Air Pollution and Children's Health

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ABSTRACT. Children's exposure to air pollution is a special concern because their immune system and lungs are not fully developed when exposure begins, raising the possibility of different responses than seen in adults. In addition, children spend more time outside, where the concentrations of pollution from traffic, powerplants, and other combustion sources are generally higher. Although air pollution has long been thought to exacerbate minor acute illnesses, recent studies have suggested that air pollution, particularly traffic-related pollution, is associated with infant mortality and the development of asthma and atopy. Other studies have associated particulate air pollution with acute bronchitis in children and demonstrated that rates of bronchitis and chronic cough declined in areas where particle concentrations have fallen. More mixed results have been reported for lung function. Overall, evidence for effects of air pollution on children have been growing, and effects are seen at concentrations that are common today. Although many of these associations seem likely to be causal, others require and warrant additional investigation. *Pediatrics* 2004;113: 1037–1043; *asthma, particles, ozone, lung reaction.*

The health effects of air pollution exposure have become an area of increasing focus in the past 30 years. A growing body of evidence has demonstrated that there are serious health consequences to community air pollution and that these consequences are not spread equally among the population. As an example of this differential susceptibility, recent studies have indicated that people with type 2 diabetes are at higher risk for cardiovascular effects of airborne particles.[1,2] Similarly, children have been shown to be at particular risk for other effects of air pollution, as detailed below.

This article cannot be a comprehensive review of the literature, because recent reviews of airborne particles and ozone alone have hundreds of pages summarizing the literature. Rather, I cover the major health effects in children that have been linked to air pollution, cite some key papers, and discuss the strength of the evidence. I particularly highlight ar-

eas where it seems that differences between adults and children, particularly in the development of the respiratory and immune system, suggest different impacts of exposure for children.

BACKGROUND

The lung is not well formed at birth, and development of full functionality does not occur until approximately 6 years of age. During early childhood, the bronchial tree is still developing. For example, the number of alveoli in the human lung increases from 24 million at birth to 257 million at age 4,[3] and the lung epithelium is not fully developed. This results in greater permeability of the epithelial layer in young children. Children also have a larger lung surface area per kilogram of body weight than adults and, under normal breathing, breathe 50% more air per kilogram of body weight than adults. This process of early growth and development, the outcome of which is important for the future health of the child, suggests that there is a critical exposure time when air pollution may have lasting effects on respiratory health.

At the same time the child's lung is developing, the child's immune system, immature at birth, is also beginning to develop. Much recent attention in asthma research has been focused on this development, in particular factors that influence the development of TH-2 (humoral immunity dominant) versus TH-1 (cellular immunity dominant) phenotypes.[4]

Another major factor that influences the relative impact of air pollution on children versus adults is exposure. Children spend more time outdoors than adults, particularly in the summer and in the late afternoon.[5] Some of that time is spent in activities that increase ventilation rates. This can increase the exposure to air pollutants compared with adults, as indoor concentrations of air pollutants of outdoor origin are usually lower.

PRE- AND PERINATAL EFFECTS OF AIR POLLUTION

Although historically air pollution has been thought of as a respiratory toxicant, recent evidence has broadened our understanding of its full range of effects. In adults, changes in cardiovascular risk factors such as C-reactive protein[6] and autonomic control of the heart[7] have led the way in broadening our understanding of the range of toxicity. With children, perhaps the most unexpected results have been a range of recent papers reporting that prenatal exposure of populations to prevailing levels of air pollution is associated with early fetal loss,[8] preterm

delivery,[9–11] and lower birth weight.[12–18] These associations may or may not be causal but clearly warrant additional study. The later Bobak study[18] is notable in that it was nested within a birth cohort study, allowing good control for social and other factors that may confound the association. Because birth certificates in most areas have extensive information on maternal medical conditions that may affect the pregnancy, as well as maternal age, education, and smoking, all of these studies are generally well controlled. Although relatively recent, there is now considerable evidence that maternal exposure to air pollution during pregnancy is associated with adverse birth outcomes. Moreover, particulate air pollution from combustion sources shares many characteristics with sidestream tobacco smoke, which is rich in particles and polycyclic aromatic hydrocarbons. A recent review by Windham et al[19] found that environmental tobacco smoke was associated with low birth weight. This provides support for the plausibility of the reported association.

The mechanisms involved are as yet unknown but may include inflammatory processes and oxidative stress, which have been linked to air pollution. For example, Salvi et al[20] reported that human volunteers who were exposed to diesel particles for 1 hour had elevated levels of peripheral white cells, as well as increased vascular cellular adhesion molecule-1 and intercellular adhesion molecule-1 in the lung epithelium. As noted before, C-reactive protein, an acute-phase inflammatory marker, was associated with air pollution exposure in adults. Ozone is a highly reactive gas, associated with oxidative stress in many studies.[21–24]

Additional support is provided by some animal studies, which provide some ideas about mechanisms. Although these tend to be at high doses, they can help to supplement the human data. Recently, Saldiva and co-workers[25,26] reported lung inflammation associated with particle and particle component exposure in rats. Carbon monoxide exposure has been associated with fetal toxicity, including intrauterine growth retardation in the rat.[27] Ozone exposure has also been shown to be fetotoxic in an animal model.[28]

Perhaps the most serious thing that can be done to a child's life is to end it. Recently, a number of studies have reported that air pollution is associated with precisely that. In thinking about air pollution and death, one is inevitably led to the great air pollution episode of December 1–5, 1952, in London. A low-level thermal inversion that trapped coal smoke in the Thames valley, coupled with a stationary front that dropped wind speed to 0, resulted in a rapid buildup of pollution to extremely high levels. Approximately 4000 excess deaths occurred in London in that week,[29] and elevated death rates continued for weeks afterward,[30] indicating that there were delayed as well as prompt effects. Although most of the deaths were in adults, infant mortality was doubled during that period.[31]

This episode is important because it establishes causality. The influenza epidemic did not arrive in England until >1 month after the episode, and in other towns in England, where the weather was as cold or colder but no inversion occurred, no increase in deaths was observed. Furthermore, the death rate increased rapidly in phase with the pollution and began to come down when the pollution came down. Hence, it is clear that at very high levels, air pollution can produce a substantial increase in deaths of children.

More recently, Woodruff et al[32] examined infant deaths in the United States and levels of inhalable particles (PM_{10}) in the air. They excluded infant deaths in the first month after birth as likely to reflect complications of pregnancy and delivery and found that PM_{10} was associated with higher death rates in the next 11 months of life. This excess risk seemed to be principally from respiratory illness, although sudden infant death syndrome deaths were also elevated.

Bobak and Leon[33] recently also examined the cross-sectional association between air pollution and infant mortality rates across towns in the Czech Republic. A significant association was seen between infant death rates and particle and SO_2 concentration. Other studies have examined day-to-day changes in air pollution and day-to-day changes in infant deaths. Saldiva et al[34] reported that infant death from respiratory disease was associated with air pollution, particularly from traffic. Loomis et al[35] similarly found respiratory deaths in infants associated with air pollution.

ACUTE EFFECTS OF AIR POLLUTION EXPOSURE

Exposure Issues

As noted above, children's exposure can be different from adults given the same outdoor concentrations. This is particularly important for exposure to ozone. Ozone is a highly reactive gas, producing oxidative damage in the lung. Because of that high reactivity, its half-life in indoor air is only 7 to 10 minutes.[36] Consequently, ozone levels are very low indoors.[5,37] This is particularly true for locations with low air exchange rates, such as air-conditioned homes and workspaces. Ozone also has a distinct temporal pattern. Because it is not directly emitted from polluting sources but produced by photochemical reactions in the atmosphere, it shows strong seasonal and diurnal variations. It is high in the summer and the afternoon and low in the night, early morning, and winter. Children tend to be outdoors in the afternoon and in the summer, which results in much higher exposure for children than adults, who are protected by their indoor environment.

In contrast, fine combustion particles, usually indexed by $PM_{2.5}$ (particles <2.5 μM in aerodynamic diameter) penetrate indoors and are not chemically quenched like ozone (or SO_2). Recent studies of the association between personal exposure to particles of outdoor origins and outdoor concentrations show that the personal exposures are much more tightly linked than for ozone,[38] although they do vary with air exchange rates of the buildings in which the person spends time. Hence children's exposure to

$PM_{2.5}$ is enhanced by their greater outdoor activity for this pollutant but to a lesser extent than for ozone.

Health Effects

There is a large body of literature associating short-term changes in air pollution with short-term changes in pulmonary health of children, often focused on individuals with asthma. Of particular interest are a series of summer camp studies[39–41]. These were innovative because the living conditions of the children in the camp meant that they were exposed all the time. For most of the day, they were outdoors, and their indoor quarters had such high air infiltration rates that indoor concentrations of outdoor pollutants were almost certainly similar to the outdoor levels. In these studies, lung function declined during air pollution episodes, which were combinations of ozone and sulfate particulates, some of which may have been acidic.

Another set of studies examined wintertime episodes. A study in Steubenville, Ohio, repeated measurements of pulmonary function in schoolchildren before, during, and after an episode of high-particulate air pollution.[42] Lung function declined during the episode. A similar study was performed in the Netherlands.[43]

These studies were followed up by a different study design that made it possible to collect large amounts of data relatively inexpensively. A panel of children would be recruited and asked to perform daily peak flow tests and usually to answer questions on symptom prevalence (wheezing, coughing, etc) for a period of several months. These measurements were then correlated with air pollution. Often but not always, these studies would be focused on children with asthma. In general, significant associations have been reported with PM_{10},[44–48] although not in every study.[49] Other summer time studies have reported associations with ozone,[50–52] including interactions with aeroallergen exposure.[53]

Of particular interest are 2 studies from the Netherlands that addressed the question of susceptibility. Van der Zee et al[54] looked at wintertime air pollution in panels of 7- to 11-year-old children. A stronger association was found between particle pollution and peak flow decrements in children with asthma symptoms, particularly those on regular medication, than with nonsymptomatic children. There was also a significant effect on bronchodilator use in the symptomatic children. A second analysis looked at more objective measures than reports of chronic respiratory symptoms as effect modifiers. Children were stratified into those with measured bronchial hyperresponsiveness and elevated immunoglobulin E and those without.[55] The association between decrements in peak flow and air pollution was primarily in the former group.

A related approach is to use administrative data to look at more serious outcomes that require physician contact. For example, Pope[56] examined hospital admissions of children in the Utah valley during 3 consecutive winters. These winters were before, during, and after a strike that closed down a steel mill in the valley that was the largest source of wintertime air pollution. There was a >50% drop in admissions of children for asthma and for pneumonia during the period that the mill was closed and when the pollution was lower. In the following year, admissions went back to previous levels. In a neighboring valley, there was no drop in pollution or admissions in the middle winter. This is as close to a clinical trial as can be found in air pollution epidemiology, and the conclusions are striking. Air pollution is related to serious asthma exacerbation and to pneumonia exacerbation. Other studies have looked at day-to-day fluctuations in hospital admissions and day-to-day changes in air pollution and reported associations with childhood hospital admissions in Ontario,[57,58] Seattle,[59,60] and elsewhere.[61,62]

A different approach is to look at physician visits. Such data are hard to obtain systematically for large populations in the United States but are more readily available in Europe. Medina et al[63] looked at emergency house calls by physicians in Paris and found that visits for asthma were associated with particulate air pollution and ozone and that the association was stronger for children.

What evidence is there that these associations are plausible? An important study by Zelikoff et al[64] showed that exposure to urban particles exacerbated pneumonia in an animal model, supporting the results of the epidemiologic studies in Utah and elsewhere. Other studies have shown ozone to be associated with altered macrophage function and epithelial injury,[65] which could plausibly modify infectivity.

Other evidence points to a role for pollution in increasing lung inflammation in children, particularly those with asthma. For example, Fischer et al[66] examined a cohort of 68 children (aged 10–11) with 7 weekly measurements of exhaled nitric oxide (NO) and found that increases in several air pollutants were associated with increased levels of exhaled NO, a good marker of lung inflammation in individuals with asthma.[67,68] Giroux et al[69] contrasted exhaled NO in children who had asthma and lived in urban areas with others who stayed in a national park in the mountains, or with children without asthma in the same city. The exhaled NO concentrations in the urban children with asthma were more than double those in the children with asthma in the national park, and their was no difference in exhaled NO between children with asthma in the park and healthy children in the city.

Finally, we have excellent evidence that changing pollution in the short term produces immediate reductions in asthma exacerbations. In addition to the Utah study cited above, a more recent study looked at asthma hospital visits in Atlanta around the period of the Olympics, when traffic was limited and air pollution was reduced. A noticeable reduction in asthma emergency visits occurred during that period of short-term traffic control.[70]

EFFECTS OF LONG-TERM EXPOSURE TO AIR POLLUTION

Although the role of air pollution in exacerbating existing illness has been well established, recent ev-

idence has implicated pollution exposure with the development of chronic disease or impairments. Evidence has been accumulating for a while about effects on lung function and bronchitic symptoms. More recently, studies have begun to implicate air pollution, particularly from traffic, with the pathogenesis of asthma.

In the late 1980s, Schwartz[71] examined the association between long-term exposure of children to air pollution and pulmonary function in the Second National Health and Nutrition Examination Survey. He found significant decrements in lung function associated with exposure.

Jedrychowski et al[72] also reported that air pollution was associated with lower levels of lung function growth in children in Poland. Horak et al[73] made repeated measurements of spirometry during a 3-year period in Austrian schoolchildren and found that after adjustment for covariates, including initial lung function, lung function growth rates were associated with PM_{10} exposure. An increase of 10 $\mu g/m^3$ in PM_{10} exposure was associated with a decrease in growth of forced expiratory volume in 1 second of 84 mL/year.

Other studies have implicated ozone exposure during childhood with reductions in lung function. For example, Künzli et al[74] collected residential address histories for freshman at the University of California at Berkeley and matched them to monitors near their homes. Cumulative ozone exposure was associated with a significant decrement in forced expiratory volume in 1 second. A similar result was found for freshmen at Yale.[75]

Dockery et al[76] reported that chronic bronchitis and chest illness in children were associated with exposure to particulate air pollution. This study compared covariate adjusted rates across 6 communities in the eastern United States with varying levels of pollution. No association was seen with asthma or wheezing. Subsequent studies in the United States[77] and elsewhere confirmed that particulate exposure was associated with higher rates of chronic cough and bronchitis symptoms in children and the lack of association with wheezing and asthma. A similar large study ($n = 4470$) comparing schoolchildren in 10 communities in Switzerland reported an adjusted odds ratio for bronchitis of 2.88 (95% confidence interval [CI]: 1.69–4.89) for PM_{10} exposure between the most and least polluted community.[78] A study of 3676 children across 12 Southern California communities reported that bronchitis was associated with PM_{10} but only among children with asthma.[77] The largest study examined 13 369 children in 24 communities in the United States and Canada.[79] Again, particulate air pollution was associated with bronchitis episodes across these communities.

A recent study that looked at eastern Germany, where there has been a reduction in pollution since the reunification, shows that this reduction has been associated with reductions in the rates of chronic cough and bronchitis symptoms in a new cohort of children.[80] This demonstrates not merely an association but that an intervention produces improvements in health. A similar dramatic effect of intervention

was seen in a study by Avol et al.[81] Using the Southern California cohort study mentioned above, they identified 110 children who moved from the study area and followed them up in their new home with pulmonary function testing identical to that in the main cohort. Subjects who moved to locations with higher PM_{10} concentrations showed lower rates of annual growth in lung function, and subjects who moved to locations with lower PM_{10} concentrations than they had left showed higher rates of growth in lung function. This effect was increased in subjects who lived in the new location for at least 3 years.

Of considerable interest are recent studies that have called into question the previous results indicating that long-term air pollution exposure (mostly to particles) was associated with bronchitis symptoms but not asthma. These studies all used central monitoring locations in each community to assess long-term exposure in those communities. Although these monitoring stations are reasonable surrogates for long-term exposure to pollutants that are relatively homogeneously distributed across the community, that is not true for all pollutants. In particular, traffic pollutants show strong gradients. Exposure to diesel exhaust varies greatly with distance from major roadways within a community.[82,83] The new studies have used measurements or models of this microlevel spatial variability in exposure within community and returned to the question of whether air pollution exposure is associated with the development of asthma.

Studnicka et al[84] examined 8 small, rural communities with no industrial sources of pollution. NO_2 was measured in each community and taken as a measure of exposure to traffic pollution. In areas without heavy industry, almost all NO_2 is attributable to traffic. Although both gasoline and diesel engines produce NO_2, diesel engines produce much more, so this surrogate is weighted toward diesel exposure. A strong association between asthma prevalence and NO_2 levels was found, with odds ratios reaching 5.81 (95% CI: 1.27–26.5), contrasting the highest and lowest exposures. Kramer et al[85] examined 317 children in 3 German communities. NO_2 measurements were made outside the homes of each of the children, and personal NO_2 measurements were collected for each child. The personal NO_2 measurements reflect exposure to both outdoor NO_2 and indoor sources (eg, gas stoves). The NO_2 outside the home reflected exposure to NO_2 from outdoor sources only and therefore was a good surrogate for exposure to traffic pollution. The NO_2 measurements outside each child's home were significant predictors of hay fever; symptoms of allergic rhinitis; wheezing; and sensitization against pollen, house dust mites, or cats. The personal NO_2 measurements, which were strongly influenced by indoor sources, were not associated with these outcomes. This indicates that traffic pollution but probably not the NO_2 from traffic is associated with atopy and wheezing. If NO_2 per se is not the relevant exposure, than diesel particles or some component of those particles, such as polycyclic aromatic hydrocarbons, may be the most important etiologic compo-

nent. In the Netherlands, residence on a high-traffic street was associated with a >2-fold increase in the risk of wheezing after control for confounders.[86]

Even more recently, Lin et al[87] geocoded the residential addresses of children who were admitted to the hospital in Erie County, New York (excluding Buffalo) for asthma, and age-matched controls who were admitted for nonrespiratory conditions. These were linked to Department of Transportation data on vehicle miles traveled on their street. The odds of asthma (adjusted for poverty level) for living within 200 m of a street with the highest tertile of traffic density was 1.93 (95% CI: 1.13–3.29), and the children with asthma were more likely to have truck traffic on their street. Another recent report analyzed data from 2 birth cohorts totaling 1756 children in Munich.[88] Geographic Information System modeling was used to estimate the concentrations of traffic-related particles and NO_2 outside the birth addresses of all of the children. These pollutants were associated with dry cough at night in the first year of life. Another case-control study of 6147 children in Nottingham, England, found increased risk of wheeze associated with living within 90 m of a roadway.[89] Although some studies showed no increased risk,[90] the overwhelming weight of the recent evidence suggests that traffic pollution is associated with the risk of developing asthma.

CONCLUSIONS

Air pollution is not the leading cause of death or morbidity in children in the developed world. However, there is increasingly strong evidence that air pollution is associated with nontrivial increases in the risk of death and chronic disease in children, worse pregnancy outcomes, and exacerbation of illnesses. It is less clear which pollutants are most responsible, but particles and ozone have the strongest associations. For the incidence of asthma, traffic pollution, particularly from trucks, seems to be the key player.

What is important to realize is that this is an easily modifiable risk. Sulfate particles, a major fraction of the particle burden in the air in urban areas, can be easily removed using scrubbers on powerplants (their largest source) at a cost that is <1% of the current price of electricity. NOx reduction, a major component of an ozone reduction strategy, can also be retrofitted onto powerplants. In Europe, catalytic converters on cars can be brought up to US standards. Traffic particles, NOx, and so forth are dominated by diesel engines. Trap oxidizers and catalysts can reduce these emissions by up to 90%. Such devices have been on gasoline-powered vehicles for decades without ending industrial civilization as we know it. For many of these control strategies, it does not matter that we are not sure which component of the pollution mix is principally responsible. Oxidative catalysts reduce carbon soot, polycyclic aromatic hydrocarbons, CO, and so forth. Given the amount of money that we spend on the treatment of asthma and the difficulty that we have in reducing allergen exposures, such straightforward approaches need serious attention.

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