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Assessing the Impact of Air Pollution on Childhood Asthma Morbidity: How, When and What to Do

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Abstract

Purpose of Review—Exposure to air pollutants is linked with poor asthma control in children and represents a potentially modifiable risk factor for impaired lung function, rescue medication use, and increased asthma-related healthcare utilization. Identification of the most relevant pollutants to asthma as well as susceptibility factors and strategies to reduce exposure are needed to improve child health.

Recent Findings—The current available literature supports the association between pollutants and negative asthma outcomes. Ethnicity, socioeconomic status, and presence of certain gene polymorphisms may impact susceptibility to the negative health effects of air pollution. Improved air quality standards were associated with better asthma outcomes.

Summary—The link between air pollution and pediatric asthma morbidity is supported by the recent relevant literature. Continued efforts are needed to identify the most vulnerable populations and develop strategies to reduce exposures and improve air quality.

Keywords

pollution; asthma; morbidity; exposure; lung function

Introduction

Asthma is the most common chronic illness of childhood, affecting over 6 million U.S. children and resulting in over 136,000 pediatric hospitalizations in 2010 (1). Multiple factors influence asthma morbidity including access to healthcare, adherence to medications, and health literacy. Allergic T helper type 2 (T_H2)-predominant asthma is the most common endotype in children and is mediated by immunoglobulin E (IgE), eosinophils, and T_H2 cytokines such as Interleukin (IL)-4, 5, and 13. Though asthma therapies targeting these components of T_H2-predominant inflammation have been successful for reducing features of asthma, they often do not completely eliminate asthma symptoms or prevent exacerbations, indicating that other non-T_H2 factors are involved in perpetuating airway inflammation and

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must be considered. Environmental exposures to indoor and outdoor pollutants influence asthma severity and control, and may play a role in asthma inception. Children are disproportionately affected by the negative health effects of air pollution. We have focused this review on the most relevant indoor and outdoor pollutant exposures in the context of pediatric asthma, including a discussion of susceptibility factors and strategies for reducing the impact of pollutant exposures on asthma morbidity in children.

How do pollutants influence childhood asthma morbidity?

Exposure to air pollutants has been consistently linked with poor asthma control in children, with numerous studies showing reduced lung function (2**–7**)(Table 1) and increased rates of rescue medication use, emergency department visits, and hospitalizations for asthma exacerbation (8*–13)(Table 2). In this section, we discuss the most recent evidence for the effects of air pollutants on pediatric asthma.

Tobacco smoke—Environmental tobacco smoke is one of the most prevalent air pollutants affecting children, with a staggering 40% of the world's children exposed to second hand smoke (SHS) from their parents smoking in the home (14). SHS exposure is associated with greater frequency of asthma symptoms, decreased responsiveness to inhaled corticosteroids (15), more severe asthma attacks (16), increased risk for asthma-related ED visits or hospitalization (16), and increased length of hospitalization (17, 18). A recent survey of Texas Children's Health Plan members found that children of mothers who smoke were more likely to report a diagnosis of asthma, filled rescue inhaler prescriptions more often, and had more asthma-related emergency department (ED) visits compared to children whose mothers did not smoke (8*). Minority children may be at even greater risk. A large study of 30,000 children with asthma in Connecticut found that the odds of being exposed to SHS were twice as high in black and Latino children than in Caucasians (19).

Traffic related air pollution—Both prenatal and postnatal exposures to traffic related air pollution (TRAP) have been shown to negatively affect lung development (2**, 20–23) and are linked to an increase in prevalence of asthma and allergic disease (24–26). TRAP encompasses a collection of gases (nitrogen dioxide [NO_2], sulfur dioxide [SO_2], benzene) and particulates (particulate matter <2.5 μm [$PM_{2.5}$] or <10 μm [PM_{10}], black carbon) associated with fossil fuel combustion. Nitrogen dioxide (NO_2) is increasingly recognized as an important indoor and outdoor pollutant associated with development of atopy, current wheezing, and lower forced expiratory volume in 1 second (FEV_1) (27). NO_2 is generated by automobiles and gas heaters and cooking ranges. Recent studies have shown a link between NO_2 exposure and reduced lung function (3*, 4*), increased need for rescue medications (28), and elevated risk and severity of asthma exacerbations (9, 11, 29). Gaffin et al reported that for every 10 ppb increase in classroom NO_2 concentration, there was a 5% reduction in FEV_1/Forced Vital Capacity (FVC) ratio; classroom NO_2 was inversely associated with Forced Expiratory Flow at 25–75% of lung volume (FEF_{25-75}) in this study (3*). Prolonged NO_2 exposure was associated with a 100 mL reduction in growth in FEV_1 over an 8 year period (20) and with severe asthma exacerbations in children (defined as requiring hospitalization or emergency room visit) (23). A systematic review examining the effects of air pollution on asthma exacerbations reported similar findings (21). Within the

Detroit urban area, 46% of air pollution-related asthma hospitalizations were attributed to NO_2 exposure (29), with greater disease burden amongst Latino and low income populations. Similar to NO_2, SO2 exposure has been linked to reductions in FEV_1 and FVC (5) and an increased rate of asthma-related ED visits (10, 30).

Particulate matter exposure is implicated in multiple cardiopulmonary disease processes and is associated with premature death (11, 29). PM_{10} exposure during the first year of life was associated with a reduction in FEV_1 of 60 mL by age 8 (23), and PM_{10} near the home was associated with increased risk of asthma-related hospitalization (31). Similarly, long term $PM_{2.5}$ exposure was associated with severe asthma exacerbations (30) and positively correlated with number of wheezing episodes in children 2–10 years of age (32). PM emissions from burning biomass are associated with increased risk for cough, shortness of breath, chest tightness (32), wheezing (33) and other respiratory symptoms. Even short-term PM exposures can be harmful, with one study showing a positive correlation between daily PM concentration and pediatric asthma-related hospital visits (12).

Ozone—Nitrogen oxides and volatile organic compounds react in the presence of sunlight to generate ozone (O_3), a by-product of photochemical smog. Both acute and long term exposure to O_3 is associated with negative pulmonary health effects including lower FEV_1/FVC ratio (4*), increased asthma-related ED visits (30, 33) and hospital admissions (13), and more severe asthma exacerbations (9). Short term O_3 exposures during the months of August and September were positively associated with hospital admission for asthma among children 5–14 years in Texas, even after controlling for pollen and viral infections (13). Children are particularly susceptible, with a nearly 10% increase in risk of ED visits for asthma for each interquartile range (IQR) increase in O_3, with the largest effect found in 6–19 year olds (33).

What factors increase susceptibility of children to pollutant-induced respiratory disease?

A recent WHO air quality model estimates that 92% of the world's population are exposed to annual mean levels of $PM_{2.5}$ in excess of WHO air quality guidelines (10 $\mu g/m^3$) (34). Not all persons are affected equally by these exposures. Factors such as age at exposure, ethnicity, socioeconomic status, gene polymorphisms, and presence of atopy may play a role in determining susceptibility to pollutant-induced respiratory disease.

Prenatal, early life, and ongoing childhood exposure to ambient air pollutants has been associated with increased risk for pulmonary disease. Significant research effort has been devoted to identification of factors that increase susceptibility to pollutants, with much interest in the effects of exposure during the perinatal period. Prenatal exposure to tobacco smoke was associated with reduced lung function in the teen years (35), but since postnatal SHS exposure often occurs with prenatal tobacco exposure, it has been difficult to assess the impact of either alone (36). To address this problem, a survey of 6–11 year olds performed spirometry and measured serum cotinine to determine current tobacco smoke exposure. Current tobacco smoke exposure was not significantly associated with airflow obstruction, but self-reported prenatal tobacco smoke exposure was associated in asthmatic children only. These findings suggest that children are most vulnerable to the effects of tobacco smoke in

the perinatal period (36). Prenatal and early life exposures to TRAP have been linked with respiratory symptoms (37), reduced lung function (2**) and development of childhood asthma (38). A potential mechanism for this effect was reported by Gruzieva et al, who found that prenatal NO_2 exposure was associated with differential methylation of antioxidant and anti-inflammatory genes in cord blood, which could potentially influence the inflammatory response to pollutant-induced lung damage (39*). Pollutant exposure, even within currently accepted air quality standards, can have an impact on lung development in early life (6*). Rice et al found that recent exposure to even low levels of ambient air pollutants $PM_{2.5}$ and black carbon and living close to a major roadway were associated with reduced lung function in mid-childhood, with those living less than 100 meters from major roads having a FEV_1 5.7% lower than children living more than 400 meters from major roads (6*). O_3 differentially influences child health, with children at higher risk for hospital admission with increases in ambient ozone concentration compared to adults (40).

Minority and low-income populations may be at increased risk for negative health outcomes from pollutant exposure. Early life particulate exposures were associated with reduced lung function in Latino and African American children with asthma, with a 5 $\mu g/m^3$ increase in average lifetime $PM_{2.5}$ associated with 7.7% decrease in FEV_1 (7**). Others have replicated these findings, demonstrating a greater impact of TRAP and ozone on lung function (5) and respiratory disease (41) in low income groups. A study of the environmental burden of disease attributable to air pollution in the city of Detroit found that Latino populations are disproportionately affected (29). Some of this effect likely results from poor housing conditions and living in closer proximity to major roadways. Bowatte et al reported that living less than 200 meters from a major road was associated with current wheeze (aOR, 1.38; 95% CI, 1.06–1.80) and atopy (aOR, 1.26; 95% CI, 0.99–1.62), and lower prebronchodilator and postbronchodilator FEV_1 (27). In addition, black and Latino children are twice as likely to be exposed to SHS than white children; children on public insurance were three times more likely to have SHS exposure (19).

Gene variants may also convey susceptibility, even to relatively low levels of pollutants. Children with a particular polymorphism in the tumor necrosis factor α gene had more significant reductions in lung function after SO_2 exposure (42). Polymorphisms in the antioxidant Glutathione S-Transferase (GST) genes have been studied as potential modifiers of response to pollutants (43, 44). One study found a significant interaction between *GSTT1* null genotype and living less than 200 meters from roadways for atopy (OR 2.66; 95%CI, 1.3–5.43), house dust mite sensitization (OR 2.59; 95%CI, 1.32–5.05), current wheeze (OR 3.00; 95%CI, 1.48–6.1), and current asthma (OR 2.92; 95%CI, 1.43–5.95) (27). The presence of atopy may also impact response to environmental pollutants in children. Cockroach-sensitized atopic children exposed to black carbon showed demethylation of proinflammatory genes including interleukin-4, and this was associated with higher FeNO, a biomarker of eosinophilic airway inflammation (45). Patients with a history of allergic rhinitis or atopic dermatitis were at greater risk of asthma-related ED visit with increases in PM_{10} exposure (33).

What can be done to reduce childhood asthma morbidity related to air pollution?

Indoor and outdoor pollutants are important modifiable risk factors for poor asthma control in children. Legislative efforts such as banning smoking in public spaces can be effective strategies for reducing the impact of this common pollutant on child health. Indoor tobacco legislation was associated with a fall in asthma-related ED visits in children in Washington D.C (adjusted rate ratio 0.83; 95%CI, 0.82–0.85) (46). However, these public smoking bans do not address the risks associated with parental smoking within the home. Faber et al published a systematic review of the benefits of WHO tobacco control policies on child health (8*), including smoke-free legislation, smoking cessation programs, and taxation of tobacco products. They found that studies evaluating smoke-free legislation demonstrated a reduction in pediatric hospitalizations for asthma and respiratory infections. Smoking cessation programs were not associated with significant changes in pediatric asthma-related ED visits but did correlate with a decrease in ED visits for upper respiratory tract infections (47). Tobacco taxation was associated with no significant change in ED visits for asthma but a decrease in ED visits for lower respiratory tract infections (47).

Home interventions for improving indoor air quality have been studied for their impact on respiratory health. A study of asthmatic children living in homes with wood-burning stoves examined the impact of improved stoves and air filters on child health (48). They found no change in asthma-related quality of life with either intervention, but addition of air filters was associated with a reduction in indoor $PM_{2.5}$ levels and diurnal peak flow variability, which the authors used to approximate airway hyperreactivity.

A prior study of antioxidants in children with asthma found some potential protective anti-inflammatory effects against ambient air pollutants, whose harmful effects are thought to be mediated in part by generation of reactive oxidants (49). A recently published study evaluated children from the Swedish BAMSE birth cohort and found a significant inverse association between dietary antioxidant intake and sensitization to allergens; however, this association was strongest in children with low exposure to TRAP, suggesting that in children exposed to higher amounts of air pollutants, dietary antioxidants may be insufficient to provide protection (50).

Others have attempted to harness the popularity of technology-based interventions for health into efforts to detect and reduce pollutant exposure. In one study, children wore sensors equipped with GPS that detected PM levels in real time in the home, during transit and in the school. Exposure to ≥ 5 $\mu g/m^3$ of PM during commute to school was associated with significantly higher urinary LTE_4 excretion and with albuterol use, more so than in the home or school environments (51*). Norwegian researchers implemented a small, inexpensive sensor for measuring real-time outdoor air quality at schools, allowing teachers to plan outdoor activities to limit exposure to air pollutants (52).

Multiple studies around the world have demonstrated benefit to child health with improved air quality. Guerrirero et al determined that reduction in outdoor NO_2 exposure near London schools could result in an average of 82 fewer asthma exacerbations per year per school (53). A longitudinal cohort study of U.S. children from 1993 to 2012 found a significant association between decreases in ambient air pollutants concentrations in California and

reduction in cough and congestion symptoms in children with and without asthma (54*). A 3.6 ppb decrease in ambient air O_3 was associated with an OR of 0.66 (95% CI, 0.50–0.86) for bronchitic symptoms, with a 16% reduction in prevalence. Similar findings were reported for a 5.8 μg/m^3 reduction in PM_{10} [OR 0.61 (95% CI, 0.48–0.78), 18.7% decrease in prevalence], a 6.8 μg/m^3 reduction in $PM_{2.5}$ [OR 0.68 (95% CI, 0.53–0.86), 15.4% decrease in prevalence], and a 4.9 ppb reduction in NO_2 [OR 0.79 (95% CI,0.67–0.94), 10.1% decrease in prevalence]. Reduction in $PM_{2.5}$ level associated with fewer asthma-related ED visits in another study (30). Ultimately, reducing the burden of pollutant-induced respiratory disease will require broad policy changes that reduce the burning of fossil fuels, increase urban green space, and mitigate the effects of climate change.

Conclusions

In this review, we have summarized the most recent scientific findings regarding the impact of air pollution on asthma morbidity in children. Air pollution clearly impacts child health, contributing to increased asthma symptoms, rescue medication use, ED visits and hospitalizations, resulting in significant social and economic burden. Further study is needed to identify factors that increase susceptibility of children to pollutants and poor asthma outcomes. Reducing exposure to air pollutants has been associated with improved respiratory health. Coordinated efforts between scientists, healthcare workers, and local, state, and federal governments are needed to successfully implement policy changes that will reduce air pollutant exposures and improve the health of children.

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Key Points

- Children are more susceptible to the negative health effects of pollutants than adults, and pollutant exposure has been linked with reduced lung function and increased asthma-related healthcare utilization.
- Timing of exposure, genetic factors, atopy, and socioeconomic status are all factors that may increase susceptibility to air pollution effects in children with asthma.
- Improvements in air quality have been associated with reduced respiratory symptoms and decreased asthma-related healthcare visits in children, though even low levels of pollutant exposure can still have negative health effects.

Table 1

Findings from recent publications examining the effects of air pollution on lung function

Reference	Study Design	Age (years)	Exposure Assessment	N	Pollutants	Outcomes	Notes
Schultz et al, 2016 (2**)	Prospective cohort	16	Average pollutant levels calculated from emissions and Gaussian disper-sion model	2,278	Nitrogen oxides (NO_x) and PM_{10}	NO_x and PM_{10} exposures in infancy were negatively associated with FEV_1 at age 16	Exposure to high levels of TRAP during first year of life associated with higher OR for FEV_1 less than lower limit of normal
Gaffin et al, 2017 (3*)	Cross sectional	4–13	Passive sampling of classrooms for 1 week periods twice a year	188	NO_2	NO_2 levels highly associated with airflow obstruction	For every increase of 10 ppb in NO_2, there was a 5% decrease in FEV_1/FVC
Ierodiakonou et al, 2016 (4*)	*Post hoc* analysis of CAMP study	9 ± 2 (Median and SD)	Daily average levels linked to postal code of residence	1,033	CO, O_3, NO_2, SO_2	Negative correlation between pollutant concentrations and FEV_1, FVC, FEV_1/FVC and PC_{20}	
Cakmak et al, 2016 (5)	Cross sectional	11 (Mean)	Yearly average city measurements; land regression model to account for neighborhood	1,528	NO_2, SO_2, $PM_{2.5}$	Significant reduction in FEV_1 for every IQR change in NO_2 in low income group; reduction in FVC for every IQR change in SO_2 in group with less than high school education	Socioeconomic status may modify effect of pollutants on lung function
Rice et al, 2016 (6*)	Prospective cohort	7.9 ± 0.8 (Mean and SD)	Distance from home to nearest roadway (for TRAP); aerosol optical depth (AOD) measure-ments (for $PM_{2.5}$)	614	$PM_{2.5}$, black carbon (BC)	Long term exposure to PM2.5 and BC were negatively associated with FVC and FEV_1, even after passage of strict regulations on air quality. FEV_1/FVC and bronchodilator response were not associated with pollutant exposure	Exposure to even relatively low amounts of pollutants was negatively associated with lung function
Neophytou et al, 2016 (7**)	Case-control	12.6 ±3.2 (GALAII) 13.7 ± 3.5 (SAGE II)	Daily average levels accounting for distance of residence from monitoring stations	1,449 Latino 519 African American	$PM_{2.5}$, PM_{10}, NO_2, O_3, SO_2	5 μg/m^3 increase in lifetime $PM_{2.5}$ lifetime exposure correlated with a 7.7% decrease in FEV1 in minority populations	Genotyping performed to estimate global genetic ancestry; No significant interaction between genetic ancestry and the association between pollutant exposure and lung function

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Table 2

Findings from recent publications examining the effects of air pollution on asthma outcomes

Reference	Study Design	Age (years)	Exposure Assessment	N	Pollutants	Outcomes	Notes
Farber et al, 2016 (8*)	Cross sectional	<18	Survey	22,470	Secondhand smoke	Significant association between SHS and ED visits in children whose mothers smoke	
Tetreault et al, 2016 (9)	Retrospective cohort	<13	Daily average levels linked to postal code of residence	162,752	NO_2, $PM_{2.5}$, O_3	Positive association between time-dependent exposure to pollutants and asthma exacerbation frequency	Stronger association with long term exposure than exposure at birth.
Schvartsman et al, 2017 (10)	Ecological time-series	<19	Daily average city-wide levels of pollutants	20,958 visits	O_3, CO, NO_2, SO_2, PM_{10}	Increase in PM_{10} and SO_2 daily levels positively correlated with number of ED visits for asthma; 7-day cumulative effect of PM_{10} and SO_2 on ED visits was much higher	Cumulative exposure had much larger effect on asthma-related ED visits than did same day exposure
Orellano et al, 2017 (11)	Systematic review	0–80	Multiple	267,415	NO_2, SO_2, PM_{10}, $PM_{2.5}$, CO, O_3	Subgroup analysis showed significant association between NO_2, SO_2, and $PM_{2.5}$ and pediatric asthma exacerbations	
Ding et al, 2017 (12)	Case crossover	0–18	Daily average city-wide levels of pollutants	2,507 visits	PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO, O_3	Increase of 10 $\mu g/m^3$ in PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO were positively associated with asthma-related hospital visits	No association between asthma-related hospital visits and O_3
Goodman et al, 2017 (13)	Time-series analysis	5 to >65	Area-specific daily average 8h maximum O_3 concentration	74,824 hospital admiss-ions	O_3	Positive correlation between pediatric asthma-related hospitalization and short-term O_3 exposure	Association was strongest in August and September, correlating with start of school year