

Exposure and allergic sensitization to cockroach allergen in East Germany

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Summary

Background Some studies suggest that the prevalence of sensitization to cockroach allergens may be higher in the United States than in Europe, but there are no comparable data from population-based studies.

Objectives To determine the prevalence of allergic sensitization to German cockroach (GCR) in German schoolchildren and to assess its clinical relevance; and to determine the exposure to the major GCR allergen Bla g 2 in non-selected homes and nurseries.

Methods The prevalence of allergic sensitization to GCR and other allergens was determined by measurement of specific IgE and skin-prick tests in a cross-sectional study of 2993 children aged 5–11 years in Dresden, Germany. The prevalence of atopic disease was determined by questionnaire, and pulmonary function and bronchial hyperresponsiveness to hypertonic saline were measured. Bla g 2 exposure was determined on floors of 187 kitchens and 47 nurseries by a commercial sandwich ELISA.

Results One hundred and twenty-seven (4.2%) of the children had specific IgE (>0.7 kU/L) against GCR. Among children with current wheeze, 8.4% were GCR-sensitized. Compared to data from the United States, the prevalence of sensitization to cockroach was similar in children without asthma (3.9%), but less frequent in asthmatic children from Dresden (6.1%). After adjustment for positive reactions to other allergens (SX1 test) no significant impact of GCR sensitization on wheeze or other symptoms and diagnoses was found. Bla g 2 was detected in 29% of the kitchens and 43% of the nurseries. None of these sites had exposure levels above the proposed threshold for causing disease of 80 ng/g dust.

Conclusion The data suggest that allergic sensitization to GCR is less frequent in asthmatics from Dresden, Germany than in US cities. The data indicate that GCR sensitization is not an independent risk factor for asthma and other atopic diseases in 5–11-year-olds from this city.

Keywords: allergic sensitization, asthma, atopy, Bla g 2, cockroach, indoor allergens

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Introduction

Allergic sensitization and exposure to cockroach allergen is a major risk factor for severe asthma in US cities [1–4].

Between 25% and 37% of asthmatic children have been reported to develop IgE-mediated hypersensitivity against cockroach allergens [4,5]. Among 100 patients presenting with asthma attacks (13 children and 87 adults) in a hospital in Chicago, 60 were sensitized to cockroach [6]. In contrast, only 5–6% of healthy children or adults examined as controls were sensitized [1,3,5]. In 41–86% of inner-city homes in the United States Bla g 1 and 2, the major allergens

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of German cockroach (GCR, *Blattella germanica*), were found in concentrations above the proposed threshold for causing disease (≥ 2 U/g dust, corresponding to 80 ng/g dust, personal communication, Dr Martin Chapman, Charlottesville, VA, USA) [1–4].

From Europe, prevalences between 13% and 16.5% were reported for children and adults with respiratory symptoms or with asthma and/or rhinitis [7–9]. An investigation of 623 adult healthy volunteers detected specific IgE against GCR (> 0.35 kU/L) in 4.7% [10]. GCR allergen exposure could be demonstrated in homes with visual evidence of cockroach infestation [9,11] and schools [12], but was low in samples from other homes and public places [13–15].

However, none of the data on prevalence of cockroach sensitization published so far in the United States and in Europe refer to a random sample from the general population. Most studies analysed subjects from risk-group or case–control studies. Because of the different inclusion criteria the prevalences found in such studies are not comparable to each other.

Therefore the first purpose of this study was to determine the prevalence of allergic sensitization to GCR in a large population-based sample of school children. Secondly, we analysed the association between GCR sensitization and atopic diseases and compared it with the role of sensitization against other allergens. In addition, we determined the exposure to Bla g 2 in homes and nurseries selected independently of visual cockroach infestation and atopic status of the inhabitants.

Methods

Cross-sectional study

Dresden, a city with 480 000 inhabitants, is located in the south-east of Germany. Between August 1995 and June 1996 all children participating in the school entry examinations ($n = 3866$) and a random sample of schoolchildren attending classes of fourth-grade classes ($n = 3668$) were studied using the Phase II modules of the International Study of Asthma and Allergies in Childhood (ISAAC) [16]. Because all school beginners were between 5 and 7 years of age at the time of investigation, and most fourth-grade pupils were between 9 and 11 years old (98.8%), we will refer in the following text to 5–7 and 9–11-year-old children, respectively.

Parental questionnaires were distributed through the community health department, which conducts the school entry examinations for 5–7-year-olds and through the schools for 9–11-year-olds. A completed questionnaire was returned by parents of 3312 (85.7%) children aged 5–7 years and of 3045 (83%) children aged 9–11 years. The questions on respiratory and allergic disorders included

those developed for the ISAAC project [17]. The focus of this analysis is on responses to the ISAAC questions on ‘wheeze in the last 12 months’ and ‘speech-limiting wheezing’ in the last 12 months. Symptoms of allergic rhinoconjunctivitis (‘sneezing or runny, or blocked nose without a cold’ and ‘itchy watery eyes’) and atopic eczema (‘itchy rash’) during the last year were also assessed via ISAAC core questions.

Furthermore, parents were asked: ‘Did a doctor ever diagnose any of the following diseases in your child? a. “asthma”; b. “asthmatic, spastic or obstructive bronchitis”; c. “bronchitis”’. Children were defined as having asthma if a doctor had diagnosed ‘asthma’ at least once or ‘asthmatic, spastic or obstructive bronchitis’ more than once. The questions on doctor’s diagnoses of asthma and bronchitis included in this study were validated against bronchial hyperresponsiveness to cold air in Bavarian schoolchildren [18]. Other questions were: ‘Has a doctor ever diagnosed hay fever in your child?’ and ‘Has a doctor ever diagnosed atopic dermatitis in your child?’ Finally, questions on living conditions and family background were evaluated.

All 9–11-year-olds and a random subsample of 5–7-year-olds ($n = 2328$) were invited to take part in skin-prick tests (SPT) and blood sampling (ISAAC Phase II modules). The SPTs were performed on the left forearm using ALK lancets and standardized allergen extracts of mixed grass pollen, mixed tree pollen, *Alternaria tenuis*, *Dermatophagoides pteronyssinus* (*D.pt.*), *Dermatophagoides farinae* (*D.f.*) and cat dander (ALK Hörsholm, Denmark). Atopic sensitization was defined as a wheal of > 3 mm to at least one allergen after subtraction of the reaction to the negative control. Specific serum IgE against GCR and a panel of aeroallergens (timothy grass, rye, birch, mugwort, *Cladosporium herbarum*, *D.pt.*, cat dander, dog dander) was determined by fluorescence enzyme immunoassay (SX1–CAP; Pharmacia, Lund, Sweden). SPTs were performed in 1360 (58.4%) children aged 5–7 years and 2260 (61.6%) children aged 9–11 years. Blood samples were drawn from 954 (41.0%) children in the younger and 2083 (56.8%) children in the older age group.

Measurements of lung function were offered only to a random subsample of the 9–11-year-old children ($n = 1999$). Spirometric measurements (Master Scope 4.1, Jäger, Würzburg, Germany) were performed according to the quality control criteria of the American Thoracic Society [19,20]. The FEV₁ and the forced expiratory flow over the middle half of the vital capacity (FEF_{25–75%}) were expressed as a percentage of predicted values based on gender and height [21]. FEV₁ values below 85% predicted or FEF_{25–75%} values below 70% predicted were defined to indicate impaired pulmonary function.

Bronchial responsiveness was assessed only in children with an FEV₁ above 75% predicted. These children inhaled

nebulized hypertonic (4.5%) saline for periods of increasing duration (0.5, 1, 2, 4, 8 min). After each inhalation period the FEV₁ was measured. Children were classified as bronchial hyperresponsive (BHR) if the FEV₁ had fallen by 15% or more from baseline [22]. 1256 children (62.8%) took part in spirometry, and the subsequent bronchial challenge was successfully completed by 1055 (52.8%) children.

A few minor but statistically significant ($P < 0.05$) differences in participation were observed. Among 5–7-year-olds participation in blood sampling differed depending whether or not the child had atopic eczema (46% vs. 53%). In 9–11-year-olds, participation in skin-prick testing was higher when the parents reported atopic diseases (72% vs. 68%).

Written informed consent was obtained from the parents for each study instrument separately. The study was part of a multi-centre project and was approved by the ethics committee of the University of Münster.

Sampling of carpet/floor dust

Between January and April 1996 we vacuumed dust from the floors of 187 kitchens in non-renovated apartment houses built between 1959 and 1969 in Dresden. This sample resulted from the voluntary participation of inhabitants of 66 apartment houses (total 765 apartments) in a study of the effects of subsequent renovation on indoor allergen exposure. The homes were located in Dresden in a residential area of 3 km² with intermediate to high living standards. The rental rates were within the range set by the local authorities [23]. In addition, between 1994 and 1996 dust samples from the living rooms of 47 nurseries were collected in Halle, a town of 300 000 inhabitants, 150 km north-west of Dresden. The nurseries were selected primarily for a study of exposure to mite allergen. In both studies the selection of investigation sites took place without regard to the atopic status of the inhabitants or to visual evidence of cockroaches. None of the inhabitants of the dwellings and none of the children in the nurseries took part in the cross-sectional survey described above.

The inhabitants were asked not to vacuum-clean their floors in the 7 days preceding the measurements. Floors (1 m²) were vacuumed by trained field workers for 2 min with a cleaner equipped with a motor capacity of at least 700 W. Dust was collected using a sampling device (ALK Copenhagen, Denmark) holding a cellulose filter (Filtrak GmbH Niederschlag, Germany, no. 60: 0.35 mm thick, pore size 30–40 µm), which retains 98% of particles over 0.7 µm in diameter and 91% of particles larger than 0.3–0.7 µm.

After collection, the dust samples were stored for a maximum of 24 h at 4–8 °C. They were then frozen at –20 °C for 48 h in order to kill living microorganisms. Thereafter the dust sample was again stored at 4–8 °C until GCR allergen extraction was performed.

Laboratory analysis of cockroach allergen concentrations

From each dust sample a representative portion of 0.2–1.0 g unsieved dust was used for analysis. This was extracted with 0.125 M ammonium–hydrogen–carbonate buffer + 0.1% sodium azide for 2 h (weight/volume: 1 : 10–1 : 40). The extract was then stored at –20 °C until the ELISA was performed.

The concentration of Bla g2 (ng/g dust) was determined by a sandwich ELISA using monoclonal antibodies (mAb) against Bla g2 (8F4 mAb, 1 µg/well) for allergen capture and rabbit anti-CR Ab (1 : 200 in 1% BSA PBS-T) for allergen detection (antibodies purchased from Indoor Biotechnologies Ltd, USA). Control curves were established by using a highly purified reference allergen extract (UVA 97/02) containing 2000 ng/mL Bla g 2 which was first diluted 1 : 6. Serial two-fold dilutions were then used to establish a range from 41.7 ng/mL down to 0.33 ng/mL. The extract of a dust sample from an apartment with visual evidence of CR infestation (kindly supplied by Dr Frédéric de Blay, Strasbourg/France) served as a positive control (in dilutions of 1 : 20 and 1 : 200).

The assay sensitivity was 0.5 ng Bla g 2/mL or 5 ng Bla g 2/g dust. The mean intra-assay coefficient of variation (CV) determined by double-positive controls on every plate was 4.1%. The interassay CV calculated with the results of duplicates of these positive controls was 12.7%.

Data analysis

The analyses were restricted to children with completed questionnaires from whom enough serum was obtained to determine both specific IgE against cockroach and aero-allergens (SX1). Because ethnicity has been shown to be a significant risk factor for the prevalence of atopic diseases in Germany [24], children with foreign nationality ($n = 11$) were excluded and only data for German children were evaluated. This reduced the number of children to 952 and 2041 with serum IgE measurements (99% of all children with blood examinations), and 910 and 1953 with SPT (79% of all children with SPT), in the younger and older age group, respectively. Measurements of lung function were analysed for 1046 children aged 9–11 years (83% of all children with lung function measurements).

The population evaluated for SPT results in this study comprised more older children (86.4% of all 9–11-year-olds with SPT compared to 66.9% of all 5–7-year-olds with SPT). Minor but statistically significant ($P < 0.05$, χ^2 test) differences were also found with respect to gender (more boys), some symptoms (more wheezing children, less children with symptoms of rhino-conjunctivitis and eczema), atopy (more SPT-positive children) and family background

Table 1. Atopic diseases and pulmonary function in the study population

	No. of 5–7-year-olds (%)	No. of 9–11-year-olds (%)
Symptoms in the past 12 months		
Wheeze	71/919 (7.7)	167/2010 (8.3)
Speech-limiting wheeze	18/924 (1.9)	44/2016 (2.2)
Symptoms of allergic rhino-conjunctivitis	52/921 (5.6)	262/1995 (13.1)*
Symptoms of atopic eczema	116/924 (12.6)	344/2018 (17.0)*
Doctor's diagnosis		
Asthma	61/916 (6.7)	152/2008 (7.6)
Hay fever	35/929 (3.8)	188/2003 (9.4)*
Atopic eczema	174/889 (19.6)	334/1969 (17.0)
Pulmonary function		
Bronchial hyperresponsiveness (4.5% NaCl)		134/879 (15.2)
FEV ₁ (% pred.) < 85%		68/1046 (6.5)
FEF _{25–75} (% pred.) < 70%		132/1031 (12.8)

* $P < 0.005$ for χ^2 test for comparison of age groups.

(more pets at home, more older siblings). The children with pulmonary function tests that were analysed in this study had low social status slightly more often than children not selected (85.7% vs. 78.8%). For all other potential confounders evaluated in the multivariate analysis and all health outcomes and sensitizations listed in Tables 1 and 2 no significant differences were found.

The crude prevalences of diagnoses and symptoms of atopic diseases, impaired pulmonary function and atopic sensitization to different allergens were calculated for both age groups. Furthermore, crude prevalences and prevalence odds ratios (OR) of diagnoses and symptoms

of atopic disease for subgroups of sensitized children were calculated.

The independent effects of sensitization to single allergens on diagnoses and symptoms of atopic diseases were assessed by multivariate logistic regression analysis. Each model consisted of two steps. In the first step a dichotomous variable characterizing the sensitization against a specific allergen was forced into the model as a predictor. In the second step, potential confounding factors such as gender, age group, birth weight, furred pets at home, maternal smoking, parental education, number of older siblings, heating and humidity in the dwelling were tested stepwise

Table 2. Atopic sensitization in the study population

	5 – 7 year olds	9 – 11 year olds
Specific IgE in serum		
Spec. IgE to German cockroach	23/952 (2.4 %)	104/2041 (5.1 %)*
Spec. IgE to aeroallergens > 0.7 kU/l**	212/952 (22.3 %)	642/2041 (31.5 %)*
Skin-prick test		
SPT reaction $\geq$ 3 mm to tree mixture	27/910 (3.0 %)	169/1953 (8.7 %)*
SPT reaction $\geq$ 3 mm to grass	62/910 (6.8 %)	296/1953 (15.2 %)*
SPT reaction $\geq$ 3 mm to <i>Dermatophagoides pteronyssinus</i>	19/910 (2.1 %)	206/1953 (10.5 %)*
SPT reaction $\geq$ 3 mm to <i>D. farinae</i>	11/910 (1.2 %)	145/1953 (7.4 %)*
SPT reaction $\geq$ 3 mm to cat	29/910 (3.2 %)	181/1953 (9.3 %)*
SPT reaction $\geq$ 3 mm to <i>Alternaria tenuis</i>	4/910 (0.4 %)	32/1953 (1.6 %)*
SPT reaction $\geq$ 3 mm to at least one allergen	104/910 (11.4 %)	508/1953 (26.0 %)*

* $P < 0.001$ for χ^2 test for comparison of age groups.

**SX1 panel (Pharmacia Sweden): timothy grass, rye, birch, mugwort, *Cladosporium herbarum*, *Dermatophagoides pteronyssinus*, cat, dog.

for their effect on the log likelihood of the regression model (forward selection, P_{in} 0.05, P_{out} 0.10). This model was modified further: in the first step the variable for specific sensitization and a dichotomous covariate for atopic sensitization ($SX1 < 0.7$ kU/L vs. $SX1 \geq 0.7$ kU/L) were forced into the model together. Then, in the second step, the potential confounders outlined above were introduced by forward stepwise selection.

Software for all calculations was SPSS (Chicago, IL, USA) for Microsoft Windows 6.01.

Results

Cockroach sensitization

The mean age ($\pm$ SD) of the study children was 5.4 (0.5) years in the younger age group, and 9.7 (0.6) years in the older age group. Fifty-two per cent were male. The prevalence of symptoms of hay fever and atopic dermatitis, and atopic sensitization to least one allergen, was significantly higher in 9–11-year-old children. In contrast, the prevalences of wheeze and doctor's diagnoses of asthma and atopic eczema did not differ between both age groups (Tables 1 and 2).

Two hundred and twenty-four children (7.5%) had specific IgE > 0.35 kU/L against GCR, and 127 children (4.2%) had specific GCR IgE > 0.7 kU/L. Of the latter, 111 (87.4%) were also sensitized against other allergens as measured by SX1 (> 0.7 kU/L) and 64 (52.5%) reacted to at least one allergen in the SPT. 8.4% (20/238) of the children with current wheeze, 12.9% (8/62) of the children with speech-limiting wheezing in the last 12 months and 6.1% (13/213) of the children with a doctor's diagnosis of asthma were sensitized against GCR (> 0.7 kU/L). For children with symptoms and diagnoses of hay fever the prevalences were 11.1% and 13.9%, respectively, for children with symptoms and diagnoses of atopic eczema 5.0% and 5.1%.

Table 3 shows that GCR-sensitized children were at a higher risk for developing doctor-diagnosed hay fever and symptoms of asthma or allergic rhino-conjunctivitis compared to children not sensitized to GCR. However, a stronger relation was found for all other types of sensitization (data for sensitization to tree pollen, *D.pt.*, cat dander and *Alternaria* not shown). No significant association of GCR sensitization and BHR or reduced pulmonary function was found.

Table 4 shows that the significant association between GCR sensitization and the diagnosis of hay fever and symptoms of asthma or allergic rhino-conjunctivitis remained virtually unchanged when controlling for potential confounders in the logistic regression model. However, when the model was adjusted for atopic sensitization ($SX1 > 0.7$ kU/L), the relation between GCR sensitization

and atopic outcomes disappeared whereas the influence of atopic sensitization remained significant (OR of current wheeze in SX1-positive subjects adjusted for GCR sensitization: 3.9; 95% CI: 2.8–5.2).

In contrast, the association of sensitization to grass pollen or *D.f.* and wheeze remained significant after adjustment for SX1 results (Table 4). The association between grass pollen sensitization, atopic outcomes and BHR remained significant after adjusting for SX1 results. Similar results were obtained when considering sensitization to tree pollen and *D.pt.* (data not shown). In cat-sensitized individuals OR remained statistically significant for symptoms of allergic rhino-conjunctivitis and all three diagnoses. In children sensitized to *Alternaria* OR remained significant for symptoms of allergic rhino-conjunctivitis and diagnosis of atopic eczema.

Among 79 children of parents with low educational status (both parents less than 10 years of school) seven (8.9%) were sensitized against GCR. Six of these seven children were also sensitized against other allergens ($SX1 > 0.7$ kU/L). In keeping with the results for the whole sample, the risk for symptoms of asthma (but not for a doctor's diagnosis of asthma or reduced pulmonary function) was increased in these GCR-sensitized children but the ORs lost significance when they were adjusted for SX1.

Bla g 2 exposure

Bla g 2 exposure was detectable (> 5 ng/g dust) in 54/187 dwellings (29%) and 20/47 nurseries (43%). The exposure in kitchens where Bla g 2 was detected ranged between 5.1 and 65.9 ng/g dust (median 12.5); the exposure in nurseries was 5.3–34.9 (9.7) ng/g dust. In none of the samples did the Bla g 2 concentration exceed the proposed threshold for causing disease of 80 ng/g dust (equivalent to 2 U/g dust). There was no significant difference of Bla g 2 levels between the following dwelling categories: dwelling space (< 30 m² vs. ≥ 30 m²/inhabitant), level of the dwelling (< 2 nd vs. ≥ 2 nd floor), heating (coal vs. others), pets in the dwelling, special bin for organic waste (yes vs. no), cleaning of kitchen/bathroom floor (1/week vs. more seldom). Visual evidence of cockroach in the dwelling was reported for only one dwelling, in which no Bla g 2 was detected.

Discussion

In this study the prevalence of cockroach sensitization was 4.2% among 5–11-year-old children in Germany. Among the 2755 children without current symptoms of asthma the prevalence was 3.9%, which is somewhat lower than the 6.0% found in control subjects in the United States [5]. However, in the US study sensitization to cockroach was

defined as a positive SPT reaction to a mixed cockroach extract (including three cockroach species, *Blattella germanica*, *B. orientalis* and *Periplaneta americana*) or detection of specific IgE against GCR in the serum. Although *B. germanica* and *P. americana* share at least one cross-reacting protein [25], the SPT mixture may evoke positive reactions in some individuals sensitized against cockroach species other than GCR. Therefore, we cannot conclude that

cockroach sensitization was less frequent in healthy children from our sample compared to the American children.

However, the prevalence of GCR sensitization was markedly lower in asthmatic subjects in our study (6.1% in children with a diagnosis of asthma, 8.4% in wheezing children) compared to children studied in the United States (25% [5], 37% [4]). Because in one of these studies the asthmatic children were recruited in emergency rooms and

Table 3. Prevalences and crude prevalence odds ratios (POR)* of atopic diseases and reduced pulmonary function for children sensitized to cockroach or other allergens

	Cockroach-IgE 0.7 kU/l	SPT positive (grass)**	SPT positive (<i>D.f.</i>)**	SX1 > 0.7 kU/l	SPT positive** (at least one allergen)
<i>Symptoms in the past 12 months</i>					
Wheeze					
Prevalence	15.7%	21.3%	22.6%	16.0%	18.2%
POR*	2.2 (1.3–3.6)	4.2 (3.1–5.7)	3.8 (2.5–5.7)	3.6 (2.8–4.7)	4.1 (3.1–5.4)
Speech-limiting asthma attack					
Prevalence	6.3%	6.8%	7.7%	4.5%	5.8%
POR*	3.4 (1.6–7.4)	5.4 (3.2–9.3)	4.9 (2.5–9.4)	4.1 (2.4–6.9)	6.1 (3.6–10.6)
Symptoms of allergic rhino-conjunctivitis					
Prevalence	29.2%	43.6%	30.1%	27.8%	33.5%
POR*	3.7 (2.5–5.6)	12.4 (9.5–16.3)	4.1 (2.9–6.0)	9.4 (7.2–12.3)	11.1 (8.5–14.5)
Symptoms of atopic eczema					
Prevalence	18.5%	27.1%	22.1%	22.4%	24.5%
POR*	1.2 (0.8–2.0)	2.3 (1.7–2.9)	1.6 (1.05–2.3)	1.9 (1.6–2.4)	2.1 (1.7–2.6)
<i>Doctor's diagnosis</i>					
Asthma					
Prevalence	10.4%	15.6%	15.5%	13.3%	14.0%
POR*	1.5 (0.8–2.7)	3.0 (2–4.2)	2.6 (1.6–4.1)	3.0 (2.3–4.0)	3.0 (2.3–4.1)
Hay fever					
Prevalence	25.0%	36.7%	21.6%	22.5%	26.3%
POR*	4.5 (2.9–7.0)	18.6 (13.6–25.6)	4.0 (2.6–6.0)	17.0 (11.8–24.7)	16.8 (11.9–23.7)
Atopic eczema					
Prevalence	21.3%	32.8%	22.5%	27.3%	28.8%
POR*	1.3 (0.8–2.0)	2.6 (2.0–3.4)	1.4 (0.9–2.0)	2.3 (1.9–4.1)	2.3 (1.9–2.9)
<i>Pulmonary function</i>					
Bronchial hyperresponsiveness (4.5% NaCl)					
Prevalence	22.2%	29.9%	28.3%	25.4%	26.1%
POR*	1.6 (0.8–3.4)	3.1 (2.0–4.8)	2.5 (1.4–4.5)	2.8 (1.9–4.1)	2.8 (1.9–4.2)
FEV ₁ (% pred.) < 85%					
Prevalence	10.5%	8.8%	7.0%	7.3%	7.3%
POR*	1.8 (0.7–4.3)	1.6 (0.8–2.9)	1.1 (0.4–2.9)	1.2 (0.7–2.0)	1.3 (0.7–2.2)
FEF _{25–75} (% pred.) < 70%					
Prevalence	16.1%	17.5%	21.4%	17.8%	17.8%
POR*	1.3 (0.6–2.8)	1.5 (0.97–2.5)	1.9 (1.1–3.6)	1.8 (1.3–2.7)	1.7 (1.1–2.5)

*Crude prevalence odds ratios (95% confidence intervals) were calculated comparing children who were sensitized against a specific allergen with those who were not.

**Positive SPT reactions to extracts of grass pollen, *Dermatophagoides farinae* (*D.f.*) or other allergens: wheal $\geq$ 3 mm after subtraction of the reaction to the negative control.

Table 4. Adjusted prevalence odds ratios* of atopic diseases and reduced pulmonary function for children sensitized to cockroach, grass or dust mites

	Cockroach sensitization	Cockroach sensitization (additionally adjusted for SX1)	Grass sensitization	Grass sensitization (additionally adjusted for SX1)	<i>D.f.</i> sensitization	<i>D.f.</i> sensitization (additionally adjusted for SX1)
<i>Symptoms in the past 12 months</i>						
Wheeze	2.0 (1.2–3.5)	1.0 (0.6–1.7)	4.5 (3.2–6.3)	2.4 (1.6–3.7)	4.5 (2.9–6.9)	2.3 (1.4–3.6)
Speech-limiting asthma attack	3.8 (1.7–8.2)	1.9 (0.8–4.2)	6.0 (3.4–10.7)	3.8 (1.8–8.1)	5.8 (2.9–11.4)	3.0 (1.4–6.3)
Symptoms of allergic rhino-conjunctivitis	3.3 (2.1–5.2)	1.2 (0.8–1.9)	12.6 (9.3–17.0)	5.4 (3.8–7.7)	3.9 (2.6–5.8)	1.3 (0.8–1.9)
Symptoms of atopic eczema	1.3 (0.8–2.2)	0.9 (0.6–1.5)	2.5 (1.9–3.3)	1.9 (1.3–2.7)	1.7 (1.1–2.5)	1.1 (0.7–1.7)
<i>Doctor's diagnosis</i>						
Asthma	1.3 (0.7–2.6)	0.7 (0.4–1.5)	3.1 (2.2–4.5)	1.9 (1.2–3.0)	2.9 (1.8–4.7)	1.6 (0.98–2.8)
Hay fever	3.5 (2.1–5.7)	1.3 (0.8–2.1)	16.3 (11.5–23.1)	6.1 (4.1–9.2)	3.6 (2.3–5.6)	1.1 (0.7–1.7)
Atopic eczema	1.3 (0.8–2.0)	0.8 (0.5–1.3)	2.5 (1.9–3.3)	1.8 (1.3–2.5)	1.4 (0.9–2.2)	0.9 (0.6–1.4)
<i>Pulmonary function</i>						
Bronchial hyperresponsiveness (4.5% NaCl)	1.4 (0.6–3.0)	0.8 (0.3–1.8)	2.8 (1.8–4.6)	1.9 (1.04–3.3)	2.8 (1.4–5.3)	1.6 (0.8–3.2)
FEV ₁ (% pred.) < 85%	1.4 (0.5–3.9)	1.4 (0.5–4.3)	1.3 (0.6–2.6)	1.5 (0.6–3.6)	0.5 (0.1–2.2)	0.5 (0.1–2.2)
FEF _{25–75} (% pred.) < 70 %	1.1 (0.5–2.5)	0.8 (0.4–1.9)	1.5 (0.9–2.4)	1.1 (0.6–1.9)	1.7 (0.9–3.4)	1.3 (0.6–2.7)

*Prevalence odds ratios (95% confidence intervals) were calculated by logistic regression analysis adjusting for the following putative confounding variables: gender, age group, birth weight, furred pets at home, maternal smoking, parental education, number of older siblings, heating, and humidity in the dwelling (first column). Alternatively, sensitization to a specific allergen was additionally adjusted for the results of the SX1 test (second column). Statistically significant ($P < 0.05$) odds ratios are printed bold. Cockroach sensitization and SX1 results were determined by measuring specific IgE in serum (> 0.7 kU/l). Sensitization against grass and *D. farinae* (*D.f.*) was determined by SPT reaction (≥ 3 mm after subtraction of the reaction to the negative control).

clinics [4] these children may represent a subgroup of patients with more severe disease. However, in our study only 12.9% (8/62) of the children whose parents reported speech-limiting wheezing in the last 12 months were GCR-positive. The differences may again be explained in part by the use of a cockroach mixture extract for SPT in the US studies. Nevertheless, it seems unlikely that such a marked difference in the sensitization of asthmatic children is due entirely to this methodical difference.

Most previous studies were performed in selected populations with low social status. We found a higher prevalence of GCR sensitization in children of parents with low educational status, but GCR sensitization was not an independent risk factor for asthma in these children. The data suggest that indoor risk factors for asthma in children of lower social status differ between Dresden and US cities. However, they need confirmation by studies in greater populations selected specifically for substandard housing styles in European cities.

The great majority of GCR-sensitized children was also sensitized against other allergens as measured by SX1 test or SPT. Only 24 children (0.8%) showed a relatively strong sensitization to GCR (> 3.5 kU/L). When the independent

influences of GCR sensitization and SX1 sensitization (as a marker of overall atopic sensitization) were adjusted for each other in a logistic regression analysis, only the influence of atopic sensitization (SX1) on wheeze and other symptoms and diagnoses of atopic disease remained significant. In contrast, sensitizations to house dust mites, grass or tree pollens, cat dander or *Alternaria* were particularly associated with some atopic symptoms and diagnoses. These findings suggest that specific sensitization to GCR is, rather, an immunological 'side-effect' of the disposition to develop allergic sensitization, which has no clinical relevance in most children of our population.

A paper by Witteman *et al.* [26] has suggested that an immunological cross-reactivity to a common protein (tropomyosin) is the reason for an apparent GCR sensitization in individuals originally sensitized to dust mites. Among 53 Turkish asthmatics sensitized to CR, 37 (70%) were also positive for mites [27]. In contrast, in our sample only 16 of 122 children with IgE against GCR (13%) reacted positively to *D.f.* in the SPT, and 12 of these 16 children were also sensitized against other allergens than GCR or mites. When adjusting for mite sensitization the associations of GCR sensitization with current wheeze (aPOR 1.8;

95% CI 1.03–3.2) and speech-limiting asthma attacks (3.3; 1.5–7.5) remained almost unchanged. We conclude that the prevalence of GCR sensitization and the associated health risks observed in this study are unlikely to be caused by a specific cross-reactivity to mite allergens.

The prevalences of GCR sensitization are probably representative for the examined age groups in Dresden, because there was no major selection bias due to non-participation in the blood examinations (atopic eczema was less frequent in participating 5–7-year-olds, but eczema was not associated with GCR sensitization). Participation in SPT was more frequent in 9–11-year-olds with parental atopy. In addition, SPT results were evaluated in a subgroup of older children with a slightly higher frequency of positive SPT because not all children with a SPT had a blood examination. However, in the children not evaluated in this study most associations between SPT reactions and health outcomes were similar to those described in Table 3. The only exception was a weaker association of SPT reactions with doctor-diagnosed asthma. We assume that it is unlikely that the observed differences in the clinical impact of sensitization to cockroach and other allergens are caused by a selection bias.

The assumption that GCR sensitization is not an independent risk factor for asthma and other atopic diseases is supported by the fact that the concentration of Bla g 2, the major allergen of GCR, was very low in kitchens and nurseries in our region. We cannot directly relate the exposure data from these sites to individual's sensitization because there is no information on the sensitization of their inhabitants. However, the very low Bla g 2 concentrations suggest that exposure to cockroach allergen in the average population of Dresden is low.

The investigated houses did not include substandard buildings in socially deprived areas. In such areas other European investigators (11) have found Bla g 2 levels comparable to those in inner-city homes in the United States. We cannot definitely exclude that such homes also exist in Dresden. However, cockroach infestation in apartments is rarely announced to public health authorities and seems to be a minor problem of public hygiene in Dresden (personal communication, Dr Hannelore Schweitzer, Institute for Hygiene and Microbiology, Technical University Dresden, former District's Institute of Hygiene Dresden).

In summary, the data suggest that the prevalence of cockroach sensitization in non-wheezy children from Dresden is not substantially lower than among non-wheezy children in the United States, but that asthmatic children from Dresden are probably sensitized less frequently against GCR than asthmatics in the United States. In most children sensitization to GCR was weak, and its impact on atopic symptoms was explained mainly by the overall disposition

of most of these individuals to develop allergic sensitization. Furthermore, only very low concentrations of the cockroach allergen Bla g 2 were detected in kitchens and nurseries from this East German region.

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References

- Pollart SM, Chapman MD, Platts-Mills TAE et al. Epidemiology of acute asthma: IgE antibodies to common inhalant allergens as a risk factor for emergency room visits. *J Allergy Clin Immunol* 1989; 83:875–82.
- Call RS, Smith TF, Morris E, Chapman MD, Platts-Mills TAE. Risk factors for asthma in inner city children. *J Pediatr* 1992; 121:862–6.
- Gelber LE, Seltzer LH, Pollart SM et al. Sensitization and exposure to indoor allergens as risk factors for asthma among patients presenting to hospital. *Am Rev Respir Dis* 1993; 147:573–8.
- Rosenstreich DL, Eggleston P, Kattan M et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 1997; 336:1356–63.
- Squillace SP, Sporik RB, Rakes G et al. Sensitization to dust mites as a dominant risk factor for asthma among adolescents living in Central Virginia. *Am J Resp Crit Care Med* 1997; 156:1760–4.
- Kang B, Jones J, Johnson J, Kang JJ. Analysis of indoor environment and atopic allergy in urban populations with bronchial asthma. *Ann Allergy* 1989; 62:30–4.
- Riario Sforza GG, Della Torre F, Antonicelli L et al. Sensitization to cockroach in Italy: a multicentric study. *Allergy Asthma Proc* 1997; 18:23–8.
- Di Felice G, Tinghino R, Barletta B, Afferni C, Iacovacci P, Pini C. Prevalence of cockroach allergy in Urban and Suburban Areas in Italy. *J Allergy Clin Immunol* 1997; 101:S24 (abstract).
- van Wijnen JH, Verhoeff AP, Schou C et al. Cockroach allergen in house dust. *Allergy* 1997; 52:460–4.
- Birnbaum J, Guilloux L, Charpin D, Vervloet D. Cockroach allergens. *Lancet* 1991; 337:249.
- De Blay F, Sanchez J, Hedelin G, Perez Infante A, Vérot A, Chapman M, Pauli G. Dust and airborne exposure to allergens derived from cockroach (*Blattella germanica*) low-cost public housing in Strasbourg (France). *J Allergy Clin Immunol* 1997; 99:107–12.
- Custovic A, Green R, Taggart SCO et al. Domestic allergens in public places II. Dg (Can f 1) and cockroach (Bla g 2) allergens in dust and mite, cat, dog and cockroach allergens in the air in public buildings. *Clin Exp Allergy* 1996; 26:1246–52.

- 13 De Andrade AD, Charpin D, Birnbaum J, Lanteaume A, Chapman M, Verloet D. Indoor allergen levels in day nurseries. *J Allergy Clin Immunol* 1995; 95:1158–63.
- 14 Fahlbusch B, Jäger L, Koch A et al. Erfassung und Analyse von Indoor- Allergenen. *Allergologie* 1995; 18:495–500.
- 15 Custovic A, Fletcher A, Pickering CAC et al. Domestic allergens in public places III. House dust mite, cat, dog and cockroach allergens in British hospitals. *Clin Exp Allergy* 1998; 28:53–9.
- 16 Weiland SK, von Mutius E, Hirsch Th et al. Prevalence of respiratory and atopic disorders among children in the East and West of Germany five years after unification. *Eur Resp J* 1999; 14:862–70.
- 17 Asher MI, Keil U, Anderson HR et al. International Study Asthma and Allergies – ISAAC: rationale and methods. *Eur Resp J* 1995; 8:483–91.
- 18 Nicolai T, von Mutius E, Reitmeir P, Wjst M. Reactivity to cold-air hyperventilation in normal and in asthmatic children in a survey of 5,697 schoolchildren in Southern Bavaria. *Am Rev Respir Dis* 1993; 147:565–72.
- 19 Ferris BG. Epidemiology standardization project III. recommended standardized procedures for pulmonary function testing. *Am Rev Respir Dis* 1978; 118:55–88.
- 20 Gardner RM, Hankinson JL, Clausen JL, Crapo RO, Johnson RL, Epler GR. Standardization of spirometry. 1987 update. Official statement of the American Thoracic Society. *Am Rev Respir Dis* 1987; 136:1285–98.
- 21 Zapletal A, Paul F, Samanek M. Die Bedeutung heutiger Methoden der Lungenfunktionsdiagnostik zur Feststellung einer Obstruktion der Atemwege bei Kindern und Jugendlichen. *Z Erkrank Atm Org* 1977; 149:343–71.
- 22 Riedler J, Reade T, Dalton M, Holst D, Robertson C. Hypertonic saline challenge in an epidemiologic survey of asthma in children. *Am J Respir Crit Care Med* 1994; 150:1632–9.
- 23 Amt für Wohnungswesen der Landeshauptstadt Dresden. Dresdner Mietspiegel 1998. Landeshauptstadt Dresden D-01001 Dresden, 1997; Wohnungen nach Ausstattung: 5.
- 24 Kabesch M, Schaal W, Nicolai T, von Mutius E. Lower prevalence of asthma and atopy in Turkish children living in Germany. *Eur Respir J* 1999; 13:577–82.
- 25 Schou C, Lind P, Fernandez-Caldas E, Lockey RF, Löwenstein H. Identification and purification of a cross reacting, acidic allergen from American (*Periplaneta americana*) and German (*Blattella germanica*) cockroach. *J Allergy Clin Immunol* 1990; 86:935–46.
- 26 Witterman AM, van den Oudenrijn S, van Leeuwen J, Akkerdaas J, von der Zee JS, Aalberse RC. IgE antibodies reactive with silverfish, cockroach and chironomid are frequently found in mite-positive allergic patients. *Int Arch Allergy Immunol* 1995; 108:165–9.
- 27 Mungan D, Celik G, Sin B, Bavbek S, Demirel Y, Misirgil Z. Characteristic features of cockroach hypersensitivity in Turkish asthmatic patients. *Allergy* 1998; 53:870–3.