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The impact of the Clean Air Act

Kristie Ross, MD, MS¹, James F. Chmiel, MD, MPH¹, and Thomas Ferkol, MD²

¹Department of Pediatrics, Rainbow Babies and Children's Hospital, Case Western Reserve University School of Medicine, Cleveland, Ohio

²Department of Pediatrics, Washington University School of Medicine, St. Louis, Missouri

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We seldom think about the air we breathe, but a catastrophe seventy years ago revealed the threat of air pollution to our health. During a five-day period in 1948, twenty people were killed and thousands sickened by a cloud of air pollution from a local factory that formed over the town of Donora, Pennsylvania [1]. This tragedy set into motion meaningful efforts to ensure that our air is life-sustaining and not life-threatening. The Clean Air Act, signed into law in 1970 and strengthened in 1990, gave the federal government the authority to enforce regulations that limit air pollution. We have learned much about the relationship between air pollution and health through thousands of epidemiologic and controlled studies. Air pollution, including particulate matter, ozone, heavy metals and acid gases, is harmful and can exacerbate respiratory conditions in children, such as asthma. In this Commentary, we will provide the facts regarding the many effects of airborne pollution on childhood lung disease. We will review the history of the current air pollution regulations, describe current initiatives that threaten these standards, and summarize the scientific evidence that demonstrates the importance for maintaining, and even strengthening, air pollution standards for the health of children.

A history of the Clean Air Act and Environmental Protection Agency [2, 3]

Key federal legislation related to clean air is summarized below (Table I). The first legislation involving air pollution was enacted in 1955, and authorized funds for air pollution research. It was followed eight years later by legislation to control air pollution. The Clean Air Act of 1970 represented a major shift in federal government responsibility for limiting the exposure of U.S. citizens to air pollution by authorizing regulations limiting

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Correspondence and request for reprints should be addressed to: Kristie Ross, MD MS, Case Western Reserve University, Rainbow Babies and Children's Hospital, 11100 Euclid Avenue, Cleveland, Ohio 44106. Kristie.Ross@UHhospitals.org.

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harmful emissions from stationary and mobile sources. At virtually the same time, the National Environmental Policy Act established the Environmental Protection Agency (EPA). The EPA is responsible for implementing the Clean Air Act regulations. The new regulations included phased-in use of catalytic converters for new automobiles beginning in 1975. Regulations have gone through several changes since first enacted; current standards regulate six criteria pollutants: lead, carbon monoxide, ozone, sulfur dioxide, particulate matter, and nitrogen dioxide (Table II).

Significant changes to the Clean Air Act were enacted in the Clean Air Act Amendments of 1990, specifically targeting four areas: acid rain, urban air pollution, toxic air emissions, and ozone depletion. The Acid Rain Program employs a cap-and-trade program, which has led to substantial reduction of sulfur dioxide (SO₂) and nitrogen dioxide (NO₂) emissions. Even the most conservative estimates indicated that benefits of the Acid Rain Program, in terms of avoided mortality, have greatly outweighed its costs by 46-to-1. Regulations in the amendments targeting ozone-depleting chemicals were phased in faster than predicted at a cost of 30 percent less than estimated. In addition, the Clean Air Act and amendments have dramatically reduced vehicle-related pollutants, and EPA officials estimate that when fully implemented in 2030, the new vehicle and fuel rules will achieve a 16-to-1 benefit-cost ratio. This year, the EPA issued final rule to limit mercury and other air toxic emissions from coal and oil-fired power plants by simply asking the industry to consistently adopt the best current pollution control practices, or maximum achievable technology (MACT) at US power plants. The Clean Air Act Amendments originally called for this rule to be completed more than a decade ago, with estimated health savings of \$59 to \$140 billion that will be reached in 2016 when the rule is fully implemented.

Despite these advances, the Clean Air Act is under threat from both the legislative and executive branches of the government. In response to a court ruling expressing concern about the spread of air pollution across state boundaries, the EPA finalized the Cross-State Air Pollution Rule this summer, which requires 27 states to reduce emissions from coal-fired power plants that export emissions to their neighbors in the form of ozone and fine particle pollution. Cost-benefit analyses found that \$800 million in annual projected costs will be offset by \$120 to \$280 billion in annual health and environmental benefits, including 34,000 premature deaths and 400,000 fewer asthma attacks by 2014 [4]. However, the Energy and Commerce Subcommittee and subsequently the House of Representatives passed a bill this year that would block the EPA from updating the standards for coarse particulate matter (PM₁₀) that have been in place since 1987, even though the agency stated that it did not intend to issue stricter standards.

Adverse effects of air pollution on children

There are several lines of evidence suggesting that the health consequences of air pollution are not distributed equally among the population. Children are more susceptible and at greater risk [5]. As compared to adults, children have unique developmental and physiologic differences that impact health and disease, differences that increase their vulnerability to air pollution [6]. Lung development begins *in utero* but continues throughout childhood in a tightly regulated process. Although early phases are critical for the differentiation of various

lung cell types and the formation of the branching airways, the later phases are characterized by continued lung maturation and growth. Because the alveolar phase of lung development continues until months to years after birth, inhaled toxins may affect lung development at any of these stages [7]. Infancy is a period of rapid growth and development, and early insults can have prolonged or permanent effects. Although outside the scope of this commentary, early insults may play a role not only in childhood pulmonary disease, but may also be important in the developmental origins of adult pulmonary diseases such as chronic obstructive pulmonary disease [8].

In addition to their developmental vulnerability, children are effectively exposed to higher levels of airborne pollutants than adults at similar environmental levels. Children tend to spend more time outside playing, especially in the summer, and are more physically active, thereby increasing their minute ventilation and exposure to outdoor air pollutants. They tend to breathe through their mouth, which bypasses nasopharyngeal filtration and allows particulates to deposit in the lung. Children also have larger alveolar surface area relative to body weight, which increases contact of the lining type 1 pneumocytes to inhaled toxic particles and gases [9, 10].

Air pollutants have been associated with pulmonary inflammation and oxidative stress [5, 11–17]. Components of air pollution have been shown in animal and human studies to influence allergic airway inflammation, including greater IgE production [18, 19], increased eosinophil activation [16, 20], and higher levels of cytokines and other inflammatory mediators [21–23]. Multiple pollutants, including particulate matter and ozone, have been associated with increased production of superoxide and other free radicals, or impaired antioxidant defense [11, 12, 14, 24–26]. Antioxidant defense capabilities are also immature in infants and young children, another factor that could contribute to susceptibility to pollutant-mediated lung injury [27]. Genetics are likely to play a role in inflammatory and oxidative responses to air pollution through multiple mechanisms. Gene by gene interactions, gene by environment interactions, and epigenetic mechanisms may all be important. Epidemiologic data suggest that there are significant interactions between polymorphisms in multiple genes important in oxidative stress responses and ambient air pollution exposures in pulmonary outcomes [28]. Epigenomics are an emerging area of study related to the health effects of air pollution. Epigenetic modifications are heritable post-translational changes in genes that impact gene expression, which may mediate some of the adverse health effects of some pollutants [29, 30]. Because these changes are heritable, pollutant exposures today may have lasting effects on future generations.

Prenatal exposure to air pollution and birth weight

Multiple studies have demonstrated a relationship between air pollution and lower birth weight [31–34] with subsequent increased risk for the development of respiratory diseases and diminished lung function. Reduced lung function in infancy predicts low lung function later in life [35], suggesting that early influences on respiratory health have lasting impact. In a communitybased prospective study of pregnant women living in four residential areas of Beijing, China, which included more than 74,000 live births with a gestational age of at least 37 weeks, maternal exposure to increased concentrations of sulfur dioxide or

particulate matter was associated with increased risk of low birth weight after adjustment for gestational age, maternal age, infant sex, and residence [36].

In the United States, researchers investigated the relationship between birth weight and air pollution in children enrolled in the Children's Health Study in Southern California [37]. The study population included 4,000 full-term children born in California between 1975 and 1987. Air pollution exposures were assessed using EPA records, and regression model covariates included maternal age, parity, months since last birth, maternal smoking status, gestational diabetes, infant sex, race and ethnicity. Ambient carbon monoxide levels in the first trimester and ozone levels in the second and third trimester were independently associated with lower birth weights and intrauterine growth retardation (IUGR). The magnitude of the effect of exposure to the highest levels of ozone on birth weight was similar to the magnitude of the effect of maternal smoking during pregnancy on birth weight.

Air pollution and infant mortality

Air pollution is associated with increased post-neonatal infant mortality, including sudden infant death syndrome (SIDS) [38–41]. Using time-series analyses, the relationship between daily air pollution levels and daily SIDS rates was studied in twelve Canadian cities over a sixteen year time period [40]. Average levels of all pollutants were well within current EPA standards for criteria pollutants (Table II). Higher levels of carbon monoxide, sulfur dioxide, and nitrogen dioxide were associated with increased incidence of SIDS, though the association with carbon monoxide lost statistical significance after adjustment for weather covariates. There was no association of ozone or particulate matter levels with SIDS.

The relationship between air pollution and post-neonatal infant mortality was assessed in 25 US counties in 1995–1997 using PM₁₀ as a marker for airborne pollutants [39]. The attributable risk for all infant mortality was 6%, and for SIDS and respiratory disease mortality in normal birth weight infants was 16% and 24%, respectively. In a separate study of infants born during 1999–2002 in all US counties with more than 250,000 residents, for every 10 µg/m³ rise in PM₁₀ levels, respiratory-related deaths increased by 16% [42]. Most concerning, these levels are well within current EPA standards for airborne particulate matter.

All-cause mortality was associated with gestational exposure to total suspended particulate matter in a birth cohort of nearly 360,000 infants born in Seoul, South Korea between 2004 and 2007 [41], using Cox proportional hazards models with time-dependent covariates, adjusting for sex, gestational age, maternal age, season of birth, maternal education, and heat index. Finally, investigators in Switzerland directly examined the effect of prenatal exposure to air pollution on respiratory physiology in an unselected birth cohort of term infants without chronic respiratory disease. At 5 weeks of age, prenatal exposure to PM₁₀ was associated with higher minute ventilation, 24.9 ml/min per µg/m³ of PM₁₀ [43].

Air pollution negatively impacts lung growth

Numerous studies using animal models have demonstrated interrupted lung development due to exposure to pollutants, reviewed elsewhere [7]. These findings are reflected in several clinical studies that showed exposure to air pollution was associated with impaired lung growth in children that may be permanent.

Two decades ago the Second National Health and Nutrition Examination Survey established an association between chronic exposure to air pollution and reduced pulmonary function [5, 44]. In a subsequent large study of fourth-grade children living near Los Angeles, exposures to nitrogen dioxide, acid vapor, and particulate matter were associated with statistically and clinically significant deficits in lung function in fourth-grade children living in twelve cities in metropolitan Los Angeles, after adjustment for sex, race, ethnicity, and pulmonary comorbidities including asthma. At the end of the four-year study period, children in the most polluted communities experienced a 3.4% reduction in forced expiratory volume in one second (FEV₁) compared with children that had the lowest exposures [45]. Moreover, children who spent greater periods of time outdoors were more negatively affected. In a follow-up study, the youngest cohort (8 years) had pulmonary function deficits that persisted into adulthood [45, 46], even after adjustment for potential confounders. Eliminating the communities with the highest and lowest exposures to airborne pollutants did not change the associations, suggesting that extremes did not drive the results. Children who lived in communities with the highest levels of PM_{2.5} were nearly five-times more likely to have abnormal lung function than their peers exposed to the lowest PM_{2.5} levels. There was an independent relationship between living near a freeway and reduced lung function [47]. In an interesting corollary study, children who moved away from sites where they were regularly exposed to high PM₁₀ levels to communities outside of Southern California with lower airborne particulate levels had improved lung function. Conversely, children who moved from lower to higher PM₁₀ exposure areas had worsening lung function [48]. Other studies have shown that prolonged exposure to pollutants is associated with impaired lung growth in children [49, 50]. Long-term ozone exposure during childhood was associated with reduced FEV₁ in late adolescence [51]. These data show that limiting exposure to pollutants can prevent persistent pulmonary function decline and potentially reverse damage from earlier exposures, strong arguments for tightening, not weakening, air quality regulations.

Air pollution and respiratory illnesses in children

Children of all ages are at risk for suffering respiratory symptoms related to air pollution exposure, but children with chronic respiratory diseases including asthma may be particularly at risk. Although asthma is a multi-factorial disease, evidence that exposure to airborne pollutants is associated with asthma inception, asthma exacerbations, and severity of asthma symptoms will be reviewed below. This is an important public health concern, as asthma is one of the most common chronic childhood conditions and its incidence is steadily increasing, now affecting 9.6% of US children [52]. Even higher rates are seen among poor and minority children, with 17% of African-American children affected. Several studies have demonstrated an association between pollution and the development of asthma [53–

56]. In a study that recruited over 3,000 healthy children in middle and high school, subjects who played three or more organized sports while living in communities with high ozone exposures had a far greater risk of developing asthma compared with children who did not participate [57]. A new, large cohort of children entering kindergarten and first grade found that the risk of new onset, physician diagnosed asthma increased with traffic-related exposure at home and at school [53]. Even low levels of ozone exposure have been associated with wheezing symptoms in infants [58]. The likelihood of wheezing in infants who live in non-smoking homes in southwestern Virginia increased 37% for every interquartile-range increase in ozone exposure. The effect was even stronger in infants born to mothers with asthma. In these investigations, the mean maximum 8-hour average of ozone exposure was 54.5 parts per billion (ppb), well below past and even current EPA standards. These were not isolated findings; in a separate study, during which ozone levels were also below EPA standards, exposure to air pollutants was associated with increased respiratory symptoms in children with asthma [59] using co-pollutant regression models.

Children with asthma residing in urban communities experience particularly high rates of asthma and associated morbidity [60]. Exposure to high levels of ambient air pollution may contribute to this disparity [61, 62]. In a large study of predominantly African- and Hispanic-American children with asthma living in seven urban low-income areas, higher five-day averages of nitrogen dioxide and PM_{2.5} were associated with lower lung function and increased respiratory symptoms. Others have demonstrated associations between ambient air pollution levels and emergency room use and hospitalization for asthma [63–65]. Using data from a large longitudinal study of the health effects of air pollutants, investigators examined short-term associations between ambient air pollution levels and emergency room visits for wheezing among children and adolescents in the metropolitan Atlanta [63]. In analyses of over 90,000 visits, three-day averages of ozone, nitrogen dioxide, carbon monoxide, sulfur dioxide, and multiple components of PM_{2.5} were seasonally associated with emergency room visits for asthma. In a retrospective birth cohort study of children born in New York State between 1995 and 1999, a rise in mean ozone concentration of just 1 ppb was associated with a 22% increase in risk of hospital admission. In another large study, ozone and PM_{2.5} exposures were associated with asthma admissions in school-age children in New York City [65], after adjusting for weather, seasonal and temporal trends, and weekday. These data indicate that elevated ambient air pollution concentrations in ranges consistent with current EPA standards contribute to burdensome and costly severe asthma exacerbations in children.

Although fewer studies have examined the association between air pollution and other lung diseases, exposure to elevated concentrations of particulate matter and ozone are associated with an increased risk of exacerbations and reduced lung function in individuals with cystic fibrosis [66].

The economic costs of air pollution

The Clean Air Act Amendments of 1990 included requirements that the EPA perform periodic benefit-cost analyses of the impact of the regulations. To date, three in-depth analyses have been performed. The first was a retrospective analysis that estimated the

benefits and costs of the initial Clean Air Act regulations before 1990 by comparing the differences between historical environmental and economic conditions observed with the Clean Air Act in place and hypothetical scenarios that projected economic and environmental conditions without the regulations in place. These analyses determined that the Clean Air Act regulations prevented 205,000 premature deaths and avoided millions of other non-fatal illnesses, including severe cardiac and respiratory diseases. When expressed in economic terms, the benefits were estimated as much as \$50 trillion as compared with implementation costs of \$523 billion [67].

Two later reports were designed to estimate the incremental direct benefits and costs of the Clean Air Act Amendments as compared with the initial Clean Air Act standards using a design fundamentally similar to the initial analysis with updated modeling techniques. The first prospective analysis was released in 1999 [68], and a follow-up prospective study estimating benefits and costs through 2020 was published earlier this year [69]. Through 2020, Clean Air Act Amendments regulations will prevent 2.4 million asthma exacerbations, 135,000 hospital admissions, and over 230,000 premature deaths. When expressed in economic terms, the report estimates that even though \$65 billion will be spent by 2020 to comply with new regulations, the US will reap more than \$2 trillion in health savings.

Discussion

We have come a long way since the catastrophic Donora Smog. We know that levels of air pollution below current standards are unhealthy, particularly for vulnerable populations, such as children with respiratory diseases [59, 62, 63, 70]. In 2004, the American Academy of Pediatrics issued a statement that argued current standards for several critical pollutants were inadequate and should be reevaluated [71]. The recent EPA recommendation to strengthen ozone standards was based on these and other valid concerns from the scientific community, and supported by the research cited in this manuscript. The effect of airborne pollutants on our children is not a national political problem -- it is a national *health* problem. Indeed, the cost of air pollution to pediatric health and our country's economic future is far too great to ignore.

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List of Abbreviations

PM₁₀	Particulate matter with diameter between 2.5 and 10µm
PM_{2.5}	Particulate matter with diameter less than or equal to 2.5µm
FEV₁	Forced expiratory volume in 1 second
IUGR	Intrauterine growth retardation
SIDS	Sudden Infant Death Syndrome

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Table 1

Selected federal legislation related to air pollution.

Year	Legislation	Notes
1955	Air Pollution Control Act	First federal legislation related to air pollution, authorized funds for research
1963	Clean Air Act	First legislation involving air pollution control, authorized program in the U.S. Public Health Service
1967	Air Quality Act	Authorized enforcement proceedings, expanded ambient monitoring studies and stationary source inspections
1970	Clean Air Act Amendments of 1970	Comprehensive regulations to limit emissions from industrial and mobile sources including a requirement to reduce automobile emissions by 90% by 1975, expanded enforcement authority
1971	Creation of the US EPA	Authorized by the National Environmental Policy Act, created to implement requirements of the CAAA of 1970
1977	Clean Air Act Amendments of 1977	Provisions were added to prevent deterioration of air quality in geographic areas that were not meeting air quality standards.
1990	Clean Air Act Amendments of 1990	Increased authority and responsibility of the federal government, targeting acid rain, urban air pollution, toxic air emissions, and ozone depletion

Table 2

Criteria pollutants.

Pollutant	Source	Averaging Time	Level
Carbon Monoxide	Traffic	8 hour	9 ppm
		1 hour	35 ppm
Lead	Metal processing industries	Rolling 3 month average	0.15 µg/m ³
Nitrogen Dioxide	High temperature combustion	1 hour	100 ppb
		Annual	53 ppb
Ozone	Sunlight on oxidants emitted by engines and industry	8 hour	0.075 ppm
Particulate Matter_{2.5}	Combustion processes, smoke, haze	Annual	15 µg/m ³
		24 hour	35 µg/m ³
Particulate Matter₁₀	Dust, soil, crushing and grinding processes, near roadways	24 hour	150 µg/m ³
Sulfur Dioxide	Industrial processes, especially coal	1 hour	75 ppb

Table 3

Health effects of air pollution on children.

Health Effect	Selected References
Altered lung development	5–7
Pulmonary inflammation	5,11–23
Pulmonary oxidative stress	11–14,24–26
Epigenetic changes	29,30
Low birth weight	31–34, 36–37
Infant mortality including SIDS	38–42
Impaired lung function	5,43–51
Asthma development and exacerbations	53–65
Cystic fibrosis exacerbations	66