STUDY POPULATION. A total of 161 children aged 4 to 12 years, 95 with asthma and 66 without asthma, were recruited from within a study of 193 children being studied for the effects of rhinovirus infection on asthma.

METHODS. The children provided 8 weekly nasal mucus samples that were analyzed for respiratory viruses by polymerase chain reaction. Upper respiratory infection and asthma symptoms, morning peak expiratory flow rates, and albuterol use were recorded on daily diary cards. Loss of asthma control was defined as at least moderate asthma symptoms and either a decrease in peak expiratory flow of ≥20% or use of albuterol for ≥2 days per week.

RESULTS. Three hundred forty-six infections were detected: rhinoviruses (62%), enterovirus (12%), H1N1 (10%), adenovirus (2%), and multiple viruses (13%). When multiple viruses were detected in a single sample, rhinovirus (80%) and H1N1 (51%) were the most common. Thirty-four percent of children were infected with H1N1; rates were higher in children with asthma (41%) than in children without asthma (24%) (odds ratio: 2.2; 95% confidence interval: 1.1–4.4; \( P = .03 \)). Asthma did not affect rates of infection with rhinovirus (90% in each group), enterovirus (30% vs 24%), adenovirus (11% vs 12%), or other viruses (6% vs 5%). Rates of loss of asthma control per infection were as follows: H1N1, 38% (9 of 24); rhinovirus, 21% (27 of 127); and the combination of rhinovirus and H1N1, 44% (4 of 9).

CONCLUSIONS. Given the increased susceptibility of children with asthma to infection, these findings reinforce the need for yearly influenza vaccination to prevent infection and raise new questions about the mechanism for enhanced susceptibility to influenza infection in asthma.

REVIEWER COMMENTS. Influenza infection is more likely to cause chest symptoms in a child with underlying asthma, but in addition, this study suggests that children with asthma also become infected at a higher rate. This increased susceptibility to infection appeared to be unique to influenza virus as opposed to rhinovirus and other viruses. Whereas the mechanism of this increased susceptibility to infection with a particular virus needs to be explored, infection with the particular virus involved (influenza) can often be prevented by vaccination.

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Rhinovirus Wheezing Illness and Genetic Risk of Childhood-Onset Asthma

PURPOSE OF THE STUDY. Genetic variations at the 17q21 locus, as well as human rhinovirus (HRV) and respiratory syncytial virus (RSV) wheezing illness, are associated with the development of asthma. This retrospective study aimed to determine the effects of these 2 factors independently and together on the risk of asthma.

STUDY POPULATION. Data were compiled from the Childhood Origins of Asthma (COAST) and the Copenhagen Prospective Study on Asthma in Childhood (COPSAC) birth cohorts as well as a group of adult volunteers. For the COAST study, 289 newborns had at least 1 parent with respiratory allergies, a history of physician-diagnosed asthma, or both and 200 were evaluated for asthma beginning at age 6 years. For COPSAC, 297 of 411 children born to mothers with a history of physician-diagnosed asthma and who had complete follow-up from the first 3 years of life and information on asthma status by age 7 years were included. Finally, 100 unrelated adult volunteers were recruited to examine the effects of HRV stimulation on gene expression patterns in peripheral blood mononuclear cells (PBMCs) along the 17q21 genes.

METHODS. Five asthma-associated 17q21 single-nucleotide polymorphisms (SNPs) were genotyped in the COAST cohort. Each SNP was evaluated for an association with the development of asthma, as well as HRV or RSV wheezing illness, by using a logistic regression model or a linear regression model. The authors also evaluated for interactions between the specific 17q21 genotypes and HRV or RSV wheezing illness as it pertains to the development of asthma. Last, this study examined genotype-specific expression of 17q21 genes in unstimulated and HRV-stimulated PBMCs by using the blood samples obtained from each adult volunteer.

RESULTS. The 17q21 variants identified in the COAST cohort were associated with HRV wheezing illness in early life, but not with RSV wheezing illness. The association of 17q21 variants and the development of asthma was seen only in children who also had been ill with HRV wheezing illnesses, suggesting a significant interaction effect between the 17q21 variant and HRV in early life. The expression of 2 of the 17q21 genes, ORMDL3 and GSDMB, was significantly increased in HRV-stimulated PBMCs compared with unstimulated PBMCs.

CONCLUSIONS. This study revealed that the association between 17q21 genotypes and asthma is restricted to only those who also had HRV wheezing illness in early childhood. There is a significant interaction between 17q21 genotypes and HRV wheezing illness in early life with respect to childhood-onset asthma.

REVIEWER COMMENTS. This study helps reinforce the idea that the pathogenesis of asthma involves complex interactions between genetic factors and environmental triggers. Whereas this report does not establish whether risk of asthma is correlated directly to wheezing illness (as both
could be related to an underlying genetic susceptibility in a subgroup of this 17q21 genotype), it certainly underscores the importance of additional studies to better understand both the roles and potential interdependence of genetic factors and illness events early in life with regard to asthma risk. Because exacerbations are most likely an important influence in perpetuating asthma, this mechanism could shed some light on why some children are at higher risk of persistent asthma, whereas, in others, asthma is more likely to remit.

Air Pollution Interacts With Past Episodes of Bronchiolitis in the Development of Asthma

PURPOSE OF THE STUDY. To evaluate whether air pollution affects the development of asthma in children with previous episodes of bronchiolitis.

STUDY POPULATION. A total of 1743 children, with a mean age of 6.83 years, were included in this study. Children were recruited from 16 elementary schools in 7 cities throughout Korea. A total of 1340 of these children were followed up 2 years later.

METHODS. All children had parental completion of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire and an allergy evaluation consisting of pulmonary function tests, skin-prick testing, and a methacholine challenge at the time of enrollment. Air pollution was calculated as an average of the concentrations of ozone, carbon monoxide, nitric dioxide, sulfur dioxide, and particulate matter <10 μm in diameter between 2001 and 2005, based on a geographic sampling system.

RESULTS. Higher exposure to ozone and carbon monoxide was associated with airway hyperresponsiveness at the time of enrollment. Previous episodes of bronchiolitis increased the child’s risk of both current wheezing and physician-diagnosed asthma. When the 2 factors were combined, the risk of airway hyperresponsiveness, wheezing, physician-diagnosed asthma, and decreased pulmonary function test results was higher.

CONCLUSIONS. In children, those who had both a history of bronchiolitis and exposure to higher amounts of air pollution were found to have a higher prevalence of asthma, heightened bronchial reactivity, and decreased lung function compared with children without these exposures.

Reduced Infant Lung Function, Active Smoking, and Wheeze in 18-Year-Old Individuals

PURPOSE OF THE STUDY. To test the hypothesis that reduced lung function in early life is associated with increased risk of persistent wheeze at age 18 years.

STUDY POPULATION. A total of 253 subjects were originally recruited at age 1 month.

METHODS. Maximal flow at functional residual capacity (VmaxFRC) was measured in 1-month-old infants who were then followed up at ages 6, 12, and 18 years. On the basis of symptoms reported, the subjects were categorized as having remittent wheeze (wheezing at earlier assessments but not at age 18 years), later-onset wheeze (wheezing at age 18 years but not earlier), persistent wheeze (wheezing at age 18 years and at least 1 earlier assessment), or no wheeze. Smoking status was also noted at age 18 years.

RESULTS. Of the subjects originally recruited, 150 were followed up at age 18 years. Thirty-seven of them had recent wheeze. Compared with the no-wheeze group (n = 96), persistent wheeze (n = 13) was independently associated with a reduced percentage of predicted VmaxFRC (mean reduction: 43%; 95% confidence interval [CI]: 13%–74%). Compared with the no-wheeze group, persistent wheeze was also associated with atopy in infancy (odds ratio [OR]: 7.1; 95% CI: 1.5–34.5), maternal asthma (OR: 6.8; 95% CI: 1.4–32.3), and active smoking (OR: 4.8; 95% CI: 1.0–21.3). When only wheeze at age 18 years was considered, a reduced percentage of predicted VmaxFRC was associated with wheeze at age 18 years only among current smokers (P = .04).

CONCLUSIONS. Persistent wheezing is associated with multiple factors, including reduced lung function at age 1 month, infant-onset atopy, maternal asthma, and active smoking. Wheeze at age 18 years, regardless of previous wheeze status, is associated with active smoking but only among those with reduced lung function in infancy.
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