

The following abstracts, from medical journals containing literature on asthma, were selected for their relevance to this Special Report.

### Asthma Therapy Guidelines and Emergency Room Use

*This retrospective cross-sectional analysis examined the relationship between national guideline recommendations regarding asthma therapy in a managed care population and emergency room/hospitalization utilization. Assessment of asthma therapy in a managed care organization serving nearly 360,000 patients, 5.2% of whom were asthmatic, demonstrated that there was a lower proportionate utilization of emergency room and hospital services in patients who were treated in accordance with asthma guideline recommendations. Pharmacy claims data on asthma patients revealed that 26.7% used inhaled corticosteroids concomitantly with a short-acting beta<sub>2</sub> agonist, with 85% of this subset using the beta<sub>2</sub> agonists in quantities at or below recommended dosages. Those not utilizing beta<sub>2</sub> agonists according to the recommended dosing guidelines had a significantly higher incidence (P = 0.001) of emergency room and hospital use. Of the 33.2% taking short-acting beta<sub>2</sub> agonists alone, 97.6% were utilizing therapy according to the dosing guidelines, but 2.4% were not. The latter subset had a significantly higher incidence (P = 0.016) of emergency room and hospital use.*

Nestor A, Calhoun AC, Dickson M, Kalik CA. Cross-sectional analysis of the relationship between national guideline recommended asthma drug therapy and emergency/hospital use within a managed care population. *Ann Allergy Asthma Immunol* 1998;81:327-330.

### Dual-Agent Therapy Versus Increased-Dose Monotherapy

*In this 24-week, multicenter, double-blind study involving 437 patients age 12 years and older, the addition of salmeterol to patients who remain symptomatic while using low-dose fluticasone was clinically and statistically superior to increasing the dose of fluticasone. Patients who had been receiving fluticasone 88 µg twice daily for 2 to 4 weeks were randomly assigned to receive either salmeterol 42 µg twice daily or fluticasone 220 µg twice daily. The primary efficacy endpoint was morning peak expiratory flow and secondary measures included forced expiratory volume in one second, asthma scores, nighttime awakenings, and supplemental albuterol use. Reported adverse events and asthma exacerbations were used to assess safety. The addition of salmeterol to fluticasone produced significantly greater improvements in lung function and symptom control than did increasing the fluticasone dose. At 24 weeks, morning peak expiratory flow was increased by 47 L/min from baseline in patients receiving salmeterol plus fluticasone as compared with 24 L/min in those receiving the higher dose of fluticasone (P = 0.001). Similarly, the percent of symptom-free days increased 26% from baseline among those receiving salmeterol plus fluticasone as compared with a 10% increase among those receiving higher-dose fluticasone (P = 0.001). Adverse event profiles were similar in both treatment groups, while those receiving salmeterol plus fluticasone had fewer exacerbations.*

Condemi JJ, Goldstein S, Kalberg C, Yancey S, Emmett A, Rickard K. The addition of salmeterol to fluticasone propionate versus increasing the dose of fluticasone propionate in patients with persistent asthma. Salmeterol Study Group. *Ann Allergy Asthma Immunol* 1999;82:383-389.

**Inhaled Steroids and Hospitalization Rates**

*As demonstrated in this population-based Swedish study, the increased use of inhaled corticosteroids from 1985 through 1993 has resulted in a decreased rate of hospitalization despite a higher prevalence of asthma in children during the same time period. In asthmatic children between the ages of 2 and 18, the number of hospital days per year gradually decreased to less than a third and hospital admissions decreased by 45%. The decrease in hospitalization was most marked in children over the age 5, in whom the number of hospital days was reduced to one fifth and admissions were halved. Although increased asthma education for parents and patients may have been a contributing factor, the authors attribute the decrease in hospitalization to the increased use of inhaled steroids. They also conclude that the use of these agents is a very cost-effective therapeutic approach.*

Wennergren G, Kristjansson S, Strannegard IL. Decrease in hospitalization for treatment of childhood asthma with increased use of antiinflammatory treatment, despite an increase in prevalence of asthma. *J Allergy Clin Immunol* 1996;97:742-748.

**Inhaled Steroids and Risk of Hospitalization**

*This retrospective cohort study of 16,941 asthmatic patients who were members of a large health maintenance organization found that inhaled steroids and, to a lesser extent, cromolyn conferred significant protection against exacerbations of asthma leading to hospitalization. Steroid-associated protection was most pronounced among patients who received the largest amounts of beta agonist. Of those with asthma, 742 (4.4%) were hospitalized for asthma. However,*

*the relative risk of hospitalization among patients receiving inhaled steroids was 0.5 after adjustment for beta agonist dispensing. Further adjustment for age, race, other asthma medications, and amount and type of ambulatory asthma care did not substantially affect the inverse relationship between inhaled steroid use and hospitalization. Cromolyn was also associated with reduced hospitalization risk, especially among children. In contrast, increased beta agonist use was associated with increased risk for hospitalization, even after adjustment for other medications and factors. The authors conclude that the use of inhaled steroids in patients requiring more than occasional use of beta agonists to control asthma symptoms is supported by the study results.*

Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA* 1997;277:887-891.

**Inhaled Salmeterol Versus Oral Zafirlukast**

*As demonstrated in this 4-week, randomized, double-blind, double-dummy, parallel-group, multicenter clinical trial, treatment with inhaled salmeterol provided significantly greater improvement in overall asthma control than oral zafirlukast in patients with persistent asthma, more than 80% of whom were receiving concurrent inhaled corticosteroids. Adolescent and adult study patients were randomized to receive either 42 µg salmeterol twice daily via a metered-dose inhaler or 20 mg oral zafirlukast twice daily. The primary efficacy measure was morning peak expiratory flow. Secondary efficacy measures included forced expiratory volume in one second, evening peak expiratory flow, asthma symptom scores, nighttime awakening, sleep symptoms, supplemental albuterol use, and asthma exacerbations. Both drugs*

produced within-group improvements from baseline in measures of pulmonary function, symptoms, and albuterol use. However, salmeterol produced significantly greater improvements from baseline compared with zafirlukast for morning peak expiratory flow (29.7 L/min versus 13.0 L/min,  $P \leq 0.001$ ), percentage of days and nights with no albuterol use (30.5% versus 11.3%,  $P \leq 0.001$ ), and percentage of symptom-free days (22.4% versus 8.8%,  $P \leq 0.001$ ). Safety profiles, which were assessed by adverse event monitoring, were similar in both treatment groups.

Busse W, Nelson H, Wolfe J, Kalberg C, Yancey SW, Rickard KA. Comparison of inhaled salmeterol and oral zafirlukast in patients with asthma. *J Allergy Clin Immunol* 1999;103:1075-1080.

#### Costs and Effectiveness of Spacer Versus Nebulizer

This randomized, double-blind, placebo-controlled trial, conducted in the emergency room of a children's hospital in New Zealand, compared the costs and effectiveness of albuterol by metered-dose inhaler and spacer versus nebulizer in young children (1 to 4 years of age) with moderate and severe acute asthma. Results indicated that the inhaler and spacer combination was a cost-effective alternative to the nebulizer. In this study, 30 children were randomized to 600  $\mu\text{g}$  albuterol by metered-dose inhaler and spacer followed by placebo delivered via nebu-

lizer. Another 30 children were randomized to placebo via metered-dose inhaler and spacer followed by 2.5 mg albuterol via nebulizer. Baseline characteristics and asthma severity were similar in both groups. Treatments were repeated every 20 minutes until it was apparent that the child no longer needed another dose of bronchodilator, or a total of 6 treatments. Efficacy measures, which were measured at baseline, after each treatment, and 60 minutes after the last treatment, included clinical score, heart rate, respiratory rate, auscultatory findings, and oxygen saturation. The spacer and nebulizer were equally effective for clinical score, respiratory rate, and oxygen saturation, but the spacer produced a greater reduction in wheezing and the nebulizer produced a greater increase in heart rate (11 beats per minute versus 0.17 beats per minute). Fewer children in the spacer group required hospital admission (33% versus 60% in the nebulizer group). The mean cost was NZ\$825 for the spacer group and NZ\$1282 for the nebulizer group, a significant difference ( $P = 0.03$ ). In addition, the authors point out, the combination of the inhaler and spacer was associated with a higher degree of patient acceptance, with 86% of the children and 85% of their parents preferring the inhaler/spacer to the nebulizer.

Lerversha AM, Campanella SG, Aickin RP, Asher MI. Costs and effectiveness of spacer versus nebulizer in young children with moderate and severe acute asthma. *J Pediatr* 2000;136:497-502.