RESULTS. Measures of asthma control and quality of life decreased as parent-reported PACCI direction moved from “better” to “worse.” Similar results were observed as the PACCI bother domain varied from “not bothered” to “very bothered,” although no associations were found with these domains and lung function. Any reported PACCI risk event was associated with poorer asthma control and PACQLQ scores.

CONCLUSIONS. The PACC is a valid measure of multiple indicators of asthma morbidity, allowing for assessment of asthma control, risk, and 2 measures of quality of life (direction and bother) in 1 questionnaire. Such measures better address the asthma guideline recommendation of the National Heart, Lung, and Blood Institute that patient experiences be assessed directly rather than extrapolated from other clinical measures. Predictive implications and effect on patient care and outcomes have yet to be determined.

REVIEWER COMMENTS. This study provides evidence that subjective parent-reported measures correlate well with other known measures of asthma control and quality of life. Given the convenience of using only 1 questionnaire for all measures, the PACC is a viable approach to ensuring multidimensional asthma care as recommended by current asthma guidelines.


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Discordance Between Aeroallergen Specific Serum IgE and Skin Testing in Children Younger than 4 Years


PURPOSE OF THE STUDY. The goal of this study was to test the yield of skin prick testing (SPT) versus allergen-specific serum IgE (sIgE) testing in identifying aeroallergen sensitization in atopic children aged <4 years.

STUDY POPULATION. The study population consisted of 40 atopic inner-city children from a pediatric asthma center in the Bronx, New York, aged <4 years who had a history of wheezing. Patients were enrolled in a randomized, prospective interventional clinical trial evaluating the efficacy of subcutaneous immunotherapy in asthma.

METHODS. Children with wheezing on >1 occasion, atopy, and having a major risk factor for developing asthma (ie, family history of eczema and/or asthma) were included in the study. The patients underwent SPT for 7 common aeroallergens, including grass pollen mix, ragweed pollen, dust mite, roach, mouse, dog, and cat. The children with both SPT and parental consent to participate in an associated clinical immunotherapy trial had sIgE levels performed by the Immulite System (Siemens AG, Munich, Germany) within 4 weeks of initial SPT testing.

RESULTS. Poor to fair agreement between the 2 methods of detecting allergic sensitization existed for all food allergens tested, except mouse, which had moderate agreement. If only SPT had been performed, 42% of the sensitizations diagnosed by using combination SPT and allergen-specific sIgE level would have been missed. In contrast, 13% of missed sensitizations were seen when allergen-specific sIgE alone was performed. Further investigation showed that at least 1 specific aeroallergen sensitization would have been missed in 80% of children who only underwent SPT. In addition, more than one-third of children in this study would have had ≥1 aeroallergen sensitization missed by undergoing allergen-specific sIgE testing alone. SPT and allergen-specific sIgE were a perfect match only in 7.5% (3 of the 40 children). Children with high total sIgE levels (≥300 kU/L) were more likely to have negative results on SPT in the face of sIgE-positive tests to the same allergen. They were also less likely to have SPT-positive results in the face of sIgE-negative test results to the same allergen. CONCLUSIONS. The results of this study suggest that when testing for aeroallergen sensitization, both forms of testing (SPT and sIgE) should be considered to make the diagnosis in children aged <4 years with high risk for asthma.

REVIEWER COMMENTS. This study suggests that some young patients would likely benefit from both SPT and sIgE testing. One limitation to the study, however, is the sample size. This study reminds us that when results of laboratory tests do not support the clinical diagnoses we suspect, further testing may help make the proper diagnosis in some cases. Further randomized controlled studies with larger sample sizes are needed to investigate the utility of both tests in the diagnosis of young children at high risk for asthma.


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Wheeze Phenotypes in Young Children Have Different Courses During the Preschool Period


PURPOSE OF THE STUDY. The goal of this study was to evaluate whether categorizing children with early wheeze based on their trigger can help predict their disease course in the preschool years.

STUDY POPULATION. Initially, 300 children aged <3 years with a history of wheeze were enrolled. Follow-up data were available on 150 of the children at age 5 years.
METHODS. The children with a history of wheeze were enrolled at <3 years of age and divided based on history into 3 groups: mild early viral wheeze (EVW), atopic multiple-trigger wheeze (MTW), and nonatopic uncontrolled wheeze. They were reassessed at 5 years of age and divided into 4 categories: asymptomatic, mild EVW, atopic MTW, and atopic uncontrolled wheeze. The evolution of clusters from infancy to school age was assessed by crossing the original phenotypes with the phenotypes obtained at 5 years of age.

RESULTS. Sixty-nine percent of children with mild EVW at 3 years of age were asymptomatic or continued to have mild EVW at age 5 years. The majority (59%) of children with nonatopic uncontrolled wheeze had the same severity at 5 years. The children with atopic MTW remained atopic at 5 years of age, and many of them developed uncontrolled wheeze (61%); none of the children in the atopic cluster developed the asymptomatic phenotype.

CONCLUSIONS. This study showed that disease progression in children with wheezing in early childhood depends largely on the expression of allergy. Children with viral wheezing had a good prognosis because most became asymptomatic or remained with mild EVW at age 5 years. On the contrary, none of the children with the atopic MTW phenotype became asymptomatic at 5 years. Many of the children who were initially in the nonatopic uncontrolled wheeze group had developed atopic uncontrolled wheeze by age 5 years.

REVIEWER COMMENTS. There is an increasing appreciation for the fact that not all patients with asthma have the same disease. This prospective study supports the finding that early phenotypic identification is important and helpful. For the most part, children in each of the different phenotypes tend to maintain their "type" of asthma into preschool years. This information is a useful prognostic indicator. Furthermore, children with atopic disease tended to do more poorly over time. It is therefore imperative to establish whether a child with wheeze has environmental allergies early on because these children show great improvement in their asthma control with allergy immunotherapy, especially if started early.

Onset and Persistence of Respiratory/Allergic Symptoms in Preschoolers: New Insights From the PARIS Birth Cohort

PURPOSE OF THE STUDY. The goal of this study was to identify wheezing and asthma phenotypes based on the time course of respiratory/allergic symptoms throughout preschool years.

STUDY POPULATION. A total of 3840 term healthy infants born between 2003 and 2006 were enrolled in a population-based birth cohort study (PARIS). Of the 3840 children initially enrolled in the cohort, 2522 children were included in the cluster analysis.

METHODS. Data (including symptoms of wheezing, dry night cough, rhinitis, and dermatitis) were collected annually from birth to 4 years of age. K-means clustering was used to group, into phenotypes, children with similar symptom trajectories over the study period. Children with complete reports for all symptoms at all time periods underwent a sensitivity analysis. Once respiratory/allergic phenotypes were identified, their relations with IgE-mediated sensitization, blood eosinophilia, and physician-diagnosed disease were studied by using logistic regression. The risk factors for belonging to these phenotypes were investigated by using multinomial logistic regression.

RESULTS. Four distinct respiratory/allergic phenotypes and 1 reference group were identified. The 4 phenotypes included 2 transient (rhinitis and wheeze) and 2 persistent ones that were associated with IgE sensitization (cough/rhinitis phenotype and dermatitis phenotype). Early lower respiratory tract infections were far more prevalent among the transient wheeze phenotype. The transient rhinitis phenotype never statistically differed from the reference group nor did the transient wheeze phenotype except for diagnosed asthma. The dermatitis phenotype had the highest prevalence of diagnosed eczema and food allergy. The cough/rhinitis phenotype showed the highest prevalence of diagnosed asthma and hay fever, which statistically differed from all the other phenotypes. The only factor associated with the transient rhinitis phenotype was postnatal exposure to environmental tobacco smoke in the home. Transient wheeze phenotype was related to male gender and contact with other children. Lastly, risk factors for both IgE-associated phenotypes encompassed parental history of allergy and potential exposure to stress and allergens, known to be associated with the development of allergic disease.

CONCLUSIONS. This study identified 4 distinct phenotypes based on the time course of respiratory/allergic symptoms in the first 4 years of life. The different phenotypes varied in terms of IgE sensitization and risk factors. The transient phenotypes were linked to irritation and infections, and the persistent phenotypes to allergy.

REVIEWER COMMENTS. This study reaches results similar to previously published studies, categorizing children into different clinical phenotypes and groups at risk for developing asthma. Most children with transient wheeze will not go on to develop asthma. In contrast, the persistent cough/rhinitis phenotype associated with IgE sensitization predicted the highest prevalence of diagnosed asthma. Thus, children with risk factors (mainly parental history of allergy), dry night cough, and/or rhinitis not associated...
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Mahta Mortezavi and Theresa Bingemann
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