questionnaires is unclear, and the lack of information about the clinical context, including baseline function, current medical treatments, and comorbidity, make it difficult to know how to extrapolate these results to practice. More broadly, these results raise the issue of how family physicians should approach the adoption of complementary therapies. This report is a well-designed effort to evaluate the efficacy of an unconventional treatment. Such efficacy trials should always precede evaluations of possible mechanisms.[1]

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Nebulized Ipratropium for Children with Acute Asthma

Qureshi F, Pestian J, Davis P, and Zaritsky A. Effect of nebulized ipratropium on the hospitalization rates of children with asthma. N Engl J Med 1998; 339:1030-5.

Clinical question **Does ipratropium, when added to beta-agonists and oral corticosteroids, decrease the rate of hospital admission among children with acute asthma attacks?**

Background Ipratropium bromide is a safe and effective medication for the treatment of acute exacerbations of asthma, but large trials have not been conducted to determine its impact on hospital admissions. This study set out to determine whether the addition of ipratropium bromide to standard emergency department therapy for asthma in children would reduce the hospitalization rate.

Population studied Asthmatic children between 2 and 18 years of age presenting to the pediatric emergency department with an acute exacerbation of asthma were eligible for the study. Children were excluded for such reasons as the use of ipratropium within 6 hours before the visit to the emergency department; having a disease known to have a chronic effect on lung function (eg, cystic fibrosis); any possible presence of an intrathoracic foreign body; a contraindication to the use of a beta-agonist; or the need for immediate resuscitation or airway intervention.

Study design and validity This was a prospective randomized double-blinded placebo-controlled trial. Of the 480 children initially identified, 46 children with mild disease were excluded because they responded to initial therapy with inhaled bronchodilators and did not receive the full study medication or placebo. All of the remaining children had a moderate or severe exacerbation, according to either their peak flow rate (50% to 70% of predicted for moderate exacerbation, < 50% of predicted for severe) or a standard, validated symptom score. Patients were assigned to receive either two 500-µg doses of nebulized ipratropium bromide or 2 vials of preservative-free normal saline (the placebo). Children were treated with nebulized albuterol every 20 minutes for 3 doses. At the time of the second dose, an oral corticosteroid was also administered (2 mg/kg of prednisone or prednisolone, to a maximum of 60 mg). Ipratropium or placebo was given with the second and third doses of albuterol. After the first 60 minutes of treatment, albuterol was given at the physician's discretion until a decision was made to admit or discharge the patient.

Outcomes measured The primary outcome was the hospitalization rate. Secondary outcomes included the number of nebulizer treatments until disposition, time to disposition, need for any visits to a medical facility within 72 hours after discharge, and changes in a variety of physiologic surrogate end points.

Results Intervention and control groups were similar other than a greater percentage of girls in the ipratropium group. There was no difference in the rate of admission for patients with moderate asthma (10.1% for ipratropium and 10.7% for the control group), but there was a significantly lower rate of admissions for patients with severe asthma (37.5% vs 52.6%, P=.02). The number of children with severe asthma who would need to be treated (NNT) with ipratropium to prevent 1 admission was 6.6 (95% confidence interval, 3.7-29.4). No children were dropped from the study because of adverse effects and readmission rates within 72 hours were similar.

Recommendations for clinical practice **Ipratropium bromide, when administered in conjunction with albuterol and corticosteroids, decreases the rate of hospital admissions in children with severe acute asthma. Furthermore, an NNT of 6.6 to prevent 1 admission demonstrates that this intervention has a clinically important impact. These results were confirmed by a recent meta-analysis.**[1] **Finally, although no economic assessment has been done, it is reasonable to assume that a significant amount of money might be saved by adding ipratropium to the regimen already in use in**

most emergency departments for the management of severe acute asthma in children.

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D-Dimer Testing in Suspected DVT

Bernardi F, Prandoni P, Lensing AWA, et al. D-dimer testing as an adjunct to ultrasonography in patients with clinically suspected deep vein thrombosis: prospective cohort study. BMJ 1998; 317:1037-40.

Clinical question **Is it safe to withhold anticoagulation from patients with clinically suspected deep vein thrombosis (DVT) who have both normal D-dimer levels and normal venous ultrasonography results?**

Background Current evidence suggests that patients with clinically suspected DVT and a normal venous ultrasound result should have a repeat ultrasound examination at 1 week to safely exclude DVT and continue without anticoagulation. Less than 2% of patients, however, will have evidence of DVT on the repeat examination. Recently developed tests for plasma levels of D-dimer, a fibrin degradation product, have shown high sensitivity and moderate specificity in diagnosing clinically suspected DVT. Highly sensitive tests are generally helpful in ruling out the presence of disease. This study examines the effectiveness of D-dimer testing in ruling out DVT after an initially normal venous ultrasound result.

Population studied This study included 946 adult outpatients with a suspected first episode of DVT. Patients were excluded who were taking anticoagulants for more than 48 hours, had symptoms of pulmonary embolism (PE), were pregnant, or who were unavailable for follow-up. The mean age was 59 years and the mean interval between onset of symptoms and testing was 8 days.

Study design and validity This was a prospective cohort study with a 3-month follow-up period. All patients had venous ultrasonography of the proximal veins. Patients with an abnormal ultrasound result received anticoagulation therapy. A rapid plasma D-dimer test (enzyme-linked immunosorbent assay) was performed on all patients with a normal ultrasound result. Patients with a normal D-dimer test result did not receive anticoagulation therapy and were not retested with ultrasonography. Those with abnormal D-dimer levels had a repeat ultrasound in 1 week. Anticoagulation was withheld if both ultrasound results were normal. At follow-up, all patients were interviewed; diagnostic testing was performed when thromboembolic complications were suspected. Only 2 patients were lost to follow-up, which is important in this type of study.

Outcomes measured The primary outcome was the rate of thromboembolic complications defined as the occurrence of PE before repeat ultrasonography and the occurrence of PE or DVT during the 3 months of follow-up.

Results The prevalence of DVT in the initial population was 27.5%. Of the 686 patients with a normal ultrasound result, 88 had an abnormal D-dimer result requiring repeat ultrasonography. Five patients had evidence of DVT at repeat testing and received anticoagulation therapy. Only 1 of the 598 patients with normal D-dimer levels and normal ultrasound results developed DVT during the 3-month follow-up period. The rate of thromboembolic complications was 0.4% (95% confidence interval, 0.0 - 0.9) in the group of patients not treated with anticoagulants. This rate of complications is at least as low as previously published rates in studies using repeat ultrasonography. The negative predictive value (NPV) is the chance that a patient with a negative test result does not have DVT. In this study the NPV for the initial ultrasonogram was 98.8%; adding a normal D-dimer test result increased the NPV to 99.8%.

Recommendations for clinical practice **Repeat ultrasound testing is not indicated in patients whose initial ultrasonography and D-dimer test results are normal. These patients can be safely followed without anticoagulation. Those patients with abnormal D-dimer test results have a 5.7% chance of having DVT and should have a repeat ultrasound examination at 1 week before the decision to continue withholding anticoagulation. While an economic analysis was not performed, fewer repeat ultrasound examinations should decrease costs while increasing convenience for patients. D-dimer testing is a useful adjunct to venous ultrasound and can be substituted for repeat ultrasound testing in excluding DVT.**

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