globulin E (IgE) or at least 2 atopic family members) and 815 newborn infants without these risk factors. The cohort of children were followed at the ages of 1, 3, 6, 12, and 18 months, and from then on at yearly intervals up to the age of 7 years. At each follow-up, parents were interviewed on respiratory symptoms, the child’s development, and assessment of childhood illnesses, including the frequency and number of antibiotic courses used. IgE to milk, egg, soy, wheat, dust mite, cat, dog, grass, and birch were determined by radioallergo-sorbent testing at age 1, 2, 3, 4, 5, 6, and 7 years. At age 7, bronchial histamine challenge was performed to assess bronchial hyperreactivity. Main outcome measures included asthma symptoms, atopic sensitization, and bronchial hyperreactivity.

Results. The number of lower respiratory tract infections in the first 3 years of life showed a positive dose-response with doctor-diagnosed asthma and bronchial hyperreactivity at age 7, with the strongest effect for >4 lower respiratory infections (odds ratio [OR]: 3.37; 95% confidence interval [CI]: 1.92–4.92). The total number of infectious diseases other than lower respiratory tract infections in the first 3 years of life was inversely related to a diagnosis of asthma by age 7 years (OR: 0.31; 95% CI: 0.11–0.85) to current wheeze at age 7 (OR: 0.55; 95% CI: 0.20–1.48), and to bronchial hyperreactivity at age 7 (OR: 0.40; 95% CI: 0.16–0.101). Children with <1 episode of rhinorrhea before age 1 compared with those with >2 episodes were less likely to have a doctor’s diagnosis of asthma at 7 years (OR: 0.52; 95% CI: 0.29–0.92) or to have wheeze at 7 years (OR: 0.60; 95% CI: 0.38–0.94) and were less likely to be atopic before the age of 5 years. Similarly, having >1 viral infection of the herpes type in the first 3 years of life was inversely associated with asthma at age 7 (OR: 0.48; 95% CI: 0.26–0.89).

Conclusion. Repeated viral infections other than lower respiratory tract infections early in life may reduce the risk of developing asthma up to school age.

Reviewer’s Comments. The “hygiene hypothesis” has been a recent hot topic in attempts to understand the role of infections in early childhood and suggestion has been made that infections may stimulate the immature immune system towards the Th1 phenotype and therefore reduce susceptibility, and bronchial hyperreactivity.

Outcome measures included asthma symptoms, atopic sensitization, and bronchial hyperreactivity.

Risk Factors for Persistence of Respiratory Symptoms in Childhood Asthma


Purpose of the Study. The purpose of the study was to evaluate the parameters and characteristics that could predict the persistence of respiratory symptoms in asthmatic children.

Study Population. A total of 279 children aged 1.7 to 20 years with asthma who had uniform therapy for a mean of 3 years.

Methods. A retrospective review was performed on records of children with asthma who were regularly followed by the outpatient clinic of Marmara University Hospital Pediatric Allergy and Immunology Department. Data were collected on the parameters at the initial encounter, including age at referral and at onset of respiratory symptoms, duration of symptoms, frequency of asthma episodes, sleep disturbances attributable to disease at referral, initial therapy, serum total immunoglobulin E (IgE) and specific allergen IgE levels/prick skin tests and lung function at onset. At the end of the study, the total number of episodes of asthma during follow-up, frequency of sleep disturbances in past 12 months, total serum IgE and lung function testing were recorded.

Results. The 279 patients had a mean age of 6.2 years at referral and 8.9 years at the end of follow-up. A total of 122 girls and 157 boys were studied. A total of 85/279 (30%) of patients had experienced no respiratory symptoms in the past 12 months at the conclusion of the follow-up. No significant differences were found between those with and without current respiratory symptoms with respect to age, sex, age at onset of symptoms, duration of follow-up, age at referral, therapeutic choice, severity of asthma, and duration of therapy. The patients with current respiratory symptoms had significantly higher total serum IgE levels and a higher number of positive specific allergen IgE levels/prick skin tests than those subjects without current respiratory symptoms (P = .0027, P = .011, respectively). Initial FEV1, FEV1/FVC, and FEV1/FVC were significantly lower in those with current respiratory symptoms (P = .005; P = .003; and P = .011, respectively). However, there was no significant difference between lung functions in both groups at the end of follow-up.

Conclusion. Risk factors for persistence of respiratory symptoms in this study population were low initial FEV1, FEV1/FVC, and FEV1/FVC, and allergic sensitivities.

Reviewer’s Comments. This study took a slightly different look at risk factors for persistence of respiratory symptoms in childhood asthma. During the study period patients received uniform treatment with inhaled budesonide. The author may have wanted to see if treatment would modify the risk factors, or in some way change the course of the patients’ asthma, but unfortunately this intent was not made clear. The study, however, shows once again that elevated IgE to specific allergens is an important risk factor in persistent asthma. Lung function measurements were similar for both groups at the end of the study. This may indicate that though treatment with corticosteroids may improve lung function, those patients with low initial measurements will not be “cured” by our current therapies.

WANDA PHIPATANAKUL, MD
Boston, MA

BRONCHODILATOR RESPONSIVENESS IN NORMAL INFANTS AND YOUNG CHILDREN


Purpose of the Study. To evaluate the baseline airway responsiveness to a bronchodilator, albuterol, in normal infants and young children using changes in maximal expiratory flow rates.

Study Population. In 2 major children’s hospitals, healthy infants <3 years old were recruited for the study. Exclusion criteria included preterm (<36 weeks’ gestation) birth, congenital malformations, or 2 or more episodes of recurrent wheezing with lower respiratory tract infections. Infants who had chronic respiratory conditions were also excluded. At the time of the study, they had to be free of
any respiratory tract symptoms and have not had a cold for the previous 2 weeks.

Methods. Questions were asked about prenatal and postnatal smoke exposure. Infant pulmonary function testing was performed at each institution using technologies well-established at each institution (Columbus Children’s Hospital, Columbus, Ohio, and James Whitcomb Riley Hospital for Children, Indianapolis, Indiana). Maximal expiratory flow-volume curves were obtained at baseline. Measurements included forced vital capacity, forced expiratory flow at 25, 50, 75, 85, and between 25 and 75% of the expired forced vital capacity (FEF25–75%, FEF50%, FEF75%, FEF90%, and FEF25–90%). The forced expired volume in 0.5 second, FEV0.5, was also measured. Albuterol was given using a metered-dose inhaler and spacer. Adequate drug delivery was assumed when the resting heart rate increased by 10%. Repeated doses of albuterol were given until the heart rate increased until a maximum of 8 puffs over 8 minutes. Measurements of pulmonary function began 10 minutes after the first dose of albuterol. A second group of infants received placebo. Response to albuterol was either a percent change in FEF75%, FEF85%, FEV0.5%, and FEF25–75%. The changes versus placebo were FEF75%, 10.6 versus −3.1%, FEF85%, 12.9 versus 0.46%, and FEV0.5 2.2 versus −1.5%. Using the method of standard deviation, 6 of 28 infants responded to albuterol. All of the responders were <1 year old. There were a total of 16 infants in the albuterol group, 6 of 16 responded to albuterol. There were no significant differences in baseline measures of pulmonary function between albuterol responders and nonresponders. Responders were significantly younger and had a higher percentage of mothers who smoke during pregnancy—4 of the 6 compared to 5 of 22 nonresponders. Albuterol responders also had a higher percentage of smoking parents. Five of 6 of the albuterol responders had parents who smoked as compared with 10 of the 22 nonresponders. When all the infants born to mothers who smoked were evaluated, the mean increase in FEF75% with albuterol was 19.8% compared with 6.3% of infants born to nonsmoking mothers.

Conclusions. Normal healthy infants who have no respiratory symptoms have baseline airflow tone that can be reversed with albuterol using measurements from a forced expiratory maneuver. Also, young infants and those exposed to maternal smoking during pregnancy had greater increases in forced expiratory flow after albuterol.

Reviewer’s Comments. The technology exists to measure airflow in infants and young children. In this article, the authors evaluate normal children and have verified the findings of a few previous studies. Cigarette smoke exposure can increase airway responsiveness in infants. The concern is that this is seen in infants who at the time of the study had no lower respiratory tract symptoms. One of the concerns is what will happen prospectively to these infants. Will they declare themselves with more severe lower respiratory tract illness in the future? Are they at risk? Did parental behavior change, did they stop smoking when shown this data?? Perhaps more reasons to discourage smoking.

FREDERICK E. LEICKEY, MD
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TOTAL SERUM IgE AND OUTCOME IN INFANTS WITH RECURRENT WHEEZING


Purpose of the Study. To evaluate the relationship between total serum immunoglobulin E (IgE) levels and the risk of allergic sensitization and persistent wheezing in a hospital-based cohort of infants with recurrent wheezing and no signs of allergy.

Study Population. Initially, 58 full-term infants who were seen in a hospital-based asthma clinic in Milan, Italy, were enrolled in the study. At the time of enrollment, the infants were between 9 months and 2 years old. The median age was 1.6 years. Inclusion criteria were a history of wheezing triggered by infections, ≥5 wheezing episodes, no history of atopy, and negative skin tests.

Methods. The children were followed until age 8 years. Skin tests were performed once per year. Testing was performed to egg, milk, wheat, cat, dog, and common aeroallergens. Serum IgE was measured between the ages of 0.5 to 3 years and then again between the ages of 3 and 6 years. An IgE level was performed 4 weeks or more after an acute respiratory illness. IgE levels were reported as IgE/z scores.

Results. Thirteen children were lost to follow-up. During the first 3 years, the remaining 45 children had a median of 10 episodes of wheezing (range: 5–34 episodes). The frequency of wheezing decreased during the next 3 years with a median of 6 and a range of 0 to 26 episodes of wheezing. In the last year of the study, only one third or 15 still experienced wheezing. Sensitization to at least 1 allergen was observed in 9 children and was detected between the ages of 5 and 8 years of age. Within this group, 5 had stopped wheezing and 4 were still symptomatic during the last year of the study. The mean IgE/z score decreased significantly (P = .0002) from 2.63 during the first 3 years to 2.02 between ages 3–6 years. The average IgE/z score at age 0.5 to 3 years was not significantly different between those with positive or negative skin tests. In those between the ages of 3 and 6, the IgE/z score was significantly higher (P = .013) in those with positive skin tests, but was not associated with recurrence of wheezing. There was no association between the IgE/z scores at entry and the number of wheezing episodes between ages 3 and 8 years or with the presence of wheezing in the last year of the study.

Conclusion. Total serum IgE in infants with recurrent wheezing and no allergy does not help predict those who are at risk for recurrent or persistent wheezing or atopic sensitization.

Reviewer’s Comments. It would be helpful for patient care and for parental concern to know which infant is at risk for persistent asthma. Serum IgE levels have been looked at in different populations, but not in those who have already declared themselves with severe disease. This study involves a small number of children, but they are those infants who have more severe disease and are followed in a specialty clinic. This is a population that does tend to have more asthma morbidity. This paper also has a few other very interesting findings. In their population, wheezing was resolved in 2/3. Skin testing was performed over consecutive years and sensitization to ≥1 allergen was only found in 9 of the 45. In this group of 9, 5 had stopped wheezing, and 4 continued to wheeze. In this population of severely affected infants, there was the tendency for the disorder to resolve and just over 10% of the group had allergy and persistent wheezing.
**Bronchodilator Responsiveness in Normal Infants and Young Children**  
Frederick E. Leickly  
*Pediatrics* 2002;110;448

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