INHIBITION OF OXYGEN METABOLISM IN EXHALED BREATHE CONDENSATE IN CHILDHOOD ASTHMA


Purpose of the Study. To determine if 2 markers of airway inflammation, leukotrieneB4 (LTB4) and cysteynyleukotrienes (cys-LTs) can be detected in the breath of children with asthma and to look at the effect of steroid treatment on these mediators.

Mary Beth Bollinger, DO
Baltimore, MD

ASTHMA IN EXERCISING CHILDREN EXPOSED TO OZONE: A COHORT STUDY


Purpose of the Study. The aim of this study was to investigate the relationship between newly diagnosed asthma and team sport participation in children exposed to different concentrations and types of air pollutants.

Study Population. A group of 3535 children, 9 to 16 years old, with no previous history of doctor-diagnosed asthma on a baseline questionnaire, were recruited from 12 southern California schools.

Methods. Interviewers administered baseline and yearly questionnaires regarding new diagnoses of asthma, asthma symptoms, and participation in any of 8 possible team sports in the past year. Air pollution monitoring stations in each community measured ozone, nitrogen dioxide, and particles <10 μm in diameter 10 (PM) every hour and PM 2.5 and acid vapor every 2 weeks. The risk of asthma was assessed relative to the number of high- or low-intensity team sports played at study entry, in communities with high or low levels of the measured air pollutants.

Results. The overall risk of developing asthma was not greater in the high-pollution communities compared with the low-pollution communities, after adjusting for baseline risk factors. In the 6 high-ozone communities, there was a 3.3-fold increased relative risk of developing asthma in children playing 3 or more team sports (95% confidence interval [CI]: 1.9–5.8) compared with those playing no sports. No increase in this relative risk was observed in children playing team sports in low-ozone communities. Across all communities, there was a 1.8-fold increased risk (95% CI: 1.2–2.8) of asthma in children who had played 3 or more team sports in the past year. Spending a large amount of time outside in high-ozone communities was independently associated with an increased risk of asthma. Exposure to pollutants other than ozone was not associated with a higher incidence of asthma.

Conclusions. The incidence of new asthma diagnoses was associated with heavy exercise in communities with high ozone levels, suggesting a contribution of outdoor exercise and air pollution to the development of childhood asthma.

Reviewers’ Comments. The results of this study suggest that increased ventilation rates of air containing high levels of ozone during heavy exercise may predispose children to developing asthma. Although playing high-intensity sports in high-ozonoe communities was associated with a greater incidence of asthma, data comparing the incidence of asthma in children playing high- and low-intensity sports was not shown. In addition, high-intensity individual sports, such as running or cycling, were not included in the questionnaires, so some children may have exercised more intensely than was documented. Ozone levels may be several-fold higher outdoors, so a comparison of the effects of outdoor and indoor exercise would have been useful. A description of asthma symptoms and the relationship of symptoms to sports participation would have been helpful to distinguish chronic wheezing from exercise-induced bronchospasm. Additional studies focusing on personal exposure to ozone, the intensity and location of exercise, and asthma symptoms will be helpful to further investigate this challenging question.

Robert A. Wood, MD
Baltimore, MD
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 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 persistent 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). LT B4 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 LT B4. 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 LT B4, 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. LT B4 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.

FREDERICK E. LEICKLY, MD
Indianapolis, IN

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 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).

ALLEN ADINOFF, MD
Aurora, CO

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 eosinophil cationic protein levels (ECP) and bron-
### INCREASED LEUKOTRIENES IN EXHALED BREATH CONDENSATE IN CHILDHOOD ASTHMA

Frederick E. Leickly

*Pediatrics* 2003;112;471

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: /content/112/Supplement_2/471.3.full.html</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subspecialty Collections</td>
<td>This article, along with others on similar topics, appears in the following collection(s):</td>
</tr>
<tr>
<td></td>
<td><strong>Allergy/Immunology</strong></td>
</tr>
<tr>
<td></td>
<td>/cgi/collection/allergy:immunology_sub</td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:</td>
</tr>
<tr>
<td></td>
<td>/site/misc/Permissions.xhtml</td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online:</td>
</tr>
<tr>
<td></td>
<td>/site/misc/reprints.xhtml</td>
</tr>
</tbody>
</table>
INCREASD LEUKOTRIENES IN EXHALED BREATH CONDENSATE IN CHILDHOOD ASTHMA
Frederick E. Leickly
Pediatrics 2003;112;471

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/112/Supplement_2/471.3.full.html