CONCLUSION. Overall, childhood infectious diseases protected against asthma persisting in later life. Pertussis and measles, however, were associated with an increased risk of incident asthma in preadolescence and adolescence, which does not support the original hypothesis. History of pneumonia was the most relevant which does not support the original hypothesis. History of incident asthma in preadolescence and adolescence, measles, however, were associated with an increased risk of ABPA. There was no gender differences between those fungal sensitized and the others. Fungal-sensitized children had a median age of 11 compared with 9 years for the others (P = .02). Their total IgE levels were higher (1049 IU/mL vs 78 IU/mL, P < .0001). Fungal-sensitized patients had worse pulmonary function testing than nonfungal sensitized, forced expiratory volume in 1 second 81.5% versus 95.5% predicted, respectively (P = .016) with similar differences when the fungal sensitized were compared with only those sensitized to nonfungal allergens. Similar magnitudes of differences were also present for forced expiratory volume in 1 second/forced vital capacity, and forced expiratory flow 25% to 75%. Aspergillus and Alternaria were the most common fungal allergens identified (84% and 72%, respectively). Severe persistence characterized 19 of the 25 (76%) fungal-sensitized patients, whereas only 13 of 39 (33%) had been so characterized among those without fungal sensitization for an odds ratio 6.33 (95% confidence interval 2.05–19.68, P = .0014).

CONCLUSION. Fungal sensitization in childhood asthma is associated with disease severity.

REVIEWER COMMENTS. This study is consistent with the observed association of Alternaria mold as a major cause of often severe seasonal allergic asthma in the Midwest, where it has even been associated with near-fatal episodes in a report from the Mayo Clinic (O’Hollaren MT, Yunginger JW, Olford KP, et al. Exposure to an aeroallergen as a possible precipitating factor in respiratory arrest in young patients with asthma. N Engl J Med 1991;324:359–363). Although controlled clinical trials of immunotherapy for pollens provide strong support for the effective decrease in clinical sensitivity to those allergens, data for molds is much more limited despite their apparent greater importance for severe asthma.

Increased H1N1 Infection Rate in Children With Asthma


PURPOSE OF THE STUDY. In 2009, H1N1 influenza resulted in 87,000 hospitalizations among children. The most common comorbidity for patients hospitalized as a result of H1N1 infection was asthma. Were children with asthma more likely to be infected with H1N1 influenza?
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
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