

Time for Allergists to Consider the Role of Mouse Allergy in Non-Inner City Children with Asthma



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Mouse allergen is endemic in the inner cities of the United States, with research predominantly in the Northeastern United States. A recent practice parameter notes the effect of mouse exposure in asthma in inner cities. However, studies are emerging that find a role of mouse allergen in non-inner cities as well. Mouse sensitization is associated with mouse allergen exposure and has been linked with adverse asthma outcomes including increased asthma symptoms, poorer lung function, and increased risk of exacerbations. There are commercially available extracts for testing for mouse sensitization although they are not standardized. Pest management studies have had varying results, but with decreased allergen exposure, there is a trend toward improved asthma outcomes. Physicians should be aware of the potential for rodent exposure and sensitization and consider screening for mouse allergy in asthmatic children, especially if they are located in the inner city, have poorly controlled asthma, or have a history of mouse infestation in their location. Evidence is emerging that this allergen should be considered in non-inner-city asthmatics as well. Finally, advocacy efforts are necessary to ensure that removal of this allergen is accomplished, when possible, in the environments of asthmatic children sensitized to mouse. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:1778-82)

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It is increasingly being recognized that mouse exposure and sensitization may play a role in asthma severity in children in the United States. Although the literature is predominantly focused

on inner cities, there are recent studies noting the role of mouse exposure and sensitization in non-inner-city children as well. A recent practice parameter discussed environmental assessment and exposure reduction to rodents,¹ and focused exclusively on the inner city. The issue of mouse exposure and sensitization is not discussed in current asthma guidelines.^{2,3}

The goal of this Rostrum is to review the prevalence of mouse exposure in homes and other common childhood environments, especially child care settings, the clinical relevance of this exposure, currently available testing for mouse allergy, the role of pest management strategies, and finally to make a case that mouse allergy should be increasingly considered in an asthmatic child, both in the inner city and non-inner city. Ongoing advocacy efforts that are required are reviewed as well.

PRESENCE OF MOUSE ALLERGEN IN THE HOME AND OTHER COMMON CHILDHOOD ENVIRONMENTS

Mouse allergen is traditionally described in the setting of inner-city homes, where it has been demonstrated in multiple studies to be endemic (Table 1). There are 2 principal mouse allergens, Mus m 1 and Mus m 2. Mus m 1 is the dominant mouse allergen, and it is found primarily in mouse urine but also present in smaller amounts in mouse epithelium.¹²⁻¹⁴ Mus m 2 is present primarily in mouse hair and dander.¹²⁻¹⁴

A study of 608 homes from the National Cooperative Inner-City Asthma Study (ICAS) found that 95% of all homes in 8 inner-city neighborhoods in the United States had detectable Mus m 1 levels in at least 1 room in the home.⁴ The highest levels were found in the kitchen (median, 1.60 µg/g) compared with the bedroom (median, 0.52 µg/g) or television room (median, 0.57 µg/g). In a sample of 100 inner-city school-aged asthmatic children in Baltimore, Mus m 1 was detected in settled dust samples in 100% of bedrooms (median, 3.8 µg/g) although once again the highest levels were found in the kitchen (median, 14.7 µg/g) followed by the television room (median, 4.7 µg/g).⁵ A subanalysis of 150 children with asthma enrolled in the ICAS from 7 inner-city areas in the United States noted mouse allergen in 80% of children's bedrooms.⁶

In addition to the presence of mouse allergen in inner-city homes, mouse allergen has been demonstrated in inner-city schools as well. A study of 11 inner-city public schools in the Northeastern United States found that Mus m 1 was detected in 81% of samples collected from 87 classrooms 3 times each throughout the school year, although mean levels varied widely (mean levels ranging from 0.21 to 133 µg/g).⁷ A study comparing allergens from schools and homes in 12 inner-city schools found significantly higher settled dust levels of mouse in schools than homes (545% higher; estimated absolute difference 0.55 µg/g; $P < .0001$).¹⁵

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Abbreviations used

CASI- Composite asthma severity index
CI- Confidence interval
FENO- Fractional exhaled nitric oxide
HEPA- High-efficiency particulate air
ICAS- Inner-City Asthma Study
IRR- Incidence rate ratio
OR- Odds ratio
PR- Prevalence ratio
SPT- Skin prick testing

Mouse allergen exposure has been traditionally described as an inner-city issue, but there are data to suggest that it is endemic in other demographic settings as well, although methodologic differences in allergen assessment exist between studies. Although the concentration of mouse allergen has been shown to vary as much as 1000-fold between inner-city and non-inner-city environments,¹⁶ several studies have found very high levels of exposure in non-inner-city environments. Analysis of the cross-sectional survey of the US population from the National Survey of Lead and Allergens in Housing (of which 80% were above the poverty level) found detectable levels of Mus m 1 in 82% of homes, although at lower levels than found in the inner-city studies (median level, 0.36 µg/g in the kitchen; 0.28 µg/g in the bedroom floor).⁹ Kitchen floor level concentrations that are commonly thought to exceed sensitization levels (>1.6 µg/g) were found in 22% of homes. A prospective study of 498 children with asthma/atopy in Boston (90.7% of whom had household incomes >\$30,000) found mouse allergen in 42% of study homes.¹⁰ A study of 257 children in suburban, middle-class neighborhoods in the United States found levels of Mus m 1 in 74.9% of bedrooms.¹¹ A study of homes of children with asthma in rural Arkansas found mouse allergen in 81% of kitchens and 97% of bedrooms although found no specific house characteristics associated with mouse allergen exposure.¹⁷

Mouse allergen can also be passively transferred from adults who have occupational exposure to their homes. A study of 50 children whose parents worked with laboratory animals compared with 40 children whose parents did not work with laboratory animals noted significantly higher levels of mouse sensitization among the children whose parents were occupationally exposed.¹⁸

IS MOUSE SENSITIZATION COMMON AND CLINICALLY RELEVANT IN ASTHMATIC CHILDREN?

Although studies have established that mouse allergen exposure is common in both inner-city and non-inner-city neighborhoods, the larger question is whether this exposure is associated with sensitization, and by extension whether this sensitization is clinically relevant in asthmatic children. Several studies predominantly in the United States, and predominantly in inner cities, have documented mouse sensitization to be both common and have clinical relevance in children with asthma. In particular, mouse sensitization has been associated with poorer lung function, increased risk of exacerbations, and poorer outcomes across a range of measures (Table II).¹⁹⁻²²

The Mouse Allergen and Asthma Intervention Trial (MAAIT) examined the rate of mouse sensitization and correlation with

asthma outcomes in 645 predominantly minority and low-income children aged 5 to 17 years with uncontrolled asthma.¹⁹ Mouse sensitization was present in 54.4% of children and associated with higher asthma treatment step levels ($P < .001$), and higher composite asthma severity index (CASI) ($P = .02$). In addition, higher environmental exposure in mouse-sensitized children was independently associated with a higher asthma treatment step ($P = .04$) and CASI ($P = .03$). The ICAS noted that sensitization rates (22%) in 150 school-aged children aged 5 to 11 years with asthma were highly correlated with mouse allergen exposure (bed or bedroom floor risk ratio 3.00; 95% confidence interval [CI]: 1.92, 4.70).⁹ Sensitization and exposure were associated with multiple measures of asthma control including maximum symptom days in past 2 weeks ($P = .02$), and nights child lost sleep because of asthma symptoms in the past 2 weeks ($P = .02$). Hospitalization rate due to asthma was significantly higher for children who were mouse sensitized and exposed (rate ratio, 1.65; 95% CI: 1.09, 2.50). A prospective cohort study of 284 students (aged 4-13 years) from 37 inner-city elementary schools in the United States noted mouse allergen in 99.5% of school dust samples, with higher levels of allergen noted in schools than in students' homes ($P < .001$).²⁴ Increased mouse allergen exposure at school was associated with increased odds of asthma symptoms (odds ratio [OR], 1.27; 95% CI: 1.05-1.54) and a 4.0 percentage point lower predicted forced expiratory volume in 1 second ($P = .002$).

A study of 546 adolescents in the Asthma Control Evaluation study found that among mouse-sensitized participants, higher mouse-specific IgE levels were associated with worse asthma control including higher levels of fractional exhaled nitric oxide (FENO), poorer lung function, and higher blood eosinophil levels, as well as increased risk of asthma exacerbations and hospitalizations.²⁰ A study of 144 children aged 5 to 17 years with asthma in Baltimore found a 51% mouse sensitization rate, which was associated with acute asthma care visits (prevalence ratio [PR], 1.33; 95% CI: 1.07-1.65), higher FENO levels ($P < .01$), and increased bronchodilator reversibility (PR, 1.54; 95% CI: 1.09-2.19).²¹ This study also looked at cockroach allergy and found that although both mouse and cockroach sensitization and exposure were associated with worse asthma outcomes, mouse sensitization/exposure was the primary contributor to these relationships.

A study of 127 school-aged children in inner-city Baltimore with symptoms of asthma noted that mouse sensitization was associated with 50% more asthma symptom days (incidence rate ratio [IRR], 1.5; 95% CI: 1.1-2.1), 80% more days of beta-agonist use (IRR, 1.9; 95% CI: 1.3-2.5), and increased emergency department visits for asthma (OR, 2.1; 95% CI: 1.1-4.1) and hospitalizations for asthma (OR, 36.6; 95% CI: 4.1-327.3) than other children.²²

There is limited evidence about the effects of mouse exposure on sensitization rates and asthma outcomes in middle-class neighborhoods. A cross-sectional survey of a sample of 831 nationally representative households in the United States found that 82% had mouse urinary protein levels in the home, and that current asthma was associated with increased mouse urinary protein levels. Within this national sample, the association of exposure and outcome was modified by atopic status, with elevated allergen exposure increasing the odds of asthma only among atopic individuals (OR, 1.93; 95% CI: 1.14-3.27).²⁵

TABLE I. Presence of mouse allergen in homes and other common environments

Study	Location	Mus m 1 levels
Phipatanakul et al ⁴	608 homes in 8 inner-city US neighborhoods	Detectable in 95% of homes with the highest levels in the kitchen
Matsui et al ⁵	100 homes in Baltimore	Detectable in 100% of bedrooms
Pongracic et al ⁶	150 homes from 7 inner-city US neighborhoods	Detectable in 80% of bedrooms
Chew et al ⁷	87 classrooms in 11 inner-city public schools in Northeastern United States	Detected in 81% of samples
Perry et al ⁸	33 head start facilities in Arkansas	Detectable in 100% of facilities
Cohn et al ⁹	831 US nationwide housing units (80% above poverty level)	Detectable in 82% of homes
Phipatanakul et al ¹⁰	498 Boston homes (90% above poverty level)	Detectable in 42% of homes
Matsui et al ¹¹	257 homes in middle-class US neighborhoods	Detectable in 74.9% of bedrooms

HOW CAN WE DETECT MOUSE EXPOSURE AND SENSITIZATION IN CHILDREN

One of the best measures of mouse exposure is parental report of mice in the home environment (Table III).^{5,9,26} Other predictors of mouse exposure noted in studies include associated evidence of cockroach infestation,¹⁰ having cracks or holes in doors or walls,⁵ evidence of food remains in the kitchen,⁵ use of floor mopping instead of vacuuming,⁹ living in a high-rise apartment or mobile home,⁹ and older age of the home.⁹ In a multivariate analysis, living in a single detached home was inversely associated with detectable kitchen mouse allergen levels (OR, 0.4; 95% CI: 0.2-0.6).²⁶ The highest levels of mouse exposure tend to occur, within the home, in the kitchen.

Skin test and specific IgE reagents are available for testing for mouse sensitization although neither are standardized.²⁷ The skin testing extract is composed of mouse epithelium, not urinary extracts, and the concentration of Mus m 1 can vary significantly between extracts.²⁷ Serum specific IgE extracts include mouse urine, epithelium, and serum.²⁷ To our knowledge, the only studies to compare skin prick testing (SPT) and mouse-specific IgE measurements are adult studies, and the literature is scant. A study of 69 mouse laboratory workers noted SPT (defined as the net orthogonal wheal diameter at least 3 mm larger than saline control) to have the highest negative and positive predictive values.²⁷ A study of 49 adult asthmatics confirmed these findings, noting that SPT (or the combination of SPT and mouse-specific IgE) had the best diagnostic capacity.²⁸ Further research into the positive and negative predictive values of SPT and specific IgE reagents, as well as standardization of SPT reagents, is required.

ARE THERE EFFECTIVE WAYS TO REMOVE MOUSE ALLERGEN FROM HOMES?

Some studies have shown an integrated pest management strategy to be effective at removal of mouse allergen from home environments. For example, a study of 18 homes of children with mouse sensitization and asthma in Boston found that an integrated management strategy reduced mouse allergen significantly compared with control homes (kitchen intervention 78.8% reduction vs control 319% increase; $P = .02$).²⁶ This study did not examine effects on asthma symptoms with this reduction. The pest management strategy included filling all holes and cracks in the home (with a copper mesh and caulk sealant), cleaning surfaces with detergent, vacuuming with high-efficiency

TABLE II. Association of mouse exposure and sensitization to asthma outcomes

Study	Association of mouse sensitization with asthma outcomes
Pongracic et al ⁶	↑ Maximum symptom days in the past 2 wk ↑ Nights child lost sleep because of asthma in the past 2 wk
Grant et al ¹⁹	↑ Hospitalization rates for asthma ↑ Asthma treatment step level ↑ Composite asthma severity index ↑ Asthma treatment step
Matsui et al ²⁰	↑ FENO levels ↑ Serum eosinophil levels ↑ Risk of asthma exacerbations ↑ Risk of asthma hospitalizations
Ahluwalia et al ²¹	↑ Acute asthma care visits ↑ Bronchodilator reversibility
Matsui et al ²²	↑ Asthma symptom days ↑ Beta-agonist use ↑ Emergency department visits for asthma ↑ Hospitalizations for asthma
Torjusen et al ²³	↑ Odds of asthma-related health care use ↑ Emergency department visits for asthma ↑ Unscheduled doctor visits for asthma

FENO, Fractional exhaled nitric oxide.

particulate air (HEPA) filtration, tracking powder (pesticide) on wall voids/pipe chases, snap traps, and familial education.

Other studies have examined as an additional outcome the effect that decreased mouse exposure has on asthma outcomes in children. The ICAS found that environmental interventions reduced mouse allergen levels (27.3% reduction on the bedroom floor; 95% CI: -46.1%, -1.9% vs 28.0% increase in the control homes; 95% CI: -6.10%, 74.5%), which was associated with less missed school (morbidity change, -0.0653; $P = .05$), decreased sleep disruption (morbidity change, -0.1535; $P = .02$), decreased reduction in activity (morbidity change, -0.1664; $P = .006$), and decreased caretaker burden (morbidity change, -0.0989; $P = .03$).⁹ The intervention consisted of HEPA filtration in the bedroom and on the vacuum cleaner, filling of access points and placement of traps, and family education about food storage and kitchen cleaning. However, symptom scores were not significantly

TABLE III. Predictors of home mouse exposure

Report of mice in the home environment ^{5,9,26}
Evidence of cockroach infestation ¹⁰
Food remains in the kitchen ⁵
Cracks or holes in doors and walls ⁵
Floor mopping instead of vacuuming ⁹
Older age of home ⁹
High-rise apartment or mobile home ⁹

changed ($P = .9$) nor were days of wheeze ($P = .63$), hospitalizations ($P = .13$), or unscheduled asthma visits ($P = .13$).

To our knowledge, there is only 1 study that evaluated different pest interventions in the same study. The MAAIT randomized families of 361 children and adolescents with asthma to an integrated pest management in their home plus education versus mouse eradication education alone.²⁹ In this study, integrated pest management consisted of rodenticide, sealant, trap placement, cleaning, allergen-proof bedding, and air purifiers. However, the study found no significant difference in asthma symptom days between the 2 groups at 6, 9, or 12 months ($P = .16$). Further research into the effects of mouse eradication alone is crucial, as integrated pest management strategies are expensive and may not be feasible, especially in inner-city communities.

In conclusion, there is emerging evidence that pest management strategies may have a role in both decreasing mouse allergen exposure and decreasing asthma outcomes in children and adolescents. However, questions remain. It is unclear which strategy is most effective, and it may be that pest management education alone is sufficient. Even among educational strategies, evidence is scant about which are the most efficacious management strategies. However, some interventions, such as housekeeping practices (proper storage of food, cleaning of areas after food ingestion, traps), are relatively inexpensive, and could be considered as a trial in homes with mouse exposure. Although professional involvement is recommended to remove mouse infestation from a home,¹ efforts aimed at affordable solutions are necessary especially in inner-city communities. Finally, the research on mouse sensitization and allergy has been predominantly focused in the Northeastern United States, and a more global recognition of this issue, and research efforts in other countries with a large burden of asthma, is required.

SHOULD PHYSICIANS BE AWARE OF THIS RISK?

Currently, although there is a practice parameter on rodent infestation,¹ there is no mention of evaluation of mouse sensitization in either the Global Initiative for Asthma³ or National Asthma Education and Prevention Program (Expert Panel Report, 3) guidelines.² In the authors' opinion, the evidence is substantial that mouse sensitization, in particular in inner-city children, is associated with asthma morbidity. As a result, in the authors' opinion, mouse sensitization should be considered and screened for, especially if there is a history of mouse sightings in the home. However, even without mouse sightings, mouse sensitization in American inner cities (especially in the Northeast) has been demonstrated to be endemic. In addition, it should be remembered that mouse exposure has been demonstrated in other environments such as daycares and schools. Testing should be considered especially in children with poorly controlled asthma. Physicians should be aware of local and

regional resources available for integrated pest management, and familiarize themselves with educational resources that could be provided to families. Finally, even among non—inner-city populations, this is an allergen that deserves some attention as studies emerge that exposure rates and sensitization rates are high in these populations as well.

WHAT STILL NEEDS TO BE DONE?

Further research into the effects of mouse sensitization on other atopic outcomes, such as eczema and rhinitis, is required (although 2 studies have demonstrated mouse sensitization to be associated with one, or both).^{30,31} A recent pooled analysis of 11 European cohort studies found no association between furry pet exposure (including rodents) during the first 2 years of life and the development of rhinitis.³² In addition, there may be differences between very early (first-year) exposure to mouse allergen and cumulative allergen exposure over years.³³

Advocacy efforts are necessary in communities where mouse allergen sensitization and exposure has been documented to be high, such as Baltimore, to provide affordable pest management strategies. Further research efforts are necessary to determine which pest management strategies are most efficacious, and potentially most economical, in order to implement them in these communities. A focus on standardization of mouse extracts may allow for more sensitive and specific testing. Research efforts are necessary to determine if mouse allergy is implicated in other atopic conditions, such as allergic rhinitis, as has been suggested by a paucity of studies. Awareness of, and research into, mouse exposure and sensitization in other countries such as Canada is required as the preponderance of research into the clinical implications of mouse allergy has been done in the United States.

Available information should be included in future asthma guidelines, including information about testing and pest management strategies. Finally, studies are required in non—inner-city populations, as we may be missing an opportunity to help children with asthma in these populations as well.

CONCLUSIONS

Studies have emerged on the role of mouse allergens from inner-city and non—inner-city populations, noting high rates of mouse allergen exposure and sensitization especially in the Northeastern United States. Mouse sensitization has been linked in multiple studies with poorer asthma outcomes including poorer symptom control and increased risk of asthma exacerbations. More research is needed on the best means of mouse allergen removal, although studies to date are reassuring for the role of both pest management strategies and family measures. Moving forward, physicians should be aware of the risk of mouse allergy and consider screening for it, both in inner-city and non—inner-city asthmatic children, especially if mice have been spotted in the home environment. Available information should be included in future asthma guidelines as well.

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