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Asthma in the Inner City and the Indoor Environment

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Inner-city residents continue to suffer disproportionate asthma morbidity despite recent progress in reducing asthma morbidity and mortality in other strata of the United States population. Although many factors are likely responsible for these disparities, studies conducted over the past decade indicate that the indoor environment is a strong contributor to poor asthma control and asthma-related health care use in inner-city populations. The term ''inner city'' generally refers to impoverished urban neighborhoods where housing is often very old and dilapidated, so that certain indoor exposures are more common and occur in higher concentrations than in suburban communities [1]. Identification of ''asthmagenic'' indoor exposures has paved the way for the development of intervention strategies aimed at reducing asthma morbidity, principally by reducing these

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exposures. This article reviews the growing body of evidence that certain indoor environmental exposures contribute to the burden of asthma in the inner city.

The major categories of indoor exposures include allergens and other biologics, such as endotoxin, as well as pollutants. The major indoor allergens include those associated with dust mites, cats, dogs, mice, rats, cockroaches, and molds. Important indoor air pollutants include particulate matter (PM), nitrogen dioxide (NO_2), secondhand tobacco smoke, and ozone.

Indoor allergens and endotoxin

Overview

Allergic sensitization is an important risk factor for asthma for both children and adults. One recent study that included children and adults estimated the population-attributable risk for allergic sensitization to be 56%. In other words, more than half of asthma cases in the United States can be attributed to allergic sensitization [2]. In the pediatric population, about 80% of school-age children with asthma have evidence of allergic sensitization to at least one common environmental allergen [3,4]. Allergic sensitization to the predominant allergen in a community confers a 4- to 20-fold increase in the risk of asthma [5–7], suggesting a causal relationship between allergen exposure and the development of asthma. Moreover, populations with more poorly controlled asthma have higher prevalence rates of sensitization than populations with well-controlled asthma. In one recent inner-city study of children with poorly controlled asthma, a staggering 94% of children had evidence of allergic sensitization [8], highlighting the potential importance of allergic sensitization as a risk factor for poorly controlled asthma. Studies have also clearly demonstrated that exposure can lead to both acute and chronic symptoms in sensitized patients with asthma [4,9–13]. Although seasonal allergens are known triggers of asthma, overall exposure to indoor allergens may be greater given the substantial amount of time spent indoors as well as the year-round presence of many indoor allergens. In addition, among inner-city children with asthma, sensitivity to indoor allergens is more prevalent than sensitivity to outdoor allergens, underscoring the relevance of indoor allergen exposure in this population [14].

Although all of the major allergens can be found in inner-city homes, the distribution of allergens depends somewhat on the geographic region of the inner city [8,15,16]. For example, the dust mite is the predominant allergen in inner-city homes of southern and northwestern United States. In contrast, pest allergens, such as rodent and cockroach allergens, are the predominant allergens in northeastern inner-city homes where dust mite allergens are less common. Some of these regional differences in allergen ecology appear to be due to differences in climate and housing stock. As such, it is important to understand which allergens are most important in a given geographic area

so that appropriate allergy testing can be performed, and tailored environmental control recommendations can be provided to patients.

Rodent allergens

Mice and rats excrete urinary allergens that are carried on small particles that readily become airborne [17–19]. The allergens are pheromone-binding proteins that are thought to have a role in mating practices [20] and are excreted in very large quantities in the urine. Although these allergens have long been known to cause occupational asthma, their role in nonoccupational asthma has only recently been described [12,21]. In fact, in some inner cities, mouse allergen appears to be an important contributor to asthma morbidity.

The domestic house mouse (*Mus musculus*) is very common, particularly in urban areas where multifamily dwellings and poorly maintained housing are common [16,22]. Mouse allergen can be found in virtually all inner-city homes, and one study found detectable airborne mouse allergen in 84% of bedrooms of inner-city children with asthma [23]. Airborne mouse allergen levels in as many as 25% of inner-city homes are similar to levels measured in occupational settings, where mouse allergen is a known cause of asthma symptoms. Mouse allergen is surprisingly prevalent in suburban communities as well, with as many as 75% of middle-class, suburban households having detectable mouse allergen levels in settled dust samples [16,24]. However, the levels in these suburban homes are 100-fold lower than the levels observed in inner-city settings. For example, the median settled-dust mouse allergen level in inner-city bedrooms is approximately 2.5 μg/g as compared with 0.02 μg/g in suburban bedrooms. Overall, as many as 75% of homes in inner cities may have clinically relevant levels of mouse allergen [12].

Sensitization to mice is also common, with 18% to 28% of inner-city children with asthma having evidence of allergic sensitization to mice [8,12,21]. Since most of these children are also exposed to clinically relevant levels of mouse allergen, more than 20% of inner-city children with asthma may be at risk for increased morbidity from mouse allergen exposure.

Recent studies have linked exposure to mouse allergen to poorer asthma control and an increased risk of asthma-related health care use among mouse-sensitized, inner-city children with asthma [10,12]. In a Baltimore study, mouse-sensitized children with more than 0.5 μg/g of mouse allergen in bedroom settled dust had more symptom days and more days of rescue medication use than children who either were nonsensitized or had lower levels of mouse allergen in their bedrooms. The sensitized and more highly exposed children were also more likely to visit the emergency department or be hospitalized for asthma than children who were either not sensitized or were exposed to lower levels of mouse allergen [12].

Any patient who reports mouse sightings or evidence of mice, such as droppings, is very likely to be exposed to significant levels of mouse allergen

in the home [22–24]. However, as with cockroach allergen, patients and families may be reluctant to admit a rodent infestation, so that a negative history is not a good predictor of lack of exposure. In addition, substantial levels of mouse allergen can be found in homes with little or no evidence of infestation, because mice nest in hidden spaces and are active at night.

Reducing exposure to mouse allergen is feasible, but can be difficult. Although several studies have found an association between the presence of a cat and lower mouse allergen levels [22,23,25], acquisition of a cat as a means of lowering mouse allergen levels has not been studied. In addition, acquisition of a cat should not be recommended as a means of reducing mouse allergen levels in patients who are allergic to both mice and cats. Integrated pest management is the best approach and includes a combination of extermination, vigorous cleaning, meticulous disposal of food remains, and sealing of holes and cracks in walls, doors, and ceilings. Using this approach, the allergen source is eliminated, the allergen reservoirs are cleaned up, and reinfestation is discouraged. In one study, integrated pest management resulted in a 75% reduction in mouse allergen levels in settled dust, while levels increased in the control group [26]. Although no studies have been conducted to determine the impact of mouse allergen reduction on asthma, the evidence to date indicates that reduction of exposure has the potential to improve asthma control and prevent asthma-related morbidity.

Rats are also common in urban areas and, although they typically do not venture indoors, rat allergen has been found in 33% of inner-city homes. In one multicenter study, 21% of inner-city children with asthma were sensitized to rats, and the children who were sensitized and exposed to rat allergen in their homes were at greater risk for asthma-related hospitalization and unscheduled medical visits than children who either were not sensitized or not exposed [13]. No published studies have examined methods of reducing household rat allergen, but a reasonable approach would include sealing holes and cracks in the home's structure, vigorous cleaning to remove reservoir allergen, and extermination.

Cockroach allergen

The two most common cockroaches found in United States homes are the German cockroach (*Blatella germanica*) and the American cockroach (*Periplaneta americana*). Cockroach allergens are carried on relatively large particles (10–40 μm) that quickly settle to dependent surfaces so that the allergens are easiest to detect in settled dust samples, but very difficult to detect in air samples. Multiple allergens from each of these cockroach species have been characterized, but inner-city asthma studies have primarily focused on the German cockroach (Bla g) allergens. Several studies have found that at least half of inner-city homes have clinically relevant levels of cockroach allergen [4,8]. Although as many as 30% of suburban, middle-class homes also contain detectable levels of cockroach allergen, the levels in

suburban homes are much lower than levels found in inner-city homes [15,27]. For example, approximately half of homes in the inner city have a Bla g 1 level greater than 8 U/g, a level associated with asthma morbidity, but only 10% to 12% of suburban homes have levels that exceed this threshold [27,28].

In inner-city populations, 30% to 70% of children with asthma are sensitized to cockroaches [8,29], and in suburban populations, sensitization rates are about 21% [27]. Cockroach allergen has also been directly linked to poorer asthma outcomes in inner-city children with asthma, including asthma-related health care use [4,8]. In the National Cooperative Inner-City Asthma Study, cockroach-sensitized children with more than 8 U/g of cockroach allergen in their bedrooms had greater morbidity than either nonsensitized or less exposed children [4]. These findings were replicated in the Inner-City Asthma Study for exposure to cockroach allergen levels greater than 2 U/g [8], suggesting that levels below 8 U/g may be sufficient to trigger asthma symptoms.

In light of these findings, it is important to assess risk of exposure in sensitized patients and make recommendations for reducing cockroach allergen exposure. Although patient report of cockroach infestation is a good indicator of significant levels of cockroach allergen exposure [15], one cannot be reassured that a patient is not exposed to significant levels of allergen if they fail to report cockroach infestation. Patients may be reluctant to admit pest infestation, and homes without evidence of active infestation often contain substantial levels of the allergen.

Substantial reductions in cockroach allergen levels can be achieved using an integrated pest management approach. Several studies have demonstrated that a combination of extermination, vigorous cleaning aimed at reducing reservoir allergen, and meticulous care in disposing of food remains can result in 80% to 90% reductions in cockroach allergen levels [30,31], although not all studies have had this degree of success [32]. One recent study pointed out the importance of using certain pest management techniques, including use of traps, to monitor and direct treatments. This same study showed that methods used by some pest management companies may be inadequate to achieve substantial and lasting reductions in allergen levels [33]. It remains unknown if cockroach allergen reduction alone has a clinical impact. However, the strong evidence that cockroach allergen exposure is linked with asthma morbidity supports recommending an integrated pest management approach to reduce exposure in cockroach-sensitized patients with asthma.

Pet allergens

Unlike cockroach allergens, cat and dog allergens are carried on small particles that remain airborne and are very adherent to surfaces and clothing [34]. These properties lead to widespread distribution, such that cat and dog

allergen can even be detected in public buildings, such as schools [35,36]. Allergen is brought to school on the clothing of children with pets at home, and the highest airborne allergen levels occur around the desks of those children with pets [35]. Cat and dog allergens are obviously found in homes with these pets, but the allergens can also be found in homes without pets, though the concentrations are typically 10 to 1000 times lower than homes with a pet [37,38].

The practice of pet keeping occurs across almost all communities in the United States, so that, in general, studies of pet allergen exposure have not focused explicitly on inner-city environments. However, a few inner-city studies, particularly recent multicenter inner-city asthma studies, provide some insight into levels of pet allergens and their potential impact on asthma in these communities. These studies have found that there is somewhat less pet ownership in inner-city homes than in suburban homes [39]. Approximately 15% of inner-city families report having a dog, and approximately 13% to 25% report having a cat [8,40], while more than half of suburban families keep pets [39,41]. Not surprisingly, cat and dog allergen levels tend to be lower in inner-city homes than in suburban homes [39]. Sensitization to cats and dogs is also common in inner-city populations with asthma. In the Inner-City Asthma Study, 44% of children were sensitized to cats and 21% to dogs [8], and the prevalence rates of sensitization in suburban or non–inner-city populations range from 50% to 80% for cats and 20% to 30% for dogs [3,39].

For both cat and dog allergens, considerable evidence supports a relationship between allergen exposure and exacerbation of asthma in sensitized individuals. Epidemiologic studies have demonstrated an increased risk of exacerbations among patients who are both sensitized and highly exposed to cat allergen [8,42]. In addition, allergen challenge studies demonstrate that cat-sensitized asthmatics develop asthma symptoms and decreased lung function in response to airborne cat allergen, even at low levels [37,43,44].

An atopic child with asthma who is sensitized to cat or dog allergen should not live with the respective pet in the home. Pet removal reduces airway responsiveness in those with pet allergic asthma [45]. Once a pet has been removed, allergen levels in settled dust fall in 4 to 6 months to those seen in homes without cats [46]. Levels fall more rapidly if extensive environmental controls are undertaken, such as removal of carpets, upholstered furniture, and other reservoirs, as well as thorough and repeated cleaning. Cat allergen may persist in mattresses for years after a cat has been removed from a home [47], so the purchase of new bedding or impermeable encasements is also recommended. Because so many sensitized patients are unwilling to remove a pet, many compromise measures have been suggested. The use of high-efficiency particulate air (HEPA) filters and vacuum cleaners results in short-term reductions in airborne cat and dog allergen levels, but no change in settled dust allergen concentrations [48–52]. No studies

to date show an effect of air filters on disease activity [46], although one study demonstrated a reduction in airway responsiveness, without change in any other clinical measure [53].

Dust mite allergens

The major dust mite allergens are carried on relatively large particles (10–30 μm) that only briefly remain airborne [54]. The mites infest fabrics and are not particularly mobile, and disturbance is required to detect the allergens in the air. The distribution of house dust mite allergens varies widely among different homes [55,56], with highest concentrations found in the bedroom, especially in the bed. Higher allergen levels are associated with increased moisture, such as in damp houses and basement bedrooms [57].

Because dust mites require higher relative humidity for survival, there are striking geographic differences in dust mite allergen levels. For example, multicenter inner-city asthma studies have found that the highest dust mite allergen levels are found in southern cities, such as Dallas, and northwestern cities, such as Seattle, where two thirds of inner-city homes have clinically relevant levels of mite allergen [8]. In contrast, only 8% to 20% of inner-city homes in New York, Chicago, and Baltimore have clinically relevant dust mite allergen levels. There also appears to be differences between suburban and inner-city homes in the same region of the United States. For example, dust mite allergen levels are approximately five-fold higher in suburban Maryland homes than in inner-city Baltimore homes. The median bedroom dust mite allergen level is 66 ng/g in inner-city Baltimore homes [58], but is 360 ng/g in suburban Maryland homes [59]. Because of these regional and community differences in dust mite allergen levels, few published studies have focused explicitly on dust mite allergen and asthma in inner-city communities.

However, based on all studies to date, the 2000 Institute of Medicine Report concluded that there are causal relationships between (1) dust mite allergen exposure and the development of asthma in susceptible children and (2) exposure and asthma exacerbations in sensitized individuals [60]. The evidence cited includes studies in various countries demonstrating an association between dust mite sensitization and asthma (with odds ratios of 6 or more) [5], bronchial provocation experiments showing allergic response [61], and studies of clinical outcomes after mite allergen avoidance [62–69].

Evidence supports dust mite allergen control measures as a reasonable approach to improving asthma in children, though whether to recommend the practices on a larger scale remains controversial. The most effective method of control is the use of allergen-proof encasings fitted to the mattress and pillow [63,70]. Of more than a dozen clinical trials of allergen-proof encasings, seven have demonstrated a reduction in mite allergen and a clinical effect [64–69]. Dust mite covers are available by mail or in retail stores, are

breathable and comfortable, and exclude nearly 100% of particles carrying mite allergen [71]. Although prior studies have found that allergen-proof bed covers can reduce mite allergen levels and improve clinical outcomes in selected populations, one recent study of over 1100 adults suggests that providing encasings to all patients with asthma may not be an effective public health intervention [72]. Washing sheets, pillowcases, blankets, and mattress pads at least weekly in warm water with detergent and with 8- to 10-minute cycles removes virtually all mite allergen [73]. Dry cleaning [74] and prolonged tumble drying [75] effectively kill mites, but are less effective at removing allergens. Vacuum cleaning reduces the bulk of household dust and reduces the overall exposure burden, but does not change the concentration of mite allergen in settled dust [76]. Second line measures for which there is evidence of mite allergen reduction include removal of wall-to-wall carpeting [77] and steam cleaning [78]. Other measures without supporting evidence include relocation of the bedroom [78] and application of acaracides [79]. The evidence surrounding dehumidifiers is inconsistent, with some studies showing a reduction in mite allergen levels [80], and others not [81].

Mold

Mold, a saprophytic fungus, requires moisture, elevated temperatures, and nutrients to grow. These conditions are often found in homes. Mold spores are small (2–10 um), and therefore can remain airborne for extend periods. Hundreds of species of mold can be found indoors. Although there has been a great deal of interest in mold exposure and its impact on respiratory health, studies have been hampered by the complexity of the assessment of mold exposure. Molds can be quantified by measuring spore counts, culturable spores, allergens, or fungal products, and it is not entirely clear which method is best for examining the impact of mold exposure on asthma. In addition, molds can cause adverse health effects through multiple mechanisms, adding to the challenge of studying the impact of mold exposure on asthma.

Despite these challenges, a growing body of evidence shows that allergic responses to inhaled mold allergens do result in increased asthma symptoms. Most of these published studies focus on the role of outdoor mold exposure and asthma symptoms, but more recent studies have focused on indoor mold exposure. The best-studied mold in asthma is Alternaria. Exposure to outdoor Alternaria has been associated with asthma symptoms, bronchial hyperresponsiveness, and severe asthma in sensitized individuals in several reports [82–85]. In a recent study, levels of indoor Alternaria were associated with an increased risk of asthma symptoms [86].

Mold exposure has been comprehensively assessed in only a few inner-city asthma studies. In the Inner-City Asthma Study, indoor culturable airborne fungi levels were correlated with outdoor levels, underscoring the importance of considering outdoor levels when assessing the relative degree

of indoor fungal exposure [87]. Homes with dampness, a cat, and cockroach infestation were more likely to have indoor fungal levels that were higher than outdoor fungal levels.

The National Academy of Sciences review of asthma and indoor air exposures [60] concluded that there is sufficient evidence of an association between fungal exposure and symptom exacerbation in sensitized asthmatics. The National Academy of Sciences also concluded that evidence is inadequate or insufficient to determine whether there is an association between fungal exposures and the development of asthma. In addition, a large body of literature suggests that damp housing, assessed by evidence of water damage or excessive moisture, is associated with respiratory symptoms and asthma severity [88]. While it is often inferred from this literature that mold is the likely culprit, damp housing is potentially a surrogate for increased pests and their allergens as well as bacteria, viruses, and fungi [88,89].

Patients with asthma should be evaluated for mold sensitization by skin testing or specific IgE testing and, if indoor fungal sources are present, steps should be taken to remove the indoor mold. Although detailed information about abatement strategies are beyond the scope of this article, information about abatement can be found in the 2004 Institute of Medicine's report, "Damp Indoor Spaces and Health" [89].

Allergen abatement recommendations in clinical care

In clinical practice, each patient must be assessed for allergic sensitization using skin testing or serum-specific IgE tests. In fact, many inner-city asthma patients have multiple allergic sensitivities and identification of the specific sensitivities will guide exposure-reduction recommendations. For example, a patient with dust mite and cockroach sensitization should be counseled to concentrate on environmental-control practices aimed at reducing exposure to these allergens, while another patient with cat and mouse sensitizations should concentrate on implementing measures to reduce exposure to these allergens. In general, strategies aimed at reducing a single allergen [32] have been less successful than multimodal interventions in reducing exposures and, consequently, improving asthma control [90,91]. The most recent National Asthma Education and Prevention Program guidelines also support a multimodal approach over a single allergen approach as an integral part of asthma management [92].

Endotoxin

Endotoxin is a proinflammatory lipopolysaccharide that makes up the outer membrane of gram-negative bacteria and produces reversible airway inflammation in animal models and human challenge studies [93–95]. Though some epidemiologic evidence in early life suggests that endotoxin exposure may protect against the development of allergic disease [96,97], other studies have found higher levels of endotoxin in homes of children

with asthma compared with control homes, suggesting that endotoxin may be a risk factor for the development of asthma [98,99]. In some farming communities, high indoor endotoxin exposure is associated with a decreased risk of wheezing and atopic asthma [96]. However, endotoxin levels in these communities may be several-fold higher than levels seen in nonfarming environments, including the inner city. In fact, several studies that have focused on nonfarming communities have reported seemingly contradictory findings. These studies demonstrated a link between increasing endotoxin concentrations and increased prevalence of wheeze in individuals at risk of developing asthma [94,100–102]. Perzanowski and colleagues specifically studied an inner-city birth cohort and demonstrated that children in homes with higher endotoxin concentration were more likely to wheeze at age 2 years (odds ratio 1.34; 95% CI 1.01–1.78) compared with children with lower endotoxin concentrations. Taken together, it appears that endotoxin is a risk factor for wheeze in nonfarming communities, including the inner city, but may protect against wheeze in early-life exposures at the highest levels seen in farming communities.

Many studies have shown that, among subjects with asthma, domestic endotoxin exposure is associated with greater asthma severity and increased morbidity, as measured by symptoms, lung function, and medication use [103–106]. Although these findings have not been replicated in inner-city populations, endotoxin levels in inner-city homes are comparable to those in other nonfarming communities where endotoxin has been associated with adverse asthma outcomes [102,107]. However, endotoxin levels in lower-income homes may be higher than those in higher-income homes. For example, in a study conducted in Denver, Colorado, lower-income homes had higher endotoxin concentrations compared with those in higher-income homes [107]. This finding may suggest that endotoxin has some link to increased asthma morbidity in lower socioeconomic homes, though further research is needed to address this hypothesis.

Despite the evidence supporting a link between endotoxin exposure and asthma morbidity, no intervention studies specifically evaluating the effectiveness of reducing endotoxin concentration on asthma morbidity have been performed. However, in a prospective randomized controlled trial, a home remediation strategy aimed at moisture reduction noted a decrease in endotoxin concentrations as well as asthma symptom days and health care use [108]. Thus, efforts at reducing endotoxin may eventually be shown to reduce asthma morbidity. However, evidence is now insufficient to support that practice.

Indoor air pollution

Indoor air pollution is a complex mixture of pollutants migrating indoors from outdoor air and pollutants generated by unique sources indoors. Even though Americans spend nearly 90% of their time indoors [109], most

scientific investigation of pollutant effects on asthma has focused on outdoor rather than indoor air pollution. Exposure to outdoor air pollutants has been associated with increased airway reactivity, asthma exacerbations, respiratory symptoms, and decreased lung function [110–113]. For some pollutants, indoor air concentrations can greatly exceed outdoor air concentrations [58,114]. Although the link between asthma and indoor air pollutants has not yet been thoroughly studied for all pollutants, research to date suggests that indoor air pollution may play a significant role in asthma morbidity. We summarize the findings of the effects of indoor air pollutants, including ozone, particulate matter, NO_2, and secondhand tobacco smoke, on asthma morbidity.

Particulate matter

PM consists of solid and liquid particles suspended in the air. For outdoor air, the Environmental Protection Agency regulates particulate concentrations through the National Ambient Air Quality Standards. These standards define acceptable outdoor particulate concentrations based on particle size, and outdoor air quality is monitored through a network of national monitoring sites. Until recently, one standards applied to particles with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) and another applied to particles with an aerodynamic diameter of less than 10 μm (PM_{10}). However, in the latest update, $PM_{2.5}$ standards were made more stringent and the PM_{10} annual standard was repealed with a new goal of implementing standards for the coarse PM fraction, defined as particles measuring from 2.5 to 10 μm ($PM_{2.5\text{-}10}$). One reason that regulations for $PM_{2.5\text{-}10}$ may supplant those for PM_{10} is that $PM_{2.5\text{-}10}$ does not overlap with the $PM_{2.5}$ measurement while the majority of PM_{10} is accounted for by particles that are smaller than 2.5 μm in diameter. Individual consideration of acceptable concentrations of both fine PM ($PM_{2.5}$) and coarse PM ($PM_{2.5\text{-}10}$) is important as particles of different sizes have different sources, composition, and deposition properties. Studies have consistently shown an association between elevated outdoor concentrations of PM and asthma morbidity, and most of these have focused on populations living in major cities [115–119].

Activities associated with elevated indoor PM include smoking, as well as cleaning (eg, sweeping) and cooking (eg, use of the stove, frying foods) [120,121]. Cigarette smoking is a substantial contributor to indoor PM as one study found that smoking households had average $PM_{2.5}$ and PM_{10} concentrations that were 33 to 54 $\mu g/m^3$ greater than those of nonsmoking households, with each cigarette smoked adding 1.0 $\mu g/m^3$ to indoor PM concentrations [58]. The observation that smoking is a major source of indoor PM is a consistent observation across numerous studies [120,122,123].

A few studies have examined the health effects of indoor PM exposure in study populations living near large cities, though it is not clear from the

reports how many of the studied homes would be considered "inner city" [119,124,125]. These studies suggest that there is a relationship between indoor PM exposure and asthma morbidity. Indoor PM has been shown to be inversely associated with lung function among children with asthma [119,124], and $PM_{2.5}$ originating from indoor sources may be more potent per unit mass in decreasing lung function compared with outdoor-derived PM [124]. Furthermore, among asthmatic children not taking inhaled corticosteroids, increases in exposure to indoor fine PM has been associated with increases in exhaled nitric oxide levels, suggesting that indoor PM may stimulate airway inflammation [124]. While these studies suggest that PM is associated with decreased lung function and increased airway inflammation, the studies to date have been relatively small and have not yet clarified whether or not there is an association with asthma exacerbations and acute health care encounters. Ultimately, studies examining the effect of PM reduction are necessary to more fully understand the potential impact of indoor PM on asthma. Although no intervention studies have explicitly targeted indoor PM, a handful of studies have incorporated HEPA filters as part of multifaceted approaches to environmental modification. These studies have demonstrated that HEPA filters are effective in lowering the concentration of indoor PM in homes of children with asthma and that, as part of a multimodality intervention to improve the home environment, they may have a modest effect in reducing asthma morbidity [91,126]. Studies that isolate the independent effect of PM reduction, and that evaluate the effectiveness of comprehensive PM reduction strategies, including source modification, ventilation, and HEPA filter placement, are still needed to better elucidate the potential benefit of PM reduction as a strategy to improving asthma health.

Nitrogen dioxide

NO_2, a common ambient air pollutant, is a product of high temperature combustion. There are many potential indoor sources of NO_2, including gas stoves, space heaters, furnaces, and fireplaces [127,128]. The National Cooperative Inner-City Asthma Study conducted in eight inner-city areas in the United States showed a link between higher levels of indoor NO_2 and increased asthma symptoms in children and decreased peak flows [129]. Similarly, Hansel and colleagues [130] showed a consistent association between higher NO_2 concentrations and increased asthma symptoms in preschool children in inner-city Baltimore. Meanwhile, another study found that indoor NO_2 exposure was associated with chest tightness and wheezing, but only in individuals living in multifamily housing units. Since this living arrangement is an indicator of lower socioeconomic status, this finding highlights the complex interaction of this exposure with poverty [131].

NO_2 may be a particular problem in the inner city where many households use gas stoves and, perhaps as indications of limited financial

resources, many of these stoves are unvented [40,58] and used for prolonged periods as a source of household heat [130]. In fact, studies assessing NO_2 concentrations in inner-city homes have demonstrated that they can be higher than those generally reported in other residential settings in the United States [40,58,129,132]. Since some evidence suggests low levels of NO_2 are not harmful but that higher levels of exposure are linked to increased asthma morbidity [129], inner-city populations may be uniquely at risk for adverse effects of indoor NO_2.

When high NO_2 concentrations are suspected, general control strategies can include source modification and ventilation. A randomized controlled trial studying the effects of reducing NO_2 in schools by replacing unflued gas heaters with flued gas or electric heaters showed a lower indoor NO_2 concentration in schools receiving the intervention compared with schools that retained the unflued gas heaters (15.5 ppb versus 47.0 ppb, $P < .001$) with a concordant lower risk of asthma symptoms (difficulty breathing [relative risk 0.41; 95% CI 0.07–0.98], chest tightness [relative risk 0.45; 95% CI 0.25–0.81] and asthma attacks [relative risk 0.39; 95% CI 0.17–0.93]) in schoolchildren [133]. While not an intervention study, observations by Kattan and colleagues [129] found a protective effect of stove vents on indoor NO_2 levels that approached statistical significance. Though definitive intervention studies in inner-city homes are warranted, we would recommend that individuals with asthma, if afforded the opportunity to choose housing, choose residences without gas stoves and heaters. For those who already have these appliances, they should be cautioned at least about the need for proper venting of the exhaust gases.

Secondhand smoke

Secondhand smoke is involuntarily inhaled tobacco smoke that contains particles and gases generated by the combustion of tobacco, paper, and additives [134]. The most recent and most comprehensive review of secondhand smoke, smoking, and asthma was published in the 2006 Report of the US Surgeon General on the Health Consequences of Involuntary Exposure to Tobacco Smoke. The surgeon general concluded that there is sufficient evidence for a causal relationship between secondhand smoke exposure from parental smoking and the onset of wheeze illness in early childhood and that there is suggestive evidence of a causal relationship between secondhand smoke exposure from parental smoking and the onset of childhood asthma [134]. The surgeon general's report also concluded that clear evidence demonstrates that secondhand smoke exposure makes childhood asthma more severe clinically. With respect to adults, the report concluded that the evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and acute respiratory symptoms, including cough, wheeze, chest tightness, and difficulty breathing, among persons with asthma [134]. There is published evidence, however, that

asthma health outcomes are worse in adults with secondhand smoke, when exposure is measured directly using nicotine badges and hair measures of cotinine and nicotine [135]. This topic is reviewed in depth in another article by Eisner elsewhere in this issue.

The prevalence of tobacco use in some urban families is alarmingly high. Data from inner-city neighborhoods in Baltimore, for example, indicate that more than 55% of homes of young asthmatics have at least one active smoker in the home [40,136]. While most exposure for young children is typically in the child's own home, 34% of children who live in nonsmoking homes may nevertheless spend time in other homes (eg, grandparents) where smoking is reported, according to another study [137].

The surgeon general's report states that "eliminating smoking in indoor spaces fully protects nonsmokers from exposure to secondhand smoke. Separating smokers from nonsmokers, cleaning the air, and ventilating buildings cannot eliminate exposures of nonsmokers to secondhand smoke" [134]. There is substantial evidence suggesting that secondhand smoke avoidance should result in improved asthma outcomes. However, studies examining the effectiveness of interventions to reduce secondhand smoke exposure show relatively insignificant effects of interventions on the smoking patterns of those who smoke near children with asthma [138,139]. There have not, to our knowledge, been clinical trials of secondhand smoke reduction in adults with asthma [134]. Recently published asthma guidelines recommend that patients who are active smokers be referred to smoking cessation programs and that all patients with asthma be counseled concerning the negative effects of smoking and secondhand smoke [92]. Substantial evidence suggests that secondhand smoke avoidance can result in improved asthma outcomes. However, effectiveness of home intervention studies attempting to reduce secondhand smoke exposure show relatively small differences in the subsequent number of cigarettes smoked in the home [138,139]. Evidence from studies of restaurants, hospitals, and other public places indicates that bans on indoor smoking can substantially reduce secondhand smoke exposure even with incomplete compliance [140]. To our knowledge, there is no evidence regarding the degree of reduction in secondhand smoke exposure that can be achieved through ventilation and air cleaning in the homes of smokers who continue to smoke indoors.

Ozone

Ambient ozone is the main contributor to indoor ozone concentrations. Therefore, indoor concentrations of ozone are directly related to outdoor concentrations and show significant seasonal variability [58]. Indoor sources of ozone are uncommon, but include ionizers or ozone generators, which are sold as air freshening or air cleaning devices, and xerographic copy machines found in offices, schools, and some home offices [60]. Epidemiologic studies of ambient ozone and experimental studies show a significant

association with asthma-related morbidity, including increases in symptoms, health care use, and airway inflammation and decreases in lung function [141–145]. The effect of indoor ozone levels on asthma morbidity has not been well studied. Similarly, the benefits of indoor ozone reduction on asthma morbidity are unknown. However, because ozone is a highly reactive gas, concentrations are generally much lower indoors relative to outdoors, even in peak ozone season, and evidence suggests that indoor ozone levels may be reduced by keeping windows and doors closed [146]. Furthermore, ozone-generating "air cleaners," "air filters," "air purifiers," and similar equipment should be avoided in the home of patients with asthma.

Summary

There is growing recognition of the importance of the indoor environment in the asthma burden in inner cities. Certain indoor allergens and pollutants are found in higher concentrations in inner-city homes, suggesting that any impact that these exposures have on asthma may be more pronounced in inner-city populations. Mouse and cockroach allergens in particular are prominent allergens in inner-city environments and contribute to asthma morbidity. Among indoor pollutants, PM, secondhand smoke, and NO_2 in particular, are found in higher concentrations in inner-city homes than in non–inner-city homes and are also known to contribute to asthma morbidity. Because multiple exposures are found in any given inner-city home, it is critical to understand how allergens, biologic pollutants, such as endotoxin, and pollutants interact. More detailed epidemiologic studies comprehensively evaluating the indoor pollutants and allergen exposures are warranted to investigate this interaction further. In addition to this line of investigation, more work still needs to be done to develop and evaluate interventions aimed at reducing indoor exposures in inner-city homes to refine current recommendations regarding environmental control practices.

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