IN Voluntary SMOKING AND ASTHMA SEVERITY IN CHILDREN: DATA FROM THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES III)


Purpose of the Study. To determine the indicators of asthma severity among children in the United States with high and low levels of tobacco exposure.

Study Population. The subjects were 523 children (age: 4–16) with physician-diagnosed asthma.

Methods. The study population was obtained from the Third National Health and Nutrition Examination Survey (NHANES III), which is a Centers for Disease and Prevention (CDC)-sponsored survey of a representative US population that underwent an extensive evaluation including a questionnaire, physical examination, lung function, and serum cotinine levels. Only children with a prior diagnosis of asthma were included in the analysis. Asthma severity was based on the frequency of symptoms. Serum cotinine levels were ranked as low (<0.115 ng/mL), intermediate (0.116–0.639 ng/mL), and high (0.64–0.20 ng/mL). Subjects that reported active smoking or had serum cotinine >20 ng/mL (indicating active smoking or use of chewing tobacco) were excluded. Cotinine levels were then compared with measures of asthma severity.

Results. Of the 13,944 children (7 years old), those without physical examinations or cotinine levels and 13 with cotinine levels >20 ng/mL were ranked as low (0.115–0.639 ng/mL), intermediate (0.64–0.20 ng/mL), and high (0.64–0.115 ng/mL) levels were ranked as low (<0.115 ng/mL), intermediate (0.116–0.639 ng/mL), and high (0.64–0.20 ng/mL). Subjects that reported active smoking or had serum cotinine >20 ng/mL (indicating active smoking or use of chewing tobacco) were excluded. Cotinine levels were then compared with measures of asthma severity.

Conclusions. The authors found that increased asthma severity was associated with higher cotinine levels. They also found that lower forced expiratory volume in 1 second (FEV1) levels and a greater proportion of children with FEV1 <80% were also associated with increased levels of cotinine. They found a mean FEV1 decrement of 8.1% in the environmental tobacco smoke (ETS)-exposed children versus 1.8% in all the children. A surprising finding was that children with higher cotinine levels were less likely to have been hospitalized for asthma in the previous year, but all other measures of severity were higher in the group.

INCREASED LEUKOTRIENES IN EXHALED BREATH CONDENSATE IN CHILDHOOD ASTHMA


Purpose of the Study. To determine if 2 markers of airway inflammation, leukotrieneB4 (LTB4) and cysteinyl leukotrienes (cys-LTs) can be detected in the breath of children with asthma and to look at the effect of steroid treatment on these mediators.
Methods. There were 4 groups of children all between the ages of 7 and 14 years. In addition to the healthy nonatopic control group \((n = 11)\), there were children with mild intermittent asthma \((n = 13)\), mild persistent asthma \((n = 13)\), and a group that contained both moderate and severe persistent asthma \((n = 13)\). The diagnosis of asthma was based on American Thoracic Society criteria. Severity classifications followed the National Heart Lung and Blood Institute/World Health Organization guidelines and the diagnosis of allergy was based on skin test responses to common allergens. Each study group was similar in age and ratio of male/female except there were considerably more boys in the moderate-severe group. The mild persistent group was on \(<400 \mu g/day\) of inhaled steroids whereas the more severe group was divided between those on \(>400\) and those on \(>1000 \mu g/day\). No one was on a leukotriene modifier. The study design involved clinical history, spirometry, and measurements of nitric oxide (NO) and leukotrienes in the breath condensate.

Results. Cys-LT was detectable in the exhaled breath of normal, nonasthmatic, nonatopic children \((18.5 \pm 0.5 \text{ pg/ml})\). Levels were significantly increased in children with mild persistent asthma \((27.9 \pm 2.8 \text{ pg/ml})\) and moderate/severe persistent asthma \((31.5 \pm 4.5 \text{ pg/ml})\). Cys-LT levels in exhaled breath of children with mild intermittent asthma were similar to the control group \((19.9 \pm 1.1 \text{ pg/ml})\). LTB4 levels were significantly increased in the breath condensates of children with mild persistent asthma \((126 \pm 8.8 \text{ pg/ml})\) and moderate/severe persistent asthma \((131.9 \pm 7.1 \text{ pg/ml})\) as compared with mild intermittent asthma \((52.7 \pm 3.8 \text{ pg/ml})\) and the control subjects \((47.9 \pm 4.1 \text{ pg/ml})\). In patients with mild persistent asthma, there was an inverse correlation between levels of cys-LT and LTB4. With increasing amounts of cys-LT there was a decrease in the amount of LT B4. The amount of exhaled NO was increased significantly in all asthmatic children compared with controls.

Conclusions. Two markers of inflammation, cys-LT and LTB4, were found to be elevated in the exhaled breath of children with mild to moderate/severe persistent asthma. These mediators were found in those already on inhaled corticosteroids. The findings support the involvement of these 2 leukotriene mediators in chronic airway inflammation. This study also shows that exhaled breath condensate may be useful in assessing inflammation in the airways of children 6 to 7 years old.

Reviewer’s Comments. For many years now we have been enthusiastic supporters of the concept that asthma is a chronic inflammatory disease of the airway. Yet, as these authors point out, we have not been able to measure what we think is important in children. Previous work on airway inflammation has involved adults undergoing rather invasive diagnostic techniques. This study introduces a noninvasive measurement of inflammation and although in small numbers clearly shows differences in inflammatory mediators in the various classifications of disease. The cys-LT are derived from mast cells and eosinophils and include mediators that are blocked by available leukotriene modifiers. All persistent forms of asthma that were treated with inhaled corticosteroids showed elevations of cys-LTs. LTB4 is derived from neutrophils. This neutrophil product is also elevated in the persistent forms of asthma. One of the take-home messages from this work is the fact that despite the use of the inhaled steroids, by-products of inflammation were detected in these children who were asymptomatic. There is also the concern or argument that deals with the presence of inflammation in all forms of asthma—the intermittent and persistent. The measures taken here did not show any of the inflammatory leukotriene mediators and only a slight increase in NO. We may have observed the introduction of a noninvasive tool to help understand the process of airway inflammation and perhaps guide therapy.

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ASSOCIATION OF FORCED EXPIRATORY VOLUME WITH DISEASE DURATION AND SPUTUM NEUTROPHILS IN CHRONIC ASTHMA


Purpose of the Study. Some patients with chronic asthma develop irreversible airflow obstruction. The aim was to assess whether reported duration of asthma and induced sputum cell counts were associated with pulmonary function in patients with asthma who did not smoke.

Study Population and Methods. Maximal forced expiratory volume in 1 second (FEV1) was determined after a steroid trial (oral prednisolone, 30 mg/day \([n = 9\) patients]; or inhaled fluticasone, 2000 \(\mu g/day\) \([n = 5\); for 2 weeks]) and 2.5 mg of nebulized albuterol. Asthma history was recorded with duration from first diagnosis. All subjects were nonsmokers, or were to have stopped smoking \(>5\) years previously and smoked \(>5\) pack-years \((n = 12)\). Induced sputum was obtained from 59 subjects for analysis of airway cell counts.

Results. Maximal FEV1 was inversely associated with asthma duration \((r = -0.47; P < .0001)\), age \((r = -0.40; P < .0001)\), and the proportion of sputum neutrophils \((r = -0.50; P = .00004)\). After adjusting for age, both duration of disease and sputum neutrophils were independently associated with maximal FEV1. Neutrophil activation, as measured by sputum myeloperoxidase levels, was positively associated with the proportion of sputum neutrophils \((r = 0.45; P = .0004)\) and inversely associated with maximal FEV1 \((r = -0.59; P < .0001)\).

Conclusions. Long disease duration may be a predisposing factor for the development of irreversible airflow obstruction in patients with chronic asthma. The negative associations of sputum neutrophil count and activation with maximal FEV1 suggest that neutrophils may be involved in the pathophysiology of irreversible airflow obstruction in asthma.

Reviewer’s Comments. Of course, one doesn’t know if the neutrophils were the cause or the result of long-standing airways obstruction. Nonetheless, the study reminds us that many adults with long-standing asthma may develop irreversible airflow obstruction over time. When that happens, I always worry that some other cardiopulmonary process is going on and start ordering all sorts of expensive tests. For those interested in this subject, the article is accompanied by a thoughtful editorial (Am J Med. 2002;112:498–500).

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SERUM ECP LEVELS AND METHACHOLINE CHALLENGE IN INFANTS WITH RECURRENT WHEEZING


Purpose of the Study. To investigate the possible correlation between eosinophilic inflammation as measured by serum eosinophilic cationic protein levels (ECP) and bron-
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