

THE ROLE OF COCKROACH ALLERGY AND EXPOSURE TO COCKROACH ALLERGEN IN CAUSING MORBIDITY AMONG INNER-CITY CHILDREN WITH ASTHMA

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ABSTRACT

Background It has been hypothesized that asthma-related health problems are most severe among children in inner-city areas who are allergic to a specific allergen and also exposed to high levels of that allergen in bedroom dust.

Methods From November 1992 through October 1993, we recruited 476 children with asthma (age, four to nine years) from eight inner-city areas in the United States. Immediate hypersensitivity to cockroach, house-dust-mite, and cat allergens was measured by skin testing. We then measured major allergens of cockroach (Bla g 1), dust mites (Der p 1 and Der f 1), and cat dander (Fel d 1) in household dust using monoclonal-antibody-based enzyme-linked immunosorbent assays. High levels of exposure were defined according to proposed thresholds for causing disease. Data on morbidity due to asthma were collected at base line and over a one-year period.

Results Of the children, 36.8 percent were allergic to cockroach allergen, 34.9 percent to dust-mite allergen, and 22.7 percent to cat allergen. Among the children's bedrooms, 50.2 percent had high levels of cockroach allergen in dust, 9.7 percent had high levels of dust-mite allergen, and 12.6 percent had high levels of cat allergen. After we adjusted for sex, score on the Child Behavior Checklist, and family history of asthma, we found that children who were both allergic to cockroach allergen and exposed to high levels of this allergen had 0.37 hospitalization a year, as compared with 0.11 for the other children ($P=0.001$), and 2.56 unscheduled medical visits for asthma per year, as compared with 1.43 ($P<0.001$). They also had significantly more days of wheezing, missed school days, and nights with lost sleep, and their parents or other care givers were awakened during the night and changed their daytime plans because of the child's asthma significantly more frequently. Similar patterns were not found for the combination of allergy to dust mites or cat dander and high levels of the allergen.

Conclusions The combination of cockroach allergy and exposure to high levels of this allergen may help explain the frequency of asthma-related health problems in inner-city children. (N Engl J Med 1997; 336:1356-63.)

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MORBIDITY due to asthma is disproportionately high among inner-city residents,¹ for reasons that are not completely understood. Proposed explanations include increased exposure to allergens,² poor air quality,³ psychosocial problems,⁴ and inadequate access to good medical care.⁴

Allergens involved in causing asthma include those derived from house-dust mites,⁵ animal dander,⁶ and mold spores.⁷ In particular, it has been suggested that exposure to cockroach allergen may be an important factor in asthma in inner-city areas,⁸ since cockroaches are ubiquitous and are highly allergenic.^{9,10} However, a clear causal relation among allergy to cockroaches, increased levels of cockroach allergen, and asthma has not been demonstrated.

As part of the National Cooperative Inner-City Asthma Study, we performed a comprehensive analysis of factors that might be associated with the severity of asthma in inner-city children. We tested the hypothesis that morbidity due to asthma is highest among children who are both allergic to a specific allergen and exposed to high levels of that allergen in bedroom dust.

METHODS

Patients

The National Cooperative Inner-City Asthma Study population consisted of 1528 children with asthma from eight major inner-city areas (Bronx, New York; East Harlem, New York; St. Louis; Washington, D.C.; Baltimore; Chicago; Cleveland; and Detroit). The children lived in neighborhoods where 30 percent or more of the households had incomes below the 1990 poverty level and had either asthma diagnosed by a physician, with symptoms during the previous year, or symptoms consistent with asthma.

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ma (cough, wheezing, shortness of breath, or a combination of these) that lasted more than six weeks during the previous year.

Recruitment took place in 13 emergency rooms and 25 clinics from November 1992 through October 1993. All the children underwent skin testing for sensitivity to allergens and pulmonary-function testing and were questioned about episodes of asthma during the previous year. We made home visits to the families of the first 663 children recruited (43 percent of the total sample). Complete information on all study variables was available for 476 of these children, who are included in the current study. The study was approved by the institutional review board of each site, and written informed consent was obtained from the children's parents or guardians.

Base-Line Evaluation

After recruitment, the children and their primary care givers were interviewed about access to health care, adherence to prescribed therapy, family psychosocial problems, home environment, cigarette smoking by household members, and demographic characteristics of the household members. Psychosocial factors were assessed with a number of different measures.

We developed a brief questionnaire to assess the availability of social support for adults caring for a child with asthma; the topics covered included information about asthma and emotional and practical support. The score on this questionnaire was the sum of all positive answers (maximum, 9). We considered a score below 7 to indicate inadequate social support.

We used a modification of the Child Behavior Checklist to assess the child's psychological adjustment.¹¹ This is a standardized, 113-item checklist completed by the parent or other care giver that generates summary scores for behavior problems and symptoms. We modified the test by eliminating 13 questions about symptoms that could be caused by asthma (e.g., difficulty sleeping) and converted the raw summary score to a T-score by means of comparison with a normative population. The mean T-score for the group was 57.3, and we used the standard level of 64 or more to indicate substantial psychological problems in the child.

We evaluated the primary care givers' mental health with the Brief Symptom Inventory, a standardized, 53-item questionnaire covering psychological symptoms, which contains three global dimensions.¹² The raw summary scores were converted to T-scores by comparison with a normative population weighted toward subjects with relatively low social status and African Americans. The mean T-score for our group was 56.02, and we used the established clinical cutoff of 63; a score above 63, or a T-score of more than 63 in any two dimensions, was considered to indicate the presence of substantial psychological problems in the care giver.

We used an abbreviated version of the Psychiatric Epidemiology Research Interview (PERI) Life Events Scale to determine the incidence of 46 stressful life events (e.g., divorce, enrollment in welfare programs, being robbed).¹³ The PERI score consisted of the total number of stressful events in the previous 12 months, and we considered a score above 5 to indicate substantial stress.

Skin Testing

Prick-puncture skin testing was performed using a Multi-Test device with allergen extracts in 50 percent glycerine (Greer Laboratories, Lenoir, N.C.).¹⁴ Subjects were tested with extracts of the house-dust mites *Dermatophagoides pteronyssinus* and *D. farinae*, cat pelt, a mixture of German cockroach and American cockroach, 10 other common aeroallergens, and histamine and buffer controls. All extracts were 1:20 (wt/vol) except dust-mite allergen (10,000 allergy units per milliliter). The resulting wheals were outlined in ink 15 minutes later, and the outline was transferred with plastic tape to paper for later measurement. The test battery was considered valid only if the diameter of the wheal produced by the negative control (buffer) was at least 1 mm smaller than that produced by the positive control (histamine). A test for a specific allergen was considered positive if the diameter of the wheal was at least 2 mm larger than the negative-control wheal.

Home Visits and Dust Collection

Bedroom dust samples were collected with a hand-held vacuum cleaner (Redivac 6735, Douglas Manufacturing, Walnut Ridge, Ariz.).⁵ An area of 1 m² beside the bed was vacuumed for two minutes, and the sample was combined with a similar sample from the mattress and bedding. Filters were removed, sealed in plastic bags, and shipped to a central laboratory (at the Department of Pediatrics, Johns Hopkins University). The inside of the front nozzle of each vacuum cleaner was washed with detergent, rinsed, and dried after each home visit.

Measurement of Allergen Levels in Settled Dust

The dust specimen was put through a sieve (with 0.3-mm mesh), and an aqueous extract was prepared from 100 mg of sieved dust in 2 ml of borate-buffered saline.^{15,16} The extracts were stored at -30°C until they were assayed for the allergens of house-dust mites (Der p 1 and Der f 1), cat allergen (Fel d 1), and cockroach allergen (Bla g 1) in monoclonal-antibody-based enzyme-linked immunosorbent assays.^{15,16} The results were expressed in micrograms per gram of dust (for Der p 1, Der f 1, and Fel d 1) or in units per gram of dust (for Bla g 1). During the analyses, the results of the two dust-mite assays were combined and expressed in terms of total Der 1 allergen. A sample of 24 coded dust extracts was assayed by Dr. Martin Chapman of the University of Virginia in Charlottesville, using an identical method; the correlation with our results for Der p 1, Der f 1, and Fel d 1 was 0.96, 0.99, and 0.95, respectively. The limits of detection of the assay were 100 ng per gram of dust for the Der 1 mite allergens, 50 ng per gram for Fel d 1, and 1 U per gram for Bla g 1. For data analysis, the level of each allergen was categorized as high or low. We defined high levels as those above 2 µg per gram for Der 1 and Fel d 1 and above 8 U per gram for Bla g 1, on the basis of proposed threshold levels for the induction of disease.^{2,5,6,10}

Collection of Follow-up Data

Three, six, and nine months after the base-line evaluation, each family was contacted to obtain information about symptoms of asthma and use of health care services. Follow-up at the three times was 90 percent, 92 percent, and 94 percent complete, respectively.

Data on morbidity during each three-month period were collected by a trained interviewer, mainly during telephone interviews with the child's primary care giver, according to a standardized questionnaire (92.6 percent of assessments by telephone, and 7.4 percent by personal interview). The interviewers were unaware of allergen levels in the homes.

The care givers were asked to measure the peak expiratory flow rate (Mini-Wright peak flow meter, Clement Clarke, Columbus, Ohio) in the child twice daily for two weeks after the base-line interview and for two weeks before each of the follow-up assessments and to record the values in diaries.¹⁷ Only 65 percent of the participating families returned all the peak-flow diaries. For each child, a summary mean peak flow rate was determined by averaging the mean values in all completed diaries (range, two to four diaries).

Assessment of Morbidity Due to Asthma

We assessed morbidity due to asthma in terms of four factors: clinical symptoms, use of health care services, activities of daily life, and effect on the parent or other care giver. The assessment period for the measures was two weeks or three months before the follow-up assessment; the period was determined in advance for each measure and was based on the anticipated reliability of the recall information. Clinical measures included the number of days with wheezing and nights of lost sleep for the child during the two weeks before each interview. Measures of the use of health care services included the number of hospitalizations for asthma and the number of unscheduled visits to a health care pro-

TABLE 1. CHARACTERISTICS OF THE STUDY POPULATION.*

CHARACTERISTIC	STUDY SAMPLE (N = 476)	NATIONAL COOPERATIVE INNER-CITY ASTHMA STUDY (N = 1528)
		no./total no. (%)
Mean (±SD) age — yr	6.17±1.69	6.16±1.69
Male sex	299/476 (62.8)	954/1528 (62.4)
Race or ethnic group		
Hispanic	78/475 (16.4)	295/1512 (19.5)
Black	371/475 (78.1)	1111/1512 (73.5)
Other	26/475 (5.5)	106/1512 (7.0)
Annual family income under \$15,000	284/430 (66.0)	835/1364 (61.2)
At least one smoker in household	275/472 (58.3)	889/1519 (58.5)
Family history of asthma	275/476 (57.8)	868/1512 (57.4)
Inadequate social support†	194/466 (41.6)	637/1499 (42.5)
Large no. of stressful life events‡	267/476 (56.1)	893/1515 (58.9)
Psychopathology in care giver§	225/456 (49.3)	732/1470 (49.8)
Psychopathology in child§	157/476 (33.0)	499/1509 (33.1)
Allergy on skin test		
Cockroach	175/476 (36.8)	460/1286 (35.8)
Dust mite	166/476 (34.9)	445/1286 (34.6)
Cat	108/476 (22.7)	312/1286 (24.3)

*Totals are the numbers of children for whom data were available.

†The range of scores for social support was from 0 to 9; a score below 7 was considered to indicate inadequate social support for the family in dealing with the child's asthma.

‡Life events were measured with the Psychiatric Epidemiology Research Interview Life Events Scale; scores ranged from 0 to 46. A score above 5 was considered to indicate a substantial number of stressful life events in the previous 12 months.

§The Child Behavior Checklist for children and the Brief Symptom Inventory for care givers are tests in which high scores indicate the presence of substantial psychological problems. The mean normalized score (T-score) on these tests is 50; we used the standard cutoff of 63. Scores above 63 were considered to indicate the presence of substantial psychological problems.

TABLE 2. BEDROOMS WITH DETECTABLE LEVELS OF ALLERGEN IN DUST.*

VARIABLE	COCKROACH ALLERGEN	DUST-MITE ALLERGEN	CAT ALLERGEN
	number (percent)		
Detectable allergen	406 (85.3)	235 (49.4)	298 (62.6)
Above high-level threshold†	239 (50.2)	46 (9.7)	60 (12.6)
	U/g of dust	µg/g of dust	
Median	8.2	0	0.09
Maximum	1190	39	167

*Dust levels of allergen were measured in 476 children's bedrooms.

†The threshold for high exposure in this study was as follows: cockroach allergen, 8 U per gram of dust; house-dust-mite allergen, 2 µg per gram of dust; cat allergen, 2 µg per gram of dust.

vider for asthma during the previous three months. The effect of asthma on activities of daily life was assessed in terms of the number of days of reduced activity (in the previous two weeks) and the percentage of school days missed (in the previous three months). To identify changes in each child's level of activity, care givers were asked, "In the past two weeks, were there any days when [the child's name] had to slow down or stop his/her activities while at home or playing with other children because of asthma, wheezing or tightness in the chest, or cough?" The effect on the care giver was measured by the number of nights the care giver missed sleep (in the previous two weeks) and the number of days the care giver had to change his or her plans (in the previous three months) because of the child's asthma. To identify changes in the activity of the care givers, they were asked, "How many days during the past three months did you have to change your daytime or evening plans because of [the child's] asthma?" For each of the eight measures of morbidity, all available follow-up values were averaged to create a mean score. All 476 participants were assessed at least twice during the three follow-up periods, and 90.5 percent were assessed in all three periods.

Statistical Analysis

Nonparametric methods were used in the analyses, since the distributions of the measures of morbidity and dust-allergen levels were skewed. Outcome measures were rank-transformed. Levels of dust allergens were classified as high or low, and analysis of covariance was used to assess the effects of allergy and exposure to allergens. This procedure has been shown to have reasonable statistical power and to be robust when values are not normally distributed and when there is heterogeneity of variances.¹⁸ Fifteen covariates were initially considered, including the child's age, race, sex, and score on the Child Behavior Checklist, the education level of the mother or other care giver, number of people in the household, household income, family history of asthma, social-support score, smoking status of the care giver, number of smokers in the household, the care giver's sex, marital status, and score on the Brief Symptom Inventory, and the score on the PERI Life Events Scale. Out of this group, sex, score on the Child Behavior Checklist, and family history of asthma were selected for inclusion in the analysis of covariance, since they were the strongest predictors of morbidity on the largest number of measures. The results and P values reported here are for this multivariate analysis.

Patients were classified in four groups with respect to each allergen tested: those who were not allergic to a given allergen and had low bedroom levels of that allergen (group 1), those who were not allergic and had high bedroom allergen levels (group 2), those who were allergic and had low allergen levels (group 3), and those who were allergic and had high allergen levels (group 4).

For each allergen and measure of morbidity, the primary hypothesis we assessed was that morbidity due to asthma would be highest among children who were both sensitive to a given allergen and exposed to high levels of that allergen in their bedrooms. We tested this hypothesis by comparing measures of morbidity in the group of children who were allergic to cockroaches and had high bedroom levels of cockroach allergen (group 4) with those in the other three groups, using a two-sided, preplanned comparison.¹⁹

RESULTS

Patients

The children had a mean age of 6.2 years (range, 4 to 9; Table 1). Overall, the study families were poor, were primarily black or Hispanic, and had a substantial number of psychosocial problems. The frequency of reactivity on skin testing was 36.8 percent for cockroach allergen, 34.9 percent for dust-mite allergen, and 22.7 percent for cat dander. The study group and the total study population of the

TABLE 3. RELATIONS AMONG SKIN-TEST SENSITIVITY, BEDROOM-DUST ALLERGEN LEVELS, AND MORBIDITY DUE TO ASTHMA.

VARIABLE	COCKROACH ALLERGEN				DUST-MITE ALLERGEN				CAT ALLERGEN			
	NEGATIVE SKIN TEST		POSITIVE SKIN TEST		NEGATIVE SKIN TEST		POSITIVE SKIN TEST		NEGATIVE SKIN TEST		POSITIVE SKIN TEST	
	Low Allergen Level (Group 1)	High Allergen Level (Group 2)	Low Allergen Level (Group 3)	High Allergen Level (Group 4)	Low Allergen Level (Group 1)	High Allergen Level (Group 2)	Low Allergen Level (Group 3)	High Allergen Level (Group 4)	Low Allergen Level (Group 1)	High Allergen Level (Group 2)	Low Allergen Level (Group 3)	High Allergen Level (Group 4)
No. of children	160	141	77	98	279	31	151	15	323	45	93	15
Hospitalizations in past year (no.)	0.14	0.08	0.10	0.37*	0.14	0.09	0.23	0.18	0.17	0.12	0.19	0.09
Unscheduled medical visits in past year (no.)	1.40	1.44	1.50	2.56†	1.43	1.85	2.05	1.78	1.43	2.31	2.11	1.86
Days of wheezing in past 2 wk (no.)	3.21	3.13	3.86	4.04‡	3.31	4.08	3.50	4.63	3.24	3.74	4.03	3.99
Nights when child lost sleep in past 2 wk (no.)	1.62	1.59	1.77	1.92§	1.63	1.80	1.74	2.22	1.61	1.95	1.95	1.26
Days when child's activity was reduced in past 2 wk (no.)	1.89	1.90	2.04	2.13	1.83	2.50	2.15	1.52	1.96	1.76	2.10	1.88
School days missed in past 3 mo (%)¶	6.12	5.14	5.60	7.65§	5.41	7.28	7.04	6.07	5.55	6.07	7.38	8.20
Days when care giver changed plans in past yr (no.)	9.11	11.07	7.22	15.52	9.01	13.98	13.25	9.82	11.09	9.32	10.20	9.78
Nights when care giver lost sleep in past 2 wk (no.)	2.08	1.98	2.11	2.33	2.00	2.52	2.21	2.26	1.99	2.35	2.52	1.33
Peak expiratory flow rate (% of predicted value)**	86.6	86.7	84.5	85.9	85.8	80.9	87.5	88.2	85.2	88.4	88.2	87.3

*P=0.001 for the comparison between group 4 and groups 1, 2, and 3 combined.

†P<0.001 for the comparison between group 4 and groups 1, 2, and 3 combined.

‡P=0.03 for the comparison between group 4 and groups 1, 2, and 3 combined.

§P=0.02 for the comparison between group 4 and groups 1, 2, and 3 combined.

¶For days of school missed, data with respect to cockroach allergen were available for 152 children in group 1, 132 in group 2, 75 in group 3, and 91 in group 4; data with respect to dust-mite allergen were available for 267, 25, 143, and 15 children, respectively; and data with respect to cat allergen were available for 302, 43, 90, and 15, respectively.

||P=0.006 for the comparison between group 4 and groups 1, 2, and 3 combined.

**For peak expiratory flow rate, data with respect to cockroach allergen were available for 115 children in group 1, 108 in group 2, 58 in group 3, and 68 in group 4; data with respect to dust-mite allergen were available for 199, 23, 116, and 11 children, respectively; and data with respect to cat allergen were available for 238, 33, 67, and 11, respectively.

National Cooperative Inner-City Asthma Study were similar (Table 1).

Bedroom Allergen Levels

The majority of bedrooms had detectable levels of the three allergens, with values of 49.4 percent of the bedrooms for dust mites, 62.6 percent for cat dander, and 85.3 percent for cockroach allergen (Table 2). However, there was a marked difference in the number of bedrooms in which allergen levels exceeded the proposed disease-induction thresholds (Table 2). Such high levels of cockroach allergen were found in 50.2 percent of the bedrooms. In contrast, 12.6 percent of bedrooms had high levels

of cat allergen, and 9.7 percent had high levels of dust-mite allergen.

Exposure to High Bedroom Levels of Cockroach Allergen and Morbidity Due to Asthma

The mean values for each measure of morbidity due to asthma in each of the four groups of children are presented in Table 3. The data reflect the multivariate analysis, with adjustment for sex, score on the Child Behavior Checklist, and family history of asthma. The only significant relations we found were for cockroach allergen. The rate of hospitalization for asthma was approximately 3.4 times as high among the children who were sensitive to cockroach aller-

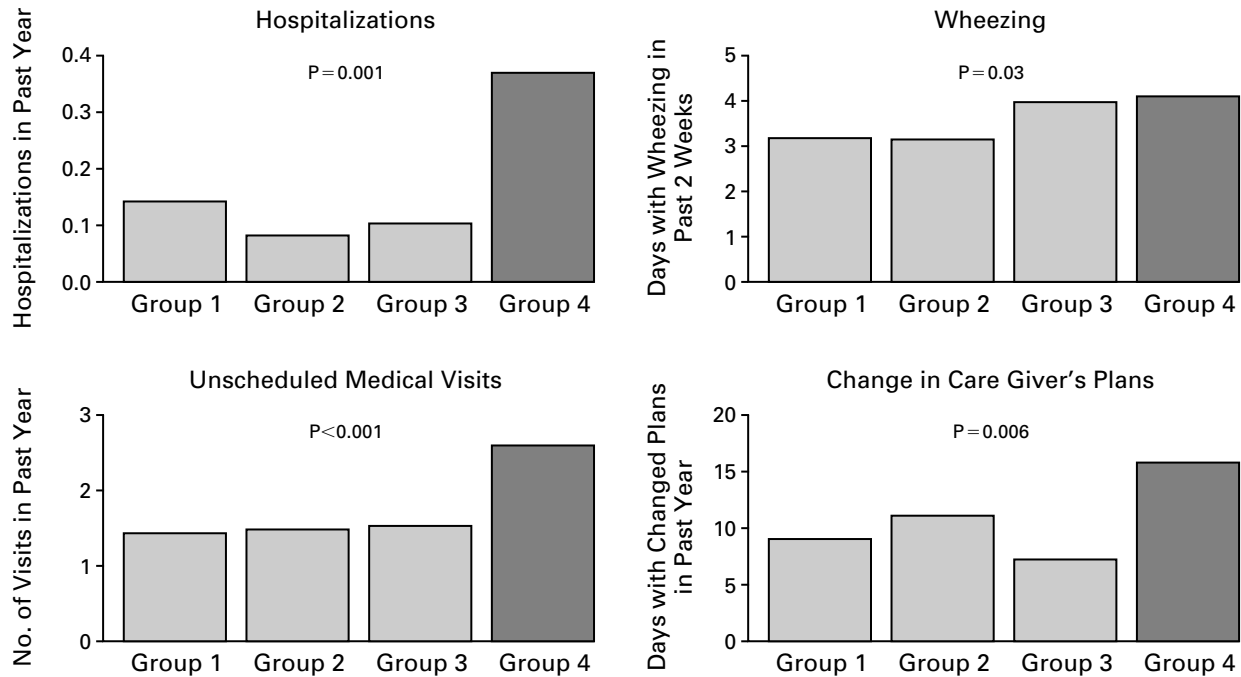


Figure 1. Morbidity among Children with Asthma, According to the Presence or Absence of Allergy to Cockroach Allergen and the Degree of Exposure.

The values shown are the means for each measure of morbidity. Group 1 is made up of children without allergy to cockroach allergen and with low levels of exposure to the allergen; group 2, children without allergy to cockroach allergen and with high levels of exposure; group 3, children with allergy to cockroach allergen and with low levels of exposure; and group 4, children with allergy to cockroach allergen and with high levels of exposure. The P values are for the comparison between group 4 and groups 1, 2, and 3 combined.

gen and exposed to high levels of this allergen in their bedrooms (group 4) as for the other three groups (0.37 hospitalization per year vs. 0.11 hospitalization per year, $P=0.001$) (Fig. 1). Similarly, this group had 78 percent more unscheduled visits to health care providers because of asthma than the mean for the children in the other groups (2.55 vs. 1.43 unscheduled visits per year, $P<0.001$) (Fig. 1).

Significant relations between allergy to cockroaches and increased cockroach-allergen levels were also found with other measures of morbidity. Children in the group with allergy to cockroach allergen and exposure to high bedroom allergen levels had more days of wheezing than those in the other groups ($P=0.03$), and their care givers had to change their own plans because of the children's asthma more often ($P=0.006$) (Fig. 1). The children also had more morbidity due to asthma as measured by the number of nights when the care giver was awakened because of the child's asthma ($P=0.006$), by the number of days of school missed ($P=0.02$), and by the number of nights when the child awoke because of asthma ($P=0.02$) (Table 3).

There was no significant difference in peak flow rates among the groups. No increase in morbidity due to asthma was associated with exposure to high

levels of cockroach allergen in the absence of allergy to cockroaches or with allergy to cockroaches in the absence of high levels of exposure to the allergen.

Sensitivity and Exposure to Dust Mites or Cat Dander in Relation to Morbidity Due to Asthma

In contrast to the findings for cockroach allergy, we did not find significant associations between morbidity due to asthma and high bedroom levels of dust-mite or cat allergen, even among allergic children. Rates of hospitalization for asthma among the four groups of children were similar (Fig. 2). Similarly, there was no association between levels of cat or dust-mite allergen and any of the other measures of morbidity due to asthma (Table 3). These analyses were performed with the same multivariate analysis used for cockroach allergen.

DISCUSSION

Among inner-city children, the highest levels of morbidity due to asthma were associated with the presence of both a positive skin-test response to cockroach allergen and current exposure to high levels of cockroach allergen in the bedroom. This association was apparent for several different measures of morbidity, notably the use of health care services,

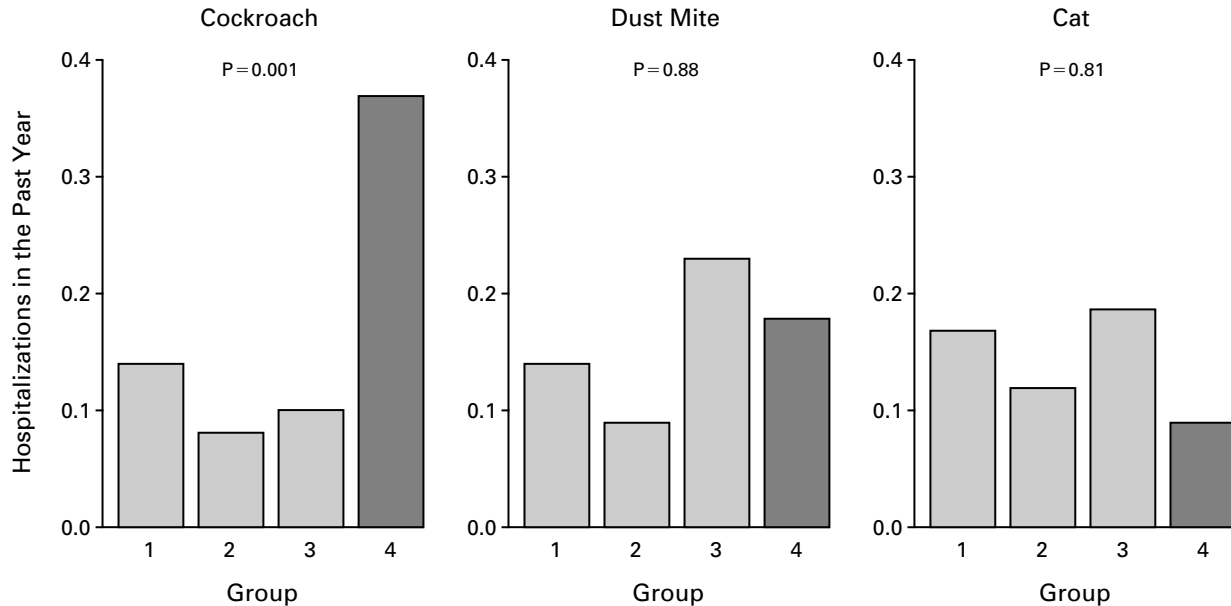


Figure 2. Number of Hospitalizations in the Past Year According to the Presence or Absence of Allergy to Cockroach, Dust-Mite, or Cat Allergen and the Degree of Exposure.

The values shown are the mean numbers of hospitalizations in the past year in each group. Group 1 is made up of children without allergy to the allergen in question and with low levels of exposure to it; group 2, children without allergy and with high levels of exposure; group 3, children with allergy and with low levels of exposure; and group 4, children with allergy and with high levels of exposure. The P values are for the comparison between group 4 and groups 1, 2, and 3 combined.

clinical symptoms, and effects on daily activities. This relation persisted after we controlled for potentially confounding psychological and sociological factors. It is possible, for instance, that high levels of cockroach allergen may be a marker for poor house-keeping or disorganization on the part of a child's care giver. However, increased exposure to cockroach allergen alone was not associated with greater morbidity, nor was cockroach allergy by itself.

The association of allergy and exposure to cockroaches with episodes of asthma is unlikely to be spurious for several reasons, including the large, diverse sample included in the National Cooperative Inner-City Asthma Study, the structured protocol of that study, and the sequential selection of homes without regard to the severity of asthma or risk factors in the children. Children from the homes we studied were representative of the overall study group both demographically and in terms of the severity of asthma, the type of treatment, and skin-test reactivity. Finally, data on morbidity were collected by interviewers who were unaware of the allergen levels in the homes.

Although we found a relation between exposure and sensitization to cockroach allergen, on the one hand, and measures of morbidity due to asthma, on the other, we did not find a relation with the peak expiratory flow rate. However, peak-flow diaries were

returned for only 65 percent of the sample. Data from a recent study using an electronic counter indicated that diaries obtained from children overestimate the number of times the peak-flow meter is actually used.²⁰ Thus, peak-flow diaries may be an unreliable measure when measurements are made by children themselves or by their parents or other care givers. Furthermore, since we did not control for the use of medications, increased or previous use of medications may have obscured otherwise significant differences in peak flow rates.

Our data confirm earlier reports showing that cockroaches are an important urban source of allergen. We found elevated concentrations of the cockroach allergen Bla g 1 in dust samples from 50.2 percent of the children's bedrooms. Similarly, other studies found high levels (>2 U per gram) of another cockroach allergen, Bla g 2, in dust from 37 to 85 percent of urban homes.^{2,10} Sensitivity to cockroach allergen is found in 23 to 60 percent of urban residents with asthma,^{2,10,21-23} and allergic persons with asthma have acute episodes when exposed to cockroach allergen in bronchial-provocation tests.⁸ In addition, sensitivity to cockroach allergen was shown to be an important risk factor for more frequent episodes of asthma in case-control studies of patients in emergency rooms.^{2,10}

Finding a relation between environmental expo-

sure to an allergen and IgE-dependent sensitization or asthma is not unexpected, but this association has been studied most extensively in regard to house-dust mites.^{24,25} A dose-response relation between exposure and sensitization can be demonstrated when different geographic regions are compared.^{26,27} For example, central Australia is hot and dry, and houses in this area have been found to have concentrations of dust-mite allergen that are 1 percent as high as those in communities in the much more humid coastal regions.²⁶ The rate of sensitization to dust mites parallels this difference in exposure.²⁶ When environments with smaller differences are studied, however, the relation between sensitization and exposure is less consistent.^{28,29}

The relation between household exposure to dust mites and asthma is less clear. Asthma is reported to be more common in regions with higher levels of dust-mite allergen,²⁶ but within the same city, most studies show that dust-mite levels do not differ significantly between the homes of people with asthma and those of nonasthmatic persons.^{2,10,29} In contrast, sensitized adults with more severe asthma in Marseilles, France, were found to be exposed to higher levels of dust-mite allergen than those with milder asthma.²⁷ In accordance with our findings with respect to cockroach allergen, levels of house-dust mites in Vancouver, British Columbia, correlated with the severity of asthma only among patients with asthma who were positive on skin tests with dust-mite allergen.³⁰

The low levels of house-dust-mite allergen in the inner-city areas we studied are somewhat surprising, since the house-dust mite has been reported to be an important allergen in many parts of the United States.³¹ A report of mite-allergen levels in inner-city homes in Atlanta found very high levels.² The lower levels found in our study may reflect the fact that dust samples were obtained between January and June and not during the fall months, when mite levels are highest. In addition, there are probably regional differences in the prevalence of dust mites.

Exposure and sensitization to animal allergens have also been found to be related to the presence of asthma. For example, sensitization to cat and dog allergens was associated with asthma in Los Alamos, New Mexico, where levels of exposure and sensitization to house-dust-mite allergen are low.³² This relation has also been reported in New Zealand.³³ In contrast, as we also found, two other studies of urban populations observed that levels of exposure to cat allergen were relatively low and not related to the incidence of asthma.^{2,10}

With respect to the frequency of allergy to cat dander, only 10 percent of the homes in our study had resident cats, as compared with 20 to 30 percent nationally. In the Atlanta study, cat-allergen levels and the frequency of undetectable levels were similar

to our findings.² The fact that so few children with asthma in our study had high levels of cat or dust-mite allergen in their bedrooms (only 7 of 476 households had mite-allergen levels above 10 U per gram of dust) makes it difficult to assess accurately the relation between current levels of these allergens and morbidity due to asthma.

In summary, our findings provide evidence that exposure to cockroach allergen has an important role in causing morbidity due to asthma among inner-city children. These results suggest that reducing exposure to cockroach allergen should be an important component of plans for the management of asthma. The implementation of intensive, multicomponent cockroach-reduction strategies, including education of patients and the use of safe insecticides and nontoxic traps, should be evaluated as a method of reducing morbidity due to asthma in this population.

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APPENDIX

In addition to the authors, the following investigators participated in the study: Albert Einstein School of Medicine, Bronx, N.Y. — E. Crain and L. Bauman; Children's Memorial Hospital, Chicago — R. Evans III, J. Lavigne, Y.D. Senturia, C.M. Weil, K.K. Christoffel, and H.J. Binns; Cook County Hospital, Chicago — M. Sullivan, J.H. Mayefsky, and M.F. McDermott; Rainbow Babies and Children's Hospital, Cleveland — C. Kercsmar, S. Redline, and S. Wade; Henry Ford Hospital and Medical Center, Detroit — J.A. Anderson, F.E. Leickly, C.L.M. Joseph, and C. Johnson; Mount Sinai School of Medicine, New York — C. Lamm, M.T. Tin, G. Butts, E. Luder, and D. Baker; Washington University Medical School, St. Louis — H.J. Wedner and G. Evans; Howard University, Washington, D.C. — A. Thomas, S. Molock, and M. Richard; National Institute of Allergy and Infectious Diseases, Program Office, Bethesda, Md. — E. Smartt, K. Weiss, and R. Kaslow; and New England Research Institutes, Data Coordinating Center, Watertown, Mass. — E. Wright, K.M. Mortimer, and S. Islam.

REFERENCES

- Gottlieb DJ, Beiser AS, O'Connor GT. Poverty, race, and medication use are correlates of asthma hospitalization rates: a small area analysis of Boston. *Chest* 1995;108:28-35.
- 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.
- Evans R III, Mullally DI, Wilson RW, et al. National trends in the morbidity and mortality of asthma in the US: prevalence, hospitalization and death from asthma over two decades: 1965-1984. *Chest* 1987;91:Suppl: 65S-74S.
- Birkhead G, Attaway NJ, Strunk RC, Townsend MC, Teutsch S. Investigation of a cluster of deaths of adolescents from asthma: evidence implicating inadequate treatment and poor patient adherence with medications. *J Allergy Clin Immunol* 1989;84:484-91.
- Sporik R, Holgate ST, Platts-Mills TAE, Cogswell JJ. Exposure to house-dust mite allergen (*Der p I*) and the development of asthma in childhood. *N Engl J Med* 1990;323:502-7.

6. Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TAE. Quantitative assessment of exposure to dog (Can f 1) and cat (Fel d 1) allergens: relation to sensitization and asthma among children living in Los Alamos, New Mexico. *J Allergy Clin Immunol* 1995;96:449-56.
7. Targonski PV, Persky VW, Ramekrishnan V. Effect of environmental molds on risk of death from asthma during the pollen season. *J Allergy Clin Immunol* 1995;95:955-61.
8. Kang B. Study on cockroach antigen as a probable causative agent in bronchial asthma. *J Allergy Clin Immunol* 1976;58:357-65.
9. Twarog FJ, Picone FJ, Strunk RS, So J, Colten HR. Immediate hypersensitivity to cockroach: isolation and purification of the major antigens. *J Allergy Clin Immunol* 1977;59:154-60.
10. Gelber LE, Seltzer LH, Bouzoukis JK, Pollart SM, Chapman MD, Platts-Mills TAE. Sensitization and exposure to indoor allergens as risk factors for asthma among patients presenting to hospital. *Am Rev Respir Dis* 1993;147:573-8.
11. Achenback TM, Edelbrock C. Manual for the Child Behavior Checklist and revised Behavior Profile. Burlington: University of Vermont, Department of Psychiatry, 1983.
12. Derogatis LR, Spencer PM. Administration & procedures: BSI manual-I. Baltimore: Clinical Psychometric Research, 1982.
13. Dohrenwend BS, Krasnoff L, Askenasy AR, Dohrenwend BP. Exemplification of a method for scaling life events: the PERI Life Events Scale. *J Health Soc Behav* 1978;19:205-29.
14. Berkowitz RB, Tinkelman DG, Lutz C, Crammie A, Smith K. Evaluation of the Multi-Test device for immediate hypersensitivity skin testing. *J Allergy Clin Immunol* 1992;90:979-85.
15. Chapman M, Aalberse RC, Brown MJ, Platts-Mills TA. Monoclonal antibodies to the major feline allergen Fel d 1. II. Single step affinity purification of Fel d 1, N-terminal sequence analysis, and development of a sensitive two-site immunoassay to assess Fel d 1 exposure. *J Immunol* 1988;140:812-8.
16. Wood RA, Eggleston PA, Lind P, et al. Antigenic analysis of household dust samples. *Am Rev Respir Dis* 1988;137:358-63.
17. Hsu KH, Jenkins DE, Hsi BP, et al. Ventilatory functions of normal children and young adults — Mexican-American, white, and black. II. Wright peak flowmeter. *J Pediatr* 1979;95:192-6.
18. Conover WJ, Iman RL. Analysis of covariance using the rank transformation. *Biometrics* 1982;38:715-24.
19. Winer BJ. Statistical principles in experimental design. 2nd ed. New York: McGraw-Hill, 1971.
20. Redline S, Wright EC, Kattan M, Kerckmar C, Weiss K. Short-term compliance with peak flow monitoring: results from a study of inner city children with asthma. *Pediatric Pulmonology* 1996;21:203-10.
21. Bernton HS, Brown H. Insect allergy — preliminary studies of the cockroach. *J Allergy* 1964;35:506-13.
22. Kang B, Sulit N. A comparative study of prevalence of skin hypersensitivity to cockroach and house dust antigens. *Ann Allergy* 1978;41:333-6.
23. Kang BC, Johnson J, Veres-Thorner C. Atopic profile of inner-city asthma with a comparative analysis on the cockroach-sensitive and ragweed-sensitive subgroups. *J Allergy Clin Immunol* 1993;92:802-11.
24. Platts-Mills TAE, Sporik RB, Wheatley LM, Heymann PW. Is there a dose-response relationship between exposure to indoor allergens and symptoms of asthma? *J Allergy Clin Immunol* 1995;96:435-40.
25. 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.
26. Peat JK, Tovey E, Toelle BG, et al. House dust mite allergens: a major risk factor for childhood asthma in Australia. *Am J Respir Crit Care Med* 1996;153:141-6.
27. Vervloet D, Penuad A, Razzouk H, et al. Altitude and house dust mites. *J Allergy Clin Immunol* 1982;69:290-6.
28. Kuehr J, Frischer T, Meinert R, et al. Mite allergen exposure is a risk for the incidence of specific sensitization. *J Allergy Clin Immunol* 1994;94:44-52.
29. Marks GB, Tovey ER, Toelle BG, Wachinger S, Peat JK, Woolcock AJ. Mite allergen (Der p 1) concentration in houses and its relation to the presence and severity of asthma in a population of Sydney schoolchildren. *J Allergy Clin Immunol* 1995;96:441-8.
30. Chan-Yeung M, Manfreda J, Dimich-Ward H, et al. Mite and cat allergen levels in homes and severity of asthma. *Am J Respir Crit Care Med* 1995;152:1805-11.
31. Arlian LG, Bernstein D, Bernstein IL, et al. Prevalence of dust mites in the homes of people with asthma living in eight different geographic areas of the United States. *J Allergy Clin Immunol* 1992;90:292-300.
32. Sporik R, Ingram JM, Price W, Sussman JH, Honsinger RW, Platts-Mills TA. Association of asthma with serum IgE and skin test reactivity to allergens among children living at high altitude: tickling the dragon's breath. *Am J Respir Crit Care Med* 1995;151:1388-92.
33. Sears MR, Herbison GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. *Clin Exp Allergy* 1989;19:419-24.

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