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

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Background: Although mouse allergen is known to cause occupational asthma in laboratory workers, its potential significance in home environments has never been studied.
Objective: This study was designed to define the prevalence of mouse sensitivity and its relationship to mouse allergen exposure and disease activity in inner-city children with asthma.
Methods: A subset of 499 subjects from the National Cooperative Inner-City Asthma Study had dust samples adequate for mouse allergen analysis, as well as valid puncture skin test (PST) results. Data were analyzed to relate mouse allergen exposure and other risk factors to mouse sensitization and asthma morbidity.
Results: Eighty-nine (18%) of the 499 children had a positive mouse skin test response. Children whose homes had mouse allergen levels above the median (1.60 μg/g) in the kitchen had a significantly higher rate of mouse sensitization (23% vs 11%, $P = .007$). Atopy was also significantly related to mouse sensitization, with 40% of those with more than 4 positive PST responses having mouse sensitivity compared with 4% of those with no other positive PST responses ($P < .0001$). When atopy and exposure were considered together, 53% of those with more than 4 positive PST responses and allergen levels above the median had a positive PST response to mouse allergen compared with 22% of those with more than 4 positive PST responses and allergen levels below the median ($P < .0001$). The relationship among mouse allergen exposure, sensitization, and any measures of asthma morbidity was not statistically significant.
Conclusions: Mouse allergen may be an important indoor allergen in inner-city children with asthma, with exposure and atopy contributing to mouse sensitization. (J Allergy Clin Immunol 2000;106:1075-80.)

Key words: *Mouse allergen, indoor allergens, inner-city asthma, sensitization, asthma morbidity*

The identification of major indoor allergens and the ability to measure these allergens in home environments have shed considerable light on the relationships among allergen exposure, allergic sensitization, and disease activity for dust mite, cat, and cockroach allergens in patients with asthma.[1-10] It is also clear from these studies that different allergens may be more important than others in certain environments. A striking example of this was the recent demonstration of the particular importance of cockroach allergen in children from the inner city with asthma, a group in which asthma morbidity is exceptionally high.

We have now had the opportunity to analyze dust samples from the National Cooperative Inner-City Asthma Study (NCICAS) for mouse allergen and have reported a high prevalence of mouse allergen in the homes of inner-city children with asthma.[11] Although mouse allergen is known to be a potent sensitizer in occupational settings, its potential importance in home environments has never been studied. The purpose of this study was therefore to evaluate the clinical significance of mouse allergen in this unique inner-city asthma population, including the prevalence of mouse sensitization, the relationships between mouse exposure and sensitization, and the potential contribution of mouse allergen to asthma morbidity. Furthermore, because previous studies have suggested that atopy[5] and other variables, such as smoking,[12] sex,[13] cockroach sensitization and exposure,[8] and psychosocial[14,15] and socioeconomic[16] factors, may also play a part in sensitization and asthma morbidity, the roles of these potential covariates were also analyzed.

METHODS

The NCICAS study population consisted of 1528 children aged 4 to 9 years from 8 major inner-city areas (Bronx, NY; East Harlem, NY; St Louis, Mo; Washington, DC; Baltimore, Md; Chicago, Ill; Cleveland, Ohio; and Detroit, Mich). As previously described, these children had a diagnosis of asthma and lived in neighborhoods where 30% or more of the households had incomes below the 1990 poverty level.[16,17] Dust samples were collected from the home by using a hand-held vacuum (Redivac 6735, Douglas Manufacturing Co). Samples were collected from 3 rooms, the child's bedroom, the television-living room, and the kitchen, by using standardized methods.[5,17] Dust samples were removed from the vacuum, sieved, and then stored at –30°C until they were extracted.

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Abbreviations used
NCICAS: National Cooperative Inner-City Asthma Study
OR: Odds ratio
PST: Puncture skin test

An aqueous extract of 100 mg of sieved dust was prepared in 2 mL of borate-buffered saline solution. The extracts were stored at –30°C until they were assayed for the major mouse allergen Mus m 1. A sandwich ELISA with an affinity-purified monospecific anti-Mus m 1 antibody was used to determine the concentration of Mus m 1.[18]

All of the children in the study received skin testing by using the prick puncture method with the Multitest device to a predefined panel of aeroallergens,[19] which included German and American cockroach, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat pelt, dog pelt, mouse pelt, rat pelt, *Alternaria tenuis*, *Penicillium* species, mixed grasses, orchard grass, white oak, maple, and giant and short ragweed obtained in 50% glycerosaline (Greer Laboratories), as previously described.[5] Mouse and rat allergen skin testing concentrations were 1:20 wt/vol. The skin test results were read at 15 minutes. A skin test panel was considered valid if the wheal from the positive control (histamine 1 mg/mL) was at least 1 mm larger than that of the negative control. A skin test response was considered positive if the panel was valid and if the mean wheal diameter of the allergen test was at least 2 mm larger than that of the negative control wheal. There were a total of 499 children who had both valid skin test data and an adequate dust sample for mouse allergen analysis whose data were analyzed in this study.

At study entry, the child and primary caretaker had a baseline evaluation that included extensive medical, environmental, demographic, and psychologic interviews.[15-17] The methods for determining the psychosocial characteristics of the households have been previously described.[15] A measure of social support had a scale of 0 to 9, with a score below 7 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, with scores ranging 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 caregivers are tests in which high scores indicate the presence of substantial psychologic problems. The mean normalized score (T score) on these tests was 50; we used the standard cutoff of 63 or greater as the criteria indicating the presence of substantial psychologic problems.

The children also underwent skin testing and spirometry. To obtain a year-long assessment of the child's asthma morbidity, each family was interviewed by telephone at 3, 6, and 9 months regarding days with wheezing, hospitalizations, days with poor sleep or reduced activity as a result of asthma, school days missed as a result of asthma, change of plans for the caretaker as a result of the child's asthma, and unscheduled medical visits for asthma.[12,13]

The comparison of the study sample with the remainder of the NCICAS population was based on an ANOVA or Mantel-Haenszel χ^2 test stratified by city. The Mantel-Haenszel χ^2 test adjusted for city was used to assess the relationship between allergen exposure (above or below the median) and mouse sensitization. The Wilcoxon rank-sum test was used to compare distributions of allergen levels among groups of patients. Logistic regression was used to assess the combined effect of allergen levels and atopy on mouse sensitization. For the analysis of morbidity data, subjects were classified as mouse sensitive and exposed if the mouse skin test response was positive and the mouse dust level in the kitchen was above the median. Subjects were classified as cockroach sensitive and exposed if the cockroach skin test response was positive and the cockroach dust level in the bedroom was above the median. An analysis of covariance with rank transformations of the morbidity measures was used to assess the effect of mouse and cockroach exposure and sensitivity on morbidity measures. The child's sex, a family history of asthma, and the child's score on the Child's Behavior Checklist were also included as independent variables on the basis of a previous analysis.[8] A P value of less than .05 was considered to be significant.

RESULTS

The children had a mean age of 6.2 years (range, 4-9 years). There were no significant differences in any demographic features between the study group and the total NCICAS study population, except for annual income (P = .012) and number of stressful life events (P = .015, Table I). Three hundred ninety-five (79%) children had at least one positive puncture skin test (PST) response, 270 (54%) had 1 to 4 positive PST responses, and 125 (25%) had 5 or more positive PST responses. Mouse sensitivity was detected in 89 (18%) of 499 children. The pattern of skin test reactivity was not different in the subpopulation of 499 children whose data were analyzed in this study and the entire study population who had valid skin test responses. The distribution of sensitization to mouse by city is illustrated in Table II, with a range from 12% in Cleveland to 27% in Washington, DC.

Those with mouse allergen levels greater than the median in the kitchen (1.6 μg/g) had a higher risk of mouse sensitization than those with levels below the median (23% vs 11%; odds ratio [OR], 2.2; 95% CI, 1.24-3.88; P = .007). A similar relationship was seen in the television-living room (OR, 1.75; 95% CI, 1.05-2.93; P = .03) but not in the bedroom (OR, 1.35; 95% CI, 0.82-2.21; P = .24; Table III). In addition, allergen levels in the kitchen were significantly higher in the homes of children with a positive mouse PST response (median, 5.8 μg/g) than in those of children with a negative PST response (median, 1.3 μg/g; P = .001). Likewise, the median levels were significantly different for the bedroom and television-living room in those with a positive and negative PST response (bedroom: 0.71 μg/g vs 0.51 μg/g, P = .033; television-living room: 1.19 μg/g vs 0.49 μg/g, P = .003).

Among other risk factors, atopy, defined by the number of other positive PST responses, was strongly related to mouse sensitization. The percentage of children with sensitization to mouse allergen increased as the degree of atopy increased (4% for no other positive PST response, 13% for 1 to 4 other positive PST responses, and 40% for those with >4 other positive PST responses; $P < .0001$). When atopy and exposure were considered together, 53% of the 62 children with more than 4 positive PST responses (excluding mouse) and allergen levels above the median in the kitchen had a positive PST response to mouse allergen compared with 21% of the 47 children with more than 4 positive PST responses and allergen levels below the median in the kitchen (P = .005 for exposure, $P < .0001$ for atopy). A similar relationship

TABLE I. Characteristics of the study population*

Characteristic	Study sample (n = 499)	NCICAS (n = 1528)
Mean ± SD age (y)	6.16 ± 1.68	6.16 ± 1.69
Male sex	315/499 (63.1%)	954/1528 (62.4%)
Race		
Hispanic	82/493 (16.6%)	295/1512 (19.5%)
Black	383/493 (77.7%)	1111/1512 (73.5%)
Other	28/493 (5.7%)	106/1512 (7.0%)
Annual income <$15,000†	296/446 (66.4%)	835/1364 (61.2%)
At least one smoker in home	287/494 (58.1%)	887/1513 (58.6%)
Family history of asthma	281/489 (57.5%)	868/1512 (57.4%)
Inadequate social support	209/488 (42.8%)	637/1499 (42.5%)
Large No. of stressful life events†	275/498 (55.2%)	893/1515 (58.9%)
Psychopathology in child	179/494 (36.2%)	531/1509 (35.2%)
Psychopathology in caretaker	238/476 (50.0%)	732/1470 (49.8%)

*Totals are the numbers of children for whom data were available.
†$P < .05$.

was seen for the television-living room ($P = .008$) but not for the bedroom ($P = .12$). Table IV illustrates these percentages of mouse sensitization with and without exposure in relation to atopy.

Fig 1 further illustrates the relationship between mouse allergen exposure, atopy, and mouse sensitization. In each of the 3 subgroups characterized by atopic status, there was a higher frequency of mouse sensitivity in children with mouse exposure (defined as a kitchen allergen level above the median) compared with those without exposure. In addition, Fig 1 shows the stepwise increase in mouse sensitivity in both the exposed and not exposed groups with increasing degrees of atopy.

In addition to the overall relationship with atopy, children with a positive PST response to cockroach also had a significantly higher prevalence of mouse sensitivity (29% vs 12%, $P < .0001$). A significantly higher percentage of children were also sensitized to mouse if there was visible evidence of mice in the home (25% vs 14%, $P = .004$). Other variables, such as age, sex, income, family history, smokers in the home, socioeconomic status, and psychosocial factors did not predict sensitization to mouse allergen.

Data were also analyzed to determine whether there were relationships among mouse sensitivity, exposure, and asthma morbidity (Table V). The data reflect multivariate analysis, with adjustments for sex, the score on the Child Behavior Checklist, and a family history of asthma. In addition, because of previous reports of the importance of cockroach allergen in the NCICAS population,[8] we used cockroach exposure and sensitivity as a covariate. Comparisons were therefore made between those who either did or did not have both sensitization and exposure to mouse, controlling for cockroach exposure and sensitization. There were no significant relationships detected between mouse sensitization and exposure for any of the morbidity variables, although there were trends toward significance for the median number of days wheezing in the past 2 weeks ($P = .1$), the number of nights when the child lost sleep in the past 2 weeks ($P = .11$), and the number of days when the child's activity was reduced in the past 2 weeks ($P = .10$).

DISCUSSION

We have previously reported that mouse allergen is widely distributed[11] in the homes of inner-city children with asthma, and in this study we attempt to further define the prevalence of mouse sensitivity, the risk factors for mouse sensitization, and the relationships among mouse exposure, mouse sensitivity, and asthma morbidity in the same population.

We found a prevalence of mouse sensitization of 18%, which compares with 37% for cockroach allergen, 35% for dust mite allergen, and 23% for cat allergen in the same study population.[8] However, although sensitivity to mouse allergen was not quite as common as the other major indoor allergens, the number of homes with detectable mouse allergen was comparable with that of homes with cockroach allergen and greater than that of homes with both cat and dust mite allergens. The combination of widespread exposure and frequent sensitization suggests that mouse allergen may be another important indoor allergen in at least some settings, such as the inner city.

The relationship between allergen exposure and sensitization to dust mite, cat, and cockroach allergen in the NCICAS patient population has been reported previously. Eggleston et al[5] showed a clear dose response between cockroach allergen levels and sensitization and also found that atopy was important in modifying the relationship between exposure and sensitization. However, they did not demonstrate the same exposure-sensitization relationship for dust mite or cat allergen. Our data demonstrate that a similar exposure-sensitization relationship exists for mouse allergen as it does for cockroach allergen and agree that the highest risk for sensitization occurs when atopic children are exposed to higher levels of allergen. This suggests that the factors underlying sensitization to mouse allergen, such as significant atopy and housing conditions conducive to mouse infestation, may be similar to those for cockroach allergen among this particular inner-city asthmatic population.

Most previous studies of cat and dog allergens in other populations have failed to detect a correlation between

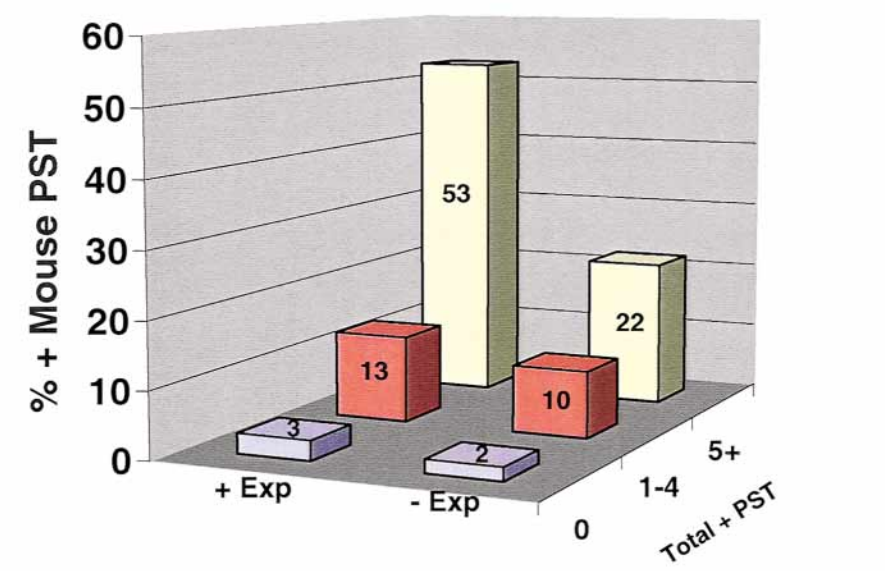

FIG 1. Interrelationships among mouse exposure, atopic status, and the frequency of sensitization to mouse allergen. Each *bar* represents a subgroup of children with or without exposure (kitchen Mus m 1 concentrations above or below the median) and atopy (total number of positive skin test responses, excluding mouse allergen). The height of the bar and the numbers on the bars represent the frequency of positive skin test responses in the children defined by these parameters.

TABLE II. Percentage of children with a positive skin prick test response to mouse allergen

Baltimore	24
Bronx	22
Chicago	11
Cleveland	11
Detroit	14
New York	17
St Louis	18
Washington, DC	27
Total	18

allergen exposure and sensitization.[5,9,10] These findings have been thought to be due to the virtually ubiquitous distribution of these allergens, making it difficult to define current allergen exposure with measures in the home. Our study is an example of a clear relationship between exposure to an animal allergen and sensitization. This may be due to the fact that this was a unique population or because there may be differences in the distribution of mouse allergen compared with that of cat and dog allergens. Further studies are needed to examine the significance of this relationship, ideally also including suburban or rural environments.

Other studies have shown that dust mite allergen exposure is associated with sensitization rates outside of the NCICAS population. Peat et al[20] found that dust mite sensitization was clearly increased in environments with high mite allergen concentrations among diverse climatic regions in Australia. Lau et al[21] found a correlation between mite allergen concentrations in mattresses and mite-specific IgE in dust mite–sensitive asthmatic subjects, whereas Kuhr et al[22] found that the incidence of positive mite PST response was strongly dependent on the atopic status of the children and the level of mite allergen in the settled dust. Furthermore, Sporik et al[23] found that the frequency of sensitization to dust mite and cockroach allergen was strongly associated with atopy and increasing domestic concentrations of these allergens, whereas the same relationship was not seen for cat allergen. The relationship of mouse allergen exposure and sensitization in our study is therefore similar to the relationships found in these dust mite studies.

We found the strongest relationship between sensitization and mouse allergen exposure in the kitchen, with less-significant associations in the television-living room and bedroom. These data differ from those for cockroach, in which the strongest relationship was seen with bedroom allergen exposure, even though the highest allergen concentrations were found in the kitchen.[5] This may have important implications regarding the nature of mouse allergen dispersion and exposure. The strategies that may be needed for effective mouse allergen control may require more attention to the kitchen, but further study is necessary to determine where mouse allergen is most clinically important.

Because other variables might increase the risk of mouse sensitization, we analyzed the data adjusting for factors such as atopy, sex, smoking in the household, psychosocial stressors, and socioeconomic status. We found that atopy had a highly significant influence on mouse sensitization. An additive effect between atopy and allergen exposure was also demonstrated, suggesting that the combination of being highly atopic and exposed

TABLE III. Relationship of mouse allergen exposure to mouse sensitization

Room	Allergen exposure*	Positive PST response to mouse (%)	*P* value†
Kitchen	Above median	23	
	Below median	11	.007
Television-living room	Above median	23	
	Below median	13	.03
Bedroom	Above median	21	
	Below median	15	.24
Any Room	Above median	21	
	Below median	12	.10

*Mouse allergen level above or below the median concentration for room.
†Mantel-Haenszel χ^2 test adjusting for city.

TABLE IV. Relationship of atopy and exposure to mouse sensitization

		Atopy†			
Room	Allergen exposure*	0	1-4	> 4	*P* value‡
Kitchen	Above median	2.6	13	53	.005 (exposure)
	Below median	2.2	10	22	<.0001 (atopy)
Television-living room	Above median	2.6	15	54	.008 (exposure)
	Below median	5.5	12	24	<.0001 (atopy)
Bedroom	Above median	4.3	14	46	.12 (exposure)
	Below median	3.4	11	33	<.0001 (atopy)
Any room	Above median	3.3	13	47	.10 (exposure)
	Below median	4.7	12	23	<.0001 (atopy)

Results indicate the percentage of children with a positive mouse PST response.
*Mouse allergen level above or below the median concentration for room.
†Number of positive skin test responses, not including mouse allergen.
‡*P* value for logistic regression, including both exposure and atopy.

TABLE V. Relationship of mouse and cockroach sensitivity and exposure to asthma morbidity

	Negative for cockroach		Positive for cockroach*		
	Negative for mouse (1)	Positive for mouse† (2)	Negative for mouse (3)	Positive for mouse† (4)	*P* value‡
No. of children	297	33	71	15	
Any hospitalizations in past year (%)	5.4	12.1	19.7	20.2	.26
Unscheduled medical visits in past year (n)	1.4	1.5	2.8	1.5	.93
Days of wheezing in past 2 wk (n)	3.2	3.6	4.1	4.9	.10
Nights when child lost sleep in past 2 wk (n)	1.6	1.8	2.0	2.5	.11
Days when child's activity was reduced in past 2 wk (n)	1.8	2.3	2.2	2.3	.10
School days missed in past 3 mo (%)§	6.0	4.8	7.7	8.1	.49
Days when caregiver changed plans in past year (n)	10.2	8.0	16.4	13.2	.45
Nights when caregiver lost sleep in past 2 wk (n)	2.1	1.9	2.4	2.7	.27

Number of children reflects the number with valid skin test responses, adequate kitchen dust samples, and asthma history and morbidity data for analysis (n = 416).
*Children with positive results for cockroach allergen had both a positive cockroach skin test response and cockroach dust levels above the median in the bedroom.
†Children with positive results for mouse allergen had both a positive mouse skin test response and mouse dust levels above the median in the kitchen.
‡Comparison between children with negative and positive results for mouse allergen, controlling for cockroach.
§For days of school missed, data with respect to mouse allergen were available for 284 children in group 1, 32 children in group 2, 66 children in group 3, and 14 children in group 4.

to high mouse allergen levels maximizes the risk for sensitization. This is similar to what has been reported for cockroach allergen,[5] again suggesting the parallel nature of the 2 allergens. We did not find any association between mouse sensitization and any of the other variables that were studied.

We also had extensive data on asthma morbidity in this population and therefore had the opportunity to analyze whether the combination of mouse sensitivity and exposure contributed to disease activity. Although there were trends suggesting some relationship between mouse allergen exposure and sensitization in some of the mor-

bidity variables (ie, number of days of wheezing and nights of lost sleep), none of these reached significance. These findings suggest that although mouse allergen exposure and sensitization may contribute to asthma severity, this relationship was not as strong as that seen for cockroach allergen in this population.

We conclude that mouse allergen may be important in the pathogenesis of asthma among inner-city children. We have demonstrated a high prevalence of exposure and have shown that allergen exposure, atopy, and sensitization to cockroach allergen were significant risk factors for mouse sensitization. Although further study is clearly needed to define its true clinical importance, in both inner-city and other environments, we believe that mouse allergen is likely to be an important indoor allergen that has thus far been underrecognized.

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APPENDIX

In addition to the authors, the following investigators from the National Cooperative Inner-City Asthma Study participated in this study. Albert Einstein School of Medicine, Bronx, NY: D. L. Rosenstreich, E. Crain, and L. Bauman; Children's Memorial Hospital, Chicago, Ill: R. Evans III, J. Lavigne, Y. D. Senturia, C. M. Weil, K. K. Christoffel, and H. J. Binns; Cook County Hospital, Chicago, Ill: M. Sullivan, J. H. Mayefsky, and M. F. McDermott; Rainbow Babies and Children's Hospital, Cleveland, Ohio: C. Kercmar, S. Redline, and S. Wade; Henry Ford Hospital and Medical Center, Detroit, Mich: D. Ownby, J. A. Anderson, F. E. Leicky, C. L. M. Joseph, and C. Johnson; Mount Sinai School of Medicine, New York, NY: M. Kattan, C. Lamm, M. T. Tin, G. Butts, E. Luder, and D. Baker; Washington University Medical School, St Louis, Mo: H. J. Wedner and G. Evans; St Louis University School of Medicine, St Louis, Mo: R. G. Slavin; Howard University, Washington, DC: F. Malveux, A. Thomas, S. Molock, and M. Richard; National Institute of Allergy and Infectious Diseases, Program Office, Bethesda, Md: P. Gergen, E. Smartt, K. Weiss, and R. Kaslow; Center for Occupational Environmental Health, Irvine, Calif: D. Baker; New England Research Institues, Watertown, Mass: H. Mitchell, K. McNiff-Mortimer, H. Lynn, and S. Islam.