using multiple environmental and biological factors. The study reinforced known clinical and demographic associations with early-life wheeze. However, the definition of wheeze phenotypes was largely based on the empirical categorization of the investigators. In addition, further information regarding disease course and outcomes was not available, and future longitudinal studies are necessary to determine the clinical relevance of the identified phenotypes in terms of stability over time and also in predicting severity and treatment response.


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The Burden of Childhood Asthma and Late Preterm and Early Term Births

PURPOSE OF THE STUDY. The goal of this study was to evaluate the association between gestational age at birth and the risk of subsequent development of childhood asthma.

STUDY POPULATION. The study population was derived from a clinical birth database of 45,030 infants born after 22 weeks’ gestation at a university hospital in Finland between 1989 and 2008. Women with live-born infants without asthma served as control subjects.

METHODS. This trial was a retrospective, observational, hospital-based birth case-controlled study in which data on 44,173 women with live-born infants were linked with data from the register for reimbursement for asthma medication for their offspring. Pregnancy factors consisting of 75 background items were recorded during pregnancy. Health care workers added information on pregnancy complications, pregnancy outcomes, and the neonatal period. The main outcome measure was asthma among the infants.

RESULTS. The study found that the risk of asthma was highest in children born before 32 weeks’ gestation compared with control subjects. There was also a significantly higher risk found for those born late preterm (33–36 weeks) and those born early term (37–38 weeks); these 2 groups contributed the most to the extra cases of asthma compared with the reference group of term infants. Delivery at ≥41 weeks was protective against developing asthma. The burden of asthma in offspring was associated mainly with early term deliveries, even though the relative risk of asthma was higher in infants born before 32 weeks. Maternal asthma and male gender had stronger effects on the risk of asthma in offspring born after 37 weeks.

CONCLUSIONS. The risk of asthma was 3.9-fold higher in children born at <32 weeks’ gestation compared with control subjects, and it remained high in those born up to 38 weeks. Delivery after 41 weeks seemed to protect against the development of asthma. The magnitude of the risk decrease depends on gestational age at birth.

REVIEWER COMMENTS. Reduction in risk of asthma development is a key goal of asthma management. This study confirmed previous reports of the association between preterm delivery and asthma in offspring. A novel finding is that the risk is still almost double in those born late preterm and that it remains significant even in those born early term compared with children born at term. This knowledge can help guide the avoidance of iatrogenic early term late preterm deliveries, especially in pregnant women with asthma. A limitation of the study is that prenatal and environmental factors after birth, which are potential risk factors for asthma development in children, were not controlled. In addition, asthma severity was not taken into account.


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Parental Psychological Distress During Pregnancy and Wheezing in Preschool Children: The Generation R Study

PURPOSE OF THE STUDY. The goal of this study was to evaluate the associations of maternal psychological distress during pregnancy with childhood wheezing in the first 6 years of life.

STUDY POPULATION. In this study, 4848 children were evaluated from the Generation R Study, a population-based cohort trial from fetal life onward in Rotterdam, the Netherlands. Subjects were born between April 2002 and January 2006.

METHODS. The Brief Symptom Inventory was used to assess maternal and paternal psychological distress at 20 weeks of gestation and 3 years after delivery. Maternal psychological distress was also assessed at 2 and 6 months after delivery. Information on wheezing was obtained annually at ages 1, 2, 3, and 4 years by using the asthma questionnaire from the International Study on Asthma and Allergy in Childhood, and information on physician-diagnosed (ever) asthma was obtained by using a questionnaire at 6 years.

RESULTS. Of mothers, 7.8% had overall psychological distress during pregnancy. Children had an increased odds ratio (OR) of wheezing overall from 1 to 4 years of life if
born to mothers with overall distress (OR: 1.60 [95% confidence interval (CI): 1.32–1.93]), depression (OR: 1.46 [95% CI: 1.20–1.77]), and anxiety (OR: 1.39 [95% CI: 1.15–1.67]) during pregnancy. Similar positive associations were observed among children of mothers with a history of asthma and atopy compared with those without such a history and among children of non-smokers versus smokers. No associations were observed between paternal psychological distress during pregnancy or maternal and paternal psychological distress after delivery and childhood wheezing or physician-diagnosed asthma.

CONCLUSIONS. This study found that children of mothers experiencing psychological distress during pregnancy had increased odds of wheezing in the first 6 years of life. This finding was independent of paternal psychological distress or psychological distress in either parent after delivery, suggesting an intrauterine programming effect on fetal lung development and resulting respiratory morbidity.

REVIEWER COMMENTS. Few studies have explored the association of maternal psychological distress on childhood wheezing and none previously in a population of this size. As the authors noted, there is a potential for bias given that children included were more often from parents with a higher educational level and less psychological distress during pregnancy than those lost to follow-up. Nevertheless, the mechanisms that may connect maternal psychological distress with childhood wheezing are currently unknown, and the potential of an intrauterine biological mechanism based on the results of this study highlight the need for further research measuring stress markers, changes in the immune system, and possible epigenetic mechanisms that contribute to intrauterine programming for atopic disease outcomes.

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Effects of Prenatal Community Violence and Ambient Air Pollution on Childhood Wheeze in an Urban Population

PURPOSE OF THE STUDY. Prenatal exposures to maternal stress and physical toxins can affect children’s respiratory development and health. This study sought to examine the effects of prenatal psychosocial stressors (exposure to community violence [ECV]) and physical (traffic-related air pollution) stressors on childhood wheeze concurrently in an urban population.

STUDY POPULATION. The study enrolled 989 women (≥18 years old) in mid- to late pregnancy (28.4 ± 7.9 weeks) receiving care at Brigham & Women’s Hospital in Boston, Massachusetts, between August 2002 and December 2009. Of these, 708 mother–child pairs completed the study and were included in the analyses.

METHODS. In this cohort study, mothers completed a multi-item survey to assess prenatal ECV, and results were summarized into a continuous scale. Prenatal exposure to black carbon was estimated based on residence during pregnancy by using land-use regression modeling; exposure to particulate matter of diameter ≤2.5 μm (PM$_{2.5}$) was estimated by using land-use regression modeling incorporating satellite data. Mothers reported child wheeze at 3-month intervals up to age 24 months, with ≥2 episodes constituting repeated wheeze. The independent effects of ECV and air pollutants on repeated wheeze were analyzed by using multivariate logistic regression. Interactions between ECV and air pollutants were examined in stratified analyses.

RESULTS. Most mothers were of an ethnic minority (55% Hispanic and 29% black) and low socioeconomic status (62% with ≤12 years of education). Eighty-seven (12%) children wheezed repeatedly. In the multivariate models, ECV (odds ratio [OR]: 1.95 [95% confidence interval (CI): 1.13–3.36]) was independently associated with wheeze, adjusting for gender, race/ethnicity, maternal education, birth season, maternal atopy, and cockroach antigen. Black carbon (OR: 1.84 [95% CI: 1.08–3.12]) and PM$_{2.5}$ (OR: 2.02 [95% CI: 1.20–3.40]) produced similar associations. In stratified analyses, a statistically significant association was shown between high prenatal ECV and increased repeated wheeze in the low black carbon and low PM$_{2.5}$ groups, suggesting an interaction between ECV and air pollution.

CONCLUSIONS. The findings suggest that increased ECV and higher exposure to air pollutants in the prenatal period independently contribute to repeated wheeze in these urban children. In addition, the stratified analyses suggest that place-based psychosocial stressors may affect the mother such that physical pollutants adversely affect the fetus, even at relatively lower levels.

REVIEWER COMMENTS. Childhood wheezing respiratory illness causes significant morbidity, particularly in urban communities of lower socioeconomic status, and characterizing its risk factors remains important. This study contributes to known associations with community violence and ambient pollution by providing additional evidence that they exert independent effects on wheeze and novel evidence that they may interact such that their effects are synergistic. Future larger scale studies are necessary to clarify these interactions, as well as to confirm that these relationships hold in the long term.
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