# ALLERGIES AND THE ENVIRONMENT (RL MILLER, SECTION EDITOR)

# **Environmental Remediation in the Treatment of Allergy and Asthma: Latest Updates**

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Abstract In the modern era, the prevalence of asthma and allergies are increasing. It has been speculated that environmental exposures are contributing to this rise. Several studies demonstrate that common indoor allergen exposures exacerbate asthma. Minimizing exposure to allergens and remediating the environment play a critical role in the treatment of asthma and allergies. The most effective environmental control measures are tailored multifaceted interventions which include education, thorough cleaning, using high-efficiency particulate air (HEPA) filters, integrated pest management, and maintenance of these practices.

 $\label{eq:Keywords} \begin{tabular}{ll} Keywords & Asthma \cdot Allergen \cdot House dust mite \cdot Cat \cdot Dog \cdot Mold \cdot Endotoxin \cdot Cockroach \cdot Rodents \cdot Environmental tobacco smoke \cdot Air pollution \cdot Home remediation \cdot Integrated pest management \\ \end{tabular}$ 

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## Introduction

It has been speculated that the increasing prevalence of asthma and allergies, over the past few decades, is attributable to an increase in environmental exposures. In the modern era, environmental exposures are important because we spend more time indoors with increasing temperatures and humidity which are ideal conditions for the growth of mold and dust mites [1]. Important indoor allergens and irritants include the house dust mite, domestic pets, mold, cockroach, mouse, environmental tobacco smoke, endotoxin, and air pollution. In this article, we will review the literature on environmental interventions in the treatment of asthma and allergies. The most effective environmental remediation strategies include multifaceted interventions tailored to specific exposures and allergen sensitizations (Table 1).

#### **House Dust Mite**

The most common species of the house dust mite (HDM) are *Dermatophagoides pteronyssinus* and *D. farinae*. The most extensive studies of allergen levels and sensitization have been conducted using the HDM. Cysteine proteases found in the HDM's gut and fecal particles are potent inducers of allergic disease [2]. Studies have demonstrated that there is a dose–response relationship between HDM exposure and allergen sensitization [3]. HDM sensitization in asthmatics is associated with an increased risk of medication use and health care utilization including asthma-related unscheduled visits and hospitalizations [4].

There are multiple studies which have examined the efficacy of HDM interventions in HDM sensitized asthmatics; however, the results are inconsistent. In a systematic review of 54 studies, the authors concluded that HDM interventions did not significantly decrease asthma symptoms compared to



Table 1 Summary of allergens and environmental remediation strategies

Allergen	Source	Environmental remediation strategies
House dust mite	Woven materials: carpet/rugs, pillows, mattresses, bedding, stuffed animals and toys	First Level:  •Wash bedding weekly in hot water and dry in a heated dryer •Encase pillows and mattresses (pore diameter <10 microns) •Vacuum with a HEPA filter bag •Keep humidity <50 % •Remove stuffed animals and toys from bedroom Second Level: •Remove upholstered furniture, drapery, carpeting or rugs Third Level: •Move from a damp location such as a basement to a higher floor
Pets (cat and dog)	Furniture, carpet/rugs, and clothing	First Level:  •Remove pet from home •Thoroughly clean upholstered furniture, walls, and carpet Second Level:  If pet not removed from the home •Remove pet from bedroom •Aggressive cleaning of upholstered furniture, walls, and carpet •Removal of upholstered furniture and carpet is ideal •Encase mattresses and pillows (pore diameter <6 microns) •Use a HEPA filter •Washing pets may be helpful (wash dog twice weekly)
Pests (mouse and cockroach)	Mainly kitchen (highest level of allergens)	First Level: Inspect to detect hiding places and food sources Store food in sealed containers Remove clutter Professional extermination with pesticides and bait traps Seal holes or cracks in the home to prevent re-infestation
Mold	Humid environments	First Level:  •Locate mold contaminated items and remove them  •Reduce humidity to <50 %  •Clean moist areas  •Repair leaks

control groups [5]. This systematic review included studies that focused on a single intervention. Woodcock et al. [6] found that using impermeable HDM bedding as a single intervention is ineffective because it does not reduce total HDM exposure. One of the studies in the systematic review conducted by Halken et al. [7] was a prospective, double-blind, placebo-controlled trial. Sixty children were randomized to receive either HDM impermeable encasings or sham encasings. The intervention group had a reduction in HDM levels which was associated with a reduction in inhaled corticosteroid (ICS) use in a 1-year period [7]. However, these findings were not replicated in a study conducted by de Vries et al. [8].

More recently, Ghitany et al. [9] conducted a randomized control trial in Egypt with 160 asthmatic children sensitized to the HDM. The children were randomized into four groups: physical, chemical, both physical and chemical interventions, or no intervention. In the physical intervention group, there was an improvement in lung function and decreased hospitalizations in a 16-week period [9].

Effective and Sustainable Interventions for HDM

Although there have been few recently published studies that focus solely on HDM intervention, the evidence suggests that the most effective long-term strategy for HDM control is a comprehensive plan. Effective strategies include cleaning regularly, washing and drying bedding weekly in high heat, using HDM impermeable encasings, maintaining humidity indoors below 50 %, and avoiding the use of carpet, upholstered furniture, and stuffed animals [2]. The more current approach to environmental remediation is multifaceted and targets multiple allergens. This is particularly important in children because they tend to be sensitized to more than one allergen [10]. We will discuss studies with more comprehensive approaches to environmental remediation at the end of this review.

# Pets

The most common domestic pets are cats and dogs. Domestic pets allergies are common in atopic individuals. The primary



cat allergen is Fel d 1, which is found in saliva, skin, and hair follicles. The major dog allergen is Can f 1, which is also found in saliva, skin, and hair follicles [2].

Cat allergen is carried on small particles, ranging from 2 to 10 microns, which allows it to remain airborne and become adherent to surfaces and clothing [11]. This allergen is found in dust samples taken from environments without cats, for example, in schools and daycares [12, 13.]. Wood et al. [14] found that after cat removal, it takes 20-24 weeks to reduce cat allergen levels in the indoor environment. After aggressive cleaning of the upholstered furniture, cat allergen decreases more rapidly [14]. Another potential reservoir of pet allergen is the mattress; thus, encasings are recommended as part of a comprehensive approach to reduce allergen levels. Regular washing of pets reduces allergen levels; however, the effects are not sustained. Washing cats demonstrated no benefit or transient benefit (not sustained beyond 1 week) [15, 16]. Hodson et. al. [17] reported, similarly, that dog washing reduced dog allergen levels; however, the results were short-lived unless the dog was washed twice a week.

There are few studies that have evaluated the effectiveness of pet allergen remediation in the treatment of asthma and allergies. In one study, excluding cats from the bedroom and using HEPA filters were found to be effective in reducing cat allergen levels; however, there was no reported improvement in asthma or allergic rhinitis symptoms [18]. Van der Heide et al. [19] conducted a 3-month HEPA filter intervention study in 20 pet-sensitized children with asthma. HEPA filter use, in the living room and bedroom, was associated with reduced airway hyper-responsiveness. However, more recently, Sulser et al. [20] conducted a similar study, over a 12-month period, and the results were not replicated; thus, HEPA filter use is less likely to improve symptoms and medication use over a sustained period of time.

Shirai et al. [21] conducted a study of 20 symptomatic patients with newly diagnosed pet allergic asthma. Ten of the 20 subjects had their pets removed from their homes. After 1-year follow up, none of the subjects in the pet removal group were on ICS compared to 9 subjects in the control group (p<.001) [21], which suggests that this is the most effective long-term strategy for environmental remediation.

More recently, we have had to address issues pertaining to hypoallergenic pets. In the past two decades, many pet companies have marketed so called "hypoallergenic" pets. We have to stress to our patients and the public that there is no scientific evidence to support the existence of "hypoallergenic" pets [22, 23]. In a study conducted by Vredegoor et al. [24], higher Can f 1 levels were found in hair and coat samples of hypoallergenic dog breeds compared to non-hypoallergenic dog breeds; however, there was no difference in dog allergen levels in settled dust and airborne samples between the two breeds.

Effective and Sustainable Interventions for Pets

The American Academy of Allergy and Immunology (AAAAI) practice parameter for furry animals states hypoallergenic cats and dogs should not be recommended for sensitized individuals [23]. The most effective long-term strategy for environmental remediation in pet-sensitized individuals is to remove the pet from the home; however, individuals are often reluctant to remove their pets from the home. HEPA filter use may be beneficial, in pet-sensitized individuals who are unwilling to remove their pets from the home, because pet allergen may be airborne in these homes [25, 26].

#### Cockroach

The most common species of cockroach that cause sensitization are *Blattella germanica* (German cockroach) and *Periplaneta americana* (American cockroach). The major allergens are Bla g 1, Bla g 2, and Per a 1, which are found in saliva, secretions, debris, and fecal material [2]. There are regional differences in the prevalence of cockroach allergen. In Gary, Indiana, detectable levels of Bla g 1 allergen were found in 98 % kitchens in 101 apartments [27]. In New Orleans, Louisiana, cockroach allergen was found in 56.6 % of homes in moderate to high levels [28]. Cockroach infestation is associated with living in densely populated areas, urban environments, inner-city communities, and low socioeconomic status [29].

In 1997, cockroach was found to be the major allergen implicated in inner-city asthma exacerbations [30]. Gergen et al. [31] in the National Cooperative Inner City Asthma Study (NCICAS) demonstrated that using professional extermination with cockroach insecticide and directed education, in the homes of 265 asthmatic children, reduced cockroach allergen levels; however, the results were not sustained in a 12-month period. Sever et al. [32] found that results were more sustained when interventions were performed by academic entomologists compared to commercial companies.

# Effective and Sustainable Interventions for Cockroach

There are a variety of techniques used for abatement of pests. Pests and pest allergens are difficult to eliminate. The goal is to reduce pest allergen in an attempt to reduce pest-related asthma morbidity and allergy symptoms. These techniques involve short-term strategies and require long-term care to prevent re-infestation. Different strategies include education, cleaning regularly, plugging holes, using traps, and applying insecticides through professional extermination services. Strategies to repair structural defects include caulking, metal mesh, or expandable spray foams and gels. The above strategies, collectively, are termed integrated pest control (IPM)



[29], and it is an effective and sustainable intervention to control cockroaches long term.

## Mouse

The major mouse allergens include Mus m 1 and Mus m 2 which are found in mouse urine, dander, and hair follicles [33]. Similar to cockroach, mouse infestations are more prevalent in urban and densely populated environments [29].

Exposure to mouse allergen is associated with a high rate of allergen sensitization [33]. High levels of mouse allergen, found in schools and homes, have been associated with increased asthma morbidity [34-37]. In the Northeastern US, Sheehan et al. [37] conducted a study examining the prevalence of mouse allergen in 4 inner-city schools. In schools with higher levels of mouse urinary protein, asthmatic students reported more asthma-related missed schools days [37]. Permaul et al. [13., 38] examined allergen exposures in 29 inner-city schools and found children with asthma were exposed to high levels of mouse allergen. Mouse allergen levels were higher (generally greater than 0.5 μg/g) in schools compared to homes. Predictors of mouse allergen in schools included visible droppings which were associated with higher mouse allergen levels in settled dust and air, particularly during the spring [38]. Matsui et al. [34] found that mouse allergen levels of greater than 0.5 µg/g, in the home of preschool inner-city asthmatics, were associated with increased asthma symptom days, medication use, and health care utilization.

Phipatanakul et al. [35] found that, in the NCICAS, 95 % of the homes had detectable levels of mouse allergen; however, there was no statistically significant association between exposure, sensitization, and morbidity [36]. More recently, in Baltimore, Ahluwalia et al. [39••] conducted a study in the homes of 144 inner-city children with asthma. They found a high prevalence of both mouse and cockroach allergen exposure/sensitization; however, mouse allergen exposure/sensitization contributed more to asthma morbidity.

IPM is an effective measure of reducing rodent infestation and rodent allergen levels. While most environmental remediation studies have focused on reducing cockroach allergen exposure in the inner-city, Phipatanakul et al. [40] performed a mouse allergen intervention using IPM in 18 homes of innercity children with asthma. The IPM intervention entailed vacuuming, using low toxicity pesticides, traps, and sealing holes. These measures were associated with a mouse allergen reduction of 78.8 % in the kitchen (p=.02) and 77.3 % in the bedroom (p<.01) [40]. Pongracic et al. [41], from the Inner City Asthma Study (ICAS), performed IPM in the homes of children with asthma and found a reduction of mouse allergen in the bedroom which was associated with less sleep

disruption and missed school days over a 12-month period, but there was no reduction in health care utilization [41]. However, in moderate to severe inner-city asthmatics, multifaceted environmental remediation strategies were found to be cost-effective because of the associated reduction in health care utilization [42]. This suggests that IPM is an effective long-term strategy particularly when it is incorporated as part of a multifaceted approach to environmental remediation.

While associations between pest allergen exposure, sensitization, and asthma morbidity have been investigated in children, there are few studies in adults. Phipatanakul et al. [43] found that women in Boston, sensitized to mouse allergen, had greater than twice the odds of asthma diagnosis. In a New York City Public housing study, living in a senior citizen building and having a physician diagnosis of asthma were associated with high mouse allergen levels in the home [44].

Effective and Sustainable Interventions for Mouse

In the AAAAI rodent practice parameters, Phipatanakul et al. [45] concluded the most effective strategies for abatement of rodents include preventing ingress, reducing clutter, and eliminating sources of food and shelter. Using bait, traps, and plugging cracks and holes are effective [29]. The use of rodenticides is not considered first-line treatment but it can be used if other interventions are ineffective; however, rodenticides should be applied by professional exterminators [45]. There is sufficient evidence to recommend IPM to reduce rodent allergen levels.

#### Mold

There are many species of mold, but common molds include *Alternaria, Cladosporium, Aspergillus, and Penicillium* [2]. Of all the molds, the most thoroughly investigated is *Alternaria*. In inner-city children with asthma, *Alternaria* sensitization has been associated with an increased risk of asthma-related hospitalization [4]. In the HEAL (Head off Environmental Asthma in Louisiana) study [46], the homes of 182 asthmatics were assessed for mold post-Hurricane Katrina in New Orleans. Most of the homes were damaged by flooding, rain water, or both. High levels of *Alternaria* were found but other molds and allergens were not elevated; however, the authors speculated that this was likely due to thorough cleaning and other environmental remediation efforts performed post-Hurricane Katrina [46].

While many studies have focused on the home, a study conducted by Baxi et al. [47••] found that there was mold in 100 % of the 180 classrooms air samples collected from 12 inner-city schools. The amount of mold varied from classroom to classroom within the same school. The most commonly



found species, at high concentrations, were *Cladosporium* (29.3 $\pm$ 4.2 spores/m³), *Penicillium/Aspergillus* (15.0 $\pm$ 5.4 spores/m³), smut spores (12.6 $\pm$ 4.0 spores/m³), and basidiospores (6.6 $\pm$ 7.1 spores/ m³) [47••].

There are few studies that have examined the effect of mold remediation in the treatment of asthma and allergies. Lingell et al. [48] conducted an environmental remediation in a school in Finland with poor air quality and high levels of mold. After installing a ventilation and exhaust system, there were lower levels of mold but this was not associated with fewer respiratory complaints. Kercsmar et al. [49] studied mold remediation in the homes of 62 inner-city asthmatics. The intervention group had aggressive mold remediation which included repair of leaks, removal of water-damaged materials, ventilation alteration, and decreasing the humidity in damp basements. In this study, the asthmatics had fewer emergency rooms and hospitalizations after mold remediation compared to the control group. This study suggests that there may be a long-term benefit from a comprehensive plan to remediate mold and reduce asthma morbidity, but more studies are needed.

In a Cochrane review of mold remediation conducted by Sauni et al. [50] of 8 studies (6,538 participants) in homes, schools, and an office building, the authors found moderate evidence for remediation in both children and adults. In children, remediating homes was associated with decreased acute care visits. In adults, mold remediation in the homes was associated with decreased asthma symptoms. However, the interventions in these studies varied from cleaning only to extensive remediation; thus, it is difficult to make comparisons.

## Effective and Sustainable Interventions for Mold

More randomized control trials are needed to make a strong recommendation for extensive mold remediation. Extensive mold remediation is expensive and there is a lack of evidence to support its use in the treatment of asthma and allergies.

# **Environmental Tobacco Smoke**

Environmental tobacco smoke (ETS) exposure is known to exacerbate asthma. In a cross-sectional study, using NHANES data, of 2,250 youths with asthma, 17.3 % reported using tobacco smoke products [51•]. Of the non-smokers, 53.2 % were exposed to second-hand smoke in their homes [51•]. Several intervention trials have targeted tobacco smoke cessation and reduction of second-hand smoke exposure in the home [52, 53, 54•, 55]. However, a Cochrane review found that most intervention studies aimed at reducing children's ETS exposure were ineffective [56].

Since children may not be able to avoid second-hand smoke, the evidence suggests HEPA filters may be useful. Lanphear et al. [54•] conducted a double-blind randomized control trial of 215 asthmatic children with known secondhand tobacco smoke exposure. The intervention group received 2 HEPA filters and the control group received 2 sham air filters. In the intervention group, there was an 18.5 % reduction in the number of unscheduled asthma visits in a 12-month follow up period (185 visits vs. 227 visits; p=.043) [54•]. There were fewer airborne nicotine particles in the intervention group. Although there was a decrease in the amount of unscheduled visits, there was no difference in serum or hair cotinine between the two groups [54•]. This suggests that the use of HEPA filters may be an effective longterm strategy for reducing health care utilization in asthmatics who cannot avoid ETS.

There has been a recent body of literature published on the potential health hazards of third- hand smoke (THS) in children. THS is smoke pollutants remaining in the indoor environment and on surfaces after active tobacco smoking has ceased. Smoke pollutants include nicotine, formaldehyde, phenol, 3-ethenylpryidine, cresols, naphthalene, and tobacco-specific nitrosamines which can undergo physical and chemical transformations [57]. These smoke pollutants can persist for weeks to months on surfaces and in settled dust. Children are more vulnerable than adults to the potential hazardous effects of THS because of their behavioral habits which include crawling and ingesting non-food items [57]. Matt et al. [58] demonstrated that urine nicotine levels in infants were higher in the homes of smokers who smoked outside the home compared to infants in homes with nonsmokers. This suggests that even smoking outside the home may be associated with adverse health effects in infants [58].

## Effective and Sustainable Interventions for ETS

The most effective measure to control ETS is avoidance of second-hand smoke; however, more studies are needed to determine the adverse health effects of THS in children with asthma. If avoidance of second-smoke is impossible, then using a HEPA filter may be a beneficial and sustainable environmental intervention.

## **Endotoxin**

Endotoxin is a component found in the cell wall of Gramnegative bacteria which is released after cell death [59]. Studies examining the associations between endotoxin and asthma are conflicting. Most of the studies focus on exposure to endotoxin and the development of asthma. In a study conducted by Sordillo et al. [60], dampness and visible water



damage were associated with elevated endotoxin levels. Endotoxin levels were reduced by weekly cleaning of the home [60]. Chew et al. [61] conducted a study measuring the levels of mold and endotoxin in homes post-Hurricane Katrina in New Orleans. They found that thorough cleaning and disposing of damaged furnishings, and dry walls, maintaining cross-ventilation, and treating surfaces with a biostat agent reduced mold and endotoxin levels [61].

In a study conducted by Sheehan et al.  $[62^{\bullet \bullet}]$ , endotoxin levels in both the schools and homes of inner-city children with asthma were measured. At each individual school, the median dust endotoxin concentration ranged from 6. to 24.0 EU/mg  $[62^{\bullet \bullet}]$ . The endotoxin levels in the classrooms were significantly higher compared to the matched samples obtained from the home bedrooms (mean log value=1.13 vs. 0.99, p=0.04)  $[62^{\bullet \bullet}]$ .

More recently, a study conducted by Matsui et al. [63] found that the effects of airborne endotoxin on asthma were modified by co-exposure to airborne nicotine or nitrogen dioxide (NO<sub>2</sub>). In the homes of children without detectable nicotine levels, higher levels of endotoxin were associated with fewer acute care visits and less oral corticosteroid use; however, there was more acute care and more oral corticosteroid use if air nicotine levels were detected, and similar results were found for NO<sub>2</sub> [63].

Effective and Sustainable Interventions for Endotoxin

More studies are needed to determine the effect of endotoxin exposure on asthma and the role of endotoxin remediation on asthma morbidity.

# **Air Pollution**

In the first 2 years of life, exposure to air pollutants has been associated with respiratory symptoms including cough and wheeze [64]. In childhood asthma, caregivers likely contribute to their child's air pollution exposure. In a Chicago-based survey, 75 % of caregivers reported idling their cars while in the community [65]. Diette et al. [66] found that inner-city homes of children with asthma in Baltimore had higher levels of indoor NO<sub>2</sub>. The authors speculated that poorly ventilated gas stoves serve as the source of indoor NO<sub>2</sub>.

In a study conducted by Hansel et al. [67] of inner-city asthmatics, ages 2–6 years old, exposure to high levels of  $NO_2$  was associated with increased asthma symptoms including cough, limited speech, and nocturnal symptoms. In a study of 148 inner-city asthmatic children, Lu et al. [70] found being overweight or obese was associated with increased asthma symptoms when exposed to fine particulate matter (less that 2.5  $\mu$ m) compared to those who were normal weight. In a double-blind crossover trial conducted by Marks et al. [71],

exposure to low nitrogen oxide unflued gas heaters in school classrooms was associated with increased respiratory symptoms in atopic children compared to the use of non-indoor-air-emitting flued gas heaters [71].

In a study conducted in Korea, after reducing particulate matter and other air indoor air pollutants, there was an associated decrease in prevalence of atopic dermatitis and improvement in eczema area and severity index (EASI) [68]. In a study conducted by Du et al. [69], using HEPA filters reduced particulate matter by 69–80 % in the homes of children with asthma. This suggests that HEPA filter use may be an effective strategy to reduce indoor air pollution but more studies are needed.

Effective and Sustainable Interventions for Air Pollution

In a review on the effects of indoor pollution on inner-city asthmatics, the authors concluded that there is sufficient evidence to suggest that reducing indoor pollutants reduces asthma symptoms [72]. More studies are needed to determine the most effective control measures and strategies for reducing indoor air pollution and the effects of remediation on asthma morbidity and allergic diseases.

# **Multifaceted Intervention Programs**

There have been few studies which examine the efficacy of multifaceted interventions in the treatment of asthma and allergies; however, based on the limited evidence available, these interventions are the most promising with regard to long-term benefit. Most children are sensitized to more than one allergen [10], and an environmental remediation approach that targets multiple allergens is an appropriate strategy. In the ICAS, Morgan et al. [73] reported a customized multi-allergen environmental intervention, based on positive skin-testing in asthmatic children, decreased asthma symptom days in the intervention group compared to the control group.

More recently, Breysse et al. [74] conducted a randomized control trial in Milwaukee to examine the impact of environmental remediation and nursing case management in the homes of asthmatics. The intervention included minor repairs of the home, thorough cleaning, and IPM. After the intervention, the control group had 72 % more total settled dust [74]. Although there was a decrease in settled dust in the intervention group, there was no significant difference in the concentration of allergens between the two groups [74].

The use of HEPA filters in targeted multifaceted interventions is effective. In an air filter review conducted by Sublett et al. [26], the authors concluded that there is sufficient evidence to suggest that air filtration decreases allergic respiratory disease progression. Air filtration is multifactorial and is impacted by the air filtering device, ventilation, source



control, and humidity. The placement of an air filter in the home as a single intervention will not address the complex interactions that effect air quality and subsequent filtration [26].

In a systematic review of 23 multifaceted home environmental intervention studies in sensitized asthmatics, the authors concluded that these interventions in children were associated with decreased asthma morbidity as measured by asthma symptom days, asthma-related missed school days, and healthcare utilization; however, there were only 3 studies in adults included in the review [75••]. Thus, more studies are needed in adults.

Additionally, we need to conduct more studies in children to identify school-specific exposures that may contribute to asthma morbidity. Our group has an on-going study, the School Inner-City Allergen Study (SICAS), to comprehensively assess allergen exposures in both the school and home environments of inner-city asthmatics, and examine correlations with asthma morbidity [76]. In SICAS, there were higher allergen levels of mouse, cat, and dog in settled dust from schools compared to homes [13••]. This suggests that schools serve as an important source of environmental exposure for children which may influence asthma outcomes.

#### **Conclusions**

In the treatment of asthma and allergies, the most effective environmental remediation strategies are multifaceted interventions. This is particularly important in children because they are typically sensitized to more than one allergen [10]. There are fewer studies conducted in adults; thus, patterns of sensitization and the role of environmental remediation in adults are not well understood compared to children. Most trials have focused on children in an attempt to develop strategies to decrease disease progression or modify disease activity early in life. Although there are limited data in adults, the evidence suggests that multifaceted environmental interventions improve outcomes in children; thus, we recommend these interventions in children. However, more studies need to be conducted in adults. The most robust studies are multifaceted randomized, double-blind, placebo-controlled environmental intervention trials that examine composite outcomes which correlate objective data such as measured allergen levels with subjective and objective measures of patient outcomes. However, these studies are lacking in the literature.

One must devise a comprehensive environmental remediation strategy targeting multiple allergens based on sensitivities and exposures to effectively treat asthma and allergies. Based on the evidence available, the most effective control measures include education, thorough cleaning, use of HEPA filters, integrated pest management, and maintenance of these practices.

#### **Compliance with Ethics Guidelines**

Conflict of Interest This work was funded in part by NIH/NIAID R-01grant AI-073964, R01AI073964-02S1, K24 AI 106822, and NIH/NHLBI grant 1U10HL098102.

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