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Environmental Issues in Managing Asthma

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Abstract

Management of asthma requires attention to environmental exposures both indoors and outdoors. Americans spend most of their time indoors, where they have a greater ability to modify their environment. The indoor environment contains both pollutants (eg, particulate matter, nitrogen dioxide, secondhand smoke, and ozone) and allergens from furred pets, dust mites, cockroaches, rodents, and molds. Indoor particulate matter consists of particles generated from indoor sources such as cooking and cleaning activities, and particles that penetrate from the outdoors. Nitrogen dioxide sources include gas stoves, furnaces, and fireplaces. Indoor particulate matter and nitrogen dioxide are linked to asthma morbidity. The indoor ozone concentration is mainly influenced by the outdoor ozone concentration. The health effects of indoor ozone exposure have not been well studied. In contrast, there is substantial evidence of detrimental health effects from secondhand smoke. Guideline recommendations are not specific for optimizing indoor air quality. The 2007 National Asthma Education and Prevention Program asthma guidelines recommend eliminating indoor smoking and improving the ventilation. Though the guidelines state that there is insufficient evidence to recommend air cleaners, air cleaners and reducing activities that generate indoor pollutants may be sound practical approaches for improving the health of individuals with asthma. The guidelines are more specific about allergen avoidance; they recommend identifying allergens to which the individual is immunoglobin E sensitized and employing a multifaceted, comprehensive strategy to reduce exposure. Outdoor air pollutants that impact asthma include particulate matter, ozone, nitrogen dioxide, and sulfur dioxide, and guidelines recommend that individuals with asthma avoid exertion outdoors when these pollutants are elevated. Outdoor allergens include tree, grass, and weed pollens, which vary in concentration by season. Recommendations to reduce exposure include staying indoors, keeping windows and doors closed, using air conditioning and perhaps high-efficiency particulate arrestor (HEPA) air filters, and thorough daily washing to remove allergens from one's person.

Keywords

asthma; pollutants; particulate matter; nitrogen dioxide; sulfur dioxide; secondhand smoke; ozone; allergens

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Introduction

Asthma is a common, complex respiratory disease that is characterized by recurrent symptoms of wheeze, cough, chest tightness, and dyspnea. There is growing evidence of environmental causes of the disease, and substantial evidence of the role of the environment, especially inhaled agents such as allergens, pollutants, and viruses, in provoking asthma attacks. Asthma is best thought of as an immunologically mediated disease, in which an abnormal immune response to inhaled agents provokes a cascade of events that lead to mucus hypersecretion, airways constriction and hyperresponsiveness, and, ultimately, symptoms. Because so much evidence points to environmental factors as triggers of the exuberant immune response, there has been much attention to identifying specific environmental factors that are most responsible for provoking asthma and developing strategies to minimize relevant exposures. Indeed, avoidance of environmental factors that provoke asthma, where feasible, is a logical way to improve asthma-related health and to minimize the need for long-term use of asthma medications.

In this paper we will summarize available evidence on the current practices for managing environmental issues with patients who have asthma. In addition, given the recent release of the latest version of the National Asthma Education and Prevention Program's Expert Panel Report 3, Guidelines for the Diagnosis and Management of Asthma (2007 NAEPP guidelines),[1] we will highlight many of the newest and most prominent recommendations of that guideline committee, especially because this latest version of these guidelines supports its statements with a formal process of grading the available evidence. Though the potential scope of this paper on the environment and asthma could be quite broad and include topics such as primary prevention and occupational exposures, for the sake of brevity we will focus the discussion on common indoor and outdoor exposures that are most relevant to people in the United States, regardless of occupation. Also, though diet and infections may be conceptualized as part of the environment, discussion of those factors is beyond the scope of this paper.

Indoor and Outdoor Environments

Management of asthma requires attention to environmental exposures that originate from both the outdoor and indoor environment, though, arguably, those originating indoors may be more relevant for certain patients with asthma. Americans spend nearly 90% of their time indoors,[2] such as the home, workplace, and school, which underscores the substantial contribution of indoor exposures to an individual's total exposure. In some cases the risk of encountering certain environmental factors known to exacerbate asthma (eg, dust mite) is only relevant in the indoor environment, whereas in other cases the indoor environment accounts for the bulk of most individuals' exposure time, although the inciting factor could be found outdoors (eg, particulate matter). Also, in contrast to the outdoors, people may have a greater ability to modify indoor environmental exposures. For example, most individuals do not have direct control over outdoor pollutant concentrations, but they may be able to decrease concentrations of specific pollutants in their homes. Because the sources of exposure differ in the indoor and outdoor environments and because interventions to limit exposure also differ, we will consider the indoor and outdoor environments separately in the following discussion.

Indoor Environmental Factors

Air Pollution

Indoor air pollution is a complex mixture of pollutants migrating indoors from outdoor air and pollutants generated by indoor sources. Since studies have shown that indoor air pollution concentrations can greatly exceed outdoor air concentrations,[3] indoor sources can be very important contributors to total indoor air pollution. Table 1 lists some indoor pollutant sources relevant to asthma. Although the link between asthma and some indoor air pollutants has not yet been thoroughly studied, research to date suggests that they may play an important role in asthma morbidity.

Particulate Matter

Particulate matter consists of solid and liquid particles suspended in the air. Particulate matter originates from a variety of natural and man-made sources. Natural sources include pollen, spores, bacteria, plant and animal debris, sea salt, and dust from the earth's crust. Man-made sources consist mostly of combustion by-products from factories, motor vehicles, and power plants. Smoking is a major contributor to indoor particulate matter. Additional sources include cooking exhaust, wood-burning stoves and fireplaces, cleaning activities that re-suspend dust particles (eg, sweeping), and penetration of outdoor particles into the indoor environment.[4,5]

Particulate matter is also characterized and regulated on the basis of particle size (Fig. 1).[6] Particles < 10 μm in diameter (PM_{10}) are capable of entering the respiratory system, and particles < 2.5 μm ($PM_{2.5}$) are capable of reaching the alveoli. The so-called "coarse fraction" particles ($PM_{2.5\text{-}10}$) are too large to reach the alveoli and therefore deposit in the proximal airways. The Environmental Protection Agency regulates particulate-matter concentrations in outdoor air, but currently there are no standards for indoor air.

Studies that have examined the effects of indoor particulate matter have found an association with asthma morbidity. For example, among children with asthma, higher indoor particulate-matter concentration is associated with decreased lung function,[7,8] greater respiratory symptoms,[9] and more frequent use of rescue medications. Particulate matter exposure may provoke inflammation in asthma, some evidence of which is the elevated exhaled nitric oxide concentration (a marker of airway inflammation) associated with an elevated $PM_{2.5}$ concentration.[8] Of particular concern is that particulate-matter concentrations in some indoor settings are even higher than those outdoors, and the particulate matter that originates indoors may, in some cases, be more harmful than that found outdoors. For example, in one study from inner-city Baltimore, investigators found that indoor $PM_{2.5}$ and PM_{10} concentrations were more than twice as high as the simultaneously measured outdoor concentrations.[5] Koenig et al[8] found that $PM_{2.5}$ originating from indoor sources was more potent in decreasing lung function than was outdoor-derived particulate matter.

Management of Indoor Particulate Matter—The evidence regarding what factors can be modified to reduce particulate matter and improve asthma health comes from observational studies and clinical trials. For example, in cohort studies of inner-city children with asthma, higher particulate-matter concentration was found with tobacco smoking and greater frequency of sweeping and stove use in the home.[4,5] Increased ventilation with more open windows led to lower in-home particulate-matter concentration. Intervention studies have shown that high-efficiency particulate arrestor (HEPA) air filters are effective in lowering indoor particulate matter (Fig. 2).[10,11] Though these studies did demonstrate a health benefit, the particulate-matter reduction was part of an overall allergen and pollutant intervention strategy, which makes it impossible to isolate the independent health effect of particulate-matter reduction with air cleaners.

The 2007 NAEPP guidelines[1] concluded that there is insufficient evidence to recommend indoor air-cleaning devices, and make no specific recommendations for indoor particulate-matter reduction. However, we believe that the best way to apply the existing evidence regarding indoor particulate matter to asthma management is to inform individual patients about what is currently known. Patients should be warned of the potential health effects of indoor particulate matter and advised to reduce or eliminate activities (such as smoking) that raise indoor particulate matter. Furthermore, for patients with a keen interest in making all possible changes to optimize their indoor environment, use of air cleaners and improved ventilation can be recommended, if financially feasible.

Nitrogen Dioxide

Nitrogen dioxide (NO_2) is a gaseous product of high-temperature combustion. It has many indoor sources, including gas stoves, space heaters, furnaces, and fireplaces, and has been linked to respiratory health effects.[12] Although some studies[13-18] have found adverse respiratory health effects from indoor NO_2, other studies have failed to confirm that association.[19-22] For example, data from the National Health and Nutrition Examination Survey III did not suggest any impact from gas stoves (the major source of indoor NO_2) on pulmonary function or respiratory symptoms in adults with asthma.[23] To the extent that gas appliances may confer a risk of respiratory symptoms, the exposure may be more complex than simply NO_2 (Fig. 3). For example, gas stoves may also increase other indoor air pollutants, such as nitrous acid, that may also adversely affect respiratory health.[13]

Studies that have specifically investigated the effect of indoor NO_2 on asthma morbidity have also had inconsistent results. Some found no association between indoor NO_2 level and respiratory symptoms,[20] but an increasing number have found a positive association with asthma morbidity. Two recent studies of asthmatic children found that higher indoor NO_2 increased the likelihood and frequency of asthma symptoms, including wheeze, chest tightness, breathlessness, and daytime and nighttime asthma attacks.[16,18] In a study of inner-city children with sthma there was a strong and significant association between higher indoor NO_2 and respiratory morbidity, including wheeze, chest tightness, breathlessness, and daytime and nighttime asthma attacks.[24,25] NO_2 exposure has also been found to impair host resistance to respiratory viruses and bacteria, by reducing bacterial clearance and impairing innate immunity.[26-28] Higher personal NO_2 exposure increased the severity of virus-induced asthma exacerbations, as measured by symptom severity and peak-flow reduction.[29]

Management of Indoor NO_2—Given the uncertainty about the association of NO_2 and respiratory health, additional studies are needed to determine whether NO_2 increases risk in people with asthma. General control strategies include source modification and ventilation. A randomized controlled trial on the effects of reducing NO_2 in schools, by replacing unflued gas heaters with flued gas or electric heaters, found that a substantial reduction in mean indoor NO_2 concentration was associated with a concordant decrease in asthma symptoms in school children.[30] The uncertainty about the utility of NO_2 reduction is apparent in the 2007 NAEPP guidelines, which found only modest support for NO_2 reduction, and this recommendation is in the context of general recommendations to reduce exposure to common indoor irritants.[1] We believe that the best way to apply the existing evidence regarding indoor NO_2 to asthma management is to take a common-sense approach. If a patient reports symptoms in the presence of an NO_2-producing device (such as a stove), we recommend that they assure that it is properly vented to the outside. And if the patient has the option to choose, we suggest they select electric rather than gas appliances. This approach to NO_2, as with most pollutants, becomes especially important for the patient who has poor asthma control or requires a high dose of medication to control symptoms.

Secondhand Smoke

Secondhand smoke is involuntarily inhaled tobacco smoke that contains particles and gases generated by the combustion of the tobacco, paper, and additives of cigarettes.[31] Secondhand smoke exposure is common in the United States, and there is sufficient evidence to suggest a causal relationship between secondhand smoke and incidence of wheezy illnesses in infants and pre-school-age children, though the causal link to asthma incidence has not been fully established. Exposure to secondhand smoke is convincingly linked to greater disease severity among children and adults with asthma.[1,31] Secondhand smoke is associated with worse lung function and greater airway inflammation, daytime and nocturnal symptoms, exacerbations, health care utilization, and intubation.[32-37]

Management of Indoor Secondhand Smoke—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 exposure of nonsmokers to secondhand smoke."[31] There is substantial evidence that secondhand smoke avoidance should improve asthma outcomes, but intervention studies that attempted to reduce secondhand smoke exposure showed relatively small effects on the smoking patterns of those who smoke near children with asthma.[38,39] There have not, to our knowledge, been clinical trials of secondhand smoke reduction in adults with asthma.[31] The 2007 NAEPP 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.[1] We recognize that not all patients can avoid secondhand smoke, and, because secondhand smoke contributes to air-borne particulate matter, which air cleaners can reduce, patients may want to consider air cleaners if secondhand smoke cannot be avoided.

Ozone

The indoor ozone (O_3) level tends be high only in warmer months of the year, because the level is mainly influenced by ozone penetration from outdoors.[40] Indoor ozone sources are uncommon, but include ionizers and ozone generators, which are sold as air-freshening or air-cleaning devices, and xerographic copy machines, found in offices and schools.[41] Epidemiologic studies of ambient ozone and experimental studies show a significant association with asthma-related morbidity, including symptoms, health care utilization, airway inflammation, and decreases in lung function.[42-46] However, the effect of indoor ozone on asthma morbidity has not been well studied, and the benefits of indoor ozone reduction on asthma morbidity are unknown.

Management of Indoor O_3—Since O_3 is a highly reactive gas, the O_3 concentration is generally much lower indoors than outdoors, even in peak ozone season. Evidence suggests that indoor ozone can be reduced by keeping windows and doors closed.[47] The 2007 NAEPP guidelines make no specific recommendations on indoor O_3 reduction.[1] We recommend a common-sense approach to indoor ozone, including avoidance of ozone-generating "air purifiers" and other ozone-generating devices in the homes of patients with asthma.

Indoor Allergens

Allergens are water-soluble glycoproteins that induce an immunoglobin E response in susceptible individuals. The allergens adhere to particles that range in size from 1 μm to > 100 μm.[48,49] Particles of that size range deposit in the upper and lower respiratory tracts, where the allergen can directly elicit an inflammatory response and respiratory symptoms.

Both indoor and outdoor allergens can cause asthma symptoms in patients who are sensitized to the allergen. Sensitization is defined as having evidence of immunoglobin E specific to the particular allergen, which can be assessed by allergy skin testing in an allergist's office, or via a serum test known as a radioallergosorbent test, the blood for which can be collected by a primary care provider or other health care provider, and the test is obtained from a commercial laboratory.

Indoor allergens are generally present year-round, so they are associated with perennial symptoms. Outdoor allergens are generally present during certain seasons and thus trigger asthma only during those seasons.

Patients may have perennial allergen-induced asthma symptoms, seasonal allergen-induced symptoms, or both. For example, a patient who presents with persistent asthma with a history of springtime exacerbations may have asthma symptoms that are triggered by both perennial and seasonal allergens. There are 5 general groups of indoor aeroallergens: furred pet, dust mite, cockroach, rodent, and mold allergens (see Table 1). The 2007 NAEPP guidelines recommend that patients be advised to reduce exposure to allergens to which they are sensitive, but particularly to note that individual steps alone are generally ineffective.[1] Avoidance requires a multifaceted, comprehensive approach, and this often requires targeting several allergens simultaneously, in some cases employing multiple proven approaches for each allergen (Fig. 4).

Furred Pet Allergens—Cats and dogs are common furred pets, although families often keep other species of furred pets as well. Cat and dog allergens can be found in virtually all homes, but, not surprisingly, homes with pets contain much higher levels of the allergens than homes without pets.[50] Furred pet allergens are also found in other settings, such as schools and other public buildings (Fig. 5),[51] and are passively transferred from one environment to another.[52] Passive transfer of cat allergens to school by children who have cats at home causes asthma symptoms in cat-sensitized classmates.[53] Both cat and dog allergens can be passively transferred, because they are carried on small particles that remain airborne and adhere to surfaces and clothing.[53-55]

Allergic sensitization to furred pet allergens is quite common, and in some populations more than 60% of children with asthma are sensitized to cat or dog allergens.[56,57] The combination of widespread exposure to pet allergens and high prevalence of allergic sensitization to these allergens suggests that a substantial proportion of patients with asthma are at risk for cat or dog allergen-induced asthma symptoms. In fact, several studies have directly linked animal allergen exposure to poorer asthma outcomes among animal-sensitized patients with asthma.[52,58]

Assessing pet allergen exposure in patients is fairly straightforward and can be accomplished by taking a history focused on pet ownership, recent relocation into a home where pets had been living, and for children in particular, pet exposure at daycare. Most, but not all, relevant sources of exposure can be identified with this approach.

Because furred pet allergens are airborne and adhere to clothing, it is impossible to eliminate exposure entirely. Pet removal is the only method of substantially reducing the animal allergen level, but it will not decline significantly for 4-6 months,[59] so clinical benefit may be slow to realize. The rate of decline may be improved by vigorous cleaning to remove allergens remaining in reservoirs, including accumulated dust, carpeting, and bedding. Allergen-proof mattress and pillow encasings sequester the allergen in the mattress and pillow and are a helpful adjunct to pet removal.

Because some families are very reluctant to give up a pet, alternative methods of furred animal allergen control have been studied and have largely proven ineffective. HEPA room-air filters can modestly reduce airborne animal allergens, but most studies have found that the allergen reduction is not sufficient to improve asthma symptoms.[59,60] Other methods, such as washing the pet, are also ineffective.[61] Citing the general lack of positive controlled trials, the 2007 NAEPP guidelines offer an expert-opinion basis for a general recommendation of either

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removal of pets from the home or isolation of the pet from the asthmatic individual if removal is not feasible.[1]

Although the effect of pet removal on asthma symptoms has not been well studied, because of the practical difficulties of conducting a randomized controlled trial of pet removal, one recently published study found a substantial reduction in inhaled corticosteroid requirements among furred-pet-sensitized adults with asthma who chose to remove their pets from their homes, compared to those who kept their pets.[62] These findings underscore that pet removal is a critical part of the treatment plan for pet-sensitized patients with asthma.

Dust Mite Allergens—Dust mites are arachnids that infest bedding, carpet, upholstered furniture, and fabric. Their main food source is human skin scales, and they grow best in warm, humid environments,[63] so they are rarely found in arid regions, such as the desert Southwestern United States, but are common in more humid regions such as the Northwestern and Southeastern United States. The predominant dust mites in the United States that have been implicated in allergy are *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus.*[63,64] The allergens are predominantly found on larger particles, in the range of 10-20 μm, which rapidly settle on dependent surfaces after disturbance.[49]

The prevalence of allergic sensitization to dust mites varies from region to region and depends on the regional prevalence of dust mites. For example, the sensitization rate among children with asthma is estimated to be 5% in the arid setting of Los Alamos, New Mexico, in contrast to as high as 66% in the more humid setting of Atlanta, Georgia.[65,66]

Like many other allergens, exposure to dust mite allergen in sensitized patients is associated with poorer lung function, greater medication requirements, and more asthma symptoms.[65,67,68] In contrast to other allergens, there is evidence that dust mite allergen leads to the development of asthma, in addition to exacerbating pre-existing asthma in dust mite-sensitized patients. A prospective cohort study found that infants exposed to high levels of dust mite allergen were significantly more likely to have asthma later in childhood than were infants who were not exposed to high levels.[69] Thus, reducing dust mite allergen exposure should both improve asthma control in sensitized patients and prevent the development of asthma in children.

Since dust mites are microscopic organisms, it is difficult to determine a patient's exposure status by history. The most practical approach is to assume that patients living in arid climates are very unlikely to have substantial exposure to dust mites, and that patients in more humid regions are at risk for substantial exposure. However, there are commercially available home test kits for dust mite allergens that can provide semi-quantitative results so the patient can assess his/her degree of exposure.

First-line dust mite control measures include installing allergen-proof mattress and pillow encasements, washing all bedding every 1-2 weeks in hot water, removing stuffed toys, vacuuming and dusting regularly, and reducing indoor humidity. All of these measures are recommended by the 2007 NAEPP guidelines.[1] These strategies reduce asthma symptoms, reduce medication requirements, and improve lung function.[66,70,71]

Removal of carpet and upholstered furniture may also be helpful, but is more expensive. Because dust mite allergens are predominantly found on dependent surfaces and are not airborne, air filters are not likely to offer any benefit. Carpet treatments have been developed that include agents that kill the mites (acaricides) and denature the allergen (denaturing agents). Although laboratory studies indicate that both of these reagents are efficacious, field studies indicate that neither agent is very effective in practice.[72,73]

A recently published study found that mattress encasements, as a single intervention, provided no health benefit to adults with asthma.[74] However, the study population included many people who would not be expected to benefit from the intervention, including people who were not sensitized to dust mite, as well as persons with other underlying lung disease, such as chronic obstructive pulmonary disease. The study provided little evidence to suggest that patients with asthma and dust mite sensitization would not benefit from a multi-pronged dust mite intervention. In fact, the evidence accumulated thus far suggests that concerted efforts to control dust mite exposure are only of clinical benefit in mite-sensitized persons with asthma and are a critical component of the treatment plan for these patients.

Cockroach Allergen—The 2 most common cockroaches found in United States homes are the German cockroach (*Blatella germanica*) and the American cockroach (*Periplaneta americana)*. Cockroach allergen is the predominant allergen in the inner city, where most homes contain detectable levels.[75] At least half of inner-city homes have a clinically relevant level of cockroach allergen. 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 in inner-city homes.[76,77]

In inner-city populations, 30-40% of children with asthma are sensitized to cockroach,[78] and in suburban populations, the sensitization rate is about 21%.[76] Cockroach allergen has also been directly linked to poorer asthma outcomes in inner-city children with asthma, including asthma-related health-care utilization.[75,79]

In light of these findings, it is important to assess risk of exposure in sensitized patients and to make recommendations for reducing cockroach allergen exposure. Although patient report of cockroach infestation is a good indicator of substantial cockroach allergen exposure,[77] one cannot be sure that a patient who denies cockroach infestation is not exposed to substantial cockroach allergen. Patients may be reluctant to admit pest infestation, and homes without evidence of active infestation often contain substantial levels of the allergen.

Substantial reduction in cockroach allergen can be achieved with an integrated pest management approach. The 2007 NAEPP guidelines recommend such an approach, though they caution to avoid use of volatile chemical agents, which can be irritating when inhaled by persons with asthma.[1] 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 reduce cockroach allergen by 80-90%.[80,81] A more recent study found that an entomologistled integrated pest management intervention reduced cockroach allergen more than did the efforts of commercial pest management companies.[82] It is unknown if this degree of allergen reduction will have 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.

Rodent Allergens—Mice and rats excrete urinary allergens that are carried on small particles that readily become airborne, like allergens from other furred animals such as cats and dogs.[83-86] The allergens are pheromone-binding proteins that are thought to have a role in mating practices[87] 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 was only recently described.[88,89]

The domestic house mouse is very common, particularly in urban multi-family dwellings and poorly maintained housing.[90] 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.[91] The mouse allergen level in some homes is similar to that in occupational settings, where mouse allergen is a known cause of asthma symptoms.

Mouse allergen is surprisingly prevalent in suburban communities as well. As many as 75% of middle-class, suburban households have detectable mouse allergen in settled dust samples,[92,93] though the levels in these suburban homes are 100-fold to 1,000-fold lower than in inner-city settings. Recent studies linked exposure to mouse allergen to poorer asthma control and higher risk of asthma-related health-care utilization among mouse-sensitized inner-city children with asthma.[88,94]

Assessing exposure to mouse allergen can be fairly straightforward. Any patient who reports mouse sightings or evidence of mice, such as droppings, is very likely to be exposed to substantial levels of mouse allergen in the home.[90-92] However, as with cockroach allergen, patients and families may be reluctant to admit a rodent infestation, so 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 when they are less likely to be seen.

Reducing exposure to mouse allergen is feasible, but it can be difficult. Integrated pest management is the best approach; it 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 re-infestation is discouraged.

In one study, integrated pest management reduced the mouse allergen level by 75% in settled dust, while the level increased in the control group.[95] Although no studies have been conducted to determine the impact of mouse allergen reduction on asthma, the evidence to date indicates that reducing exposure should improve asthma control and prevent asthma-related morbidity. Noting this lack of clinical-trial evidence to date, the 2007 NAEPP guidelines offer an expert-opinion recommendation to use measures to reduce infestation, as part of a general recommendation about reducing exposure to relevant furred animal allergens.[1]

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 rat, 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 were children who were not sensitized or exposed.[96] 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.

Mold Allergens—There is a very large number of mold species, and very few have been well studied with regard to their effects on asthma. Molds can be found in both indoor and outdoor environments. *Aspergillus* and *Penicillium* species are among the most common indoor molds, and *Alternaria* can be found in both indoor and outdoor environments.

Molds have been extremely difficult to study because of their complexity, and a full discussion of their impact on asthma is beyond the scope of this article. However, major allergens have been isolated from a few molds, and sensitization to *Alternaria* has been linked to the development of asthma, as well as to asthma severity in Midwestern and Southwestern United States populations.[97,98] It is important to note, however, that *Alternaria* is found in all regions of the country.[99] In a nationwide study, higher dustborne *Alternaria* allergen levels were associated with higher risk of wheeze.[100]

Because molds prefer warm, moist environments, mold growth can be decreased by interventions that reduce moisture and humidity, such as dehumidification, air conditioning, and increased ventilation. Humidifiers and vaporizers increase indoor humidity and can become colonized with mold, so they should not be used in homes of people with asthma. For mold that is already present, thorough cleaning with fungicides is recommended. If cleaning is not possible, the item should be disposed of.

Keeping windows closed and running the air conditioner may help reduce exposure to outdoor sources of mold. A HEPA room-air filter may also help, but this intervention has not been studied.

Water leaks can contribute to the growth of indoor molds, so it is sensible to prevent and eliminate water leaks wherever possible. When outdoors, patients should avoid heavy exposure to moldy vegetation and use a properly fitting particulate mask when working with moldy material. Although there have been no randomized trials of mold abatement in persons with asthma, there is adequate evidence to recommend these basic interventions to reduce exposure for mold-sensitized patients with asthma. Given the association of indoor fungi and respiratory symptoms in some studies, the 2007 NAEPP guidelines recommend considering measures to control indoor dampness and mold.[1]

Outdoor Environmental Factors

Air Pollution

There are several outdoor air pollutants that can affect asthma, including particulate matter, O_3, NO_2, and SO_2 (Table 2). Except for SO_2, the general sources and characteristics of these pollutants are the same as those described above for indoor air pollution. Additional relevant information is contained in this section, as it pertains to outdoor sources and the effects of these pollutants. Generally, individuals have little control over the outdoor environment, so the following recommendations center mostly on avoiding the outdoor environment on days when specific pollutant levels are high. Patients should be cautioned to avoid exertion on those days and to stay indoors, and, when feasible, in an air-conditioned environment.

Particulate Matter

Particulate matter exposure in outdoor air is linked to higher mortality in the general population.[101] Those with underlying cardiopulmonary disease may be even more susceptible to the effects of inhaled particulate matter, as evidenced by increased hospitalizations after short-term increases in particulate-matter concentration.[57] Among asthmatics, ambient particulate matter has been linked to exacerbations, chronic symptoms, and decline in lung function.[49,82,83] Though most studies have focused on the fine-particulate-matter fraction, outdoor coarse particulate matter is associated with a greater risk of hospitalization for childhood asthma than outdoor fine particulate matter.[77]

Ozone

Ozone is a highly reactive gas that is generated at ground level by a chemical reaction of sunlight on mixtures of NO_2 and hydrocarbons from fossil fuel combustion.[102] Major sources include vehicular traffic, power plants, and industrial operations. Sunlight and hot weather create ground-level ozone in a harmful concentration in the air, and ozone is the primary constituent of “summertime smog.” Ozone can increase airway inflammation and hyperresponsiveness.[103,104] Ozone exposure is associated with reduced lung function, increased symptoms, increased rescue medication use, and increased risk of asthma exacerbation.[105,106] Among people with allergic asthma, ozone exposure may interact with allergens to cause a greater asthmatic response.[107,108] The 2007 NAEPP guidelines recommend, as with other outdoor pollutants, that individuals should avoid exercise or exertion outdoors when the O_3 level is high.[1]

Nitrogen Dioxide

NO_2 is formed from primary emissions of oxides of nitrogen. Automobile exhaust is the main source of ambient NO_2 in most urban environments. Other sources include local industry, power plants, and forest fires. There is growing evidence that elevated ambient NO_2 is associated with increased asthma symptoms, exacerbations, and hospitalizations, and with lower lung function, particularly in vulnerable populations, including young children and the elderly.[109-112] A reduction of traffic density in a geographic region was associated with reduced asthma morbidity,[113,114] which may be partially mediated by the lowering of NO_2 exposure.

Sulfur Dioxide

Sulfur dioxide (SO_2) is an ambient air pollutant mainly formed by the combustion of high-sulfur coal or oil. Indoor SO_2 sources are not common, and when present indoors SO_2 is rapidly adsorbed onto household surfaces, so personal SO_2 exposure is mainly due to ambient air pollution.[115] Experimental studies suggest that SO_2 can decrease lung function in exercising adults with asthma.[116-118] The 2007 NAEPP guidelines recommend that patients with asthma avoid exercise outdoors on days when air pollutants, including SO_2, are high.[1]

Pollen Allergens

Pollen and mold allergens are the predominant outdoor allergens. Mold allergens were addressed above, in the section on indoor allergen, so this section will focus on pollen allergens. Tree, grass, and weed pollen are present in all regions of the United States and cause seasonal asthma exacerbations (see Table 2). Tree pollen is produced primarily in the spring, though the levels peak at slightly different times, depending on the regional climate. Grass pollen peaks in the summer, and weed pollen peaks in the fall. Again, the peak of these seasons varies by region, so understanding the timing of pollen seasons in one's region is helpful when evaluating a patient with seasonal asthma exacerbations.

Pollen allergen sensitization is common. For example, a population-based study found that more than 25% of the United States population is sensitized to ragweed, and a similar proportion is sensitized to grass pollen.[119] The well-known phenomenon of pollen-induced asthma is characterized by a predictable increase in asthma symptoms during the relevant pollen season in a sensitized patient.

Unfortunately, it is very difficult to reduce pollen allergen exposure during the pollen season. Recommendations for exposure reduction include staying indoors, keeping windows and doors closed, using air conditioning, and perhaps HEPA room-air filters. After spending time outdoors, pollen-allergic patients should wash their hands and face, and should wash their hair daily to remove allergens. Many of these measures are also suggested by the 2007 NAEPP guidelines.[1]

Summary

Environmental control practices are a sensible, evidence-based component of the overall management of asthma. Control of the environment requires attention to exposures that originate from both the outdoor and indoor environments. The indoor environment notably contains particulate matter, NO_2, secondhand smoke, and O_3, and allergens from furred pets, dust mites, cockroach, rodents, and molds. The 2007 NAEPP guidelines recommend eliminating indoor smoking and improving ventilation. Though the guidelines state that there

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is insufficient evidence to recommend air cleaners, these devices, along with reducing activities that generate indoor pollutants, may be sound practical approaches to improving the health of individuals with asthma. The guidelines are more specific about allergen avoidance; they recommend identifying allergens to which an individual is immunoglobin E sensitized. Further, the guidelines emphasize multifaceted, comprehensive strategies to reduce exposure.

Outdoor air pollutants can impact asthma, and guidelines recommend that individuals with asthma avoid exertion outdoors when concentrations of certain pollutants are elevated. Outdoor allergens include tree, grass, and weed pollens, which vary in concentration by season. Recommendations to reduce exposure include staying indoors, keeping windows and doors closed, using air conditioning, and perhaps HEPA room-air filters, as well as thorough daily washing to remove allergens from one's person.

Though there are still considerable research opportunities to identify additional means to improve the environment for the sake of asthma health, research to date has shown that careful attention to these specific environmental controls can improve the health of people with asthma.

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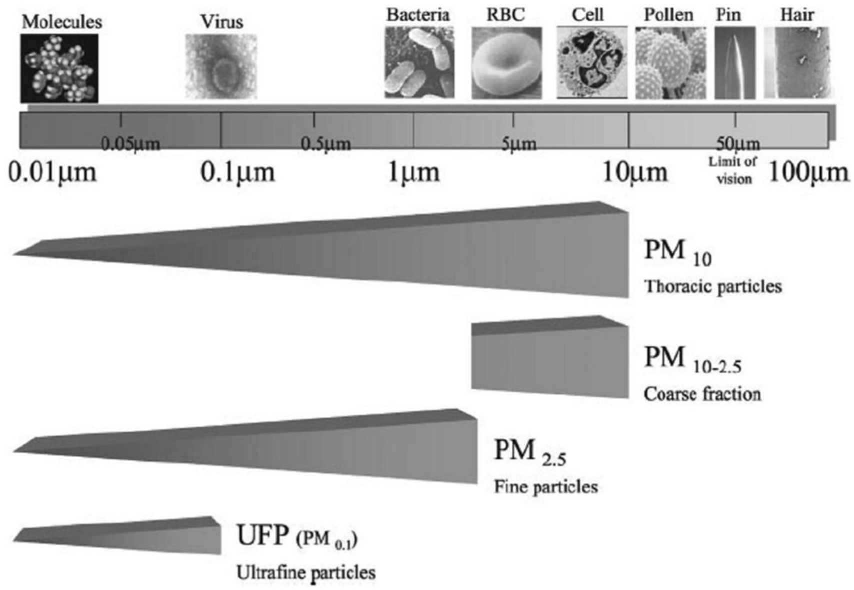

Fig. 1.

Characterization of particulate matter (PM) based on size. Particulate matter < 10 μm (PM_{10}) can enter the human thorax, whereas PM < 2.5 μm ($PM_{2.5}$) can reach the alveoli. RBC = red blood cell. (From Reference 6, with permission.)

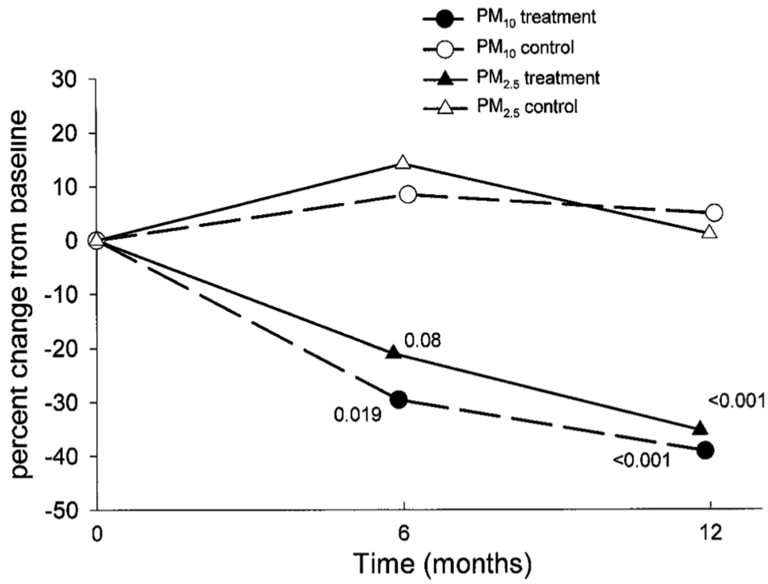

Fig. 2.
Change in particulate matter (PM) concentration in the bedrooms of children with asthma. The rooms of the intervention subjects had high-efficiency particulate arrestor (HEPA) air cleaners. The study was conducted in inner-city Baltimore, Maryland. There was substantial and sustained reduction in both of the particulate-matter size ranges (< 10 μm [PM_{10}] and < 2.5 μm [$PM_{2.5}$]) in the filtered-air rooms. (From Reference 10, with permission.)

Fig. 3.
A gas stove in the home, without proper venting. (Photograph courtesy of Karen A Callahan RN MSc, Department of Pediatrics, Johns Hopkins University, Baltimore, Maryland.)

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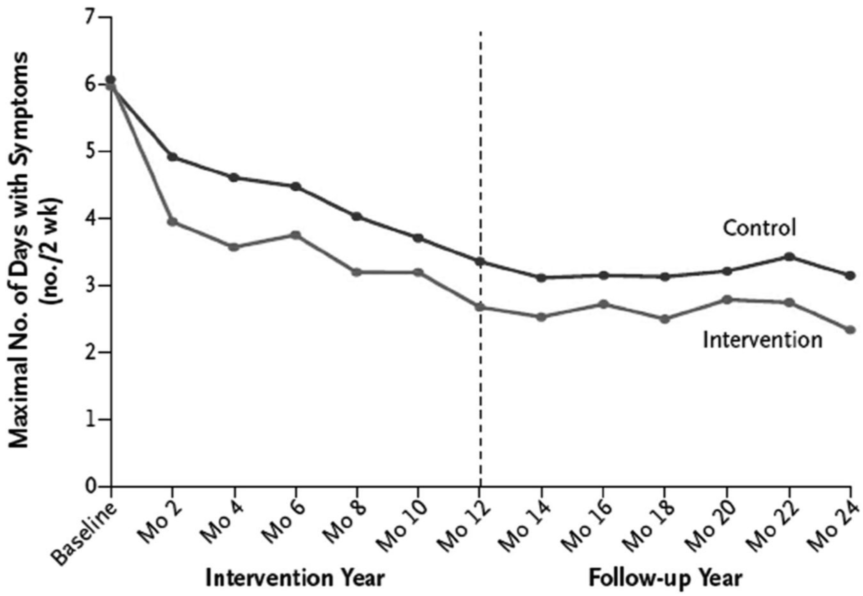

Fig. 4.

Effect of a multi-faceted intervention on the number days with asthma symptoms. There was a modest reduction in symptoms over the 12 months of the active intervention, and the reduction persisted during the 12 follow-up months after the intervention. (From Reference 11, with permission.)

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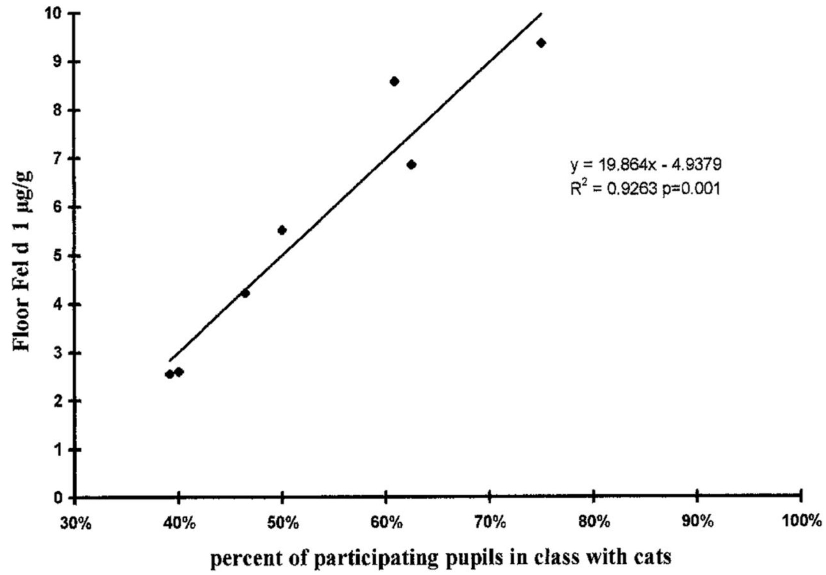

Fig. 5.

Results from a study in New Zealand schools. There was a strong correlation between the level of cat allergen (Fel d 1) on the classroom floor and the percent of students who had cats in their homes. (From Reference 51, with permission.)

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Table 1

Major Indoor Environment Factors That Affect Asthma

Pollutants
Particulate matter
Nitrogen oxides
Secondhand smoke
Ozone
Allergens
Furred pets
Cats
Dogs
Others
Dust mites
Cockroaches
Rodents
Mice
Rats
Molds

Table 2

Major Outdoor Environment Factors That Affect Asthma

Pollutants
Particulate matter
Ozone
Nitrogen oxides
Sulfur dioxide
Allergens
Pollens
Trees
Grasses
Weeds
Molds