

How Environmental Exposures Influence the Development and Exacerbation of Asthma

Ruth A. Etzel, MD, PhD

ABSTRACT. Environmental exposures may increase a child's risk of developing asthma and also may increase the risk of asthma exacerbations. This article reviews several environmental exposures and suggests whether they contribute to asthma prevalence, asthma exacerbations, or both. Outdoor air exposures and violence are not likely to cause the increase in asthma prevalence. Exposure to outdoor air pollutants primarily leads to increased exacerbations, sometimes manifested as asthma clusters. Clinicians should be alert for space-time clusters of asthma exacerbations in the community, because these clusters may suggest a modifiable point-source exposure. Indoor air exposures are more strongly linked to the increase in asthma prevalence. Exposure to dust mites and tobacco smoke are risk factors for the development of asthma and may also exacerbate existing asthma. Effective measures to prevent exposures to these pollutants are available. With proper management, the amount of environmental exposures can be decreased. Whether decreasing these exposures will result in decreases in asthma prevalence and exacerbations is not yet documented. *Pediatrics* 2003;112:233–239; *asthma, indoor air pollution, outdoor air pollution.*

ABBREVIATION. ppb, parts per billion.

Rates of asthma morbidity and mortality are increasing.^{1–7} From 1980 to 1994, the prevalence of asthma in the United States increased 75%.⁸ Asthma is more prevalent among black children than among white children.^{2,9} Black children are hospitalized for asthma at a higher rate than are white children, although much of this difference is likely attributable to poverty rather than to race.^{10,11}

From a public health perspective, it is useful to consider 2 separate dimensions of the asthma problem. The first is that the proportion of children in whom asthma has been diagnosed is increasing. Environmental exposures are among the many possibilities that have been proposed to explain the increase. The second component of the asthma problem is the increase in asthma attacks among children who already have asthma. Environmental exposures are also among the many possible explanations for this increase.

From the Department of Environmental and Occupational Health, School of Public Health and Health Services, George Washington University, Washington, DC.

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Address correspondence to Ruth A. Etzel, MD, PhD, 4320 Diplomacy Dr, Ste 2630, Anchorage, AK 99508. E-mail: retzel@earthlink.net

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For the purposes of this article, the home environment includes exposures inside the home (eg, dust mites, cats and dogs, cockroaches, environmental tobacco smoke, molds) and also exposures in the neighborhood of the home (eg, outdoor air pollutants, violence). A child's home environment contributes to the risk of developing asthma and the subsequent risk of having asthma attacks^{12–14}; a recent study indicated that violence may also contribute to the risk of asthma attacks.¹⁵ Children who live in poverty are often exposed to violence. Whether children who live in poverty are more heavily exposed to indoor and outdoor air pollutants than are children who do not live in poverty is not known.

It is essential for clinicians to be knowledgeable about environmental precipitants of asthma, because this information may help them to counsel patients and their parents. Ideally, clinicians would focus their energy on primary prevention of asthma (prevention of the initial onset of asthma). At this time, however, the effectiveness of many primary prevention strategies is unknown. As a result, most clinicians have relied on secondary prevention (ie, trying to prevent exacerbations in children with known asthma, in part by decreasing environmental exposures, which cause worsening of symptoms). What is not widely recognized, however, is that the effectiveness of many secondary prevention measures is also unknown.

The purpose of this article is to review the evidence regarding the link between environmental exposures and asthma prevalence and exacerbations. The realization that environmental exposures could lead to asthma attacks has its origins in studies of clusters of asthma.

Much of what we now know about the relation between outdoor air exposures and asthma came to light as a result of asthma clusters in communities. Clinicians should be alert for space-time clusters of asthma exacerbations in the community, because these clusters may suggest a modifiable point-source exposure.^{16–19} Specific outdoor air pollutants linked to clusters of asthma are described in the following paragraphs.

EXPOSURE TO OUTDOOR AIR POLLUTANTS

Exposure to Castor Bean Dust

One of the first studies to document the relationship between air pollution and asthma was an investigation of an asthma cluster in Ohio. In the late 1920s, a cluster of asthma affecting 200 patients oc-

curred in Toledo.¹⁶ Most affected patients lived within a 1-mile radius of a castor bean mill, which also produced linseed oil. Many of the patients claimed that their attacks coincided with the odor of linseed oil coming from the mill when the wind blew in the right direction. When the health department investigated the possibility that linseed oil might be causing the asthma attacks, they considered it unlikely because the seed was too heavy to become windborne. The mill, however, not only manufactured linseed oil but also expressed castor oil from castor beans. The castor beans produced a fine dust that was readily carried by the wind into the surrounding neighborhoods. The outbreak of asthma attacks in Toledo was documented to have been caused by the inhalation of castor bean grinding dust, and the epidemic disappeared after the factory stopped processing castor beans.¹⁶ Asthma epidemics also have been documented to occur in other locations in the United States, including Brooklyn, New York,²⁰ but the cause of these epidemics is elusive.

Exposure to Grain Dust

Beginning in 1953 and continuing for nearly 20 years, Charity Hospital in New Orleans experienced asthma epidemics. These epidemics often involved >100 asthma-related visits to the emergency department in a single 24-hour period. In 1955, >350 patients with asthma were treated in the emergency department in a period of <24 hours; 2 patients died. In early November 1960, >200 people with asthma sought care in the emergency department in a single day. Epidemics such as this continued to occur until 1968, when they stopped, for reasons that were not fully understood. A large number of possible causes were studied.²¹⁻²⁵ One of the first hypotheses was that the asthma outbreaks might be attributable to inhalation of particles from a waste dump site where spontaneous underground burning was occurring.^{21,26} When the waste dump was removed, the asthma outbreaks continued.^{22,27} Other possibilities were suggested, including fire smoke emissions and aeroallergens.²⁸ Grain dust was also considered,²⁹ because a large amount of grain from Midwestern farms is shipped on barges down the Mississippi River and exported through New Orleans. Along the short stretch of the river between Baton Rouge and the Gulf of Mexico, there are >60 loading facilities. In 1968, the year the epidemics stopped, the grain elevators in New Orleans were modernized. The modernization included the addition of new dust control equipment, such as air filters on the silos. It is likely that these filters prevented soy dust from reaching the city's residents. An ecologic study documented that the asthma epidemics occurred on days when barges carrying soybeans were unloading in the New Orleans harbor.³⁰

Exposure to Soybean Dust

In the early 1980s, emergency department physicians in Barcelona, Spain, documented that sudden increases in visits for acute severe asthma overwhelmed the emergency services on certain days.

Between 1981 and 1987, 1155 emergency department visits by 687 people occurred on 26 asthma epidemic days. Careful daily surveillance was undertaken, with documentation of the place, day, and time when each person seeking emergency department care at each of 4 large hospitals experienced an asthma attack. Geographic mapping of the place where most emergency department visitors experienced attacks on epidemic days demonstrated that symptoms were most likely to start in the central part of the city, near the harbor. Epidemic asthma was found to occur only on weekdays, never on weekends. Furthermore, on epidemic days, most people experienced their attacks in the middle of the day, usually between 11 AM and 1 PM. After studying each of the products loaded or unloaded from ships in the harbor, it was determined that the outbreaks of asthma were caused by inhalation of soybean dust released from silos during the unloading of soybeans at the city harbor.^{17,18} In 1997, filters were placed on the silos, decreasing the amount of soybean dust emitted into the ambient air. No additional epidemics of asthma were reported in Barcelona.¹⁹

Exposure to Wood Smoke

Smoke from bush fires has been linked to increases in emergency department visits for asthma in Sydney, Australia,³¹ and smoke from forest fires has been linked to increases in emergency department visits for asthma in California.³² These and other studies indicate that localized outdoor air pollution may play an important role in asthma.

Exposure to Ambient Air Pollution

Ambient (outdoor) air pollution may be deleterious to the health of children with asthma.³³⁻⁴⁰ Some children with asthma (as well as some children without asthma) have decreases in lung function after exposure to ozone.⁴¹⁻⁴⁵ Ozone, a pollutant that is formed primarily by vehicular exhaust and is the principal component of urban smog, is associated with asthma exacerbations in some children with reactive airway disease. Levels of ozone are usually greatest on hot summer days, and the levels tend to reach their peak in the late afternoon. Exposure to ambient sulfur oxides and suspended particulates may also lead to pulmonary function decreases in children.⁴⁶⁻⁵²

Nitrogen dioxide is an oxidant gas that can penetrate deep into the lungs and damage delicate lung tissues. Some studies have shown a relationship between nitrogen dioxide and respiratory symptoms. Shima et al⁵³ have demonstrated that the prevalence of bronchitis, wheezing, and asthma increased with each increase of 10 parts per billion (ppb) in indoor nitrogen dioxide concentrations among girls but not among boys.

Epidemiologic studies have documented that the relationship between air pollution and hospital admissions for respiratory illnesses may be the largest among people in inner cities.⁵⁴ White et al⁵⁵ demonstrated that the average number of emergency department visits for asthma or reactive airways disease among inner-city children in Atlanta was 37%

greater on days when the maximum ozone levels exceeded 11 ppb. Tolbert et al⁵⁶ showed that the relative risk for a pediatric emergency department visit increased by 1.04 per increase of 20 ppb in the maximum 8-hour ozone exposure level.

Although ambient air pollution may exacerbate asthma among individual children, a large international study suggests that outdoor air pollution is not a major factor in the development of asthma in populations.⁵⁷ It is not likely that outdoor air pollution could account for the increasing asthma prevalence in children.

EXPOSURE TO INDOOR AIR POLLUTION

Exposure to indoor air pollutants may have a more important effect on the development of childhood asthma than may exposure to outdoor air pollutants.⁵⁸ Many allergens and irritants (from smoke, cockroaches, mites, molds, cats, and dogs) are found indoors.^{58–61} In the United States, most children spend the majority of each day (average 20 hours) inside buildings.⁶² Indoor air pollution has become a particular problem since the energy crisis of the 1970s, which led to the construction of more energy-efficient buildings with less air circulation.

The Institute of Medicine recently released a report, "Clearing the Air," on the relationship between indoor air pollution and asthma.⁵⁸ The report described the quality of the evidence supporting the relationship between certain indoor pollutants and asthma development and exacerbations. Five levels of evidence were identified: sufficient evidence of a causal relationship, sufficient evidence of an association, limited or suggestive evidence of an association, inadequate or insufficient evidence to determine whether an association exists, and limited or suggestive evidence of no association. Indoor air pollutants for which there is sufficient evidence of a causal relationship and sufficient evidence of an association are described in this article and are summarized in Table 1.

Exposure to Environmental Tobacco Smoke

Exposure to environmental tobacco smoke is a risk factor for the development of asthma and for asthma attacks in children with existing disease. The Institute of Medicine concluded that there is sufficient evidence of an association between exposure to environmental tobacco smoke and the development of asthma and sufficient evidence of a causal relation-

ship between exposure to environmental tobacco smoke and exacerbations of asthma.⁵⁸

Birth certificate data for 1999 indicate that 12.3% of women who gave birth reported smoking during pregnancy.⁶³ Exposure to tobacco smoke products in utero is a risk factor for wheezing in the first year of life.⁶⁴

Approximately 42% of children 2 months to 11 years of age live in a home with at least 1 smoker.⁶⁵ An estimated 8.7 to 12.4 million US children younger than 5 years are exposed to cigarette smoke at home.⁶⁶ Children who have asthma and whose parents smoke have more frequent asthma attacks and more severe symptoms.^{67–80} One study suggested that if parents expose their children with asthma to less cigarette smoke, then their asthma symptoms may be less severe.⁸¹ More studies are needed on the effectiveness of decreasing the amount of environmental tobacco smoke to which children are exposed. Nonetheless, the Centers for Disease Control and Prevention has conducted systematic reviews on 11 interventions to decrease the amount of environmental tobacco smoke to which children are exposed and has made recommendations regarding the use of these interventions.⁸²

Indoor Exposure to Dust Mites

The Institute of Medicine has concluded that sensitization to house dust mites is an important risk factor for asthma development and also asthma exacerbations.^{58,83–85} Household interventions can decrease children's exposure to dust mites. Plastic mattress covers are an effective measure to decrease dust mite infestation of bedding. Several randomized controlled trials have demonstrated a significant decrease in concentrations of mite allergen on mattresses covered by polyurethane casings.^{86,87}

Vojta et al⁸⁸ recently conducted a randomized trial of physical interventions to decrease house dust mite allergen levels in low-income urban homes. They studied bedroom carpet interventions in 11 homes. Six homes received intensive vacuuming only, and 5 homes received dry steam cleaning and intensive vacuuming. Although both groups of homes had significant decreases in house dust mite levels in the bedroom carpets, only the homes that had received dry steam cleaning had decreases in house dust mite levels that persisted for up to 8 weeks after the intervention. They also studied bed interventions in 11 homes. All 11 beds received allergen-impermeable

TABLE 1. Relationship Between Indoor Exposures and Asthma Development and Exacerbations

| Indoor Exposure | Asthma Development | Asthma Exacerbations |
|-----------------------------|--------------------|----------------------|
| House dust mite | Increased | Increased |
| Environmental tobacco smoke | Probably increased | Increased |
| Cockroach | Maybe increased | Increased |
| Cat | Maybe increased | Increased |
| Dog | Maybe increased | Probably increased |
| Molds | ? | Probably increased |
| Oxides of nitrogen | ? | Probably increased |
| Ozone | ? | Probably increased |
| Particulates | ? | Probably increased |
| Sulfur dioxide | ? | Probably increased |

box springs, mattresses, and pillow covers. The bedding in 6 homes was laundered weekly by a professional service, and the bedding in the other 5 homes was laundered at home. Both interventions resulted in significant decreases in house dust mite levels in the beds. They also evaluated the effects of dry steam cleaning versus intensive vacuuming of upholstered furniture. Both interventions were about equally effective in decreasing dust mite levels in upholstered furniture.

Other investigators have shown little or no impact of house dust mites on asthma. Lau et al⁸⁹ showed no correlation between levels of house dust mites and asthma in children at 7 years of age. Gotzsche et al⁹⁰ performed a meta-analysis of 23 studies of house dust mite control measures in the management of childhood and adult asthma. Five of the 23 studies showed a decrease in dust mite exposure. When all studies were considered, the results did not show any clinical benefit from measures to reduce dust mites.^{90,91} The same was true when only the 5 trials that showed a decrease in dust mite exposure were considered. Additional studies of effectiveness of dust mite reduction techniques in homes of children with asthma are needed.

Exposure to Cockroaches

The Institute of Medicine concluded that cockroach allergens are causally related to asthma attacks.⁵⁸ Cockroach droppings may be one of the most underappreciated allergens in the indoor environment.⁹² Multicenter asthma studies funded by the National Institutes of Health have brought to light the importance of cockroach allergens in causing morbidity among inner-city children with asthma. Cockroach allergens not only increase the risk of asthma attacks but also may increase a child's risk of developing asthma.^{58,93} In a study among 235 children in Boston, children who lived with higher levels of cockroach antigen (as measured by *Bla g* levels from kitchen samples) were 4 times more likely to have a new diagnosis of asthma than were children from homes with a low level of cockroach antigen.⁹³

Exposure to Cats

The Institute of Medicine concluded that exposure to cats is causally related to asthma exacerbations among children with asthma.⁵⁸ Recent studies,^{94,95} however, have shown that the presence of a cat in the house may decrease the risk of developing asthma. The reasons for this apparently contradictory finding are being investigated.

Exposure to Molds

Indoor Exposure

The Institute of Medicine concluded that exposure to molds is associated with asthma exacerbations.⁵⁸ Some molds may invoke an allergic response (resulting in asthma or allergic rhinitis) in susceptible children. Exposure to molds may lead to allergic sensitization.⁶¹ At least 60 species of molds have spores thought to be allergenic.⁹⁶ Species of particular concern are *Penicillium*, *Aspergillus*, *Cladosporium*, and

Alternaria. On exposure to these species, nasal congestion, runny nose, sneezing, conjunctivitis, lacrimation, wheezing, chest tightness, and shortness of breath may occur. Thirty percent of patients with respiratory allergies seem to be particularly sensitive to molds. Children are the most sensitive population.⁹⁷⁻⁹⁹ Strong associations have been found between mold or dampness and respiratory symptoms (eg, wheezing, sore throat, runny nose)^{97,98,100-105} and doctor-diagnosed asthma.¹⁰⁶⁻¹⁰⁸

Outdoor Exposure

Fungal concentrations in outdoor air vary according to the season and weather conditions.¹⁰⁹ In subarctic climates, patients with mold allergies have more serious symptoms during spring and autumn when outdoor mold concentrations are usually highest.¹¹⁰ The 1997 National Heart, Lung, and Blood Institute *Guidelines for the Diagnosis and Management of Asthma* suggest that clinicians who care for children with asthma inquire about molds in the home environment and suggest methods to decrease the amount of mold to which children are exposed.¹¹¹

Exposure to environmental molds has been documented to play a role in asthma-related mortality.¹¹² Airborne molds have been linked to asthma deaths among 5- to 34-year-olds in Chicago.¹¹³ The odds of an asthma death occurring on days with mold spore counts of ≥ 1000 spores/m³ was 2.16 times higher (95% confidence interval: 1.31-3.56) than that on days with mold spore counts <1000 spores/m³.

Exposure to Violence

A potential risk factor for asthma that has recently been recognized is violence. Stress may potentiate the allergic response to allergens by increasing the release of inflammatory mediators and the subsequent cascade of inflammatory events characteristic of chronic asthma.^{15,114}

PROTECTIVE FACTORS

Several risk factors have been identified as protective against asthma. Ball et al¹⁴ showed that exposure of young children to older children at home or to other children in child care settings protects against the development of asthma and frequent wheezing later in childhood. They hypothesized that within the first 6 months of an infant's life, the immune response of children without atopy shifts from one associated predominantly with type 2 helper T cells, such as that in adults with atopic illnesses, toward one based more on cytokines derived from type 1 helper T cells, such as that in adults without atopy.^{14,115} A recent study has shown that long-term and early-life exposure to stables and farm milk induces a strong protective effect against development of asthma, hay fever, and atopic sensitization.¹¹⁶

PREVENTION

The aforementioned studies have documented that specific interventions can decrease environmental exposures in homes of children with asthma. Despite the growing body of evidence, many children and their families, particularly children who live in pov-

erty and rely on emergency departments as their primary source of health care, may not be receiving adequate counseling about how to avoid environmental exposures. A variety of excellent educational materials have been developed to teach parents and children with asthma about the importance of their environment, and several excellent reviews of indoor environmental controls in asthma management have been published.¹¹⁷⁻¹¹⁹

To prevent unnecessary exposures to outdoor air pollution, clinicians who care for children should be aware of the implications of municipal smog alerts and provide appropriate guidance to children with asthma and their parents regarding exercise during periods of high pollution.^{120,121}

With proper management, many environmental exposures can be decreased. What has yet to be documented is whether this will result in decreased morbidity from asthma. Studies to investigate this hypothesis are currently under way.

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Ruth A. Etzel

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