METHODS. Children were followed prospectively every 8 weeks with noninvasive measures of airway inflammation including exhaled nitric oxide (eNO), sputum induction with bronchial hyperreactivity testing, and exhaled breath condensate. Physicians who were unaware of the results of inflammatory measures made reductions in the steroid dose on the basis of clinical assessment and spirometry. Multiple logistic-regression models were used to determine the usefulness of noninvasive inflammatory markers in predicting successful steroid reduction.

RESULTS. Seventy-five percent of patients tolerated a reduction in steroid dose for at least 2 months; however, 15 (38%) of the 40 patients’ conditions subsequently failed ICS dose reduction and experienced an asthma exacerbation. All children with absence of sputum eosinophils successfully tolerated dose reduction. Increased eNO ≥22 ppb (odds ratio: 6.3; 95% confidence interval: 3.75–10.58) and increased sputum eosinophils ≥3% (odds ratio: 1.38; 95% confidence interval: 1.06–1.81) were significant predictors of failed ICS dose reduction.

CONCLUSIONS. Noninvasive measures of airway inflammation may be useful tools in optimizing treatment of children with asthma.

REVIEWER COMMENTS. These findings suggest that noninvasive measures of airway inflammation are potential adjuncive tools that can be used in pediatric patients who appear clinically stable. However, their clinical usefulness may be limited by several factors. Sputum induction was not successfully performed in 25% of the children, and some measures including bronchial hyperreactivity and breath condensate did not prove to be useful predictors in this study. In addition, criteria for predicting failure were met in 6 (21%) of 28 and 19 (39%) of 49 occasions for sputum eosinophil and eNO cutoffs, respectively, when the child was successfully weaned on the basis of clinical judgment. Conversely, use of noninvasive markers would have prevented an attempt to wean steroids on >70% of occasions when patients subsequently experienced an exacerbation. Inflammatory markers as sole predictors of success or failure will likely result in both significant undertreatment and overtreatment with ICSs. Treatment algorithms that include noninvasive airway inflammatory markers in conjunction with clinical markers are likely the best approach to optimize therapy in children who appear clinically stable.

The Influence of Pulmonary Function Testing on the Management of Asthma in Children

PURPOSE OF THE STUDY. Seventy-five percent of the asthma care in the United States is provided by primary care generalists. The National Asthma Education and Prevention Program guidelines recommend spirometry to assess management once the peak flow has stabilized. The purpose of this study was to assess how pulmonary-function tests (PFTs) performed during a patient encounter influence management decisions beyond the history and physical examination alone.

STUDY POPULATION. A total of 367 asthmatic patients were enrolled during their visit to a pediatric pulmonary clinic. The patients were 4 to 18 years old (mean: 10.4 years), and 60% were male. Patients were excluded if PFTs could not be performed on them, if they had a pulmonary diagnosis other than asthma, or if they had used albuterol within 4 hours.

METHODS. History of asthma symptoms was obtained, and a physical examination was performed. Spirometry was performed before the provider assessment. Peak expiratory flow rate (PEF) was also obtained. The results of the PFTs were not known to the provider at the time of the assessment and initial decision-making. The provider then reviewed the spirometry results and revised the initial recommendations if necessary. Changes in management were analyzed with respect to demographic data and spirometry. The diagnostic accuracy of PEF to detect abnormal lung function was determined.

RESULTS. Eight percent of the patients had mild intermittent asthma, 21% mild persistent asthma, 57% moderate persistent asthma, and 14% severe persistent asthma. Spirometry results were normal in 55% of the visits. Abnormal spirometry occurred equally in boys and girls. Sixty percent of the abnormal results were new compared with previous baseline measurements. The likelihood of an abnormal PFT increased with increasing severity classification. Ten percent of those in the group with mild intermittent asthma had abnormal PFTs, compared with 74% of those with severe persistent asthma. PFT results changed management in 15% of the visits. When spirometry did not change the treatment, the providers were more likely to have already decided to maintain therapy (58%). When spirometry did change treatment, providers were more likely to increase medications (75%). PEF was moderately inaccurate in detecting abnormal spirometry.

CONCLUSIONS. In a clinical setting, even asthma care experts tended to overestimate the degree of asthma control as...
measured by airway obstruction. Spirometry results in this study were just as likely to be abnormal in patients with a normal history and physical examination.

REVIEWER COMMENTS. The next logical question is: Does decision-making enhanced by spirometry result in better outcomes such as decreased symptoms, improved functioning and sleep, fewer exacerbations requiring steroid rescue, and less use of urgent asthma care services? When assessing asthma control, one should always consider comorbidities and adherence issues before stepping up therapy.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2006-0900AAA

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Titrating Steroids on Exhaled Nitric Oxide in Children With Asthma: A Randomized, Controlled Trial
Pijnenburg MW, Bakker EM, Hop WC, De Jongste JC.
Am J Respir Crit Care Med. 2005;172:831–836

PURPOSE OF THE STUDY. To evaluate whether titrating inhaled corticosteroids (ICSs) on the fraction of nitric oxide in exhaled air (FeNO) improves asthma management in children.

STUDY POPULATION. A total of 85 children (aged 6–18 years) with asthma who had been using ICSs at a constant dose for at least 3 months.

METHODS. Children were randomly allocated to 1 of 2 groups stratified for baseline FeNO and dose of ICSs. In one group, ICS doses were determined by FeNO and symptoms according to an algorithm; in the other group, only symptoms influenced ICS dosing. The study duration was 12 months, with 5 visits at 3-month intervals. FeNO was measured at each visit, and the ICS dose was then adapted to FeNO and/or symptom scores that were recorded during the previous 2 weeks.

RESULTS. The cumulative ICS dose was not different between groups. Within the FeNO group, no significant change in FeNO was found, whereas in the symptom group there was a significant increase in FeNO (P = .035). In the FeNO group, hyperresponsiveness improved more than in the symptom group (2.5 vs 1.1 methacholine doubling dose; P = .04). Eight prednisone courses were prescribed for 7 patients in the FeNO group versus 18 courses in 10 patients in the symptom group, but this difference was not statistically significant (P = .60). There was no difference between groups in forced expiratory volume in 1 second (FEV1) or symptom scores.

CONCLUSION. In children with asthma, 1 year of steroid titration on FeNO did not result in higher steroid doses and did improve airway hyperresponsiveness and inflammation.

REVIEWER COMMENTS. I am still not sure what to make of eNO. If monitoring FeNO and making treatment decisions on the basis of the values leads to better asthma outcomes, then it would be a useful tool. Because the FeNO group did not end up receiving a higher cumulative ICS dose, we have to assume that they got more when they needed it and less when they did not. However, the clinical results seem inconsistent. I suppose it is a good thing to have a higher methacholine PD20 (the dose provoking a 20% fall in FEV1) and a lower FeNO, but I would have been happier to see a difference in FEV1 and symptom scores, or if the difference in the number of episodes requiring prednisone courses had been statistically significant. Although I am not sure that I can share the authors’ conclusion that “the time has come to introduce FeNO in to the routine assessment of children with asthma,” I believe we should pay attention to future studies on FeNO monitoring and clinical asthma outcomes.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2006-0900BBB

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Use of Exhaled Nitric Oxide Measurements to Guide Treatment in Chronic Asthma

PURPOSE OF THE STUDY. To determine if measurement of exhaled nitric oxide (FeNO) adds to guideline-driven asthma management for patients with chronic asthma.

STUDY POPULATION. A total of 110 patients (aged 12–75 years) with chronic asthma on inhaled corticosteroids (ICSs) for at least 6 months using stable doses for 6 weeks were initially evaluated. Exclusion criteria included ≥4 courses of oral prednisone in the previous 12 months, admission to the hospital because of asthma in the previous 6 months, ICU admission at any time in the past, or >10 pack-years (an average of 1 pack of cigarettes smoked per day for >10 years) of cigarette smoking.

METHODS. This was a single-blind, placebo-controlled study. In phase 1 the ICS dose was adjusted on the basis of FeNO or guidelines-based algorithms. When the optimal dose was determined, patients were managed for 12 months.

RESULTS. There were 46 patients in the FeNO group and 48 patients in the guideline group who completed the
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Michael S. Kaplan
Pediatrics 2006;118;S32
DOI: 10.1542/peds.2006-0900AAA

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