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.

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Titrating Steroids on Exhaled Nitric Oxide in Children With Asthma: A Randomized, Controlled Trial

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 (FEV$_1$) 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 PD$_{20}$ (the dose provoking a 20% fall in FEV$_1$) and a lower FeNO, but I would have been happier to see a difference in FEV$_1$ 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.

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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
study. The final ICS dose for fluticasone was 370 μg/day (95% confidence interval [CI]: 263–477 μg) in the FeNO group and 641 μg/day (95% CI: 526–756 μg; \( P = .003 \)) in the guideline group. The rate of exacerbations per patient per year was 0.49 (95% CI: 0.31–1.49) in the FeNO group, compared with 0.9 (95% CI: 0.31–1.49; \( P = .27 \)) in the guideline group. There was no difference in the number, frequency, or time of first exacerbation between groups. There was no significant difference in nighttime awakenings, bronchodilator use, percent symptom-free days, or number of oral corticosteroid courses. There also was no difference in percent sputum eosinophils or pulmonary-function tests.

CONCLUSIONS. With the use of FeNO, control of asthma can be obtained with a lower ICS dose.

REVIEWER COMMENTS. The values for FeNO differ from other studies because a flow rate of 250 mL/second was used instead of 50 mL/second. The control group had downward titration of dose on the basis of symptoms, which was achieved only in a minority of patients. This may have magnified the observed difference in the ICS dose. This and subsequent studies suggest that markers of airway inflammation are becoming accepted as important surrogate markers of asthma control.

Patterns of Quick-Relief and Long-term Controller Medication Use in Pediatric Asthma


PURPOSE OF THE STUDY. To simultaneously examine adherence to long-term controller and quick-relief medications and to contrast patterns of medication use in children with asthma.

STUDY POPULATION. There were 75 children aged 8 to 16 years diagnosed with persistent asthma and prescribed quick-relief and long-term medications by metered-dose inhaler. Participants were a subsample of a larger adherence study.

METHODS. This was a cross-sectional, 1-month follow-up study. The primary outcome measure was adherence to both medications as measured by electronic monitoring devices. A classification framework for contrasting adherence patterns between medication classes was developed to identify cases for individual analysis.

RESULTS. High levels of nonadherence to long-term controller medications (median: 46% of prescribed doses taken) and variable patterns of quick-relief medication use (range: 0–251 doses over the month) were documented, but consistent relationships between patterns of medication use across both classes were not found. Individual cases identified by the classification scheme il-
# Use of Exhaled Nitric Oxide Measurements to Guide Treatment in Chronic Asthma

Bradley E. Chipps

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