Original Article

Mouse Sensitization and Exposure Are Associated with Asthma Severity in Urban Children

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What is already known about this topic? Mouse sensitization and allergen exposure have been linked to poor asthma *control*.

What does this article add to our knowledge? In this study, mouse sensitization and allergen exposure are also associated with asthma *severity*, which is a predictor of poor outcomes in adulthood.

How does this study impact current management guidelines? Intervening upon mouse sensitization or exposure in this population has the potential to reduce asthma severity.

BACKGROUND: Mouse sensitization and exposure are associated with uncontrolled asthma, but whether they are associated with asthma severity, an intrinsic disease characteristic and long-term outcome predictor, is unclear.

OBJECTIVE: To examine relationships between mouse sensitization and/or exposure and asthma severity in urban children.

METHODS: A total of 645 children (5-17 years) with uncontrolled asthma underwent mouse sensitization evaluation. Sensitized children had mouse allergen measured in bedroom dust. Relationships between mouse sensitization, allergen levels, and asthma severity measures (treatment step and Composite Asthma Severity Index [CASI]) were examined using regression models adjusted for age, sex, atopy, study site, race, ethnicity, and insurance.

RESULTS: The study population was predominantly minority (69.6% black, 20.8% Hispanic), low income (61.8%), and mouse sensitized (54.4%). Mean ± SD treatment step was 3.2 ± 1.6, equivalent to medium-dose inhaled corticosteroid. Mean ± SD CASI was 6.5 ± 3.4, reflecting moderate persistent asthma. Mouse sensitization was associated with higher treatment step (3.5 vs 2.9, mouse-sensitized vs nonsensitized, $P < .001$), independent of potential confounders (β [95% CI], 0.36 [0.07-0.64]; $P = .01$). Mouse sensitization was associated independently with CASI (β [95% CI], 0.82 [0.16-1.47]; $P = .02$). Among mouse-sensitized participants, higher bedroom floor and bed Mus m 1 were independently associated with treatment step (β [95% CI], 0.26 [0.09-0.43]; $P = .002$ and β [95% CI], 0.22 [0.01-0.43]; $P = .04$), respectively. Higher bedroom floor Mus m 1 was independently associated with CASI (β [95% CI], 0.43 [0.05-0.81]; $P = .03$).

CONCLUSIONS: Mouse sensitization and exposure are associated with asthma severity, among low-income, minority children. Further studies are needed to determine whether reducing allergen exposure among mouse-sensitized patients with asthma can reduce severity, ultimately altering childhood asthma natural history. © 2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2016;■:■-■)

Key words: *Inner-city asthma; Childhood asthma; Mouse sensitization; Mouse allergen; Indoor allergens*

Although asthma controller medication is very effective in improving asthma control and reducing morbidity, studies have shown repeatedly that inhaled corticosteroids have little effect on the natural history of the disease.[1,2] In addition, allergen immunotherapy appears to have little effect on the natural

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Abbreviations used
CASI- Composite Asthma Severity Index
FVC- Forced vital capacity
MAAIT- Mouse Allergen and Asthma Intervention Trial

history of disease among children with asthma,[3-5] and there is limited long-term data on the effect of omalizumab on the natural history of asthma. There is a need, then, to develop a better understanding of the modifiable risk factors for poor long-term outcomes to develop approaches aimed at altering the natural history of the disease. Studying risk factors for long-term outcomes is difficult because the natural history of childhood asthma plays out over several decades. However, examining current asthma *severity* among children can lend insight into outcomes in adulthood because asthma *severity* in childhood is a predictor of poor outcomes in adulthood.[3,6-9]

Because indoor allergen exposure causes airway inflammation and decrements in lung function among sensitized children with established asthma,[10,11] it is possible that it is responsible for greater disease *severity*, which is a strong predictor of long-term outcomes, including adult lung function and asthma that persists in adulthood.[3,6,7] Although many previous studies have examined relationships between allergic sensitization and/or exposure and asthma *control*, few studies have examined relationships between allergen sensitization and/or exposure and asthma *severity* among children with established asthma. Because childhood asthma *severity* is a predictor of worse long-term outcomes, the question of whether an indoor allergen, such as mouse or cockroach allergen, contributes to asthma *severity* has important implications for the potential role of allergen exposure reduction in modifying the natural history of the disease. We therefore tested the hypothesis that indoor allergen sensitization and/or exposure contributes to asthma *severity* by examining relationships between mouse allergen sensitization and/or exposure and markers of disease *severity* in a population of low-income, predominantly minority children and adolescents with persistent asthma. We also examined the relationship between cockroach allergen sensitization and markers of disease *severity* because cockroach is also known to be associated with asthma morbidity in this population.[12]

METHODS

Study population and recruitment procedures

As part of screening for a multicenter, randomized controlled trial of an environmental intervention, the Mouse Allergen and Asthma Intervention Trial (MAAIT), 746 children aged 5 to 17 years with persistent asthma and a recent exacerbation completed a screening clinic visit. Six hundred forty-five children had valid skin test data and were included. The analyses related to mouse and cockroach sensitization. Participants with a mouse-specific IgE level of 0.10 kU/L or more or a positive mouse skin test result (wheal size $\geq$ 3 mm) were eligible for the baseline home visit. Four hundred ninety-five participants completed the baseline home visit, and 461 of these participants met the more stringent criteria for mouse sensitization of a mouse-specific IgE level of 0.35 kU/L or more or a positive mouse skin test result and comprised the analysis population for the exposure analyses (Figure 1).

Recruitment occurred between December 2010 and August 2014. Participants were recruited from pediatric emergency rooms, primary care clinics, and specialty clinics and had physician-diagnosed asthma at least 1 year before the screening visit. *Persistent asthma* was defined as use of a long-term controller medication or fulfillment of National Asthma Education and Prevention Program guidelines for persistent disease.[13] An *exacerbation* was defined as an asthma-related emergency room or urgent care visit, overnight hospitalization, or oral steroid burst in the last 12 months. Children were screened for eligibility over the phone and those who met initial inclusion criteria were invited for a screening clinic visit. The study was approved by the Johns Hopkins Medicine and Boston Children's Hospital institutional review boards. Written, informed consent was obtained from parents or guardians of participants.

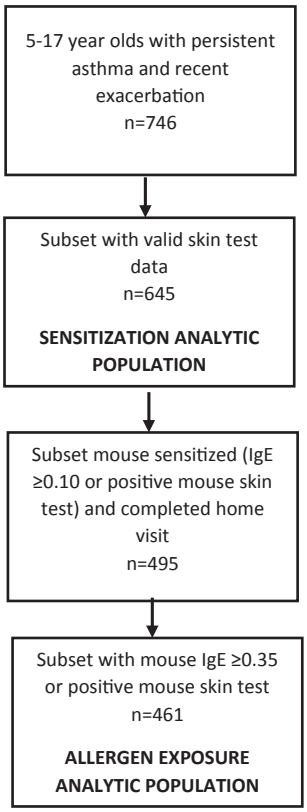

FIGURE 1. Flow diagram depicting derivation of study population used for the sensitization and exposure analyses.

Clinic visit procedures

A questionnaire was administered to collect socioeconomic, clinical, and environmental data. Trained research assistants administered the asthma symptoms and health care use questionnaire to primary caregivers of children aged 5 to 11 years and to adolescents aged 12 to 17 years.[12,14] Questionnaires that captured sociodemographic and home environmental data were administered to the primary caregiver. Medication use was captured by a questionnaire and information obtained from medications that were brought to the clinic visit by study participants.

Participants underwent skin testing for 14 aeroallergens using the MultiTest II device (Lincoln Diagnostics, Decatur, Ill): dog, cat, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, rat epithelia, German cockroach, American cockroach, mouse epithelia, tree mix, grass mix, *Alternaria*, *Aspergillus*, common ragweed, and