

sensitive molecular methods for virus detection, and the results suggest that bacteria might contribute to wheezing episodes in children at high risk. Interventional strategies geared toward these microorganisms might be useful to further our understanding of wheezing and asthma development in these children. Given the paucity of information on evidence-based strategies in young children for treating wheezing episodes, clinical trials for evaluating antimicrobial agents and other interventions for wheezing episodes should be considered and are currently being evaluated among large clinical trial networks.

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Causal Direction Between Respiratory Syncytial Virus Bronchiolitis and Asthma Studied in Monozygotic Twins

Poorisrisak P, Halkjaer LB, Thomsen SF, et al. *Chest*. 2010;138(2):338-344

PURPOSE OF THE STUDY. To compare the long-term outcome of asthma, allergy, and pulmonary function in monozygotic twin pairs discordant for severe respiratory syncytial virus (RSV) disease.

STUDY POPULATION. There were 37 monozygotic twin pairs discordant for RSV hospitalization at a mean age of 10.6 months evaluated in the study. The twins were born between January 1, 1994, and December 31, 2003, and enrolled through the Danish Twin Registry.

METHODS. Hospitalization was used as a marker of disease severity. Participants were studied at a mean age of 7.6 years. The study included clinical examinations, lung-function testing, fractional exhaled nitric-oxide levels, determination of an asthma diagnosis, use of asthma medication, and results of skin-prick tests to common inhalant allergens.

RESULTS. The prevalence of asthma among the twins was 18%. The twins did not differ with respect to current asthma, use of inhaled corticosteroids or β_2 agonists, atopic dermatitis, fractional exhaled nitric oxide, baseline lung function, bronchial responsiveness, or sensitization ($P > .1$ for all comparisons).

CONCLUSIONS. There was no significant difference within cohabiting monozygotic twin pairs discordant for hospitalization for RSV bronchiolitis in infancy on the development of asthma and allergy, which argues against a specific viral effect.

REVIEWER COMMENTS. This study examined the question of which came first: not the chicken or the egg but whether severe RSV bronchiolitis causes wheezing or whether

someone with a predisposition to asthma suffers a more severe response to RSV. This study's results argue against a specific effect of severe RSV infection in the development of asthma and allergy. Another recent study report based on 8280 twin pairs showed that a model in which asthma "causes" RSV hospitalization fit significantly better than a model in which RSV hospitalization "causes" asthma. We guess the chicken came first.

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Allergic Sensitization Is Associated With Rhinovirus-, but not Other Virus-, Induced Wheezing in Children

Jarti T, Kuusipalo H, Vuorinen T, et al. *Pediatr Allergy Immunol*. 2010;21(7):1008-1014

PURPOSE OF THE STUDY. Building on recent studies that have suggested a link between early wheezing caused by rhinovirus and the development of asthma, these researchers sought to characterize the relationship of respiratory viral infections with atopy in hospitalized wheezing children.

STUDY POPULATION. The authors studied a subgroup from among a previously described cohort of 293 hospitalized wheezing Finnish children aged 3 months to 16 years who had comprehensive virology performed ($N = 247$; median age: 1.6 years). Subjects with recent oral corticosteroid use, chronic disease, or ICU treatment were excluded.

METHODS. Respiratory viral infections were evaluated through a nasopharyngeal aspirate and blood sample at baseline and after 2 to 3 weeks. A combination of viral culture, antigen detection, immunoglobulin G (IgG) and IgM measurement, and polymerase chain reaction was used to evaluate for respiratory syncytial virus, human rhinovirus, enteroviruses, human bocavirus, and a broad panel of additional respiratory viruses. Atopy was assessed through serum-specific IgE testing to several common food allergens, cat, dog, horse, birch, mugwort, timothy grass, mold, and dust mite.

RESULTS. Allergen-specific IgE sensitization was closely related to sole rhinovirus infection (odds ratio: 3.5; $P = .0002$). In contrast, sole respiratory syncytial virus infection was negatively associated with sensitization (odds ratio: 0.087; $P = .027$). No significant associations with atopy were found with the remaining viruses or with those with multiple concurrent viral infections.

CONCLUSIONS. Acute wheezing in early childhood caused by human rhinovirus is associated with an increased risk

of allergic sensitization and, therefore, an increased risk of developing future asthma.

REVIEWER COMMENTS. A limitation of this study lies in the fact that all subjects were hospitalized for their wheezing, thereby representing a minority of children with rhinovirus infection. Nevertheless, when considering the asthma predictive index, the evidence presented from this study suggests that a history of rhinovirus infection, especially severe infection, could be considered an additional risk factor for the development of asthma.

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Association of Childhood Obesity With Atopic and Nonatopic Asthma: Results From the National Health and Nutrition Examination Survey 1999–2006

Visness CM, London SJ, Daniels JL, et al. *J Asthma*. 2010;47(7):822–829

PURPOSE OF THE STUDY. Previous work has suggested that obesity is related to asthma through an allergic inflammation pathway. These researchers sought to examine the role of C-reactive protein (CRP) in the association between obesity and asthma among a nationally representative sample of US children and young adults.

STUDY POPULATION. The sample came from the 1999–2006 National Health and Nutrition Examination Survey (NHANES) and specifically included children aged 2 to 19 who had information on BMI and asthma status ($N = 16\,074$).

METHODS. Atopy was measured by using allergen-specific serum immunoglobulin E; asthma status was measured through self-report of diagnosis by a physician; and BMI was calculated on the basis of height and weight measurements. Multiple logistic regression analysis was used to examine the association between BMI and asthma status.

RESULTS. Nearly 10% of the children reported current asthma. A higher proportion of atopic compared with nonatopic children reported current asthma (15.8% vs 6.4%; odds ratio [OR]: 2.71 [95% confidence interval (CI): 1.98–3.72]). There was a strong relationship between BMI and CRP levels ($r = 0.41$). Obese children had a 1.68 odds (95% CI: 1.33–2.12) of having current asthma. Among nonatopic children, those in the obese category were more than twice as likely to have current asthma (OR: 2.46 [95% CI: 1.21–5.02]); however, there was no association between overweight or obesity and asthma among atopic children. Increased CRP levels were asso-

ciated with an increased odds of having asthma among nonatopic children (OR: 1.45 [95% CI: 1.16–1.81]) but not among atopic children (OR: 0.97 [95% CI: 0.65–1.44]).

CONCLUSIONS. The association of overweight and obesity with asthma was stronger among nonatopic children. Overweight might lead to systematic inflammation that, in turn, leads to an increased risk of asthma in nonatopic people.

REVIEWER COMMENTS. There is growing evidence that the rise in both obesity and asthma might be related. This study was cross-sectional and limits our understanding of the causal relationship between obesity and asthma. However, it contributes to advancing the evidence in this area by examining the mechanisms through which obesity and asthma might be related—in this case, through nonallergic disease. Future studies can build on these findings by examining these associations prospectively.

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Risk of Asthma in Young Adults Who Were Born Preterm: A Swedish National Cohort Study

Crump C, Winkleby, Sundquist J, Sundquist K. *Pediatrics*. 2011;127(4). Available at: www.pediatrics.org/cgi/content/full/127/4/e913

PURPOSE OF THE STUDY. To evaluate whether those who were born prematurely were more likely to be prescribed asthma medications in young adulthood than those who were born at term.

STUDY POPULATION. This was a national cohort study of all singleton infants born in Sweden from 1973 through 1979 ($N = 622\,616$) and followed to ages 25.5 to 35.0 to determine whether asthma medications were prescribed in 2005–2007.

METHODS. Asthma-medication data were obtained from all outpatient and inpatient pharmacies throughout Sweden. Outcome was defined as prescription of (1) both a β_2 agonist inhalant and a glucocorticoid inhalant or (2) a combination inhalant containing a β_2 agonist and other drugs for obstructive airway diseases.

RESULTS. Young adults who were born extremely prematurely (23–27 weeks' gestation) were 2.4 times more likely to be prescribed asthma medications than those who were born at term (95% confidence interval: 1.41–4.06). No association was found between later prematurity (28–32 or 33–36 weeks' gestation) and asthma medications in young adulthood.

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Edwin Kim and A. Wesley Burks

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