Environmental exposures and asthma morbidity in children living in urban neighborhoods

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Abstract

A substantial disparity in asthma prevalence and morbidity among urban children compared with their nonurban counterparts has been recognized for more than two decades. Because of the nature of urban neighborhoods, pest allergens, such as cockroach and mouse, are present in high concentrations in US urban housing and have both repeatedly been linked to asthma morbidity in sensitized children. In addition, there is a growing body of evidence demonstrating that concentrations of many pollutants are higher indoors than outdoors in both US and European urban communities and that exposures to indoor pollutants such as particulate matter (PM) and nitrogen dioxide (NO\textsubscript{2}) are independently associated with symptoms in children with asthma. Although environmental interventions are challenging to implement, when they reduce relevant indoor allergen and pollutant exposures, they are associated with clear improvements in asthma. Other modifiable risk factors in urban childhood asthma that have emerged include dietary and nutritional factors. Overweight and obese children, for example, may be more susceptible to the pulmonary effects of pollutant exposure. Insufficiency of vitamin D and folate has also emerged as modifiable risk factors for asthma morbidity in children. The identification of these modifiable risk factors for urban childhood asthma morbidity offers a ripe opportunity for intervention.

Keywords

childhood asthma; folate; indoor allergens; indoor pollutants; mouse allergen
the type and condition of housing stock and the proximity to pollution sources such as traffic, psychosocial stressors, and other factors associated with poverty (3).

**Indoor allergens**

Although common indoor allergens, such as furry pet and dust mite allergens, are present in urban homes and can contribute to asthma morbidity, this review will focus on pest allergens which are more specific to urban neighborhoods. Because of the nature of US inner-city housing, pest allergens are frequently detected in inner-city homes and are often present in high concentrations. The poor housing conditions, and shared walls and floors/ceilings of multifamily dwellings provide an optimal environment for cockroaches, mice, and rats. There are several species of cockroach, but the predominant species in US inner-cities are the German and American cockroaches, with the German cockroach allergen being the most common and the best studied (4–6). These studies have found that cockroach allergen is detectable in 85% of inner-city US homes (4) and that approximately 2/3 of inner-city children with asthma demonstrated skin test sensitivity to cockroach, making them susceptible to the effects of cockroach allergen exposure (4, 7, 8). In fact, cockroach-sensitized children exposed to higher levels of cockroach allergen in their homes have greater asthma morbidity across a range of morbidity measures than nonsensitized or nonexposed children. Cockroach allergen exposure has also been reported in European urban communities, including high levels in cockroach-infested public housing units in France (9). However, in general, sensitization rates in European studies are much lower than in US studies and may be due to cross-reactivity rather than to a primary IgE response to cockroach (10–12). One study in Poland, however, found that almost a quarter of asthmatic children were sensitized to cockroach and that most of their homes had detectable cockroach allergen. There was also an association between cockroach sensitization and more severe asthma, suggesting that cockroach exposure and sensitization may be clinically relevant in at least some European communities (13).

The role of rodent allergen exposure, however, was not well studied until the past decade. Initial studies reported a prevalence of detectable mouse allergen of 95% in inner-city homes (14), but non-inner-city studies also demonstrated a surprisingly high prevalence of mouse allergen of 75–80% (15, 16). The striking difference between inner-city and non-inner-city homes was in the concentration of mouse allergen found. In suburban homes, concentrations of Mus m 1, the major mouse allergen, were in the range of ng/g of settled dust, while in inner-city homes, mouse allergen concentrations were in the mcg/g range. Studies that have sampled air from bedrooms of children with asthma have found that 85–90% of bedrooms have detectable airborne mouse allergen (17, 18), with 25% having airborne concentrations similar to those found in some laboratory mouse facilities (19). However, it is important to note that mouse allergen, such as other indoor allergens, has a specific geographical distribution with Northeastern and Midwestern US cities having much higher mouse allergen concentrations than Western US cities (20). On an even more granular scale, mouse allergen can also have a specific distribution within a city (21). Whether the geographical heterogeneity of mouse allergen is due to the age or type of housing stock, or other factors, is not known.

Although multicenter studies report mouse sensitization prevalence of 18–22% (20, 22), in some cities, the mouse sensitization prevalence is 50% or more, with higher prevalence found in populations with greater asthma severity (18). Several studies have convincingly demonstrated a strong association between exposure to mouse allergen and asthma morbidity among mouse-sensitized children (18, 20, 23). Not only do sensitized and exposed children have more asthma symptoms and more acute healthcare visits for asthma than nonexposed or nonsensitized children, but they also have higher exhaled nitric oxide levels.
worse lung function, and are more likely to have bronchodilator reversibility, demonstrating an effect on pulmonary inflammation and physiology in addition to symptoms and exacerbations (24).

More recent studies have focused on trying to understand the clinical relevance, if any, of mouse allergen levels measured from specific locations within the home. In the Mouse Allergen and Asthma Cohort Study, there was a stronger association between bed mouse allergen levels and asthma-related acute visits than mouse allergen levels in dust samples taken from the bedroom floor or the kitchen and air samples taken from the bedroom (18). In this study, the shape of the dose–response relationship between mouse allergen exposure and asthma morbidity was also examined. A linear relationship between bed mouse allergen exposure and asthma morbidity was found among mouse-sensitized, but not non-mouse-sensitized, participants (Fig. 1). Taken together, these findings suggest that any incremental reduction in home mouse allergen levels would result in a corresponding reduction in risk of asthma morbidity and that efforts to target the bed exposure compartment may augment the effects of interventions aimed at eliminating the mouse infestation. The role of mouse allergen exposure in causing asthma is less clear than its role in symptoms and exacerbations in inner-city children with established asthma. However, birth cohort studies have found that parental report of mouse exposure in the first year of life, and sensitization to mouse at 2–3 years of age were associated with greater risk of wheeze in early life (25, 26).

There have been only a few studies in European cities examining mouse allergen exposure, and the prevalence of mouse allergen in home dust and sensitization to mouse varied, but was generally lower than that observed in US inner-city populations. In a study of Strasbourg public housing, 60% of homes had detectable mouse allergen, but the concentrations were 1000-fold lower than concentrations observed in US inner-city homes (27). In one Italian study, approximately 5% of patients seen by allergists were sensitized to either rat or mouse, and a much smaller percentage reported mouse infestation (28). One Polish survey of inner-city asthmatics found that 35% were mouse-sensitized and sensitization was associated with detectable mouse allergen in settled dust, although mouse allergen concentrations were still orders of magnitude lower than those observed in US inner-city homes (29).

**Indoor pollutants**

Although outdoor pollutants have been linked to adverse respiratory effects in urban children with asthma (30) and are known to penetrate indoors and contribute to indoor pollution, there is a growing body of work demonstrating that concentrations of many pollutants are higher indoors than outdoors and that exposure to indoor pollutants is independently associated with asthma symptoms in urban children with asthma.

The best studied indoor pollutants include airborne particulate matter (PM), nitrogen dioxide (NO₂), and second-hand smoke exposure. Airborne particulate matter (PM) is typically measured in different size fractions, so that fine PM is considered PM with an aerodynamic diameter of 2.5 microns or less (PM₂.₅) and coarse PM is considered PM with an aerodynamic diameter greater than 2.5 microns and up to 10 microns (PM₂.₅–₁₀). Both fine and coarse PM comprise PM₁₀. Secondhand smoke (SHS) exposure is composed of many substances, which are both particulate and gaseous in nature. SHS contributes predominantly to the fine particle (PM₂.₅) fraction of airborne particulate matter, and the most commonly measured gaseous component of SHS is airborne nicotine.

Indoor PM concentrations in urban homes are higher than concentrations in nonurban homes (31) and can be as much as twice as high as outdoor concentrations (32–35). Smoking, sweeping, and stove use contribute significantly to both PM₂.₅ and PM₁₀ indoors (32).
indoor PM$_{2.5}$ and PM$_{2.5-10}$ exposures are associated with more asthma symptoms and rescue medication use in urban children with asthma (32). NO$_2$ is the byproduct of combustion reactions, and homes with gas-powered appliances have higher levels of NO$_2$ than homes without gas-powered appliances. Indoor NO$_2$ levels are also higher than outdoor NO$_2$ levels in urban homes. In many US cities, gas stoves and heat are prevalent, and some families will use their gas stoves and ovens for heat. In contrast to PM, outdoor NO$_2$ has little to no influence on indoor NO$_2$ concentrations. Exposure to indoor NO$_2$, such as indoor PM, is associated with more asthma symptoms in urban children (36), although one study found that this was only true among nonatopic urban children (37).

Second-hand smoke exposure is relevant in urban childhood asthma as more than half of inner-city US children with asthma live with a smoker as compared to a US national smoking prevalence among adults of 20%. (http://www.cdc.gov/nchs/fastats/smoking.htm) Although some studies have reported no effect of SHS exposure on asthma symptoms or asthma-related healthcare use (37), others have found a clear association between SHS exposure and asthma morbidity in children (38), and prenatal and SHS exposures are associated with incident wheeze and asthma in children (39). A recent public smoking ban in UK was associated with a marked reduction in childhood asthma hospitalizations, suggesting a causal link between second-hand smoke exposure and childhood asthma morbidity (40). Another source of indoor pollutants that has been linked to childhood respiratory disease is burning of biomass fuel for cooking, which produces high concentrations of particulate and gaseous pollutants and bioaerosols. Most of the studies focusing on cook stoves have been in developing countries, and use of a variety of alternative fuels and ventilation is associated with lower indoor pollutant concentrations and improved respiratory health (41).

**Environmental interventions**

Now that a clearer picture of the environmental causes of asthma morbidity in urban children has emerged, there has been greater focus on designing environmental interventions that could serve as an integral part of a patient's asthma management. Intervention studies have focused on targeting-specific allergens, such as cockroach or mouse allergen, or pollutants, such as second-hand smoke exposure. Others have tested the efficacy of a multifaceted intervention tailored to each study participant's panel of triggers, which are identified through allergy testing and assessment of home exposures. Although these interventions are challenging to implement, when they reduce relevant indoor exposures, they are associated with clear improvements in asthma.

The most notable example of a successful environmental intervention is the Inner-City Asthma Study (8), which enrolled 937 inner-city children with atopic asthma. In this randomized controlled trial, the active intervention group received a 1-year, multifaceted environmental intervention that was tailored to the study participants' sensitivities and exposures. The active intervention group had an almost immediate reduction in asthma symptoms that persisted for an additional year beyond the active intervention period, and the improvements in symptoms were associated with the degree of reduction in dust mite and cockroach allergen levels. The findings were striking in that the magnitude of improvement, as compared to the control group, was similar to that observed with controller medication, but unlike controller medications, the effects of the intervention persisted well beyond the active intervention period. This study highlights the feasibility and efficacy of environmental interventions in urban children with asthma and re-enforces the importance of incorporating environmental control practices into the management of urban children with asthma. Although not all aspects of the intervention are relevant to all urban communities, at least some of the interventions should be appropriate for all urban communities.
There have been several randomized controlled trials of indoor pollutant interventions as well. Although the Inner-City Asthma Study environmental intervention trial did not report the effects of the intervention on indoor pollutant levels, it is notable that portable high-efficiency particulate air (HEPA) purifiers were a component of the intervention, so that it is likely that the reductions in allergen levels that were observed were also accompanied by reductions in indoor pollutants, such as PM. In another study, inner-city children with asthma were randomized to a multifaceted intervention or a control group (42). The intervention was similar to the one in the Inner-City Asthma Study, and included deployment of a portable HEPA purifier, but both indoor PM$_{2.5}$ and PM$_{10}$ levels were measured. This study demonstrated a marked reduction in both PM$_{2.5}$ and PM$_{10}$ levels as well as an improvement in asthma symptoms in the active treatment group. In a follow-up trial, inner-city children with asthma who lived with a smoker were randomized to one of three groups: (1) two HEPA purifiers and a behavioral intervention aimed at reducing the child's exposure to SHS, (2) two HEPA purifiers, or (3) control (43). The behavioral intervention was no more effective than the air purifiers, but the air purifier groups had $\sim$40% decline in both PM$_{2.5}$ and PM$_{2.5-10}$ levels and an improvement in some symptoms outcomes. Taken together, these studies indicate that deployment of portable HEPA purifiers not only reduces indoor airborne particulate pollution, but also improve asthma control, even for children living with a smoker. Although these studies provide strong evidence for the incorporation of an individually tailored, multifaceted environmental intervention as an integral part of management of inner-city children with asthma, one question that remains unclear is whether community-level interventions that target the predominant allergen(s) responsible for asthma morbidity in that community would be effective in reducing asthma morbidity. There remain, unfortunately, obstacles to implementation of comprehensive environmental interventions as a part of patient care, perhaps the largest of which is that these services are not covered by health insurance in the USA. This is particularly notable because the population that would arguably have the greatest benefit from environmental intervention is the same population that contributes most to asthma-related healthcare costs, but cannot afford to pay out of pocket for these services. Although these services are covered to some extent in some settings in Europe, access to, and coverage of, these services is not widespread (44).

**Other modifiable risk factors and susceptibility factors**

There are additional characteristics of low-income, minority children that may contribute directly or indirectly to their disproportionate asthma morbidity. For example, overweight and obesity is more common in inner-city children and adolescents than their non-inner-city counterparts. Approximately 30% of inner-city children with asthma are obese (45, 46), while the percentage of the general population of US children who are obese is 18%. Although the impact of overweight and/or obesity on asthma in this population is not entirely clear, overweight and/or obesity may be associated with more severe disease. There are several biologically plausible mechanisms for a relationship between obesity and worse asthma, but the mechanisms for this association are poorly understood.

In addition, several observations regarding overweight and obese children suggest that they may be more susceptible to the pulmonary effects of pollutant exposure. Overweight and obese children, for example, have greater tidal volumes than their normal-weight counterparts, and pulmonary deposition of airborne pollutants appears to be greater in these children (47). Obesity may also be associated with a reduced capacity to handle oxidative insults such as pollutant exposure, so that inflammatory effects of pollutants are greater in obese patients. Because obesity is associated with resistance to corticosteroids, it is also possible that the inflammatory response induced by pollutant exposure is less responsive to inhaled corticosteroids (48). In fact, some evidence does point to an interaction between
weight status and pollutant exposure. In one cohort of inner-city asthmatics, both indoor PM$_{2.5}$ and NO$_2$ exposures were associated with more symptoms in overweight and obese children than in normal-weight children (Fig. 2) (46). A large population-based study in China also found that overweight/obese children were more susceptible to the respiratory effects of outdoor pollutant exposure than normal-weight children (49). Given the high indoor pollutant concentrations and high prevalence of overweight/obesity among inner-city children, this combination of risk factors may be responsible for a substantial portion of asthma morbidity.

Inner-city populations are also at risk of insufficiencies or frank deficiencies in micronutrients. Two micronutrients, vitamin D and folate, have emerged as potential modifiable risk factors for asthma morbidity in children in general (50–52). Moreover, inner-city children in particular are at risk of lower vitamin D and folate levels, so that these micronutrients may contribute to asthma morbidity in inner-city children. Psychosocial factors associated with poverty also contribute to asthma morbidity (53). Limited financial resources, low health literacy, and limited emotional support are just some of the many poverty-related factors that are implicated in inner-city asthma.

Conclusions

Urban communities are characterized by a complex environment that has a profound influence on the risk of asthma morbidity, likely explaining a substantial proportion of the high level of morbidity among urban children. Specifically, work over the past decade has provided clear evidence that the pest allergens, pollutants, and poverty-related psychosocial factors play a major role in perpetuating the morbidity in this population (Fig. 3). The indoor allergens implicated in asthma morbidity are very community-specific, so community-level studies are needed to identify the allergens of greatest public health relevance within any given community. The growing evidence from randomized controlled trials that environmental interventions targeting indoor allergens and pollutants improve asthma should be leveraged to lobby for insurance coverage for these interventions, and future work should focus on refining these interventions and studying the effectiveness of community-level environmental interventions.

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Figure 1.
Predicted lines for relationships between bed mouse allergen exposure and predicted probability of an acute visit for asthma. The red line represents children who were not sensitized to mouse and the blue line represents children who were sensitized to mouse. Adapted from (18), Torjusen et al., Indoor Air, © 2012 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.
Figure 2.
Surface plot of relationships between indoor particulate matter exposure, body mass index, and probability of cough without a cold. Adapted from (46). Reprinted from *Journal of Allergy and Clinical Immunology*, Vol. 131, Lu et al., ‘Being overweight increases susceptibility to indoor pollutants among urban children with asthma’, pages 1017–1023, copyright 2013, with permission from Elsevier.
Figure 3.
Schematic of complex relationships between environmental exposures, susceptibility factors, and clinical manifestations of asthma.