with infection should be referred to an allergist early on for allergy testing. Identification of IgE sensitization should change management in a child with a higher risk of developing asthma.


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Morphological Changes in Eosinophils Are Reliable Markers of the Severity of an Acute Asthma Exacerbation in Children


PURPOSE OF THE STUDY. The goal of this study was to determine if morphologic changes in blood eosinophils can be used for early identification of the severity of an acute asthma exacerbation in children.

STUDY POPULATION. Children were selected sequentially in an emergency care unit or asthma outpatient clinic. They comprised a group of 15 healthy children (5 girls and 10 boys; ages 4–14 years) without asthma or a personal or familial history of allergy, a group of 15 asthmatic children with variable disease severity (3 girls and 12 boys; ages 2–12 years) seen at a symptom-free period, and a group of 40 children with acute asthma exacerbations (14 girls and 26 boys; ages 2–13 years). There were no statistically significant differences in age or gender among the 3 groups examined.

METHODS. One milliliter of blood was collected from the subjects without anticoagulant, and 40 μL was placed directly on each slide field. Cells were allowed to adhere and were stained; a morphologic assessment was then conducted by evaluating 200 eosinophils by using microscopy (in duplicate for each subject). Microscopic fields were randomly selected, and the slides were identified only at the end of the evaluation. Morphologic changes were compared by using the Mann-Whitney test, and correlation between the severity of the asthma exacerbation and the percent changed eosinophils was tested with Spearman’s correlation.

RESULTS. The proportion of activated eosinophils was higher in asthmatic symptom-free children compared with the control group and was highest in those with acute asthma exacerbation. Significant morphologic changes were noted in several criteria: emissions of multiple pseudopods, presence of cytoplasmic vacuoles, spreading, and presence of a cluster of free eosinophil granules (P < .001). In addition, mild/moderate exacerbations could be distinguished from severe exacerbations (P < .0001) by using all of the aforementioned criteria except for the clusters of free eosinophil granules. Considering the extreme values as cutoffs for the respective sample distribution, the minimum percentages of eosinophils that indicated a risk of a severe acute exacerbation were ≥14% for those emitting a single pseudopod and 8% for multiple pseudopods, 17% for cytoplasmic vacuoles, 28% for eosinophils releasing a large quantity of granules, and 66% for spread eosinophils. Sensitivity and specificity were highest for spread of eosinophils (100% and 96%, respectively).

CONCLUSIONS. The results of this study show that quantifying morphologic changes in eosinophils is a feasible and reliable way to identify the severity of an asthma exacerbation and may therefore prove useful in the clinical management of patients.

REVIEWER COMMENTS. This study represents a novel approach to utilizing observed changes in eosinophil morphology to assist in clinical evaluation. It does require technical skill but only a small blood sample that would be practical in many settings. Additional prospective studies would be helpful to confirm the utility of this approach.

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Exhaled Volatile Organic Compounds Predict Exacerbations of Childhood Asthma in a 1-Year Prospective Study


PURPOSE OF THE STUDY. The goal of this study was to investigate whether exhaled volatile organic compounds (VOCs) in exhaled breath are able to predict asthma exacerbations and to assess which combination of VOCs is the most predictive.

STUDY POPULATION. Children with asthma aged 6 to 16 years from the outpatient clinic of the Department of Pediatric Pulmonology, Maastricht University Medical Centre, were included. All children were known to have had a diagnosis of asthma for at least 6 months.

METHODS. A 1-year longitudinal study was performed in 40 children with asthma. At 2-month intervals, exhaled nitric oxide fraction, VOC profiles in exhaled breath samples, lung function, and symptoms were determined. VOC profiles were analyzed by using gas chromatography–time-of-flight mass spectrometry.

RESULTS. Thirty-eight of 40 children completed the study. Sixteen children experienced an exacerbation. A total of 3434 different VOCs were detected in exhaled breath. The most optimal model of baseline measurements versus exacerbation within patients was based on 6 VOCs (sensitivity: 100%; specificity: 93%). The model of baseline values of patients with an exacerbation compared with
those without consisted of 7 VOCs (sensitivity: 79%; specificity: 100%). The nitric oxide fraction and lung function were not predictive for exacerbations.

CONCLUSIONS. VOC profiling from exhaled breath is able to predict exacerbations of childhood asthma.

REVIEWER COMMENTS. This longitudinal study is the first to analyze the ability of VOCs in exhaled breath to predict asthma exacerbations. The result indicates that a combination of 6 or 7 VOCs was able to predict exacerbations of childhood asthma both between and within patients with high sensitivity and specificity. The advantage of VOC analysis in exhaled breath is that sample collection is noninvasive and inflammatory markers are measured simultaneously. However, there was no mention of asthma severity classification. Therefore, it was not possible to explore the role of VOCs in different degrees of asthma severity. Biochemical origin and pathophysiological function of identified compounds in VOCs need to be clarified. In addition, validation studies in a larger population are needed to confirm the optimal combination of VOCs.

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Childhood Asthma Hospitalizations in the United States, 2000-2009


PURPOSE OF THE STUDY. The goal of this study was to examine temporal trends in the US incidence of childhood asthma hospitalizations, in-hospital mortality, mechanical ventilation use, and hospital charges between 2000 and 2009.

STUDY POPULATION. This serial, cross-sectional analysis included a nationally representative sample of children hospitalized with acute asthma. The Kids Inpatient Database was used to identify children aged <18 years with asthma by using International Classification of Diseases, Ninth Revision, Clinical Modification, code 493.xx.

METHODS. Outcome measures were asthma hospitalization incidence, in-hospital mortality, mechanical ventilation use, and hospital charges. Temporal trends of each outcome, accounting for sampling weights, were analyzed. Hospital charges were adjusted for inflation to US 2009 dollars.

RESULTS. The 4 separate years (2000, 2003, 2006, and 2009) of national discharge data included a total of 592,805 weighted discharges with asthma. Between 2000 and 2009, the rate of asthma hospitalization in US children decreased from 21.1 to 18.4 per 10,000 person-years (13% decrease; \( P_{\text{trend}} < .001 \)). Mortality declined significantly after adjusting for confounders (odds ratio for comparison of 2009 with 2000: 0.37 [95% confidence interval: 0.17–0.79]). In contrast, there was an increase in the use of mechanical ventilation (from 0.8% to 1.0% [28% increase]; \( P_{\text{trend}} < .001 \)). Nationwide hospital charges also increased from $1.27 billion to $1.59 billion (26% increase; \( P_{\text{trend}} < .001 \)); this increase was driven by a rise in the geometric mean of hospital charges per discharge, from $5940 to $8410 (42% increase; \( P_{\text{trend}} < .001 \)).

CONCLUSIONS. Between 2000 and 2009, significant declines in asthma hospitalization and in-hospital mortality were noted among US children. In contrast, mechanical ventilation use and hospital charges for asthma increased significantly over this same period.

REVIEWER COMMENTS. This article is a very interesting analysis of trends in hospital mortality, mechanical ventilator use, hospital charges, and childhood asthma hospitalizations in the United States between 2000 and 2009. These data demonstrate that asthma hospitalizations and mortality declined significantly. There was an increase in mechanical ventilation use over this time period, which might reflect a more aggressive approach to management of severe asthma exacerbations in children. Although the results of this study suggest that progress has been made in reducing the impact of severe acute asthma in children in the United States, overall charges per discharge for asthma hospitalizations increased markedly; nationwide hospital charges increased by 26%. This increase most likely reflects more aggressive management of sicker patients. The large asthma burden in the United States presents an ongoing public health and health education challenge, and further studies are needed to find more cost-effective strategies and in-patient protocols to meet this challenge.

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Asthma Outcomes and Costs of Therapy With Extrafine Beclomethasone and Fluticasone


PURPOSE OF THE STUDY. The investigators sought to compare asthma outcomes and costs of extra-fine hydrofluoralkane (HFA)-beclomethasone (QVAR) and fluticasone (Flovent HFA).

STUDY POPULATION. Patients aged 12 to 80 years with asthma were followed up for at least 1 year before (baseline year) and 1 year after (outcome year) the index date. Some patients received a first prescription of inhaled corticosteroids (ICS) as QVAR or Flovent on the index date. Other patients were receiving 1 of these 2 options as step-up therapy on the index date.
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