

Household mouse allergen exposure and asthma morbidity in inner-city preschool children

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Background: Inner-city children experience disproportionate asthma morbidity, and suspected reasons include indoor environmental exposures.

Objective: To determine if mouse allergen exposure is a risk factor for asthma morbidity.

Methods: Preschool children with asthma were recruited from inner-city Baltimore, MD. Skin testing was performed and blood was collected at the baseline visit for quantification of mouse allergen specific IgE. A questionnaire evaluated symptoms, medication, and health care use at baseline, 3 months, and 6 months. A trained technician collected dust samples from the child's home for analysis of Mus m 1 at baseline, 3 months, and 6 months. Outcomes were compared between mouse-sensitized, highly exposed children and all other children.

Results: A total of 127 children had complete data for mouse sensitization status and bedroom settled dust mouse allergen levels at baseline. The mean age of the children was 4.4 years, 92% were African American, and 26% were sensitized to mouse. Mouse-sensitized children exposed to higher levels of Mus m 1 ($>0.5 \mu\text{g/g}$) had 50% more days of symptoms (incidence rate ratio [IRR], 1.5; 95% confidence interval [CI], 1.1–2.1) and 80% more days of β -agonist use than other children (IRR, 1.8; 95% CI, 1.3–2.5). Children in the sensitized and highly exposed group were also more likely to have an unscheduled physician visit (odds ratio [OR], 3.1; 95% CI, 1.6–6.3), emergency department visit (OR, 2.1; 95% CI, 1.1–4.1), and hospitalization (OR, 36.6; 95% CI, 4.1–327.3) than other children. These associations between mouse allergen exposure and asthma symptoms and morbidity remained statistically significant after adjusting for potential confounders, including atopy and cockroach sensitization and exposure.

Conclusions: In mouse-sensitized inner-city children, exposure to mouse allergen may be an important cause of asthma morbidity.

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INTRODUCTION

Inner-city children with asthma, particularly those of African American race, continue to have disproportionate rates of morbidity and mortality from asthma. Although some inner-city asthma morbidity has been attributed to environmental factors, such as cockroach allergen exposure¹ and environmental tobacco smoke,^{2,3} other environmental factors, which are just beginning to be examined, may contribute to asthma morbidity.

Rodent allergens, for example, may play an important role in asthma morbidity, because exposure and sensitization to these allergens are common.^{4–8} In occupational settings, where exposure can be high, rodent allergen exposure is clearly related to asthma symptoms.^{9,10} In a national study of inner-city homes of children with asthma, exposure to rat allergen among rat-sensitized children was associated with higher rates of hospitalization and unscheduled medical visits for asthma.¹¹ Since mouse allergen exposure has also been related to symptoms in occupational settings,^{12,13} and rat and mouse allergens are similar in their airborne distribution and particle size,^{14,15} mouse allergen may be an important contributor to asthma morbidity outside the occupational setting. In addition, mouse allergen is virtually ubiquitous in inner-city homes, and sensitization rates as high as 18% have been found in inner-city children.^{5,6,16}

Despite the fact that exposure and sensitization to mouse are commonplace in the inner city, it is still unclear whether mouse allergen exposure is a cause of inner-city asthma morbidity. To address this question, we conducted a prospective cohort study, collecting repeated measures of mouse allergen exposure and asthma outcomes in inner-city preschool children with asthma.

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MATERIALS AND METHODS

Study Population and Recruitment Procedures

Recruitment for this study, a part of the Center for Childhood Asthma in the Urban Environment, occurred between September 2001 and December 2003. Participants were recruited from the health systems that provide care to most residents of East Baltimore, MD. Inclusion criteria were (1) age between 2 and 6 years, (2) residence within the catchment area, (3) physician-diagnosed asthma, and (4) symptoms of asthma and/or medication use for asthma in the previous 6 months. The study was approved by the Johns Hopkins School of Medicine Institutional Review Board.

Home Environmental Evaluation

During the home environmental visit, environmental technicians completed an inspection checklist,¹⁷ and settled dust was collected for mouse allergen analysis. A household dust sample was collected from each of the following rooms using a standardized vacuum method: kitchen, television-living room, and child's bedroom (including the bed and bed linens).¹⁸ Protein was extracted from the filters and dust samples using a standardized protocol, and Mus m 1 was quantified by sandwich enzyme-linked immunosorbent assay (ELISA) using immunosorbent purified sheep anti-Mus m 1 (supplied by Dr J. Ohman).¹⁴ The limit of detection for the Mus m 1 ELISA was 2.2 ng/g. The home environmental evaluation and sample collection were repeated at 3 and 6 months.

Clinical Evaluation

During the baseline clinic visit, each child underwent skin prick testing (Multi-Test II, Lincoln Diagnostics, Decatur, IL) to 14 aeroallergens: American and German cockroach, dust mite mix, cat dander, dog hair-dander, mouse epithelia, rat epithelia, 3 pollens (Eastern Oak mix, grass mix, and ragweed mix), and 4 molds (*Helminthosporium*, *Alternaria*, *Penicillium*, and *Aspergillus*). Atopy was defined as at least 1 positive skin test result to the panel of allergens tested. Serum samples were analyzed for mouse allergen specific IgE by CAP radioallergosorbent test (RAST). A mouse urine CAP-RAST value greater than 0.35 kU_A/L was considered a positive result. A positive skin test result was defined as a wheal size of at least 2 mm greater than the negative control, as in previous childhood asthma studies.^{6,19} Mouse sensitization was defined as either a positive skin test result to mouse epithelial extract or a positive mouse urine CAP-RAST result. Questions from the International Study of Asthma and Allergies in Childhood²⁰ and the Children's Health Survey for Asthma²¹ were used at the baseline, 3-month, and 6-month visits to evaluate indicators of poor asthma control, such as nocturnal awakening, exercise-induced symptoms, rescue medication use, and unscheduled physicians visits, emergency department (ED) visits, and hospitalizations.

Statistical Analysis

Because Mus m 1 was present in 100% of bedrooms, we compared a lower exposure group to a higher exposure group.

Since previously published findings indicated that a settled dust concentration of Mus m 1 that exceeds 0.5 $\mu\text{g/g}$ is predictive of detectable airborne Mus m 1, we defined higher exposure as a bedroom Mus m 1 level greater than 0.5 $\mu\text{g/g}$.¹⁶ Lower exposure was defined as Mus m 1 exposure of 0.5 $\mu\text{g/g}$ or less, which reflected the lowest quartile of exposure in our population.

We used an approach taken in previous studies^{1,6,11} and stratified participants into 4 groups based on exposure and sensitization status: the negative sensitization/lower group included those with no evidence of sensitization to mouse allergen and a bedroom Mus m 1 level of 0.5 $\mu\text{g/g}$ or less; the negative sensitization/higher group included those with no evidence of sensitization to mouse and a bedroom Mus m 1 level greater than 0.5 $\mu\text{g/g}$; the positive sensitization/lower group included participants with either a positive skin test or CAP-RAST result to mouse and a bedroom Mus m 1 level of 0.5 $\mu\text{g/g}$ or lower; and the positive sensitization/higher group included participants with either a positive skin test or CAP-RAST result to mouse and a bedroom Mus m 1 level greater than 0.5 $\mu\text{g/g}$. Mouse sensitization status was fixed at all time points, but exposure status was time dependent so that a participant's assigned sensitization/exposure group could vary over time.

The χ^2 test was used to compare proportions, and the *t* test was used to compare continuous data. Logistic regression and generalized estimating equations were used to generate marginal models of the relationships between sensitization/higher exposure and the repeated dichotomous outcome measures (hospitalization, ED visit, and unscheduled physician visit). Negative binomial regression and generalized estimating equations were used to model the relationships between sensitization/higher exposure and repeated measures of days of symptoms or medication use. Multivariate regression was used to adjust for potential confounding variables. Cockroach sensitization and exposure were adjusted for in the final models using a single dichotomous variable that indicated if an individual was sensitized to cockroach and was exposed to more than 8 U/g of Bla g 1 in the bedroom.¹ All analyses were performed with StataSE statistical software, version 8.0 (Stata Corp, College Station, TX). Statistical significance was defined as $P < .05$.

RESULTS

Study Population

Of the 150 children recruited for the study, 127 (85%) had complete data for mouse sensitization status and bedroom settled dust mouse allergen levels at baseline. Most of the participants were male (58%), were African American (92%), and had public health insurance (90%) (Table 1). Ninety-two percent of participants reported wheezing during the 12 months before the baseline visit, and 68% were atopic. Overall, 44% of children had skin test sensitivity to cockroach, 33% to cat, 27% to rat, 26% to dust mite, and 13% to dog. Twenty-seven percent had skin test sensitivity to a mold and

Table 1. Characteristics of Children With Asthma

Characteristics	No. (%) of children (N = 127)
Race/ethnicity	
African American	117 (92)
White	4 (3)
Other	6 (5)
Sex	
M	74 (58)
F	53 (42)
Health insurance type	
Public insurance	112 (88)
Private	12 (9)
Self-pay or other	3 (2)
Educational attainment of caregiver	
Eighth grade, some high school	48 (38)
High school graduate	55 (43)
Some college or more	24 (19)
Housing type	
Row house or apartment	118 (93)
Detached or semidetached home	9 (7)
Smoker in the home	
Yes	71 (56)
No	56 (44)

32% to a pollen. Thirty-five children were sensitized to mouse; 23 had a positive skin test result to mouse and 26 had a positive mouse urine CAP-RAST result. Ninety-one percent of the mouse-sensitized participants had at least 1 other positive skin test result.

Caregivers reported that their children spent most of the time inside their homes, where allergen levels were measured. Specifically, participants were only away from their homes for a mean of 5.4 hours per day and were only outdoors for a mean of 2.1 hours per day. At baseline, Mus m 1 was detected in 100% of bedrooms, and levels in the bedroom, kitchen, and television room were strongly correlated (bedroom and television room: $r = .79$; bedroom and kitchen: $r = .67$; television room and kitchen: $r = .72$; $P < .001$ for all correlations). The median Mus m 1 level in bedroom settled dust was 2.5 $\mu\text{g/g}$ (interquartile range [IQR], 0.6–8.8 $\mu\text{g/g}$). Der p 1 was detected in only 5% of bedrooms, and Der f 1 levels were low, with a median of 41 ng/g (IQR, below detection to 327 ng/g). Fel d 1 and Can f 1 levels were also relatively low (median, 470 ng/g; IQR, 189–9,188 ng/g; and median, 124 ng/g; IQR, below detection to 473 ng/g, respectively). Sixty-seven percent of participants were also exposed to Bla g 1, and the median bedroom Bla g 1 level was 2.6 U/g (IQR, below detection to 14 U/g).

Asthma Symptoms and Health Care Use

At baseline, 22 children (17%) were in the negative sensitization/lower exposure group, 72 (57%) were in the negative sensitization/higher exposure group, 8 (6%) were in the positive sensitization/lower exposure group, and 25 (20%) were in the positive sensitization/higher exposure group. Because exposure status was reassessed at 3 and 6 months, the composition of these sensitization and exposure groups varied

over time. For example, a mouse-sensitized study participant could have moved between the positive sensitization/lower and positive sensitization/higher groups, and a nonsensitized participant could have moved between the negative sensitization/lower and negative sensitization/higher exposure groups at subsequent study visits. In addition, because of attrition, there were 127 study participants at baseline, 110 (87%) at the 3-month visit, and 116 (91%) at the final 6-month study visit.

Both asthma symptoms and asthma-related health care use were more common among participants who were in the mouse-sensitized/higher-exposure group than the others. In the initial cross-sectional analyses at each time point, the sensitized/highly exposed group tended to have more days of symptoms, slowed activity, exercise-induced symptoms, and short-acting β -agonist use than the other groups (Table 2). For example, at the baseline study visit, the sensitized, higher-exposure group had used a short-acting β -agonist an average of 5.8 days during the previous 2 weeks compared with 3.4 days for the nonsensitized or non-highly exposed group (Table 2). Although these findings were not statistically significant across all outcomes at all time points in the initial analyses, the associations observed in the final longitudinal data analyses that accounted for repeated measures of exposure and outcomes were statistically significant. In addition, the associations between mouse allergen exposure and asthma outcomes were independent of cockroach sensitization/exposure, public health insurance, study visit, atopy, age, and sex (Table 3). Specifically, the sensitized, highly exposed group reported significantly more days of symptoms (incidence rate ratio [IRR], 1.5; 95% confidence interval [CI], 1.1–2.0), days of slowed activity as a result of asthma (IRR, 1.5; 95% CI, 1.1–2.2), days of exercise-induced symptoms (IRR, 1.6; 95% CI, 1.1–2.2), days of cough (IRR, 1.6; 95% CI, 1.1–2.4), and days of short-acting β -agonist use (IRR, 1.8; 95% CI, 1.3–2.5) than the others. Thus, sensitized, highly exposed children had 50% more days of symptoms and slowed activity, 60% more days of exercise-induced symptoms, and 80% more days of rescue medication use than the nonsensitized or non-highly exposed children. The association between mouse sensitization/higher exposure and nocturnal symptoms was not statistically significant after controlling for the potential confounders (IRR, 1.3; 95% CI, 0.9–1.8).

Asthma-related health care use was also more common among the mouse-sensitized/higher-exposure group than the other groups (Table 4). Unscheduled physician visits, ED visits, and hospitalizations were all more common in this group. For example, at the 3-month study visit, 8 (31%) of the 26 children in the sensitized, higher-exposure group had had an unscheduled asthma-related physician visit in the previous 3 months compared with 9 (9%) of the 102 nonsensitized or non-highly exposed children. There were a total of 10 hospitalizations in this study population, and 9 of the 10 occurred in children who were sensitized and highly exposed to mouse. After adjusting for cockroach sensitization and exposure, public health insurance status, atopy, age, sex, and study visit, the children in the sensitized/higher-exposure group were

Table 2. Days of Symptoms and β -Agonist Use and Mouse Sensitization/Exposure Status

	Negative mouse sensitization/lower exposure	Negative mouse sensitization/higher exposure	Positive mouse sensitization/lower exposure	Positive mouse sensitization/higher exposure	P value*
Days of symptoms, mean					
Baseline	2.0	2.1	1.9	2.8	.37
3 mo	2.5	2.2	3.8	4.5	.01
6 mo	2.7	2.3	0.7	3.0	.32
Days of slowed activity, mean					
Baseline	1.6	1.9	2.4	2.6	.38
3 mo	3.7	1.5	0	3.8	.06
6 mo	2.3	1.6	0.7	1.8	.85
Days of exercise-induced symptoms, mean					
Baseline	0.8	1.6	1.6	2.5	.14
3 mo	2.8	1.6	0	3.1	.13
6 mo	1.3	1.1	0	1.6	.32
Days of cough, mean					
Baseline	1.4	1.1	2.4	2.1	.66
3 mo	1.1	0.8	0.4	2.6	.004
6 mo	1.3	1.0	0	1.2	.74
Nights of wakening, mean					
Baseline	2.3	1.9	2.4	1.2	.41
3 mo	2.0	1.5	0	3.4	.02
6 mo	2.2	1.3	0.3	2.4	.20
Days of short-acting β -agonist use, mean					
Baseline	3.4	3.4	3.6	5.8	.04
3 mo	3.9	2.7	2.8	5.5	.02
6 mo	3.8	2.5	0.5	4.8	.03

* *t* test comparing mouse-sensitized, highly exposed children to all others.

Table 3. Asthma Symptoms and Health Care Use Among Mouse-Sensitized, Highly Exposed Children*

	OR or IRR (95% CI)	Adjusted OR or IRR (95% CI)†
Health care use		
Unscheduled visit	3.1 (1.6–6.3)	3.1 (1.5–6.5)
ED visit	2.1 (1.1–4.1)	2.1 (1.0–4.3)
Hospitalization	36.6 (4.1–327.3)	69.9 (5.8–838.9)
Asthma symptoms		
Days of symptoms	1.5 (1.1–2.1)	1.5 (1.1–2.0)
Days of slowed activity	1.6 (1.1–2.2)	1.5 (1.1–2.2)
Days of exercise-induced symptoms	1.7 (1.2–2.4)	1.6 (1.1–2.2)
Days of cough	1.6 (1.1–2.3)	1.6 (1.1–2.4)
Nights of wakening	1.5 (1.1–2.1)	1.3 (0.9–1.9)
Days of β -agonist use	1.8 (1.3–2.4)	1.8 (1.3–2.5)

Abbreviations: CI, confidence interval; ED, emergency department; IRR, incidence rate ratio; OR, odds ratio.

* Values are ORs for health care use and IRRs for asthma symptoms.

† Adjusted for age, sex, atopy, cockroach sensitization and exposure, public health insurance, and study visit.

significantly more likely to have an unscheduled physician visit (odds ratio [OR], 3.0; 95% CI, 1.4–6.3), an ED visit (OR, 2.0; 95% CI, 1.0–4.2), and hospitalization (OR, 70.6; 95% CI, 5.5–909.6) compared with the others (Table 3).

In contrast, cockroach sensitization or exposure was not associated with asthma symptoms, short-acting β -agonist use, or health care use. For example, cockroach-sensitized children exposed to higher levels of cockroach allergen did not have more days of symptoms (IRR, 0.9; 95% CI, 0.6–1.2),

nights of wakening (IRR, 1.0; 95% CI, 0.7–1.5), or days of β -agonist use (IRR, 0.9; 95% CI, 0.6–1.2) than other children. Similarly, they were not more likely to visit the ED (OR, 1.2; 95% CI, 0.6–2.4) or be hospitalized (OR, 1.2; 95% CI, 0.2–6.7) than other children.

DISCUSSION

This study provides evidence to implicate exposure to mouse allergen as a cause of asthma morbidity in the inner city. For

Table 4. Asthma-Related Health Care Use and Mouse Sensitization/Exposure Status

	No. (%) of children				<i>P</i> value*
	Negative mouse sensitization/lower exposure	Negative mouse sensitization/higher exposure	Positive mouse sensitization/lower exposure	Positive mouse sensitization/higher exposure	
Unscheduled physician visit					
Baseline	5/22 (23)	11/72 (15)	1/8 (13)	6/25 (24)	.39
3 mo	2/25 (8)	7/54 (13)	0/5 (0)	8/26 (31)	.01
6 mo	4/25 (16)	3/60 (5)	0/6 (0)	7/25 (28)	.005
ED visit					
Baseline	5/22 (23)	16/72 (22)	3/8 (38)	7/25 (28)	.64
3 mo	4/25 (16)	6/54 (11)	1/5 (20)	9/26 (35)	.01
6 mo	5/25 (20)	6/60 (10)	1/6 (17)	7/26 (27)	.09
Hospitalization					
Baseline	0/22 (0)	0/72 (0)	1/8 (13)	3/25 (12)	.005
3 mo	0/25 (0)	0/54 (0)	0/5 (0)	5/26 (19)	<.001
6 mo	0/25 (0)	0/59 (0)	0/6 (0)	1/26 (4)	.06

Abbreviation: ED, emergency department.

* χ^2 test comparing the mouse-sensitized, highly exposed group to all others.

mouse-sensitized inner-city preschool children with asthma, exposure to settled dust bedroom mouse allergen levels above 0.5 $\mu\text{g/g}$ was associated with multiple measures of poor asthma control, including symptom days, short-acting β -agonist use, and unscheduled physician visits, ED visits, and hospitalization. These findings implicate household mouse allergen exposure as another potential explanation for the striking disparities in asthma that are seen for inner-city children, especially African Americans.

To our knowledge, only one previous study, the National Cooperative Inner-City Asthma Study (NCICAS), has examined mouse allergen exposure and asthma morbidity among inner-city children with asthma. In that study, although there was a positive association between allergen exposure and some measures of morbidity, none of the associations was statistically significant.⁶ In the current study, however, exposure to higher levels of *Mus m 1* was significantly associated with poor asthma control and asthma-related health care use. In the NCICAS, the site of the exposure was the kitchen, whereas in the current study, we collected dust from the child's bedroom. We selected the bedroom as a potentially more relevant site of exposure for young children, because they spend more time there and, while asleep, are in close contact with the surface from which we sampled. In fact, one study found that bedroom allergen exposure was more strongly associated with risk of allergic sensitization than allergen levels in other rooms in the home,²² suggesting that allergen concentrations in the bedroom may be more closely related to true exposure than concentrations found in other rooms.

Cockroach allergen exposure was not associated with either poor asthma control or asthma-related health care use in our study but was associated with asthma morbidity in the NCICAS population. The reasons for these differences are unclear but could be a reflection of the differences in the ages

of the respective populations. Although another study found an association between cockroach allergen exposure and recurrent wheeze in young children, allergic sensitization data were not collected, so it is unclear if the association was due to an allergic response or confounding by unmeasured psychosocial factors or other allergen exposures.²³ In addition, our study population was exposed to higher levels of mouse allergen and lower levels of cockroach allergen, in general, than the NCICAS population. Therefore, conditions may have been optimal for detecting a mouse effect in the Baltimore-based study and optimal for detecting a cockroach effect in the NCICAS. Whatever the reasons for the apparent differences in the 2 studies, the impact of household mouse allergen exposure on asthma morbidity may be substantial and merits further study.

Even though mouse allergen exposure is likely to be associated with a number of risk factors for poor asthma control, such as poor housing conditions and markers of low socioeconomic status,^{4,16,24} our findings suggest that exposure to mouse allergen is directly linked to poor asthma control and not simply a marker for these other risk factors. If the observed association between mouse allergen exposure and poor asthma control was due to low socioeconomic status or other psychosocial variables that are associated with higher levels of mouse allergen, we would expect that the unsensitized children who were exposed to higher levels would have more symptoms and health care use than those exposed to lower levels of mouse allergen. Instead, the children in the unsensitized/higher-exposure group had similar estimates of poor asthma control and morbidity as the unsensitized/lower-exposure group, providing further evidence that exposure to higher mouse allergen levels has a direct effect on asthma control.

Our study population consisted of preschool children with asthma, defined by (1) a health encounter for wheezing, (2)

caregiver report of a physician-confirmed asthma diagnosis, and (3) recent symptoms. Although some of the younger children could be transient wheezers whose asthma symptoms will resolve as they approach school age, most (67%) of the children were atopic, a predictor of persistent wheeze.²⁵⁻²⁷ Furthermore, the differences in asthma control and morbidity between exposure/sensitization groups were not likely due to differences in asthma phenotype (transient vs persistent wheezing), because adjusting for atopy had little effect on our findings.

It is conceivable that caregivers of children with poorly controlled asthma may have undertaken greater efforts to exterminate pests in their homes, potentially lowering their households' mouse allergen levels. However, this type of selection bias would have attenuated, rather than enhanced, the association that was found between mouse allergen exposure and poor asthma control. Because our study population did not include a nonexposed group and the sample size was modest, we were unable to determine if mouse allergen levels below 0.5 $\mu\text{g/g}$ could be considered safe or if there was a dose-response effect of mouse allergen exposure on asthma control and morbidity. The recruitment process for this study may have selected more severe asthmatic patients overall, since children were initially selected based on a health encounter for wheezing, so that milder asthmatic patients who did not visit their physician's office for wheezing would have been excluded. Because of a potentially more severe asthma population, our findings may not apply to preschool children with very mild asthma. Our study population was also racially, socioeconomically, and geographically homogeneous, so it is unclear if these findings can be generalized to other populations, such as older children, adults, or non-African Americans. On the other hand, the homogeneity of our study population is a significant strength in that the association of mouse allergen exposure and poor asthma control is unlikely to be attributable to confounding by differences in geographic location, socioeconomic status, or race.

The study design and analysis in this study provide stronger evidence of allergen exposure and health effects than those used in previous studies. Previous studies have relied on an evaluation of household allergen exposure at one point in time and have related that measure of exposure to outcomes during a variable period—from 2 weeks to 1 year.^{1,6,11} Those analyses assume that one exposure reflects typical exposure, and this approach does not allow for time-varying health status relative to changing exposure levels. In the current study, household mouse allergen exposure and asthma outcomes were evaluated repeatedly at baseline, 3 months, and 6 months. In this way, outcomes within an individual person vary as a function of time-varying exposure. This method overcomes the problem of assuming that a single exposure measure represents a constant level of exposure (which is unlikely to be true). This time-dependent analysis adds strength to the causal inference by allowing a person's symptoms to change along with changing levels of exposure.

The results of this study provide compelling evidence that household mouse allergen exposure and asthma morbidity are related and underscore the potential impact of mouse allergen exposure on asthma morbidity among inner-city children. Mouse allergen exposure and sensitization should be evaluated in future inner-city environmental studies, and efforts should focus on developing feasible environmental interventions and studying the impact of exposure reduction on asthma morbidity. In addition, clinicians should evaluate asthmatic children for mouse sensitization through skin testing or in vitro laboratory testing and recommend avoidance measures in sensitized children.

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