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REVIEW

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The influence of urban exposures and residence on childhood asthma

Torie L. Grant | Robert A. Wood

Division of Pediatric Allergy, Immunology, and Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Correspondence
Torie L. Grant, 600 N Wolfe Street, Blalock 430, Baltimore, MD 21287, USA.
Email: tgrant12@jhmi.edu

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Abstract

Children with asthma who live in urban neighborhoods experience a disproportionately high asthma burden, with increased incident asthma and increased asthma symptoms, exacerbations, and acute visits and hospitalizations for asthma. There are multiple urban exposures that contribute to pediatric asthma morbidity, including exposure to pest allergens, mold, endotoxin, and indoor and outdoor air pollution. Children living in urban neighborhoods also experience inequities in social determinants of health, such as increased poverty, substandard housing quality, increased rates of obesity, and increased chronic stress. These disparities then in turn can increase the risk of urban exposures and compound asthma morbidity as poor housing repair is a risk factor for pest infestation and mold exposure and poverty is a risk factor for exposure to air pollution. Environmental interventions to reduce in-home allergen concentrations have yielded inconsistent results. Population-level interventions including smoking bans in public places and legislation to decrease traffic-related air pollution have been successful at reducing asthma morbidity and improving lung function growth. Given the interface and synergy between urban exposures and social determinants of health, it is likely population and community-level changes will be needed to decrease the excess asthma burden in children living in urban neighborhoods.

KEYWORDS
air pollution, asthma disparities, childhood asthma, pediatric urban asthma, pest allergen exposure, social determinants of health, urban asthma, urban exposures

1 | INTRODUCTION

Children living in urban areas are at higher risk of developing asthma and have increased asthma morbidity. Increased asthma prevalence and morbidity in urban communities have been observed across North America and Europe as well as in Asian, African, and South American countries.[1–9] In the United States (US), the terms urban and inner city refer to centrally located neighborhoods, often in historic cities, characterized by concentrated poverty and predominantly racial and ethnic minority populations. In 1991, the National Institute of Allergy and Infectious Diseases (NIAID) began funding research aimed at addressing the increased asthma burden in inner cities.[9]

Children living in urban neighborhoods are at increased risk of exposures known to be associated with asthma and asthma morbidity, such as pest allergens and mold as well as indoor and outdoor pollutants.[10] Additionally, children living in urban neighborhoods experience disadvantageous social determinants of health including increased poverty, poor housing quality, increased rates of obesity, and increased stress, all of which can contribute to asthma risk and morbidity.[11] The purpose of this manuscript is to review exposures which are unique to children with asthma living in urban neighborhoods and how

these exposures contribute to the increased asthma burden (Figure 1), and discuss opportunities for intervention which could help to mitigate asthma disparities among urban children with asthma (Table 1).

2 | INDOOR ALLERGENS AND MICROBES

Indoor allergen and microbial exposures have been recognized for decades as contributors to pediatric urban asthma. In particular, pest allergens, such as mouse and cockroach allergens, are major causes of urban pediatric asthma morbidity in the United States.[1,12–15] Low-income children living in urban homes are disproportionately at risk of pest infestation and allergen exposure due to housing disrepair in inner cities.[16–18] Additionally, pest allergen concentrations are significantly higher in urban homes as compared with suburban homes.[19] In the United States, mouse allergen has been found in 95% of home dust samples from a multicenter asthma study, the National Cooperative Inner-City Asthma Study, with higher concentrations of mouse allergen being found in homes with concomitant cockroach infestation.[20] Furthermore, urban children with asthma are often exposed to mouse allergen at school and day care, with one study out of Boston, Massachusetts detecting mouse allergen in 99.5% of schools sampled.[21] Cockroach allergen exposure is also very common in US urban centers, with the National Cooperative Inner-City Asthma Study detecting cockroach allergen in >85% over homes, with concentrations considered to be "high" found in >50% of children's bedrooms.[13]

Mouse allergen exposure in European homes is not as well-studied or characterized and may be less clinically relevant.[10,22] A study out of Strasburg, France found in-home rodent allergen concentrations to be lower than rodent allergen concentrations found in US homes,[23] with a recent Dutch study finding no association between self-reported asthma and detectable mouse allergen.[22] However, cockroach allergen may be a more important urban pest allergen in Europe. A separate study out of Strasburg, France found high concentrations of cockroach allergen in low-cost public housing.[24] Similarly, study out of Poland found higher cockroach concentrations in older homes, homes without central heat, and low-income homes.[25]

Pest allergen exposure, especially when combined with sensitization, has been repeatedly associated with asthma morbidity. Numerous studies in the United States have demonstrated the association between both mouse and cockroach allergen exposure and increased asthma morbidity, including increased asthma symptoms and exacerbations, increased acute visits and hospitalizations for asthma, and lower lung function in urban children with asthma.[12–14,26–28] The above-mentioned study of Polish children with asthma found cockroach exposure to be associated with more severe asthma and lower lung function.[25]

In addition to increased exposure to pest allergens, children in urban neighborhoods are also at increased risk of exposure to mold, which has also been associated with housing disrepair and low-income housing.[29] Exposure to mold and dampness has been associated with childhood wheezing and childhood asthma[30,31] and mold sensitization and exposure has been associated with asthma symptoms, exacerbations, urgent visits for asthma, and lower lung function in urban asthmatic children.[32–34]

Key Message

Multiple factors contribute to the excess asthma burden in children living in urban communities, including pest allergen, mold, and air pollution exposures as well as disparities in social determinants of health. It is likely that population-level, rather than individual-level, interventions will be needed to meaningfully decrease pediatric urban asthma risk and morbidity.

While exposure to pest allergens in children with asthma is a clear risk factor for asthma morbidity in children with established disease, there is evidence suggesting that exposure to pest allergens in early life may in fact be protective against wheezing and childhood asthma development. In a US study of urban children who were at high risk of asthma development, the Urban Environment and Childhood Asthma (URECA) study, early-life exposure to both mouse and cockroach was associated with a decreased risk of wheeze at age 3[35] and a decreased risk of asthma diagnosis at age 7.[36] Perhaps more interesting, not only did these children have high allergen exposures in the first year of life, but they were also exposed to higher levels and a more diverse bacterial content in house dust,[35,36] suggesting the microbiome associated with pest allergens may be the actual protective factor against wheeze and childhood asthma.

Endotoxin, a lipopolysaccharide (LPS) found in the outer membrane of gram-negative bacteria, is often used as a marker of bacteria or microbial exposure. Endotoxin exposure in children to date has yielded mixed and complicated results. For example, a study of infants in New York City found endotoxin exposure was associated with an increased risk of wheezing, but a decreased risk of eczema.[37] However, in studies of rural, farming communities in both the United States and Europe, high endotoxin exposure is associated with decreased risk of asthma.[38,39] The difference in asthma outcomes in urban versus rural endotoxin exposure could partly be explained by higher exposure levels in rural areas, but likely is more complex owing to other exposures associated with urban versus rural residence.

Additionally, endotoxin exposure and its effects on asthma are often linked to and even modified by other exposures. In a national US survey, exposure to endotoxin was associated with wheezing, finding low income, cockroach sightings, pets in the homes, Mexican American race, and age less than 18 years to be predictors of higher endotoxin concentrations in house dust.[40] In a study of primarily low-income, Black participants with asthma, the effect of endotoxin on asthma morbidity, including acute visits and oral steroids for asthma, was modified by air nicotine and nitrogen dioxide (NO_2) concentrations.[41] For children living in homes with high air nicotine concentrations, endotoxin exposure was associated with increased acute visits for asthma. Conversely, children living in homes with lower NO_2 concentrations, endotoxin exposure was associated with

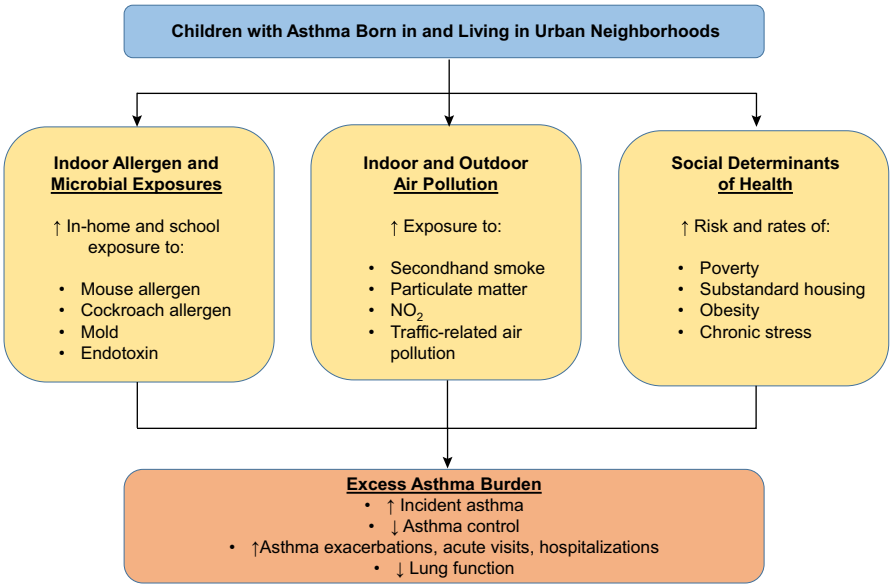

FIGURE 1 The relationship between urban risk factors and the excess asthma burden in children with asthma living in urban neighborhoods

increased acute visits for asthma.[41] Lastly, endotoxin exposure has also been associated with childhood asthma morbidity in urban schools with increased exposure in school being associated with increased asthma symptoms.[42]

As this fascinating story has developed over the past 30–40 years, it is clear that urban pest allergen and mold exposures are major risk factors for asthma morbidity in children with existing asthma, especially for children with high levels of exposure to allergens to which they are sensitized. It was, therefore, unexpected to find that high levels of pest allergen exposure in early life appear to be protective against asthma development, although this finding may be modified by, or even primarily driven by, the microbial exposures that coexist in these same households. This information, much like the data regarding protective effects of high levels of endotoxin exposure in early life, all lend support to the notion that the hygiene hypothesis may be just as relevant in urban areas as it was initially shown to be in farming communities.

3 | INDOOR AND OUTDOOR URBAN POLLUTANTS

Children living in urban areas are exposed to high levels of both indoor and outdoor air pollution, both of which have been extensively linked to asthma risk and asthma morbidity. The primary and most well-studied sources of indoor air pollution for urban children with asthma are secondhand tobacco smoke (SHS), particulate matter (PM), and nitrogen dioxide (NO_2).[43]

Children living in US urban centers are at risk for secondhand smoke exposure as multiple studies have found ≥50% of urban children are exposed to SHS.[10,44–46] This percentage is higher than expected, as currently 12.4% of US adults and 8.1% of US adolescents are active smokers,[47] illustrating both higher rates of tobacco use and overcrowding in urban households. Moreover, persons living in poverty, children under age 11, non-Hispanic Blacks, persons living in rental housing, and those with less than a high school education are more likely to be exposed to SHS.[48] Following a public smoking ban, childhood SHS exposure has decreased considerably in England over the last 20 years.[49] However, SHS exposure remains high in the United Kingdom and many other European countries, with notable exposure at primary school entrances (46%) and outdoor playgrounds (41%) in multinational European studies,[50,51] with higher SHS exposure being associated with lower income areas in both studies. While some studies have failed to show an association between exposure to SHS and asthma, the majority of studies, including a 2012 systematic review and meta-analysis, show a clear association between prenatal and childhood SHS exposure and an increased risk of wheezing and incident asthma.[52] The URECA study also showed prenatal smoke exposure was associated with increased asthma diagnosis in urban children at risk of asthma.[36] Additionally, SHS exposure may attenuate the effect of inhaled corticosteroids for the treatment of asthma in urban children,[53] making asthma controller medications less effective and contributing to increased asthma symptoms. Lastly, SHS exposure during childhood also has long-term respiratory health effects beyond pediatric asthma, with parental smoking being associated with lower lung function at age 53 and an increased risk of adult obstructive lung disease.[54]

Particulate matter is also a significant source of indoor air pollution for children with asthma living in urban centers. The primary source of indoor PM in urban homes is tobacco smoke, but other sources include cooking, heating, sweeping, and candle or incense burning.[55,56] Outdoor PM can also be a significant source of indoor PM[55] through open windows, doors, cracks, and poor housing repair. Urban indoor PM concentrations are significantly higher than those found in suburban homes[19] and can even be higher than outdoor urban PM.[57] Indoor PM exposure has been associated with increased asthma symptoms and exacerbations in urban children.[43,56,57] Nitrogen dioxide (NO_2) is also an important component of indoor air pollution which has been associated with childhood asthma. Gas heating and gas stoves are the major sources of in-home

NO_2, and urban families may use gas stoves as a source of heat during the winter when other heat sources are not available.[10,58] In-home NO_2 concentrations are often higher than outdoor NO_2 concentrations, with higher in-home NO_2 concentrations being associated with increased asthma symptoms and decreased peak flows in urban children with asthma.[58,59]

In addition to indoor air pollution, children living in urban communities also have higher exposure to outdoor air pollution. Traffic-related air pollution (TRAP) and energy generation are the main sources of outdoor air pollution.[60] Multiple longitudinal studies, including birth cohort studies, have described a strong association between outdoor air pollution, particularly TRAP, and incident asthma, increased asthma symptoms, hospitalization for asthma, and lower lung function.[61–68] Urban children with asthma who live near major highways have been found to have increased exacerbations and poorer asthma control,[65,69] with idling cars and buses in dense urban traffic and near schools contributing to higher urban air pollution.[65,70] Poor indoor air quality in urban schools is also mostly owing to high levels of outdoor air pollution.[71] In the United States, low-income racial and ethnic minority populations are at greater risk of being exposed to high pollution levels in urban areas, with historic redlining being associated with higher current air pollution levels.[72] In recent years, PM from wildfires has also become a significant source of outdoor air pollution.[73] In California, US, wildfires during the 2017 season led to an excess of asthma hospitalizations in the San Francisco Bay Area.[74]

In summary, exposure to both indoor and outdoor air pollution are high in urban areas and contribute to excess asthma incidence and morbidity. Urban pollution exposure disparities represent important opportunities for intervention, which are discussed in a later section of this review.

4 | SOCIAL DETERMINANTS OF HEALTH (SDOH) IN URBAN NEIGHBORHOODS

While indoor allergen exposures, microbial exposures, and air pollution are tangible and measurable urban risk factors for asthma, several other population-level characteristics contribute to asthma disparities and the excess asthma burden in children living in urban communities. Social determinants of health (SDoH) are non-medical influences that affect health outcomes[75] and include the conditions in which people are born, grow up, go to school and work, live, and age. SDoH are becoming increasingly recognized as important risk factors for pediatric urban asthma.[11,76] Here, we will discuss poverty, housing, obesity, and stress in the context of pediatric urban asthma.

In the United States, urban areas have high rates of poverty, with racial and ethnic minority populations having the highest rates of poverty in both urban and rural areas.[77] Income level in the United States is inversely related to asthma prevalence, with those living in the greatest degree of poverty having the highest asthma prevalence.[78] In a study of urban children with asthma in Baltimore, Maryland, there was an increase in odds of prevalent asthma per unit decrease in the household income to poverty ratio.[79] Low income is also associated with asthma exacerbations and asthma morbidity.[80] Poverty's effects on asthma are likely multifactorial, encompassing disparities in housing, education, employment, exposure to pests and pollution, limited health literacy, and access to health care.[11]

Housing quality is an important SDoH, with racial and ethnic minority populations being more likely to reside in housing considered substandard or in poor repair, which contributes to environmental health disparities.[81] Substandard urban housing is a risk factor for mouse and cockroach exposure as poor housing conditions contribute to pest infestation,[16–18] which has been highlighted above as being associated with asthma risk and morbidity. Similarly, living in homes with visible mold in the main living areas has been associated with pediatric asthma risk, asthma symptoms, and persistent asthma.[30]

Next, pediatric urban asthma patients have higher rates of obesity.[10,82] In the United States, Black children have the highest rates of early childhood (age 9 months to kindergarten entry) obesity.[83] Obesity in childhood has been linked to incident asthma and asthma morbidity[84] and lower lung function[85] in large-scale studies. Of further interest, being overweight or obese has been associated with increased susceptibility to urban exposures such as pollution and SHS,[82,86] and may further increase asthma morbidity.

Lastly, children and caregivers living in low-income, urban communities experience high levels of chronic stress, which is often multifactorial, involving high rates of income, job and food insecurity, exposure to violence, incarceration, and social disadvantage.[87] Early-life exposure to stress and maternal stress have both been associated with childhood asthma diagnosis.[36,88] Moreover, chronic stress has been associated with poor asthma control and asthma exacerbations in Black and other racial and ethnic minority children with asthma.[89,90] Chronic stress may influence asthma through chronic hypothalamic-pituitary-adrenocortical activation and a decrease in β2 adrenergic and glucocorticoid receptors.[91] This chronic activation and receptor downregulation may then lead to a decrease in responsiveness to asthma medication and an increase in asthma symptoms.[91] Chronic stress may also mediate the effects of SDoH on asthma in urban children, but the degree to which SDoH influence or explain asthma disparities is not clear.

5 | OPPORTUNITIES FOR INTERVENTION

Given the increased risk of asthma and increased asthma morbidity associated with children living in urban neighborhoods, interventions aimed at improving the urban environment in an effort to improve pediatric asthma health have been attempted for several decades. On the individual level, attempts at reducing indoor pest allergen exposure have produced mixed and often disappointing results. It can be difficult to achieve sustained allergen reduction in the urban setting. Multimodal approaches are necessary and have been successful at reducing cockroach allergen exposure and asthma symptoms in multicenter study of urban children with asthma.[92] Conversely, similar methods were not successful

TABLE 1 Community-level and population-level opportunities for intervention to improve pediatric urban asthma

Improving the state of repair of public housing in an effort to decrease pest infestation and exposure as well as mold exposure
Smoking bans in public places where children are at highest risk of SHS exposure
Outdoor air quality measures to reduce TRAP and idling vehicles in urban neighborhoods and near urban schools
Legislation, research, and public programs aimed at reducing urban, racial and ethnic disparities in income, housing, obesity rates, chronic stress exposure, and other SDoH

Abbreviations: SDoH, social determinants of health; SHS, secondhand smoke; TRAP, traffic-related air pollution.

at reducing mouse allergen exposure in a separate study of urban pediatric patients with asthma; however, participants who did experience a reduction in mouse allergen exposure, regardless of group assignment, did have an improvement in asthma symptoms.[93] A secondary analysis of this study found that significant reduction in mouse allergen exposure was associated with improved lung function growth over 1 year.[94] Yet, a different multifaceted allergen reduction study of children with asthma in New York City reported reduction in allergen exposure, but no change in asthma controller medication.[95] It is unclear as to why some studies have been successful in reducing allergen exposure and impacting asthma outcomes, while others either did not reduce allergen exposure or impact clinical outcomes. It is possible that the poor state of housing repair and high levels of infestation are limiting factors in the success of allergen exposure reduction methods in certain urban neighborhoods and community-level, rather than individual-level, approaches to improve housing conditions and pest infestation should be considered.

Population-level approaches to reduce urban pollutant exposures have been successful. As an example, in Scotland, the enactment of a smoking ban in public places has been associated with a decrease in asthma hospitalizations in children under age 15.[96] Follow-up of the public smoking ban in the United Kingdom has found decreased SHS exposure in children, including in children living in rental housing.[49] Public smoking bans aimed at reducing SHS in areas with high rates of children, such as public housing, school entrances, and playgrounds, could meaningfully affect childhood SHS exposure and reduce asthma risk and morbidity.

Another example of a successful population-level approach to reducing urban asthma risk and morbidity has been measures taken to reduce TRAP and improve outdoor air quality in California. Reduction in California air pollution has been associated with a decrease in incident pediatric asthma and an improvement in pediatric lung function growth.[97,98] Similar regulations in other densely populated urban centers with high TRAP could meaningfully reduce urban asthma disparities.

Lastly, making population-level changes to help reduce inequities in SDoH, such as high poverty, housing disrepair, higher rates of obesity, and chronic stress, will be needed to help reduce the excess asthma burden in urban children.

6 | CONCLUSION

Multiple environmental exposures and influences contribute to the increased incidence of asthma and excess asthma morbidity among children with asthma living in urban communities. Indoor pest allergen and mold exposures have been repeatedly linked to increased asthma diagnosis, symptoms, and exacerbations in urban children. However, data in high-risk urban populations found early-life pest allergen exposure, along with microbial and endotoxin exposures, to be associated with a decreased risk of wheezing and asthma,[35,36] illustrating that the association is more complex than previously thought. Individual-level allergen exposure reduction in urban children with asthma has proven challenging and yielded inconsistent results in allergen and asthma outcomes. Community-level interventions targeting housing disparities leading to pest infestation are likely needed to meaningfully change urban pest allergen exposure.

Population-level interventions have been successful at reducing childhood SHS and TRAP exposure with associated improvements in incident asthma, pediatric asthma hospitalizations, and childhood lung function growth.[96–98] However, children living in urban neighborhoods, in particularly racial and ethnic minority children, continue to be exposed to high levels of indoor and outdoor air pollution. Similarly, urban children with asthma are disproportionately affected by disadvantageous social determinants of health, including poverty, poor housing, increased rates of obesity, and chronic stress. While these disparities have been described in the literature, the extent to which and how individual SDoH influence pediatric urban asthma is unknown.

The environmental exposures and influences affecting pediatric urban asthma are complex and intertwined. Ultimately, community-level and population-level changes targeting pest allergen, mold, and air pollution exposures in conjunction with community-level and population-level changes to decrease income, housing, and other social inequalities will be needed to meaningfully change pediatric urban asthma risk and morbidity.

PEER REVIEW

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ORCID

Torie L. Grant https://orcid.org/0000-0002-5311-1527

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