

Long-term outcome after bronchiolitis: No association with the invasiveness of the infection

To the Editor:

Carroll et al¹ published in the Journal their interesting results from a retrospective population-based study on the association between the severity of bronchiolitis in infants less than 12 months old and asthma at 4.5 to 5.5 years of age. Among over 90,000 children, 18% had an infant bronchiolitis visit. The adjusted odds ratio for asthma was 1.86 for outpatients, 2.41 in the emergency ward, and 2.82 in the inpatient group, suggesting a dose-response relationship between the severity of bronchiolitis and later asthma.

We have prospectively followed up over a period of 25 years a group of 83 children who were hospitalized for bronchiolitis at <24 months of age in 1981 and 1982. Chest radiograph was studied in all cases on admission, and an infiltration was found in 46 (57%) children (rtg-pos cases) and not found in 35 children (rtg-neg cases).² No child had lobar pneumonia suggestive of a severe bacterial infection.

Sixty-eight (84%) children attended the control visit at 4.5 to 6.0 years of age.³ Seventeen (25%) were considered to have asthma (9/37 rtg-pos and 8/31 rtg-neg cases, $P = 1.00$).

Sixty-two (77%) children attended the control visit at 8.5 to 10 years of age.⁴ Only 9 (15%) children were considered to have asthma (4/37 rtg-pos and 5/25 rtg-neg cases, $P = .465$). Subnormal lung function was present in 17 (27%) children (22 rtg-pos and 11 rtg-neg cases, $P = .286$).

Sixty-five (80%) children attended the postquestionnaire study at 14 to 16 years of age.⁵ Asthma was present in 10 (14%) children (5/41 rtg-pos and 5/30 rtg-neg cases, $P = .753$).

Fifty-four (67%) children attended the control visit at 18.5 to 20 years of age.⁶ Asthma was present in 16 (29.6%) children (10/32 rtg-pos and 6/22 rtg-neg cases, $P = 1.00$). Subnormal lung function was present in 19 of 53 (35.8%) children (11 rtg-pos and 9 rtg-neg cases, $P = 1.00$).

Fifty-nine (72.8%) children attended the postquestionnaire study at 26 to 28 years of age.⁷ Asthma was present in 12 (20.3%) children (8/32 rtg-pos and 4/27 rtg-neg cases, $P = .37$).

Castro-Rodríguez et al⁸ analyzed the association between radiologically confirmed pneumonia at <36 months of age and the incidence of asthma and lung function abnormalities at 6 and 11 years of age in the Tucson birth cohort of 888 children (55 pneumonia cases). Early childhood pneumonia increased the asthma risk at both 6 years (3.3-fold) and 11 years (2.8-fold) of age, and the risk was higher than that in children with respiratory infection with no pneumonia. Likewise, early childhood pneumonia was associated with subnormal lung function at both ages. Two thirds of the patients with pneumonia also wheezed, and respiratory syncytial virus was identified in one third, but the authors did not present the outcomes separately for these subgroups.

This supplementary analysis of our prospective long-term postbronchiolitis follow-up data did not confirm the importance of severity¹ and/or of invasiveness⁸ of bronchiolitis in predicting the later outcome of the patients. In our other cohort, the disease severity by clinical scoring in infants hospitalized for wheezing had no association with childhood asthma risk until the median age of 12.3 years.⁹ Invasive infections like respiratory syncytial virus bronchiolitis were merely associated with a

beneficial outcome compared with less invasive rhinovirus infections.¹⁰

Eija Piippo-Savolainen, MD^a

Marja Ruotsalainen, MD^b

Matti Korppi, MD, PhD^a

From ^athe Department of Pediatrics, Kuopio University Hospital, Kuopio, Finland; and

^bthe Pediatric Research Center, Tampere University and University Hospital, Tampere, Finland. E-mail: matti.korppi@uta.fi.

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Reply

To the Editor:

In response to our recent article,¹ Piippo-Savolainen et al² share data from their well studied cohort of 83 subjects followed from early childhood for more than 25 years for asthma and other pulmonary outcomes. Several factors make it difficult to make comparisons to our recent findings from the work highlighted by Piippo-Savolainen et al,² including the small sample size, the fact that their study was neither designed nor powered to address our study questions, differences between studies in how exposure and outcome variables were defined, and the lack of both a spectrum of bronchiolitis severity and a comparison group without bronchiolitis.

Our population-based retrospective birth cohort study, the Tennessee Asthma Bronchiolitis Study (TABS), was designed to investigate the relationship between infant bronchiolitis and early childhood asthma. The definition of the risk factor of interest, bronchiolitis during infancy, differs significantly

between the studies. Our measure of bronchiolitis severity was based on level of health care for bronchiolitis, including clinic visits, emergency department visits, and hospitalizations, as determined by bronchiolitis diagnosis using the International Classification of Diseases, Ninth Revision, Clinical Modification, with the risk period only during infancy. Our inclusion of a comparison group of infants, who had no visit for bronchiolitis in their first year, allowed for the hypothesis-driven investigation of whether there was a severity-response relationship between the most advanced level of health care for bronchiolitis and subsequent early childhood asthma risk and morbidity. Piippo-Savolainen et al² have followed 83 children who were all hospitalized for bronchiolitis at <24 months. Piippo-Savolainen et al² also compare results from subanalyses aimed at investigating the relationship of what they term "invasiveness" of the child index illness as determined by infiltrate on chest radiograph, and subsequent asthma outcomes to previously published work by Castro-Rodríguez et al.³ Our study was not designed to investigate this question.

In regard to the authors' concluding comments regarding asthma after nonrespiratory syncytial virus bronchiolitis, we have previously shown that bronchiolitis occurring during rhinovirus-predominant months was associated with an estimated 25% increased risk of early childhood asthma compared with bronchiolitis occurring during respiratory syncytial virus-predominant months.⁴ This work supports recent findings that early rhinovirus-wheezing illnesses are associated with higher risk of subsequent asthma than other viruses.⁵ However, as we have seen in our Tennessee Children's Respiratory Initiative prospective investigation, the burden of respiratory syncytial virus bronchiolitis during infancy is much greater than rhinovirus bronchiolitis. Therefore, the expected number of asthma cases after infant respiratory syncytial virus bronchiolitis would likely be much greater.

Importantly, the work by Piippo-Savolainen et al² does highlight what has been demonstrated in other longitudinal investigations, that the proportion of children who persist in having a postinfant bronchiolitis asthma phenotype may vary with age through childhood.⁶⁻⁸ The report of the high prevalence of subnormal lung function after infant infection in their cohort is also interesting. This suggests that either early severe viral respiratory infections may lead to lung function abnormalities, or infants with abnormal lung function are predisposed to develop these infections. Clinical trials aimed at preventing severe viral infections during infancy will ultimately elucidate the nature of the association between infant viral respiratory tract illnesses and the development of early childhood asthma.

Kecia N. Carroll, MD, MPH^{a,e}
Tebeb Gebretsadik, MPH^b
Marie R. Griffin, MD, MPH^{c,d,f,h,j}
Tina V. Hartert, MD, MPH^{c,g,i}

From the Departments of ^aPediatrics, ^bBiostatistics, ^cMedicine, and ^dPreventive Medicine, and the Divisions of ^eGeneral Pediatrics, ^fGeneral Internal Medicine, and ^gAllergy, Pulmonary and Critical Care Medicine, ^hCenter for Education and Research on Therapeutics, ⁱCenter for Health Services Research, Vanderbilt University School of Medicine; and ^jthe Mid-South Geriatric Research Education and Clinical Center, and Clinical Research Center of Excellence, Veterans Affairs Tennessee Valley Health Care System, Nashville, Tenn. E-mail: tina.hartert@vanderbilt.edu.

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