LTB4 is derived from neutrophils. This neutrophil product with inhaled corticosteroids showed elevations of cys-LTs. Modifiers. All persistent forms of asthma that were treated include mediators that are blocked by available leukotriene modifiers. 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 μg/day of inhaled steroids whereas the more severe group was divided between those on >400 and those on ≥1000 μg/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 ± 0.5 pg/mL). Levels were significantly increased in children with mild intermittent asthma (27.9 ± 2.8 pg/mL) and moderate/severe persistent asthma (31.5 ± 4.5 pg/mL). Cys-LT levels in exhaled breath of children with mild intermittent asthma were similar to the control group (19.9 ± 1.1 pg/mL). LTB4 levels were significantly increased in the breath condensates of children with mild persistent asthma (126 ± 8.8 pg/mL) and moderate/severe persistent asthma (131.9 ± 7.1 pg/mL) as compared with mild intermittent asthma (52.7 ± 3.8 pg/mL) and the control subjects (47.9 ± 4.1 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 SPUMT 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 μg/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(s) = −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(s) = 0.45; P = .0004) and inversely associated with maximal FEV1 (r(s) = −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-
ASSOCIATION OF FORCED EXPIRATORY VOLUME WITH DISEASE DURATION AND SPUTUM NEUTROPHILS IN CHRONIC ASTHMA
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