Mouse allergen is the major allergen of public health relevance in Baltimore City

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Background: Cockroach and mouse allergens have both been implicated as causes in inner-city asthma morbidity in multicenter studies, but whether both allergens are clinically relevant within specific inner-city communities is unclear.
Objective: Our study aimed to identify relevant allergens in Baltimore City.
Methods: One hundred forty-four children (5-17 years old) with asthma underwent skin prick tests at baseline and had clinical data collected at baseline and 3, 6, 9, and 12 months. Home settled dust samples were collected at the same time points for quantification of indoor allergens. Participants were grouped based on their sensitization and exposure status to each allergen. All analyses were adjusted for age, sex, and serum total IgE level.
Results: Forty-one percent were mouse sensitized/exposed, and 41% were cockroach sensitized/exposed based on bedroom floor exposure data. Mouse sensitization/exposure was associated with acute care visits, decreased FEV_1/forced vital capacity percentage values, fraction of exhaled nitric oxide levels, and bronchodilator reversibility. Cockroach sensitization/exposure was only associated with acute care visits and bronchodilator reversibility when exposure was defined by using bedroom floor allergen levels. Mouse-specific IgE levels were associated with poor asthma health across a range of outcomes, whereas cockroach-specific IgE levels were not. The relationships between asthma outcomes and mouse allergen were independent of cockroach allergen. Although sensitization/exposure to both mouse and cockroach was generally associated with worse asthma, mouse sensitization/exposure was the primary contributor to these relationships.
Conclusions: In a community with high levels of both mouse and cockroach allergens, mouse allergen appears to be more strongly and consistently associated with poor asthma outcomes than cockroach allergen. Community-level asthma interventions in Baltimore should prioritize reducing mouse allergen exposure. (J Allergy Clin Immunol 2013;132:830-5.)

Key words: *Inner-city asthma, childhood asthma, mouse allergen, cockroach allergen, indoor allergens*

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Asthma is one of the most common diseases of childhood, and it is known to have a high prevalence among urban minority children.[1,2] Urban minority children also display more asthma morbidity than nonurban nonminority children. The cause for this is believed to be multifold, but the major indoor allergens (dust mite, cat, cockroach, and mouse) have repeatedly been shown to be major contributors to asthma morbidity in this population.[3-14] Because mouse, cockroach, cat, and dust mite allergen levels vary across and even within cities in the United States,[6,15,16] it is generally thought that this spatial variability in indoor allergen levels provides insight into which allergens are most clinically relevant within a geographic area. For example, if there are high prevalences and concentrations of certain allergens within a given community, the assumption is that these particular allergens are the ones that contribute to asthma morbidity in that community. As such, the prevailing thought is that both cockroach and mouse allergens are major causes of asthma morbidity in US inner cities that have high levels of these 2 pest allergens.[17] However, there are scant data to support this assumption because the multicenter inner-city asthma studies conducted to date have not, by design, focused on site-specific allergen exposure and asthma morbidity.[5,6,15]

It is also well known that sensitization and exposure to any particular allergen rarely occurs in isolation in childhood asthma, yet many inner-city asthma studies examine the effects of sensitization and exposure to a single allergen, often without adjusting for other allergens.[15,18] Although it is quite plausible that being sensitized and exposed to multiple allergens can have greater adverse effects than being sensitized and exposed to any single allergen, the combined effects of sensitization and exposure to these allergens on inner-city asthma health have not been evaluated.

Determining the specific allergen profile most highly associated with asthma morbidity within a community is not only important for managing patients with asthma and allergies from that community but also informs the development of community-level asthma interventions that would aim to reduce levels of the key allergen or allergens in the community as a whole. Therefore we aimed to identify the profile of allergens of greatest public health relevance in 1 inner-city community, Baltimore City, and to

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Abbreviations used
FENO: Fraction of exhaled nitric oxide
FVC: Forced vital capacity
PR: Prevalence ratio

estimate the combined effects of these allergens on asthma health. To accomplish these objectives, we examined relationships between exposure and sensitization to indoor allergens and asthma health in a prospective cohort study of 150 Baltimore City children and adolescents with persistent asthma.

METHODS

Study population

One hundred fifty Baltimore City children (5-17 years old) with persistent asthma were enrolled and followed for 1 year as part of the Mouse Allergen and Asthma Cohort Study. The primary objective of this study was to evaluate relationships between mouse allergen exposure and clinical markers of asthma and to evaluate the relationships between other indoor allergen exposures, particularly cockroach, and clinical markers of asthma. Participants were recruited from the Johns Hopkins Emergency Department, an institutional review board–approved database of past study participants who had consented to being contacted for future studies, and miscellaneous sources, including health fairs and word of mouth, from April 2007 to June 2009. Participants had to have received a diagnosis of asthma from a physician at least 1 year before the baseline study visit. Participants had to be receiving a controller medication or meet the criteria for persistent asthma, as defined by the National Asthma Education and Prevention Program guidelines (National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program; 2007). Participants were eligible if they had experienced an asthma exacerbation in the previous year. An asthma exacerbation was defined as requiring a trip to the emergency department or a physician's office because of asthma symptoms or an oral corticosteroid burst in the last 12 months. Smokers were excluded. Smoking status was determined based on the results of rapid urine cotinine screening. Participants with a positive rapid urine cotinine test result at baseline did not continue in the study. Participants also had to sleep in the same home for at least 4 nights each week to be enrolled in the study. Clinical assessments were performed at baseline and every 3 months thereafter. Exposure assessments were also performed at baseline and every 3 months within ±2 weeks of clinical assessment. Written informed consent was obtained, and the study was approved by the Johns Hopkins Institutional Review Board.

Clinical assessments

Allergy skin testing was performed at the baseline clinic visit with the MultiTest II device (Lincoln Diagnostics, Decatur, Ill). The allergens tested were dog, cat, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, rat epithelia, German cockroach, American cockroach, mouse epithelia, oak, grass mix, *Alternaria tenuis*, *Aspergillus fumigatus*, common ragweed, and *Cladosporium herbarum* (Greer Laboratories, Lenoir, NC). A skin test result was considered positive if the net orthogonal wheal diameter was 3 mm or greater.[19] The net orthogonal wheal diameter was obtained by subtracting the orthogonal wheal diameter of the negative control from the orthogonal wheal diameter of the skin test in question. Blood was collected at baseline, and serum total and specific IgE levels were quantified with the ImmunoCAP system (Thermo Fisher, Uppsala, Sweden).

Spirometry was performed at each clinic visit with a KoKo spirometer (nSpire Health, Longmont, Colo), and percent predicted values were determined by using Hankinson equations. Bronchodilator reversibility was defined as having a 12% or greater increase in FEV_1 15 minutes after administration of 2 puffs of short-acting β-agonist. Fraction of exhaled nitric oxide (FENO) levels were measured at each clinic visit with the NIOX Mino (Aerocrine, Solana, Sweden), according to the manufacturer's instructions. FENO levels were always measured before spirometry.

Questionnaires that captured medication use, asthma symptoms, and health care use were administered at all clinic visits. The questionnaires were designed to capture symptoms and medication use over a 2-week period.[5,6,15] Data on asthma-related health care use were collected for the preceding 3-month period. An acute visit was defined as any unscheduled visit for asthma-related symptoms.

Exposure assessments

Settled dust samples from the bed and bedroom floor were collected with a handheld vacuum cleaner and a Mitest dust collector (Indoor Biotechnologies, Charlottesville, Va). Protein was extracted from the settled dust samples, and Mus m 1, Bla g 1, Der f 1, and Fel d 1 content was quantified by means of ELISA. The limit of detection for the assay was 2.2 ng/g for Mus m 1, 0.39 U/g for Bla g 1, 21 ng/g for Der f 1, and 63.4 ng/g for Fel d 1.

Statistical analyses

Participants were stratified by sensitization and exposure status for the allergens of interest. For each allergen, sensitization and exposure status was modeled as a dichotomous predictor variable, with sensitization and exposure being coded a 1 and nonsensitization or nonexposure being coded a 0. There were separate models for each allergen. For dichotomous outcomes, such as acute care visits and reversibility, binomial regression models with a log link and generalized estimating equations were used. For continuous outcomes, such as FEV_1/forced vital capacity (FVC) ratio, linear regression models with generalized estimating equations were used. For continuous outcomes, predicted outcome values were generated from the regression models. Participants were considered sensitized if the net wheal for a particular allergen extract was 3 mm or larger. Participants were considered exposed if their house dust samples for a particular visit contained at least the following levels of allergen: Bla g 1, 1 U/g; Mus m 1, 1 μg/g; Der f 1, 2 μg/g; and Fel d 1, 8 μg/g.[3,4,14,15,20-22] These thresholds were based on thresholds determined to be clinically relevant in previously published studies. Dog allergen was not explored in our analyses because subjects in this population were much less frequently sensitized to dog (26% of participants with positive skin test results) compared with the other allergens (51% to 64% of participants with positive skin test results for all other allergens explored). Final models were adjusted for age, sex, total IgE level, and type of health insurance. Health insurance was a dichotomous variable of public health insurance versus private insurance or self-pay, and it was used as a marker of socioeconomic status.

Initial analyses focused on identifying the indoor allergens that were associated with markers of poor asthma health. To examine the combined effects of sensitization and exposure to these 2 allergens, participants were stratified into sensitization and exposure categories as follows: (1) sensitized and exposed to neither cockroach nor mouse, (2) sensitized and exposed to cockroach but not mouse, (3) sensitized and exposed to mouse but not cockroach, and (4) sensitized and exposed to both mouse and cockroach. We then modeled relationships among these 4 sensitization/exposure categories and the asthma outcomes of interest using generalized estimating equations. Predicted outcome measures were generated from the models. Final models were adjusted for age, sex, total IgE level, and type of health insurance. All analyses were performed with STATA SE 11.0 software (StataCorp, College Station, Tex). A P value of less than .05 was considered statistically significant.

RESULTS

Study population

A total of 150 participants were enrolled, and 144 had at least 1 visit with valid cockroach, mouse, dust mite, and cat allergen exposure data. The population was predominantly African American, low income, and poorly educated. Most of the participants had been to the emergency department in the last 12 months because of an asthma exacerbation. The frequency of short-acting β-agonist use was high, with participants using short-acting