Neonatal Bronchial Hyperresponsiveness Precedes Acute Severe Viral Bronchiolitis in Infants

PURPOSE OF THE STUDY. To determine if host factors in neonates expressed as bronchial hyperresponsiveness precede later development of acute severe bronchiolitis. Previous studies showed that abnormal neonatal pulmonary function was associated with asthma by age 7 years.

STUDY POPULATION. This study was nested in the Copenhagen Prospective Studies on Asthma in Childhood, a prospective study of a birth cohort of 411 neonates born to mothers with a history of asthma. Infants were enrolled at 1 month of age. Exclusion criteria included symptoms of lower airway infection, mechanical ventilation before inclusion, gestational age of <36 weeks, and any congenital abnormality or systemic illness.

METHODS. Infant lung function was measured in 402 subjects and bronchial responsiveness to methacholine was determined in 363 subjects by using the raised-volume rapid thoracoabdominal compression technique. These tests were conducted in 1-month-old neonates before they had developed any respiratory symptoms. The cohort was prospectively monitored for respiratory symptoms with daily diary cards and clinical examination at the research clinic every 6 months. Infants were also evaluated for acute respiratory symptoms and given a diagnosis of acute severe bronchiolitis according to a fixed algorithm.

RESULTS. Thirty-four (8.5%) of the infants had acute severe bronchiolitis before age 2 years. Twenty-one (62%) were hospitalized and 23 (67%) were diagnosed with respiratory syncytial virus. Children who later had severe bronchiolitis had a 2.5-fold increased responsiveness to methacholine as determined by a PD15 (provocation dose of methacholine producing a 15% decrease in transcutaneous oxygen pressure) at 1 month compared with control subjects (median PD15 in cases versus control subjects: 0.13 vs 0.33 μmol; P = .01). Differences in baseline airflow were not significant for forced expiratory volume at 0.5 seconds (mean z score for cases versus control subjects: −0.18 vs −0.01; P = .36) and forced expiratory flow at 50% of forced vital capacity (mean z score for cases versus control subjects: −0.37 vs −0.09; P = .13).

CONCLUSIONS. Bronchial hyperresponsiveness in an at-risk population of asymptomatic neonates precedes the later development of acute severe bronchiolitis. This finding suggests a preexisting host factor that would indicate an increased risk of an adverse reaction to common respiratory tract viruses.

Interaction Between Asthma and Lung Function Growth in Early Life

PURPOSE OF THE STUDY. Children with asthma have reduced lung function. This study addresses the question: Are they born that way?

STUDY POPULATION. Prospective birth cohort of 411 children from Denmark whose mothers had a physician’s diagnosis of asthma.

METHODS. At age 1 month, subjects’ spirometric and bronchial responsiveness to methacholine was obtained by thoracic compression technique. At age 7 years, subjects’ lung function was measured by using spirometry. Asthma was diagnosed prospectively, from daily diary cards and clinic visits every 6 months, if the following were noted: recurrent episodes of troublesome lung symptoms typical of asthma, need for rescue use of inhaled β2-agonist, and response to inhaled corticosteroids.

RESULTS. Children with asthma by age 7 years (14%) already had a significant airflow deficit as neonates (forced expiratory flow at 50% reduced by 0.34, z score, P = .03), which progressed (0.82 z score, P < .0001) by age 7 years, suggesting that ~40% of the airflow deficit associated with asthma is present at birth, whereas 60% develops with clinical disease. Bronchial responsiveness to methacholine in neonates was associated with the development of asthma (P = .01).
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