although this study and others clearly show that evidence of pet sensitivity are major risk factors for the diagnosis of asthma.

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THE PATTERN OF ATOPIC SENSITIZATION IS ASSOCIATED WITH THE DEVELOPMENT OF ASTHMA IN CHILDHOOD


Purpose of the Study. Asthma eventually develops in only one third of atopic children. The aim of this study was to prospectively investigate the pattern of atopic sensitization typically associated with the development of asthma in childhood.

Study Population. A cohort of 1314 children followed from birth to the age of 7 years in the German Multicenter Allergy Study.

Methods. Parental questionnaires on asthma and atopic symptoms were completed 6 times up to the age of 2 years and from then on yearly. Determination of specific immunoglobulin E to 9 food and inhalant allergens was performed yearly, and at the age of 7 years, a bronchial histamine challenge was conducted.

Results. Onset of atopic sensitization in children with current asthma at the age of 7 years was significantly earlier than in children without current asthma (39.4% before age 1 year vs 21.0%; P = .015). Early atopic sensitization without any sensitization to inhalant allergens at the age of 7 years conferred no increased risk for asthma at this age. Only those children sensitized to inhalant allergens by the age of 7 years were at a significantly increased risk of being asthmatic at this age (odds ratio 10.12; 95% confidence interval [CI]: 3.81–26.88). However, even in this group of persistently sensitized children, the risk of being asthmatic at the age of 7 years was only increased if a positive parental history of asthma or atopy was present (OR: 15.56; 95% CI: 5.78–41.83), with the effect being strongest for maternal asthma.

Conclusion. The results indicate that an underlying factor pertaining to asthma and maternal transmission may determine both a certain pattern of sensitization and the expression of asthma.

Reviewer’s Comments. This study challenges our current understanding of the natural history of childhood asthma. The notion of a progressive atopic march assumes that early atopic sensitization to food allergens is a risk factor for subsequent inhalant sensitization, which, in turn, is regarded as a risk factor for the development of asthma. However, recent epidemiologic studies showed no consistent protective effect of reduced food or inhalant allergens, as well as no positive effect of increased inhalant allergen levels on the development of asthma. This study supports the hypothesis that the development of childhood asthma and atopy run in parallel if certain perinatal or hereditary influences prevail, rather than being subsequent stepping stones in a progressive atopic march.

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PREDICTORS OF ASTHMA 3 YEARS AFTER HOSPITAL ADMISSION FOR WHEEZING IN INFANCY


Purpose of the Study. To evaluate whether early antiinflammatory therapy after a wheezing episode in infancy can prevent the development of asthma.

Study Population. A total of 89 infants <2 years old without a history of premature birth or chronic cardiopulmonary disease who had been hospitalized for wheezing.

Methods. This was a randomized, controlled study in which wheezing infants were divided into 3 treatment groups: cromolyn sodium 20 mg nebulized qid for 8 weeks followed by 20 mg nebulized tid for 8 weeks; budesonide 500 μg nebulized bid and 250 μg nebulized bid for 8 week successive periods; or no therapy. If clinically indicated, maintenance therapy was begun after the initial 16 weeks of antiinflammatory therapy. The presence of virus was assayed in nasal lavage specimens using standard techniques. The children were followed for 3 years, and at the conclusion of the study, asthma (total of 3 episodes of physician-diagnosed wheezing) was assessed, and skin prick tests (SPTs) were performed.

Results. Administration of antiinflammatory medication for 4 months after the initial wheezing episode had no significant effect on the development of asthma. Asthma activity to indoor allergens, particularly cat or dog epithelial danders, was predictive of developing asthma. Conversely, a decreased risk of asthma was seen both in patients with a furred pet at home during infancy and in patients in whom the original wheezing episode was caused by respiratory syncytial virus (RSV) infection.

Conclusions. Early antiinflammatory therapy for 4 months after bronchiolitis does not prevent the development of asthma. In this study, the presence of RSV bronchiolitis was associated with a decreased incidence of asthma. Although the authors comment that the prospective design is a strength of the study, they note that the study was not blinded. The focus only on hospitalized children with wheezing also limits the scope to episodes of severe wheezing.

Reviewers’ Comments. Although this study demonstrates that early antiinflammatory therapy does not prevent later development of asthma, it does not answer the question of how such therapy might modulate airway remodeling or severity of asthma. In addition, the findings of this study are limited by the fact that their definition of asthma (3 wheezing episodes by age 3 years) includes both “transient” and “persistent” wheezers. The incidence of asthma after RSV bronchiolitis was high (22%); however, infants who wheezed without RSV infection were at greatest risk (61%) of developing asthma by age 3 years. Additional studies are needed to confirm whether RSV-negative wheezing in infancy is in fact a major risk factor for asthma.

Michelle Montalbano, MD
James Gern, MD
Madison, WI

EARLY CHILDHOOD INFECTIOUS DISEASES AND THE DEVELOPMENT OF ASTHMA UP TO SCHOOL AGE: A BIRTH COHORT STUDY


Purpose of the Study. To investigate the association between early childhood infections and subsequent development of asthma.

Study Population. A total of 1314 children born in 1990 followed from birth to the age of 7 years.

Methods. A total of 499 newborn infants were recruited with risk factors for atopy (elevated cord blood immuno-
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 the 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: 0.16–1.01). 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 to develop towards the Th1 phenotype and therefore reduce the risk of asthma and atopy. This study found that although lower respiratory infections may increase the risk of developing asthma, upper respiratory infections may actually reduce the risk and may further support this “hygiene hypothesis.” Additional long-term studies such as this would be useful in our understanding of the complicated mix of environmental and genetic factors that play important roles in the development of atopy and asthma.

Wanda Phipatanakul, MD
Boston, MA

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 fol-

lowed 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 follow-up. 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 = 0.0027, P = 0.01, respectively). Initial FEV₁, FEF₂₅–₇₅%, and FEV₁/FVC were significantly lower in those with current respiratory symptoms (P = 0.005; P = 0.003; and P = 0.011, 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 FEV₂₅–₇₅%, and allergen 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 symptom was not initial referred. 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 = 0.0027, P = 0.01, respectively). Initial FEV₁, FEF₂₅–₇₅%, and FEV₁/FVC were significantly lower in those with current respiratory symptoms (P = 0.005; P = 0.003; and P = 0.011, respectively). However, there was no significant difference between lung functions in both groups at the end of follow-up.

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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
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Pediatrics 2002;110;447

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