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ASTHMA AND AIR POLLUTION

INTRODUCTION

The increasing prevalence of and mortality from asthma, especially among minority urban populations, have made it a renewed focus of public health attention. Asthma is considered a chronic condition that is marked by both bronchial hyperresponsiveness and inflammation in the tissues in the airways[1].

Asthma hospitalizations among U.S. children increased by 4.5% per year between 1979 and 1987, and the death rate from asthma increased 31% in the same time period[2]. From 1978 through 1989, asthma mortality in the U.S. increased with a near doubling in the mortality rates in both nonwhites and whites; the mortality rates for nonwhites were 4 times those of whites[3].

In contrast, a survey of hospital admissions and death from asthma in Canada found no nationwide increase in death rate from asthma between 1980 and 1989, though the rate of hospitalization for asthma increased greatly in that time period.[4] A large cross-sectional study of asthma prevalence in children in Canada indicates that higher asthma rates are found on the east coast. Surveyed parents reported that 4.7% of children overall had physician-diagnosed asthma. Asthma was most common in the two Maritime provinces (7.6%) and least common in British Columbia (3.3%) and Quebec (3.4%)[5].

A monthly review and summary of the scientific literature on human health effects and environmental pollutants, with an emphasis on pollutants of the Great Lakes ecosystem. Prepared under the direction of the Health Professionals Task Force of the International Joint Commission. This does not represent the official position of the International Joint Commission.

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Asthma prevalence has been found to be higher in urban areas. A survey of inner-city children in New York City showed that 14.3% reported ever having asthma, and 8.6% reported current asthma, a rate twice that of the general U.S. population (4.3%)[6]. A study of asthma mortality in Chicago found an overall asthma mortality rate of 16.42 deaths per million from 1980 to 1988 for persons aged 5 to 34 years; this is approximately three times the rate for the general U.S. population[7]. Rates were highest among poor black persons. Targonski et al.[8] studied asthma mortality among persons aged 5 to 34 years in Chicago from 1968 to 1991, and found a 337% increase in mortality for African Americans, while there was no significant increase among Whites. A study of asthma hospitalization among 5- to 14-year old Medicaid patients in Michigan also found much larger increases among urban black children, from 3.2 per 1000 in 1980 to 7.1 per 1000 in 1984[9].

The root causes for the continued increases in asthma prevalence and severity are under debate. The environmental factors that have been associated with increased asthma symptoms have generally not increased during recent decades; in the case of outdoor air pollutants, concentrations have decreased in the developed nations. Martinez et al.[10] studied a cohort of children from infancy to six years of age, and found that, for most children, wheezing does not increase the risk of asthma later in life. However, for a group of children with elevated immunoglobulin (IgE) levels and a family history of asthma, wheezing appears to be related to a predisposition to asthma. The authors could not determine whether the increased allergic sensitization was due to exposure at an early age or a predisposition to allergic sensitization.

CRITERIA POLLUTANTS

The U.S. Clean Air Act of 1970 established six pollutants as "criteria" pollutants -- sulfur dioxide, nitrogen oxides, carbon monoxide, ozone, particulate matter and lead. The resulting network of monitoring stations has provided a substantial database of pollution levels in many U.S. and Canadian cities which has been used in numerous studies of airborne pollution effects on respiratory function. There is little evidence of associations between asthma and either lead or carbon monoxide; evidence for associations with the remaining four pollutants is summarized below.

Although air pollution levels tend to be higher in urban centers, there is also substantial transboundary movement of pollutants in the Great Lakes region. Researchers in New York and Ontario[11] have estimated that regional air pollution transported across the Great Lakes from the U.S. contributed strongly to the high acid aerosol concentrations measured in the city of Toronto.

Particulate Matter. There is considerable evidence that increases in particulate matter are associated with increased respiratory mortality and hospital admissions for asthma. The current U.S. standard for PM_{10} is 150 ug/m^3 (24-hour average); a recent review of epidemiological studies indicates that the lowest observable effect level for asthma is above 50 ug/m^3 for PM_{10} and about 25-75 ug/m^3 for $PM_{2.5}$[12]. A review by researchers at Harvard[13] combined results from several studies and concluded that each 10 ug/m^3 increase in PM_{10} was associated with an approximate 3% increase in asthma attacks, bronchodilator use, and lower respiratory symptoms. A recent study at Harvard School of Public Health[14] found that both increases in "particle-strong acidity" and a 20 ng/m^3 increase in respirable particle ($PM_{2.1}$) concentration on the previous day were associated with a 0.5 l/min decrease in peak flow rate. However, a study of respiratory effects in 18 U.S. and 6 Canada cities found an increase in bronchitis, but not asthma or wheeze, in cities with higher levels of particle-strong acidity[15].

Ozone. As reviewed by Koren[16], ozone has been associated with increased hospitalization rates for asthma, but it has been difficult to separate the effects of ozone from those of other pollutants such as acid aerosols. Compared with the current U.S. standard of 0.12 ppm (24-hour average), the recent review by Lebowitz[12] indicates that the lowest effect level for asthma occurs at 0.08 ppm. In a recent clinical study,[17] asthmatic subjects exposed to 0.16 ppm ozone were signifi-cantly more sensitive to ozone exposure than nonasthmatics.

Sulfur dioxide. Koren[16] summarized clinical studies which have indicated that asthmatics may develop significant increases in airway resistance with brief exposures to sulfur dioxide at concentrations as low as 0.25 ppm; the U.S. standard is 0.14 ppm(24-hour). A recent study[18] of 14 asthmatics exposed to SO_2 while exercizing found increasing symptoms and lung function responses in concentrations above 0.5 ppm. However, Lebowitz[12] found that the lowest effect level from two epidemiological studies was 200 ug/m^3 (0.08 ppm).

Nitrogen dioxide. Clinical studies , summarized by Koren[16], have indicated that some asthmatics are inherently more responsive to NO_2 than others. NO_2 differs from the other three pollutants in that it may be found in higher concentration indoors, due in part to NO_2 production from gas stoves or heaters. A metaanalysis of data from 11 studies showed a significant association between estimated NO_2 exposure and illness[19]. Lebowitz[12] reviewed epidemiological studies, and found the results too conflicting to determine a lowest observable effect level.

AIRBORNE ALLERGENS

A number of studies have found that asthma symptoms can be triggered by increases in levels of allergens such as pollens or mold spores.[20] In one recent panel study, researchers at Harvard[14] collected daily peak flow rates and asthma symptoms from a group of children, along with daily outdoor pollutant and aeroallergen levels. They found, in addition to significant associations between particulate pollution and decreased respiratory function, evidence that mold spore concentration independently reduces lung function. A 10,000 spores/m^3 increase in *Cladosporium* was found to be associated with a 1.0 l/min decrease in morning peak flow rate, while a 60 spores/m^3 increase in *Epicoccum* was associated with a 1.5 l/min decrease in morning peak flow rate.

TOXIC AIR POLLUTANTS

As described earlier, most research on air pollution and asthma has focused on the criteria pollutants. A team of University of Cincinnati[21] researchers reviewed what is known about "air toxics" and asthma, and propose a list of 30 compounds that could have the highest impact on asthma and respiratory health. The list of compounds includes: (1) known occupational asthmagens, such as some isocyanates and aldehydes and several metals; (2) known skin allergens with a potential for inhalation exposure, such as hydrazine or chromium compounds; and (3) respiratory irritants, such as hydrochloric acid and phosphine. The authors report results of a study in which rats were exposed to formaldehyde and acrolein, and found that the effect of an 8-hour exposure was greater that what would be predicted by estimation from effects seen with 2-hour exposures, which emphasizes the need to assess effects from long-term exposures at low pollutant levels.

INDOOR ENVIRONMENTAL FACTORS

It has been estimated that people in industrialized nations spend 65% of their time in their homes.[22] Some pollutants, including nitrogen dioxide and some organic compounds, can be present in higher concentrations in indoor air than outdoor air. Researchers in Norway[23] found that increased bronchial responsiveness was associated with indoor allergens, particularly house dust mites, rather than outdoor allergens. In addition, household characteristics, such as dampness or mold growth, humidifier use, presence of tobacco smoke, presence of wall-to-wall carpet and use of gas or wood stoves, have been found to be significantly associated with asthma and respiratory symptoms in a number of studies.[22, 24, 25, 26] Norback et al.[22] found asthmatic symptoms to be significantly more common in homes where house dust mites were present (OR=5.3; 95% CI 1.2-22.8).

Although there has been little research on indoor pollutant concentrations and asthma, there is some evidence of an association. Researchers in Sweden[22] measured levels of formaldehyde and VOCs, along with other indoor factors, in homes of 47 asthmatics and 41 nonasthmatic subjects. Mean formaldehyde concentrations were 29 and 17 ug/m^3 in homes with and without subjects reporting nocturnal breathlessness. The mean levels of total VOCs in the living room were 780 ug/m^3 and 300 ug/m^3 in homes of subjects with and without reported nocturnal breathlessness. All groups of VOCs (such as terpenes, n-alkanes) were found in significantly higher concentrations in the homes of subjects reporting nocturnal attacks of breathlessness, compared to subjects without nocturnal breathlessness.

INTERACTIVE EFFECTS

Pollutant interactions. The concentrations of criteria pollutants are often correlated, and ambient air nearly always contains a mixture of pollutants. Some recent clinical studies have indicated that pollutants in combination have additive effects. Frampton et al.[27] found that asthmatics were significantly ($p<0.05$) more susceptible to lung function changes when exposed to sulfuric acid aerosol followed by ozone exposure. Liekauf et al.[21] suggest that ozone measurements can be used in estimating exposure to toxic air pollutants, especially reactive hydrocarbons.

Pollution/allergens: Gilmour[28] reviewed animal and human studies indicating that exposure to pollutants may heighten sensitization to allergens. Increased allergic sensitivity has been found in animal studies with exposure to ozone, nitrogen dioxide or sulfur dioxide; the pollutant exposure levels were higher than those found in ambient conditions. In one clinical study on humans with exposure to 0.12 ppm ozone (the U.S. air quality standard) some subjects showed increased bronchial responsiveness following antigen challenge. However, a second study, using 0.5 ppm ozone, found no significant difference in responsiveness, but it was noted that allergic individuals had much stronger responses than nonallergic individuals. In the author's lab, exposure of rats to 5 ppm nitrogen dioxide (about 100 times the U.S. standard for annual average NO_2) resulted in greater immune responsiveness and severity of pulmonary inflammation. The proposed mechanisms for this effect include reduced lung immune response resulting in longer residence time for allergens in the lung, or oxidant-induced release of inflammatory substances in lung tissue resulting in heightened sensitization to allergens.

Rain/Allergens: A recent report from London[29] supports previous studies in noting the occurrence of an "epidemic" of emergency room admissions for asthma following a thunderstorm, with a sudden drop in air temperature. Number of lightning strikes, increase in rainfall, fall in temperature, rise in air pressure and relative humidity were associated with increased asthma presentations to the emergency room. A change in pollen concentration (both rise and fall) was also found to be a significant predictor. It has been proposed that rainfall or moisture in the air exacerbates the effects of pollen. As summarized by Knox[30], pollen grains rupture by osmotic shock in rainwater, releasing hundreds of starch granules from each grain, and inhalation challenge tests have shown that starch granule suspensions are capable of eliciting immune responses in allergic people.

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