

Childhood Origins of Adult Lung Disease as Opportunities for Prevention



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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

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Learning objectives

1. To define early-life exposures and risk factors for lung disease in adulthood.
2. To identify interventions that have been shown to improve respiratory health across the lifespan.

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Prenatal and childhood exposures have been shown to impact lung development, lung function trajectory, and incidence and prevalence of respiratory disease. Early life may serve as a window of susceptibility to such exposures, with the potential to influence lifelong respiratory health. Risk factors encountered in early life with potentially durable impact on lung health include prematurity, respiratory viral illness, allergen sensitization and exposure, tobacco use and exposure, indoor and outdoor pollution, diet, and obesity. These exposures vary in the extent to

which they are modifiable, and interventions aimed at reducing harmful exposures range from individual-level behavior modification to policy initiatives implemented to promote population health. For many exposures, including tobacco-related exposures, multilevel interventions are needed. Future research is needed to provide insight as to early-life interventions to promote optimal lung growth and prevent development of chronic respiratory disease. Clinicians should play an active role, assisting individual patients in avoiding known detrimental exposures including maternal smoking during pregnancy and initiation of active smoking. Clinicians can be empowered by evidence to support policies promoting reduction of population-level risk factors, such as restriction on electronic cigarette sales and legislation to uphold air quality standards, to encourage attainment of maximal lung function and reduce risk of chronic lung disease. © 2020 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology (*J Allergy Clin Immunol Pract* 2020;8:849-58)

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INTRODUCTION

Lung development begins *in utero*, continues through adolescence into early adulthood, and is influenced by a myriad of exposures that impact lung function trajectory and risk of

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Abbreviations used*COPD- Chronic obstructive pulmonary disease**NO₂- Nitrogen dioxide**PM- Particulate matter**PUFA- Polyunsaturated fatty acid**RSV- Respiratory syncytial virus**SHS- Secondhand smoke*

disease.¹ Environmental exposures, adverse dietary intake, and obesity have been linked to impaired lung growth and development, failure to reach normal plateau, risk for childhood asthma, and accelerated decline in lung function after the plateau in early adulthood has been reached—factors that increase risk for subsequent adult asthma and chronic obstructive pulmonary disease (COPD).²⁻⁴ Childhood may represent a period of increased sensitivity to multiple exposures, because of the ongoing development of airways and alveoli, the high proportion of lung surface area relative to a child's overall size, and the activities common among children that influence exposure. Understanding the implications of exposures on respiratory development and risk of subsequent disease that continues through adulthood is critical to developing strategies to promote maximal respiratory health by mitigating harmful exposures and promoting protective ones.

Cohort studies provide unique insights into factors that influence the trajectory of lung growth, the peak of development, and the rate of decline with aging subsequent to early adulthood. Birth cohorts and cohorts beginning in early childhood have shown that early-life exposure to tobacco smoke, early allergic sensitization, low birth weight/nutrition, recurrent episodes of recurrent wheezing, respiratory syncytial virus (RSV) infection, and air pollution exposure are associated with reduced lung growth and lower FEV₁.⁵⁻¹¹ Cohort studies that have assessed factors that predict lung function trajectories from early adulthood to later life have demonstrated that low FEV₁, bronchial hyperresponsiveness, presence of childhood asthma, and active smoking are risk factors for lower peak lung function and accelerated declines in lung function in adulthood, as well as for adult asthma and COPD.¹²⁻¹⁶ These findings suggest that early-life exposures have longstanding potential impacts, and interventions to prevent or mitigate harmful exposures may have durable benefits (Figure 1).

PREMATURITY

Prematurity is a well-known risk factor for reduced FEV₁, childhood wheezing, asthma, and COPD,¹⁷⁻²⁰ and may increase susceptibility to the deleterious effects of respiratory infections and tobacco exposure on the developing lungs.²¹ Moreover, preterm birth disrupts normal lung development because fetal lungs continue to mature through the 38th week of gestation. Lung injury associated with prematurity and subsequent chronic lung disease may arise from intrauterine exposures, such as infections and stress, or from postbirth exposures including mechanical ventilation, oxygen toxicity, steroids, infections, volume overload, and nutritional deficiencies.²¹ Bronchopulmonary dysplasia, defined as the need for supplemental oxygen for 28 days or more postnatal, confers additional risk for lower lung function, asthma, and future COPD.^{22,23} Prevention of preterm birth is complex and

crosses multiple disciplines, but remains a critical step in preventing adverse pulmonary outcomes later in life.

RESPIRATORY INFECTIONS

Birth cohorts have demonstrated that lower respiratory tract infections in infancy and early childhood are associated with lower lung function trajectories.^{5,6,24} In the Tucson Children's Respiratory Study,⁶ those in the low lung function trajectory were twice as likely to have had RSV lower respiratory infection compared with those with normal lung function trajectory. The causal mechanism remains unclear,²⁵ and some studies have suggested a synergistic interaction between early-life infection and exposure to smoking that leads to lower and reduced recovery of lung function during adolescence and early adulthood.¹⁴ Lower respiratory tract infection in early childhood, particularly with RSV or human rhinovirus, has also been implicated as a risk factor for asthma development in childhood and young adulthood^{24,26-28} and increased risk for subsequent COPD.⁴ There are little data on the primary prevention of asthma through vaccination, with a recent live attenuated influenza vaccine study showing no difference in asthma at the age of 3 years,²⁹ and challenges in safe and effective vaccine development for RSV and human rhinovirus persist.^{30,31} Preventive strategies targeting high-risk groups have included studies of the mAb palivizumab for the prevention of RSV infection in preterm infants, which reduced wheezing in the first year of life,³² but did not affect the risk of asthma at the age of 6 years.³³ Although there is no current evidence that vaccination prevents chronic lung disease, vaccination, including the annual influenza vaccine, remains an important component of health care for children at the individual and population levels to reduce respiratory morbidity and mortality.

ALLERGENS

Allergic sensitization is associated with lower lung function in children^{34,35} and adolescents,³⁶ with polysensitization decreasing lung growth from the age of 3 to 11 years.³⁷ Sensitization, in particular to perennial indoor allergens such as cat, dog, cockroach, mouse, house-dust mite, and molds, is extensively associated with childhood wheezing and the subsequent risk of asthma.^{36,38-42} Early allergic sensitization appears to confer a higher risk for asthma development; sensitization to aeroallergens in the first year of life is strongly associated with asthma at the age of 6 years,^{26,41,43} and aeroallergen sensitization at the age of 3 years is associated with asthma in adolescence.⁴⁴ Multiple studies demonstrate a synergistic relationship between allergen sensitization and virus-associated wheezing in the development of asthma.^{26,45-47} Although primary prevention of allergic sensitization is difficult, known protective factors include certain bacterial exposure, living on a traditional farm, and increased number of siblings.⁴⁸⁻⁵¹ In allergen-sensitized children with rhinitis, there is evidence that allergen immunotherapy may prevent the development of asthma,^{52,53} with both US and European guidelines recommending the consideration of allergen immunotherapy for primary asthma prevention.^{54,55} In addition, there is a current study underway that is examining the use of omalizumab for the primary prevention of asthma in children aged 2 to 3 years with a history of wheezing, allergic sensitization, and a first-degree relative with asthma or allergy.⁵⁶

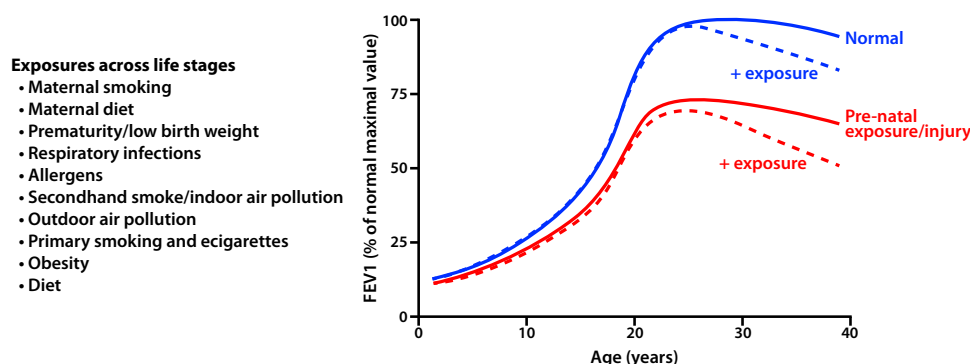


FIGURE 1. Environmental exposures and lung function across the lifespan.

Early allergen exposure to indoor allergens has been associated with asthma development,⁵⁷⁻⁶¹ with potential implications for lung health in adulthood, though in total the data demonstrate inconsistent directionality. Recent observational data from a high-risk urban cohort actually describe an inverse association between exposure to mouse, cockroach, and cat in the first 3 years of life and risk of asthma at the age of 7 years,⁶² and multiple systematic reviews looking at the association between cat and dog exposure and asthma development have mixed results⁶³⁻⁶⁵; this may be in part due to microbial exposures associated with pet ownership. Studies aimed at primary asthma prevention through allergen avoidance also yield inconsistent results,⁶⁶⁻⁷¹ with those demonstrating a reduction in asthma taking a multifaceted approach to allergen avoidance, including dietary measures.⁷⁰⁻⁷² Currently, there are no specific recommendations regarding early allergen exposure avoidance for asthma risk reduction.

There is emerging evidence that intervening on allergen exposure may improve lung function growth in allergen-sensitized patients with asthma. A recent multicenter study found that reduction of mouse allergen exposure among mouse-sensitized urban children and adolescents with asthma was associated with greater FEV₁ growth over 1 year compared with those who did not experience allergen reduction, suggesting that allergen exposure reduction may alter lung function trajectory in allergen-sensitized patients with asthma.⁷³ Further long-term studies are needed to see whether this improved lung function growth is sustained over time, translating to adulthood, and whether similar results are seen in other populations and with other allergens.

TOBACCO SMOKE

Maternal smoking during pregnancy is a modifiable determinant of childhood and adult respiratory health, yet up to 75% of women who smoked before becoming pregnant continue to smoke throughout pregnancy.⁷⁴ Prenatal smoke exposure is associated with abnormal lung development, lower lung function at birth and into adulthood, respiratory infections, increased incidence of wheezing and asthma, and epigenetic changes.⁷⁵⁻⁸⁶ Maternal smoking during pregnancy is also the largest preventable cause of preterm birth, an independent risk factor for abnormal lung development.⁸⁷ A 2012 systematic review of 79

studies looking at prenatal and postnatal smoke exposure in children implicates maternal smoking during pregnancy as having the strongest effect on incident childhood asthma (85% increased odds)⁸⁰ and evidence suggests that these effects may persist into adulthood.⁸³

Smoking cessation programs targeting pregnant women and antismoking legislation can be effective strategies to reduce the number of women who continue to smoke during pregnancy.^{88,89} Nicotine replacement therapies are effective in promoting smoking cessation in late pregnancy⁹⁰; however, nicotine is also known to be associated with adverse pregnancy outcomes.^{75,78,79} Tailored strategies to achieve smoking cessation that balance risks and benefits, including behavioral and US Food and Drug Administration–approved pharmacotherapy, are particularly needed for pregnant women who smoke.⁹¹

Secondhand smoke

Secondhand smoke (SHS) exposure throughout childhood is linked to lower lung function in childhood and adulthood, wheeze at younger than 2 years, and increased risk of asthma.^{75-78,80,85,92} The effects of SHS exposure in childhood persist into adulthood, with increased risk of wheeze and lower lung function observed in adults up to the age of 44 years.^{6,7,92,93} A prospective study that followed more than 2500 children over 6 decades from the age of 7 to 53 years with spirometry demonstrates that parental smoking during childhood is a determinant of low lung function trajectories, low lung function in adulthood, development of COPD, and asthma-COPD overlap.^{5,94} Vulnerable populations with the highest prevalence of SHS exposure include children who are younger than 11 years, non-Hispanic blacks, living below the poverty line, and living with nonhomeowners in apartments and multiunit buildings.⁹⁵⁻⁹⁸ Because maximal lung function during early adulthood is a determinant of asthma and COPD,^{12,99-101} reduction of SHS exposure during childhood, with special attention to vulnerable populations, is an opportunity to reduce chronic lung disease.

Policies aimed at reducing SHS exposure demonstrate respiratory health benefits. A meta-analysis including studies from North America and Europe investigating the implications of smoke-free legislation suggests a 10% postlegislation reduction in preterm birth rates and pediatric hospital admissions for asthma, known risk factors of adult asthma, with preterm birth also being a risk factor for COPD.¹⁰²⁻¹⁰⁴ In expanding efforts, cities and

municipalities continue to increase smoking bans in public places¹⁰⁵ and in February 2017, the US Department of Housing and Urban Development implemented a smoking ban in public housing.¹⁰⁶ Clinicians can supplement policy efforts with individual counseling, focusing efforts on promoting smoke-free homes and cars.¹⁰⁷

Active smoking

Cigarette smoking in adolescence impedes the final stages of lung growth, is associated with airflow obstruction among 10- to 18-year-old smokers,¹⁰⁸ and accelerated decline in lung function subsequently. There is evidence that active smoking may modify and amplify the detrimental effect of adverse early-life exposures on lung function.¹⁴ Active smoking is strongly associated with the development of asthma.^{2,109-111} Adolescents smoking 7 cigarettes a day for a week and 300 cigarettes or more per year have a 3.9-fold increased risk of new-onset asthma compared with nonsmokers, with those additionally exposed to cigarette smoke *in utero* having an 8.8-fold increased risk of new-onset asthma.¹⁰⁹ Smoking in adolescence and young adulthood is an important risk factor for adult lung disease, including asthma and COPD.²⁻⁴ Primary prevention of smoking as well as smoking cessation in children and adolescents should be a high priority for all providers.^{3,101}

Electronic cigarettes/vaping

Electronic cigarette (e-cigarette) use, also known as vaping, increased a staggering 900% among high school students from 2011 to 2015; e-cigarettes are now the most commonly used tobacco product among teens and young adults.¹¹² E-cigarettes deliver aerosolized nicotine, flavoring, and other chemicals including heavy metals, ultrafine particles, volatile organic compounds, and known carcinogens, and are considered unsafe for children, adolescents, and nonsmokers.^{112,113} E-cigarettes can also be used to deliver marijuana or other illicit drugs. Although marketed to reduce conventional cigarette use, evidence is mixed^{114,115} and e-cigarettes are not approved by the Food and Drug Administration for smoking cessation. E-cigarettes likely present a gateway in adolescence, with multiple studies showing both initiation of and increased conventional cigarette use after first using e-cigarettes.¹¹⁶⁻¹²¹

Because e-cigarettes are a relatively new exposure, there is little known about their long-term respiratory effects. However, there is increasing evidence of alarming acute effects. As of early September 2019, the Centers for Disease Control and Prevention declared a multistate outbreak of severe lung disease and respiratory distress in the setting of e-cigarette use, with several hundred cases of possible vaping-induced lung injury, including reports of irreversible lung damage and fatalities.¹²² A study of e-cigarette use among 11th and 12th graders demonstrated increased acute respiratory symptoms among users,¹²³ raising concern about future adult lung disease risk. The long-term consequences of vaping-induced lung injury are unknown, but likely include adult lung disease, making stringent regulation of e-cigarette advertising and sales to children and adolescents paramount. Public smoking bans should include vaping. Primary care and subspecialty physicians should routinely screen for e-cigarette use, counseling patients and parents of the potential for addiction, lung injury, and uncertain future risks. Parents should be encouraged to refrain from vaping around their

children the same way they are discouraged from smoking around their children.

INDOOR AIR POLLUTION

In addition to SHS, particulate matter (PM) and nitrogen dioxide (NO₂) can come from specific indoor sources, such as cooking and heating. Indoor burning of biomass fuels, which generates both particulate and gaseous pollutants, is associated with low birth weight; increased risk of childhood respiratory infections, which influence lung development^{124,125}; and risk for developing COPD.¹²⁶⁻¹²⁸ Exposure worldwide is often the heaviest for women and their young children related to cooking practices. Although international studies have been the main focus of indoor biomass pollution health effects, there are many areas in the United States where wood and coal are commonly used for fuel and contribute to indoor air pollution.¹²⁹ Studies of children with asthma in the United States have shown an association between PM and NO₂ and increased respiratory symptoms,^{130,131} but studies of long-term effects on lung development are lacking. Interventions, such as clean cook stove interventions in international settings, demonstrate mixed results, and there are challenges related to sustainability and to defining strategies with definitive health benefits.¹²⁵ Air purifier intervention trials conducted in the United States demonstrate improvement in respiratory symptoms, but are often part of multimodal interventions and lack long-term health outcome data.¹³²⁻¹³⁴ Given that individuals spend the overwhelming majority of their time indoors, improving indoor air quality is a potential opportunity to reduce the risk of impaired lung development among children and development of chronic respiratory disease, but studies are needed to provide evidence of long-term health benefits for interventions aimed at reducing the source of pollution and filtering air to reduce the existing pollution.

OUTDOOR AIR POLLUTION

Birth cohort studies and cohort studies of children, collectively monitoring tens of thousands of individuals, demonstrate that outdoor air pollution exposure is associated with impaired lung development.^{8-10,135-139} There is some evidence that prenatal air pollution exposures may influence the development of asthma in early childhood¹⁴⁰ and there is substantial evidence of an association between traffic-related air pollution exposure and risk for development of childhood asthma, including meta-analyses of studies throughout the world.^{141,142}

Outdoor air pollution is regulated under the Clean Air Act, targeting 6 criteria pollutants: PM, NO₂, ozone, sulfur dioxide, carbon monoxide, and lead. Sources of outdoor air pollutants include natural sources (eg, wildfires)¹⁴³ as well as industrial and motor vehicle emissions. As air quality standards have become more stringent over time, reductions in outdoor air pollution concentrations, particularly PM_{2.5} and NO₂, have provided a “natural experiment” to study associated health benefits of the policy initiatives. Studies from southern California have demonstrated that improvements in air quality have been associated with improvements in children’s lung growth, decreases in bronchitic symptoms, and reductions in incident asthma.¹⁴⁴⁻¹⁴⁶ Studies have also demonstrated that reduction in air pollution is associated with an attenuated rate of decline in lung function from early adulthood.¹⁴⁷ Taken together, these findings strongly suggest that maintaining current regulatory standards for air

quality and policy initiatives aimed to improve air quality over time represent an opportunity to improve respiratory health across the life span.¹⁴⁸ Such initiatives include those to mitigate climate change; reduction in fossil fuel emissions has the simultaneous benefit of outdoor air pollution reduction. Air quality monitors and public alert systems to communicate poor air quality days can increase awareness, and individuals, particularly pregnant women and children, should be advised to avoid vigorous activity outdoors on days with poor air quality. These measures may reduce acute exposure, but the effectiveness of such interventions in conferring long-term benefits to reduce chronic pulmonary disease remains unknown.

DIET

Dietary intake and nutritional status during the prenatal period, perinatal period, and early childhood years are associated with consequences for lung development and respiratory health. Maternal malnutrition is associated with impaired early lung development affecting both the airways and parenchyma, though data are largely derived from animal models.¹⁴⁹ Even intermittent episodes of severe acute malnutrition in infancy and early childhood are associated with lower FEV₁ and forced vital capacity, with preserved FEV₁/forced vital capacity ratio.¹⁵⁰ These changes have the biologic potential to impact peak lung growth and thus susceptibility to disease in adulthood; access to adequate quantity and quality of nutritious foods is critical to pediatric, and later adult, lung health.

Epidemiologic investigations demonstrate that dietary behaviors, including longer duration of breast-feeding and choice of healthier foods (ie, the Mediterranean diet pattern and fruit and vegetable intake), are, respectively, linked with improved lung function in childhood and adolescence^{11,151-153} and less asthma/respiratory symptoms¹⁵⁴⁻¹⁵⁷; however, evidence is correlative. Individual micronutrient levels and supplementation (including antioxidant vitamins and supplements such as vitamins C and E, flavonoids, and even folate¹⁵⁸⁻¹⁶¹) demonstrate varying results, perhaps because of intake in combination and/or variability in baseline sufficiency of these vitamins among tested populations. Two micronutrients, vitamin D and omega-3 polyunsaturated fatty acids (PUFAs), carry the weight of positive evidence to date, have been tested in trial populations, and are reviewed here.

Observational evidence supports a role for prenatal vitamin D in childhood wheeze, asthma risk, and lung function, and thus the potential to influence respiratory health in later life. Low vitamin D level in cord blood is associated with early wheezing¹⁶² and respiratory symptoms,^{162,163} and low maternal vitamin D is linked with lower lung function and incidence and prevalence of asthma in childhood.^{164,165} Furthermore, insufficient vitamin D levels in childhood (5-18 years) are associated with lower lung function,¹⁶⁶ and lower vitamin D level is associated with childhood asthma prevalence, severity, and risk of exacerbation.^{167,168} These relationships are supported by biologic plausibility. Vitamin D and its numerous isoforms play a role in immune defense, suppression of inflammatory cytokine production, inhibition of airway smooth muscle proliferation and regulation of fetal lung development, and blockage of molecular pathways involved in airway remodeling.¹⁶⁹⁻¹⁷⁴ Randomized controlled trials provide causal evidence. Vitamin D supplementation in the prenatal period results in reduced risk of wheeze/asthma in childhood.^{175,176} Vitamin D supplementation

in children with asthma leads to reduced exacerbation frequency, and several pediatric supplementation trials suggest that benefit is greatest for children with lower baseline levels.¹⁷⁷⁻¹⁷⁹ Taken together, vitamin D sufficiency, and supplementation in the deficient, has the potential to positively impact early childhood respiratory morbidity and plausibly later adult respiratory health.

Observational studies support a link between low intake of omega-3 during pregnancy and wheeze and asthma in offspring.^{180,181} Omega-3 PUFAs are the precursors of anti-inflammatory molecules known as proresolving mediators, found in the lung and systemic circulation,¹⁸² providing mechanistic rationale for observed associations. A large clinical trial of maternal omega-3 supplementation at 24-week gestation demonstrates a relative risk reduction of 30.7% for asthma/persistent wheeze in the intervention group through the age of 5 years,¹⁸³ with the strongest effect among women with the lowest baseline omega-3 blood levels. A second trial of maternal fish oil (rich in omega-3 PUFAs) supplementation in the third trimester demonstrates lower probability of asthma medication prescription in the first 18 to 19 years of life, though no difference in lung function.¹⁸⁴ A meta-analysis of omega-3 supplement trials in the postnatal and early childhood period (birth to 5 years) failed to demonstrate an association with the risk of asthma,¹⁸⁵ though notably the authors included only 5 of 14 studies identified, in part due to heterogeneity. Individual studies report reduced prevalence of wheeze,¹⁸⁶ circulating inflammatory markers,¹⁸⁷ and variable reduction in asthma severity^{187,188} with supplementation. The weight of the evidence suggests that omega-3 PUFAs are beneficial in the prenatal period, and supports a need for further study of the respiratory benefits in postnatal and pediatric populations.

Nutrient supplementation may also act to mitigate the proinflammatory effects of other exposures outlined in this review. Both higher omega-3 intake and higher serum levels of vitamin D are observationally linked to reduced detrimental effects of indoor air pollution on pediatric asthma symptoms.^{189,190} Although data regarding a primary effect of antioxidant vitamin supplementation on neonatal and pediatric respiratory health are lacking, a randomized clinical trial of vitamin C supplementation (500 mg/d) given to pregnant smokers found that infants of women who received vitamin C supplementation had better lung function and reduced wheezing in the first year of life.¹⁹¹ Vitamin C supplementation may therefore present a harm reduction strategy for infants of pregnant women who continue to smoke, whereas vitamin D and omega-3 intake represent potential targets to reduce pediatric respiratory morbidity due to air pollution exposures, plausibly translating to improved later adult respiratory health.

Although vitamin D supplementation is recommended for deficient children¹⁹² and has demonstrated respiratory benefits, further evidence is needed to support formal recommendations for maternal or child supplementation specific to pediatric and later adult pulmonary health. Future studies are needed to further delineate proposed mechanisms by which diet and nutrients may affect lung growth and development via modification of inflammation/oxidative stress,^{171,182} the microbiome,¹⁹³⁻¹⁹⁵ and body composition/obesity.^{196,197} Inclusion of respiratory outcomes in maternal and pediatric dietary future intervention studies and longer follow-up times would address gaps in the current understanding of dietary interventions and implications for adult disease.

OBESITY

Obesity and body composition, while a potential mediating or modifying exposure within the diet paradigm, also may have an independent effect on asthma morbidity.¹⁹⁶ Childhood overweight and obesity is associated with airway dysynapsis, an incongruence between (slower) growth of the airways relative to the lung parenchyma, which is linked to increased asthma morbidity.¹⁹⁸ Obesity is linked to asthma incidence and asthma morbidity, even within pediatric populations.¹⁹⁹ Overweight and obesity may modify susceptibility to air pollution and tobacco exposure, suggesting that among children at risk for air pollution exposure and obesity, there may be multiple intervention targets to improve lung development and prevent disease.²⁰⁰⁻²⁰² Existing evidence suggests that weight loss interventions may be beneficial for children with asthma, but there is heterogeneity among studies.²⁰³ Bariatric surgery has demonstrated benefit in relieving, and even potentially curing, asthma in adult populations²⁰⁴ and may be a future consideration for intervention in morbidly obese adolescents. In the context of the obesity epidemic, studies are needed to understand the long-term respiratory effects of being overweight and obese; future studies of weight loss interventions would be enhanced by inclusion of standardized respiratory outcomes, and studies designed to specifically quantify the potential synergistic effects of healthy diet and weight loss are needed.

CONCLUSIONS

Early adverse childhood exposures, beginning *in utero*, predispose children and young adults to lower lung function, wheezing, childhood asthma, and pulmonary disease in adulthood, including asthma and COPD. Responding to the science surrounding the respiratory implications of early-life exposures requires a combination of population- and individual-level approaches. Policy change has the potential for broad impact and is a key aspect of limiting deleterious exposures in outdoor and public spaces. However, individual-, family-, and community-level behavior change is essential to maximize benefit. Clinicians must take an active role in educating families and patients regarding the potential immediate and long-term implications of environmental exposures, assisting patients and caregivers in achieving recommendations, and in advocating for optimization of conditions for lung growth and development.

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