JOURNAL WATCH
PEDIATRICS & ADOLESCENT MEDICINE

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Measuring exhaled nitric oxide can guide the treatment of asthma ►

The decision to titrate the dose of inhaled corticosteroids (ICS) in patients with asthma is usually based on asthma symptoms and pulmonary function tests (PFTs), but these tests are difficult to do and of uncertain accuracy. Investigators in New Zealand randomly assigned 97 patients (age range, 12 to 73 years) with persistent asthma to dose adjustment of fluticasone based on either conventional guidelines (disease symptoms and PFTs) or measurement of exhaled nitric oxide. Exhaled nitric oxide reflects bronchial-wall inflammation, airway hyper-responsiveness, and induced-sputum eosinophilia.

After a 3- to 12-month run-in phase to establish optimal ICS dose, patients were followed for 12 months, with visits every 2 months for adjustment of the fluticasone dose. Compared with controls, those in the nitric oxide group were receiving a significantly lower dose of ICS at the end of the study (370 μg/day vs. 641 μg/day) without compromising asthma control. There were no significant differences between the groups in nighttime waking, pulmonary function, levels of airway inflammation, or use of bronchodilators or prednisone. Although there was a 46% difference in asthma exacerbations favoring the nitric oxide group, this difference did not reach statistical significance (0.49 vs. 0.90 episodes per patient per year).

Comment ► Although an inexact science, titration of inhaled corticosteroids is a key component of asthma management. Exhaled nitric oxide measurements offer promise because they are accurate and easy to perform. This approach may reduce exposure to ICS and is likely the way children with asthma will be monitored in the future. Its adoption will likely be dependent upon reimbursement eligibility and more research on its use in young children.

Howard Bauchner, MD
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▲ Smith AD *et al.* Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *N Engl J Med* 2005;**352**:2163–73.

BNP can distinguish heart from lung disease in infants ►

Brain natriuretic peptide (BNP) level is a good predictor of congestive heart failure (CHF) in adults, but it is unclear whether BNP level distinguishes between heart failure and respiratory disease in infants. Israeli investigators prospectively measured plasma levels of N-BNP (amino terminal fragment of BNP) in 35 infants (mean age, about 10 months) who presented with either CHF (based on clinical symptoms and echocardiography) or respiratory disease (bronchiolitis or pneumonia).

The two groups of infants differed significantly and distinctly in plasma N-BNP levels: The 17 infants with CHF had levels that ranged from 5736 pg/mL to 99,700 pg/mL. In contrast, levels ranged from 76 pg/mL to 1341 pg/mL in the 18 infants with respiratory disease. The range in a group of 13 control infants was 88 pg/mL to 292 pg/mL. N-BNP levels were 100% accurate in distinguishing infants with cardiac disease from those with respiratory disease.

Comment ► In this study, plasma N-BNP levels accurately distinguished between infants with CHF and those with respiratory disease. Rarely is any diagnostic test found to be 100% accurate. As experience with N-BNP in children increases, we likely will see both false-positives and false-negatives. Nonetheless, the test appears to be helpful in distinguishing cardiac from pulmonary disease in infants.

Howard Bauchner, MD
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▲ Cohen S *et al.* Amino-terminal pro-brain-type natriuretic peptide: heart or lung disease in pediatric respiratory distress? *Pediatrics* 2005;**115**:1347–50.

Travelers' diarrhea: a new approach ►

Rifaximin, a nonabsorbable antibiotic, was recently FDA-approved for the treatment of travelers' diarrhea. It also is used for treatment of bacterial overgrowth syndromes and for hepatic encephalopathy. Rifaximin is active against *Escherichia coli*, but not against salmonella, shigella, or campylobacter. In this manufacturer-supported study, investigators tested rifaximin's efficacy for preventing travelers' diarrhea in 219 U.S. students (age, ⩾18 years) who presented to a school clinic in Mexico without diarrhea.

The primary outcome was progression to travelers' diarrhea (passage of at least three unformed stools in 24 hours and at least one sign of enteric infection).

Students were randomized to receive rifaximin (200 mg one, two, or three times daily) or placebo for 2 weeks. During this period, the incidence of diarrhea was significantly higher in the placebo group than in all rifaximin groups combined (54% vs. 15%). Side effects were minimal, and their incidence was similar in the rifaximin and placebo groups.

Comment ► This study provides clear evidence that rifaximin is safe and efficacious for short-term prophylaxis against travelers' diarrhea in countries where *E. coli* is the predominant travelers' pathogen. Efficacy will vary in countries with a high prevalence of other pathogens. Although this study involved adult students, rifaximin should be safe for children because it is nonabsorbable. Physicians and families will need to compare the risks and benefits of this prophylaxis with that of over-the-counter preparations (e.g., Pepto-Bismol). Most importantly, we need to advise traveling families that no prophylaxis is 100% efficacious and that they remain at risk for parasitic and resistant bacterial infections. The best advice is still to ''boil it, peel it, cook it, or forget it!''

Peggy Sue Weintrub, MD
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▲ DuPont HL *et al.* A randomized, double-blind, placebo-controlled trial of rifaximin to prevent travelers' diarrhea. *Ann Intern Med* 2005;**142**:805–12.

Melanoma is different in children ►

Melanoma is rare in children, but a failed or delayed diagnosis may adversely affect outcomes. Investigators in Italy reviewed data from 33 children younger than 14 years who were diagnosed with melanoma at a single institution during a 25-year period.

All patients were white, and none had a family history of melanoma. The median age at diagnosis was 11 years (range, 3–14 years). Melanoma developed from congenital nevi in seven children and from an acquired nevus in two children. The most

common sites of origin were the extremities. Fourteen of 28 tumors with clinical descriptions had amelanotic lesions (9 pink or pink-white, 5 red), 13 were brown, and 1 was black. Most tumors were raised and resembled pyogenic granulomas. Tumor borders were well defined in 29 children. Nine children had lymph-node involvement, and three had metastases (one with bone and lung metastases at diagnosis). All but five children underwent adequate excision of the primary tumor. Twenty cases required repeat surgery to obtain adequate margins. Event-free and overall survival rates were 60% and 70%, respectively, at 5 years and were 56% and 66% at 10 years. Outcomes were significantly better in children younger than 10 years than in older children (5-year event-free survival, 90% vs. 47%). Only 1 of 10 children younger than 10 years had a recurrence.

Comment ► The common diagnostic criteria for melanoma in adults (ABCD; Asymmetry, Border irregularity, Color variability, Diameter >6 mm) are useless in children. The results of this study suggest that children younger than 10 may have better outcomes than older children, but pediatricians must keep a sharp eye out for small raised tumors in all children.

F. Bruder Stapleton, MD
Published in *Journal Watch Pediatrics and Adolescent Medicine* June 13, 2005

▲ Ferrari A *et al.* Does melanoma behave differently in younger children than in adults? A retrospective study of 33 cases of childhood melanoma from a single institution. *Pediatrics* 2005;**115**:649–54.

Orlistat aids weight management in adolescents ►

Can reducing intestinal fat absorption by pharmacotherapy aid weight management in adolescents? This multicenter, randomized double-blind placebo-controlled study compared the efficacy and safety of orlistat, a gastrointestinal lipase inhibitor, in conjunction with a hypocaloric diet, exercise, and behavioral therapy in 539 obese adolescents (BMI ⩾2 percentage points above the 95th percentile).

Mean BMI decreased in both the treatment and placebo groups during the first 12 weeks; however, at 52 weeks BMI had increased to above baseline in the placebo group, while the orlistat group's BMI was 0.55 points below baseline ($P=0.001$). Similarly, body weight increased by 3.14 kg in the placebo group but only by 0.53 kg in the orlistat group ($P<0.001$). Waist size, hip circumference, and diastolic blood pressure also were significantly lower in the orlistat group.

More than 94% of the participants in each group reported adverse events, but only one serious adverse event, acute cholelithiasis, was possibly related to orlistat therapy. Gastrointestinal symptoms, such as fatty/oily stool, oily spotting and evacuation, abdominal pain, fecal urgency, and flatus with discharge, occurred more often in the orlistat group. Pubertal development, lipids, and bone density did not differ between the two groups.

Comment ► Weight management in obese adolescents is notoriously difficult. These results show that a gastrointestinal lipase inhibitor may help stabilize weight in obese adolescents, albeit with significant gastrointestinal side effects. Possible variations in diet, exercise, and behavioral therapy were not reported. Although a successful tool for weight management is welcome, orlistat's effect on quality of life and its tolerability in adolescents remains to be determined.

F. Bruder Stapleton, MD
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▲ Chanoine J-P *et al.* Effect of orlistat on weight and body composition in obese adolescents: a randomized controlled trial. *JAMA* 2005;**293**:2873–83.