

The indoor environment and its effects on childhood asthma

Sharon K. Ahluwalia and Elizabeth C. Matsui

Division of Allergy and Immunology, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Correspondence to Elizabeth C. Matsui, MD, MHS, Department of Pediatrics, Division of Allergy and Immunology, Johns Hopkins University School of Medicine, 600 North Wolfe Street, CMSC 1102, Baltimore, MD 21287, USA
Tel: +1 410 955 5883; fax: +1 410 955 0229; e-mail: ematsui@jhmi.edu

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Purpose of review

Indoor pollutants and allergens cause asthma symptoms and exacerbations and influence the risk of developing asthma. We review recent studies regarding the effects of the indoor environment on childhood asthma.

Recent findings

Exposure to some indoor allergens and second hand smoke are causally related to the development of asthma in children. Many recent studies have demonstrated an association between exposure to indoor pollutants and allergens and airways inflammation, asthma symptoms, and increased healthcare utilization among individuals with established asthma. Genetic polymorphisms conferring susceptibility to some indoor exposures have also been identified, and recent findings support the notion that environmental exposures may influence gene expression through epigenetic modification. Recent studies also support the efficacy of multifaceted environmental interventions in childhood asthma.

Summary

Studies have provided significant evidence of the association between many indoor pollutants and allergens and asthma morbidity, and have also demonstrated the efficacy of multifaceted indoor environmental interventions in childhood asthma. There is also a growing body of evidence suggesting that some indoor pollutants and allergens may increase the risk of developing asthma. Future studies should examine mechanisms whereby environmental exposures may influence asthma pathogenesis and expand the current knowledge of susceptibility factors for indoor exposures.

Keywords

childhood asthma, indoor allergens, indoor pollution

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Introduction

There is strong evidence that environmental exposures lead to asthma exacerbations in children and growing evidence that some exposures can cause asthma. Major categories of indoor exposures include indoor pollutants such as particulate matter (PM₁₀ and PM_{2.5}), nitrogen dioxide (NO₂), and second hand smoke (SHS); and indoor allergens such as dust mite, cat, dog, mouse, cockroach, and molds. In this article, we review the effects of each of these indoor exposures on childhood asthma and the mechanisms by which they may act.

Indoor pollutants

Exposure to ambient air pollutants has been shown to cause increased airway reactivity, asthma exacerbations, respiratory symptoms, decreased lung function, and

altered host defense [1–4]. However, because indoor air pollution concentrations can greatly exceed outdoor air pollution concentrations [5], indoor pollutants may have a greater influence on asthma. In addition, Americans spend nearly 90% of their time indoors [6], leading to a greater duration of exposure to indoor pollutants than to outdoor pollutants. Therefore, indoor environmental exposures must be considered when evaluating young patients who either have asthma or are at risk for developing asthma.

Particulate matter

Particulate matter consists of solid and liquid particles that are suspended in the air. Particulate matter is further categorized into coarse PM₁₀ (aerodynamic diameter less than 10 µm, capable of entering the respiratory system) and fine PM_{2.5} (aerodynamic diameter less than 2.5 µm, capable of entering the alveoli).

Particulate matter generated from indoor sources (such as cooking exhaust, wood-burning stoves and fireplaces, and cleaning activities that re-suspend particles) may be more potent in decreasing lung function than particulate matter generated from outdoor sources [7–9]. Previous studies and a recent meta-analysis have concluded that exposure to high indoor particulate matter concentrations is associated with decreased lung function and respiratory symptoms in children [9,10,11[•]]. Particulate matter can provoke lung inflammation, and for children with asthma, exposure to high levels of PM_{2.5} in schoolyards (outdoor) and in classrooms (indoor) has been associated with elevated measurements of fractional exhaled nitric oxide (FeNO) [12[•]]. Whereas a causal link between exposure to particulate matter and the development of asthma has not been established, there is emerging evidence that such a relationship may exist. In one study [13[•]], children exposed to particulate matter *in utero* or in the first year of life were found to be at increased risk of having asthma at age 3–4 years, as compared with children who did not have such exposures. Although this study pertains to outdoor particulate matter, indoor particulate matter is composed in part of outdoor particulate matter travelling to the indoors. Thus, this collective evidence supports the role of particulate matter exposure in the development of asthma and as an exacerbating factor in patients with established asthma.

High-efficiency particulate air (HEPA) filters have been shown to be effective in lowering the concentration of indoor particulate matter, and this may have a modest effect on reducing asthma symptoms [14[•],15,16]. Other portable air filtration technology, such as the use of electrostatic filter material, is commercially available, but has not been well studied. Further studies aimed at comprehensive particulate matter reduction are still needed to understand the potential benefit of particulate matter reduction on asthma health.

Nitrogen dioxide

Nitrogen dioxide is a common air pollutant, and there are many potential indoor sources of NO₂, including gas stoves, space heaters, furnaces, and fireplaces. It is unclear whether NO₂ exposure contributes to the risk of developing asthma because similar NO₂ concentrations have been found in homes of children with and without asthma [17–19]. However, a recent study [13[•]] found that children exposed to ambient NO₂ *in utero* or in the first year of life had an increased prevalence of asthma in early childhood.

The link between indoor NO₂ exposure and asthma exacerbation is more clear, with several recent studies [20,21,22[•],23^{••}] showing that NO₂ exposure is associated with increased respiratory symptoms in children with

asthma. One study showed a stronger association between NO₂ and increased respiratory symptoms for nonatopic asthmatics than for atopic asthmatics [21].

It has been postulated that NO₂ may cause respiratory symptoms through its oxidizing potential. NO₂ has been shown to produce extracellular reactive oxygen species that can induce airway symptoms through interaction with antioxidants in the epithelial layer of the lung [24,25]. This may represent one mechanism through which NO₂ may cause increased respiratory symptoms in patients with allergic asthma.

There is some evidence to support the efficacy of NO₂ reduction interventions in reducing asthma symptoms. In one interventional study [26], mean indoor NO₂ was decreased by over 60% through the replacement of unflued heaters with flued heaters in classrooms, and a concordant decrease in asthma symptoms was noted among the affected schoolchildren. Further studies aimed at the reduction of NO₂ are still needed, but strategies aimed at reducing NO₂ levels may reduce asthma morbidity.

Second hand smoke

Second hand smoke exposure is very common in the USA, and the causal relationship between SHS exposure and asthma incidence and morbidity in children is well established [27–32]. SHS exposure *in utero* through maternal smoking is linked to decreased lung function, recurrent wheeze, and increased incidence of asthma in infants [33–36]. Furthermore, one recent study [37^{••}] demonstrated an association between in-utero smoke exposure and increased risk of corticosteroid resistance among adolescents with asthma, highlighting the potential long-term effects of in-utero SHS exposure.

Studies aimed at reducing SHS exposure for children through maternal and other in-home smoking have met with limited success [38,39]. However, a recent epidemiologic study [40[•]] in Scotland demonstrated a reduction of 18.2% per year in the rate of asthma-related hospitalizations for children following the implementation of a smoking ban in public places. Prior to the legislation, these rates were increasing by 5.2% per year. This study provides support for public health level interventions in the prevention of asthma morbidity.

Indoor allergens

Allergic sensitization is an important risk factor for childhood asthma, conferring a 4–20-fold increase in the risk of asthma [41–43]. Children who become sensitized to a perennial allergen during the first 3 years of life are more likely to have decreased lung function at age 13 years as compared with their nonsensitized counterparts; and

those with concomitant exposure to the allergen have the worst lung function [44]. In some populations, such as inner-city children with asthma, sensitivity to indoor allergens is more prevalent than sensitivity to outdoor allergens [45]. This evidence underscores the importance of indoor allergens in childhood asthma.

Mouse allergen

Mice excrete urinary allergens that are carried on particles that readily become airborne [46]. Several studies have demonstrated that almost all inner-city homes and more than three-quarters of suburban homes have detectable mouse allergen levels [47–51]. It is estimated that 18–50% of inner-city youth are sensitized to mouse allergen [52•,53,54]. Sensitization to mouse allergen is less common in rural and suburban areas [50,55].

For children who already have a diagnosis of asthma, mouse sensitization and exposure are associated with increased hospitalizations, increased respiratory symptoms, decreased lung function, and increased airways inflammation [52•,53,56]. Sensitization to mouse has been causally related to early wheeze in one cohort, suggesting that mouse allergy could increase the risk of developing asthma [57].

Integrated pest management (IPM) (extermination, vigorous cleaning, meticulous food disposal, and sealing of holes and cracks in housing structures) is the best approach to mouse allergen reduction. In one study [58], this approach resulted in a 75% reduction of mouse allergen levels in settled dust, whereas levels increased in the control group. A reduction in mouse allergen levels by at least 50% has been associated with reductions in missed school, fewer days of decreased activity, and fewer nights of sleep loss for caretakers among mouse-sensitized inner-city children [56], suggesting that IPM may benefit mouse-sensitized children with asthma.

Cockroach allergen

At least half of inner-city homes have clinically relevant levels of cockroach allergen. As many as 30% of suburban, middle class homes also have detectable levels of cockroach allergen, but the levels in suburban homes are generally much lower than in inner-city homes [59,60]. In inner-city populations, 60–80% of children with asthma are sensitized to cockroach [61,62], and in one suburban population, the sensitization rate was 21% [59]. Sensitization to cockroach allergen has been linked to the development of wheeze in young children [57]. Cockroach allergen has also been directly linked to poorer asthma outcomes in inner-city children with asthma, including increased asthma related healthcare utilization [62,63].

Substantial reduction in cockroach allergen can be achieved with an IPM approach, as demonstrated by studies in which IPM reduced cockroach allergen levels by 80–90% [64,65]. The effects of these reductions on asthma morbidity are unknown; however, the strong link between cockroach allergen exposure and asthma morbidity supports recommending an IPM approach to reduce exposure in cockroach-sensitized patients with asthma.

Pet allergens

Pet allergens can be found in virtually all homes, but the concentrations are 10–1000 times lower in homes without pets than in homes with pets [66,67]. Cat and dog allergens can also be found in a wide distribution of places, including public buildings such as schools [68,69]. Allergic sensitization to cat and dog is quite common, and pet allergen exposure has been linked to poorer asthma outcomes in animal-sensitized patients with asthma [70,71].

There has been a particular interest in the role of pet exposure in the development of allergic sensitization and asthma in children since some studies have suggested that pet exposure may be protective against allergy [72–74]. A follow-up of one of these earlier studies demonstrated that indoor pet exposure for children was associated with lower total IgE levels at age 18 years, but only among atopic patients [75•], indicating that the protective effect of early life pet exposure that was observed at 6–7 years [74] was mostly lost by 18 years. In contrast to these studies, a recent study [76•] in Norway found that cat allergen exposure during early life led to an increased risk of asthma at age 10 years, but not to an increased risk of animal sensitization. Further studies are needed to determine the role early life pet allergen exposure may play in the development of asthma. Until that time, there is not sufficient evidence to recommend early exposure to or removal of pets from the homes of children at risk for the development of asthma.

Dust mite allergens

The prevalence of allergic sensitization to dust mites varies regionally and depends on the local prevalence of dust mites which, in turn, is highly dependent on the humidity of the climate. Dust mite allergen exposure has been causally linked with the development of asthma in susceptible children [41] and with causing asthma exacerbations in sensitized individuals [19]. To help control dust mite exposure, the 2007 National Asthma Education and Prevention Program (NAEPP) guidelines recommend installation of allergen-proof mattress and pillow encasements, washing of all bedding every 1–2 weeks in hot water, removal of stuffed toys, reduction of indoor humidity, and regular vacuuming and dusting. These

strategies reduce asthma symptoms and medication requirements, and improve lung function [77,78].

A controversial 2008 meta-analysis [79] reported that dust mite control measures do not improve clinical outcomes in patients with dust mite allergy. In his 2008 opinion piece, Platts-Mills [80] suggested that a meta-analysis on this subject is implausible given the variability in methods among studies on this topic and that current practices of dust mite control should not be changed. Since then, others have also suggested that further clinical investigation is required prior to discontinuing use of dust mite allergen control measures [81]. Thus, it appears prudent to continue to recommend dust mite control measures in individuals with dust mite sensitization and exposure.

Molds

Assessing the effects of mold exposure on asthma is complex because of the sheer number of molds, the variety of methods through which they are quantified, and the fact that molds can cause adverse health effects through multiple mechanisms. Despite these challenges, there is growing evidence that allergic responses to inhaled mold allergens are associated with increased asthma symptoms.

Alternaria, found both indoors and outdoors, is the best studied mold in asthma. Exposure to *Alternaria* has been associated with increases in asthma symptoms, bronchial hyper-responsiveness, and severe asthma in sensitized individuals [82–84]. In one study [85**] of children with asthma, exposure to high levels of indoor *Penicillium* was associated with increases in symptoms and healthcare utilization. Furthermore, the same study found that being sensitized to one or more mold(s) was positively associated with increased frequency of asthma symptoms. Poor asthma control in children has also been linked to the presence of visible mold or mold odor in the home [86*].

Controlling mold in the home is difficult; however, reduction of mold levels may be beneficial in controlling asthma symptoms. In a recent review [87*] of housing interventions designed to improve asthma-related outcomes, it was concluded that sufficient evidence exists to recommend a combined approach of removing moldy items and eliminating leaks and moisture sources in homes to help reduce asthma symptoms.

Mechanisms and susceptibility factors

Indoor environmental exposures may cause airway inflammation and symptoms in children with established asthma by a variety of mechanisms. Although allergens act through an IgE-dependent mechanism, the mechanisms by which indoor pollutants may act are less well

understood. Many pollutants are known oxidants and may elicit inflammation by direct generation of free radicals on exposure to airway epithelium [25]. There is also evidence that pollutants can affect epigenetic changes that may influence the risk of allergy and asthma. One study [88*] of asthmatic children in Fresno found that children with asthma who were exposed to high levels of air pollution had increased methylation of fork-head box P3 (FOXP3) and decreased chemotaxis of T-regulatory cells compared with healthy children and nonexposed asthmatic children. And, most relevantly to this review of the indoor environment and childhood asthma, in-utero tobacco exposure has been associated with DNA hypermethylation in infants [89]. These studies suggest that pollutants can affect epigenetic changes that could, in part, be responsible for the health effects associated with pollution exposure.

Recent studies [90–92] have also identified genetic susceptibility factors for pollutant exposure. The possession of various polymorphisms of the glutathione transferase gene coupled with exposure to pollutants has been postulated to partially determine an individual's risk for developing asthma. In one study [93*], children with both high mold exposure and two copies of a particular single-nucleotide polymorphism (SNP) for the CHIT1 gene (which encodes an enzyme that cleaves chitin) were at an increased risk of hospitalization for asthma exacerbation. These studies, along with others, form a strong and growing evidence base pointing to the importance of genetic susceptibility factors for environmental exposures.

Conclusion

The evidence regarding the ill-effects of indoor air pollutants and allergens on asthma morbidity in children is strong. For children with known asthma, it is important to assess their allergic sensitivities and provide counseling regarding the impact of their indoor environment on their respiratory health. Causal relationships between exposures to pollutants and allergens and the subsequent development of asthma have been demonstrated most strongly for dust mite allergen and SHS. Further studies are needed before recommendations can be made regarding primary prevention through environmental modification or avoidance. Finally, further research is needed regarding the interaction of genetics with environmental exposures. This area of research holds the promise for development of patient-targeted therapies in asthma care.

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