtful incidence of sensitization was not demonstrated. It can be speculated that doubtful incidence might in part represent a measurement error ("diluting" the true incidences) and in part a transitory phase in the natural course of sensitization. Both potential explanations for doubtful incidence are suggested by quantitative rather than qualitative differences regarding the risk factors for doubtful and definite incidence in the explanatory models (■Table II).

A *Der p* I concentration of 9 µg/gm is identified as being the lowest statistically significant exposure limit with regard to definite incidence in the total population (■Fig. 2). However, this analysis does not adequately account for an effect modification caused by an initial sensitization to non-mite allergens or to *Df* (■Figs. 3 and ■4, ■Table III). A cutoff limit of 2 µg/gm appears to be relevant for children with this predisposition. In 40.1% of the group displaying this predisposition, the *Der p* I concentration was found to be above 2 µg/gm. If no initial non-*Dpt* reaction was seen, only an extremely high cutoff point (≈90 µg/gm) provided a significant relative risk, and only a relatively small proportion of 2.6% of these children were exposed to *Der p* I concentrations above this level.

In contrast to the incidences (no initial wheal reaction to *Dpt*), hardly any effect could be found for an increase from doubtful to definite sensitization (■Table II). This could indicate that these children are indeed already sensitized in the doubtful state and therefore switch to the definite state regardless of any potential risk factors. Furthermore, it should be noted that this analysis compares individuals showing an increase in their reaction to those who remain doubtfully sensitized; that is, in the references, a weak but reproducible reaction to *Dpt* is present.

Exposure to dust mite allergens has been suggested as being a risk factor for clinical manifestations.⁴ This study, however, addresses dust mite allergen exposure as a risk factor for specific sensitization. A protective effect of dust mite allergen avoidance was suggested in a study that started with intervention at birth.¹⁷ The measurements of *Der p* I in the households suggest a greater decrease in the allergen load in the case of prophylaxis, resulting in concentrations below 10 µg/gm.¹⁷ However, the study was not designed to separate the potential single effects of mite allergen and concomitant food allergen avoidance. In a 10-year follow-up study, only a weak relationship between *Der p* I exposure at birth and the degree of sensitization to *Dpt* at the end of the study was reported.¹⁸ Yet none of the children who had been exposed to less than 2 µg of *Der*

p I per gram of dust showed sensitization.¹⁸ Cross-sectional data may well demonstrate that atopic children and young adults living in homes with *Der p* I concentrations exceeding 2 µg/gm have significantly higher serum IgE levels to *Dpt* compared with the less exposed population.⁶ However, it remains unknown whether a concentration cutoff point for the estimation of exposure should be regarded as a satisfactory interventional aim and, if so, whether this applies to all segments of populations.

The present population-based study with school-age children demonstrates an increased risk of exposure to the *Der p* I allergen for the incidence of sensitization to *Dpt*. This effect is strongly modified by preceding sensitizations to other common inhalant allergens. For a school-age population, which has this additional risk factor, predictive importance regarding incidence of specific sensitization can be ascribed to the concentration limit of 2 µg/gm *Der p* I. Our data thus suggests that an exposure limit of 2 µg of *Der p* I antigen per gram of dust should be regarded as a minimal avoidance aim for primary prevention in children who are identified as showing responsiveness to other inhalant allergens.

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References

1. Montgomery Smith J. Epidemiology and natural history of asthma, allergic rhinitis and atopic dermatitis (eczema). In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, eds. Allergy: principles and practice. 3rd ed. St. Louis: CV Mosby Company, 1988;2:891-929.
2. Juhlin-Dannfeldt C. About the occurrence of various forms of pollen allergy in Sweden. Acta Med Scand 1948;26:563-77.
3. Hagy GW, Settipane GA. Risk factors for developing asthma and allergic rhinitis. J ALLERGY CLIN IMMUNOL 1976;58:330-6.
4. Platts-Mills TAE, de Weck AL. Dust mite allergens and asthma: a worldwide problem. J ALLERGY CLIN IMMUNOL 1989;83:416-27.
5. Ehnert B, Lau-Schadendorf S, Weber A, Buettner P, Schou C, Wahn U. Reducing domestic exposure to dust mite allergen reduces bronchial hyperreactivity in sensitive children with asthma. J ALLERGY CLIN IMMUNOL 1992;90:135-8.
6. Lau S, Falkenhorst G, Weber A, et al. High mite-allergen exposure increases the risk of sensitization in atopic children and young adults. J ALLERGY CLIN IMMUNOL 1989;84:718-25.
7. Kuehr J, Frischer T, Karmaus W, et al. Early childhood risk factors for sensitization at school age. J ALLERGY CLIN IMMUNOL 1992;90:358-63.
8. Ford AW, Seagroatt V, Platts-Mills TAE, Lowenstein H. A collaborative study on the first international standard of *Dermatophagoides pteronyssinus* (house dust mite) extract. J ALLERGY CLIN IMMUNOL 1985;75:676-86.
9. Lind P, Hansen OC, Horn N. The binding of mouse hybridoma and human IgE antibodies to the major fecal allergen *Der p* I of *Dermatophagoides pteronyssinus*: relative binding site locations and species specificity studied by solid-phase inhibition assay with radiolabeled antigen. J Immunol 1988;140:4256-62.
10. Andersen PK. Multistate models in survival analysis: a study of nephropathy and mortality in diabetes. Stat Med 1988;7:661-70.
11. Cupples LA, D'Agostino RB, Anderson K, Kannel WB. Comparison of baseline and repeated measure covariate techniques in the Framingham Heart Study. Stat Med 1988;7:205-18.

12. SAS Technical Report P-200. SAS/STAT software: CALIS and LOGISTIC procedures. Cary, North Carolina: SAS Institute Inc, 1990.
13. Platts-Mills TAE, Thomas WR, Aalberse RC, Vervloet D, Chapman MD. Dust mite allergens and asthma: report of a second international workshop. *J ALLERGY CLIN IMMUNOL* 1992;89:1046-60.
14. Lau S, Weber A, Wahn U. Longitudinal study on house dust mite allergens [Abstract]. *N Engl Reg Allergy Proc* 1988;9:282.
15. Barbee RA, Lebowitz MD, Thompson HC, Burrows B. Immediate skin-test reactivity in a general population sample. *Ann Intern Med* 1976;84:129-33.
16. Kuehr J, Karmaus W, Frischer T, et al. Longitudinal variability of skin prick test results. *Clin Allergy* 1992;22:839-44.
17. Arshad SH, Matthews S, Gant C, Hide DW. Effect of allergen avoidance on development of allergic disorders in infancy. *Lancet* 1992;339:1493-7.
18. Sporik R, Holgate ST, Platts-Mills TA, Cogswell JJ. Exposure to house-dust mite allergen (*Der p 1*) and the development of asthma in childhood. A prospective study. *N Engl J Med* 1990;323:502-7.

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Articles with References to this Article

This article is referenced by these articles:

Prevention of allergic disease during childhood by allergen avoidance: The Isle of Wight prevention study

Journal of Allergy and Clinical Immunology, The
February 2007 • Volume 119 • Number 2

Syed Hasan Arshad, Belinda Bateman, Alireza Sadeghnejad, Carole Gant, Sharon M. Matthews

Genetic epidemiology of health disparities in allergy and clinical immunology

Journal of Allergy and Clinical Immunology, The
February 2006 • Volume 117 • Number 2
Kathleen C. Barnes

Primary prevention of asthma and allergy

Journal of Allergy and Clinical Immunology, The
July 2005 • Volume 116 • Number 1
Syed Hasan Arshad

Exposure to indoor allergens in day-care facilities: Results from 2 North Carolina counties

Journal of Allergy and Clinical Immunology, The
July 2005 • Volume 116 • Number 1

Samuel J. Arbes, Michelle Sever, Jigna Mehta, Nicholas Collette, Brittany Thomas, Darryl C. Zeldin

Associations between specific serum IgE response and 6 variants within the genes *IL4*, *IL13*, and *IL4RA* in German children: The German Multicenter Atopy Study

Journal of Allergy and Clinical Immunology, The
March 2004 • Volume 113 • Number 3

Xin Liu, PhD^a, Terri H. Beaty, PhD^a, Philipp Deindl, BS^b, Shau-Ku Huang, PhD^c, Susanne Lau, MD^b, Christine Sommerfeld, MSc^b, M. Daniele Fallin, PhD^a, W.H. Linda Kao, PhD^a, Ulrich Wahn, MD^b, Renate Nickel, MD^{b*}

House dust mite allergen in US beds: Results from the first national survey of lead and allergens in housing

Journal of Allergy and Clinical Immunology, The
February 2003, part 1 • Volume 111 • Number 2

Samuel J. Arbes, Jr, PhD^a, Richard D. Cohn, PhD^b, Ming Yin, PhD^b, Michael L. Muilenberg, MS^c, Harriet A. Burge, PhD^c, Warren Friedman, PhD^d, Darryl C. Zeldin, MD^a

Airborne dust and allergen generation during dusting with and without spray polish

Journal of Allergy and Clinical Immunology, The
January 2002, part 1 • Volume 109 • Number 1

Karen L. Jerriem, PhD^a, Lindsey F. Whitmore, PhD^a, John F. Hughes, PhD^a, Malcolm T. McKechnie, PhD^b

Allergic Rhinitis and Its Impact on Asthma

Journal of Allergy and Clinical Immunology, The
November 2001, part 2 • Volume 108 • Number 5

Jean Bousquet, MD, PhD, Paul van Cauwenberge, MD, PhD, Nikolai Khaltsev, MDIn collaboration with the World Health Organization

Exposure to cockroach allergen in the home is associated with incident doctor-diagnosed asthma and recurrent wheezing

Journal of Allergy and Clinical Immunology, The
January 2001 • Volume 107 • Number 1

Augusto A. Litonjua, MD, MPH, Vincent J. Carey, PhD, Harriet A. Burge, PhD, Scott T. Weiss, MD, MS, Diane R. Gold, MD, MPH

House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program*

Journal of Allergy and Clinical Immunology, The
January 2001 • Volume 107 • Number 1

Karen Huss, RN, DNSc^a, N. Franklin Adkinson, Jr, MD^a, Peyton A. Eggleston, MD^a, Christopher Dawson^b, Mark L. Van Natta, MHS^b, Robert G. Hamilton, PhD^c

Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma

Journal of Allergy and Clinical Immunology, The
December 2000 • Volume 106 • Number 6

Wanda Phipatanakul, MD^a, Peyton A. Eggleston, MD^b, Elizabeth C. Wright, PhD^c, Robert A. Wood, MD^bThe National Cooperative Inner-City Asthma Study*

The relevance of allergen exposure to the development of asthma in childhood

Journal of Allergy and Clinical Immunology, The
February 2000, part 2 • Volume 105 • Number 2

Thomas A. E. Platts-Mills, MD, PhD, Gary Rakes, MD, Peter W. Heymann, MD

The environmental predictors of allergic disease

Journal of Allergy and Clinical Immunology, The
January 2000, part 1 • Volume 105 • Number 1

Erika von Mutius, MD

Relationship of indoor allergen exposure to skin test sensitivity in inner-city children with asthma

Journal of Allergy and Clinical Immunology, The
October 1998, part 1 • Volume 102 • Number 4

Peyton A. Eggleston, MD^a, David Rosenstreich, MD^b, Henry Lynn, PhD^c, Peter Gergen, MD^f, Dean Baker, MD, MPH^d, Meyer Kattan, MD^e, Kathleen M. Mortimer, MPH^c, Herman Mitchell, PhD^c, Dennis Ownby, MD^g, Raymond Slavin, MD^h, Floyd Malveaux, MD, PhD^{i*}

Association between Der p 1 concentration and peak expiratory flow rate in children with wheeze: A longitudinal analysis

Journal of Allergy and Clinical Immunology, The
September 1998 • Volume 102 • Number 3

Bin Jalaludin, MPH^a, Wei Xuan, MSc^b, Ajsa Mahmic, GradDipEd^c, Jennifer Peat, PhD^d, Euan Tovey, PhD^d, Stephen Leeder, PhD^d

Preventive effect of bedding encasement with microfine fibers on mite sensitization

Journal of Allergy and Clinical Immunology, The
January 1998 • Volume 101 • Number 1

Kenji Nishioka, MD^a, Hiroshi Yasueda, PhD^b, Hirohisa Saito, MD, PhD^{b,c}
Tokyo and Kanagawa, Japan

Indoor allergens and asthma: Report of the Third International Workshop

Journal of Allergy and Clinical Immunology, The
December 1997, Part 1 • Volume 100 • Number 6

Thomas A. E. Platts-Mills, MD, PhD, Daniel Vervloet, MD, Wayne R. Thomas, PhD, Robert C. Aalberse, PhD, Martin D. Chapman, PhD
Charlottesville, Va., Marseille, France, Amsterdam, The Netherlands, and Perth, Australia

Exposure to indoor allergens in early infancy and sensitization

Journal of Allergy and Clinical Immunology, The
August 1997 • Volume 100 • Number 2

Abul Kashem M. Munir, MD, MPH, PhD, N-I, Max Kjellman, MD, PhD, Bengt Björkstén, MD, PhD
Linköping, Sweden

Indoor allergen exposure is a risk factor for sensitization during the first three years of life

Journal of Allergy and Clinical Immunology, The
June 1997, Part 1 • Volume 99 • Number 6

Ulrich Wahn, MD^a, Susanne Lau, MD^a, Renate Bergmann, MD^a, Michael Kulig, MD^b, Johannes Forster, MD^c, Karl Bergmann, MD^d, Carl-Peter Bauer, MD^e, Irene Guggenmoos-Holzmänn, MD, PhD^b
Berlin, Freiburg, and Munich, Germany

Sensitization to hen's egg at the age of twelve months is predictive for allergic sensitization to common indoor and outdoor allergens at the age of three years

Journal of Allergy and Clinical Immunology, The
May 1997 • Volume 99 • Number 5

Renate Nickel, MD^a, Michael Kulig, MD^b, Johannes Forster, MD^c, Renate Bergmann, MD^a, Carl Peter Bauer, MD^d, Susanne Lau, MD^a, Irene Guggenmoos-Holzmänn, MD, PhD^b, Ulrich Wahn, MD^a
Berlin, Freiburg, and Munich, Germany