Federal update

From the AHRQ

Report assesses management of acute exacerbations of chronic obstructive pulmonary disease

Researchers at Duke University Evidence-based Practice Center analyzed data on the management of acute exacerbations of chronic obstructive pulmonary disease (COPD) from 1966 through 1999, for the Agency for Healthcare Research and Quality. The report will be the basis for a guideline being developed by three medical organizations.

The report assesses the evidence currently available on the diagnosis, prognosis, and management of acute exacerbation of COPD and on the use of noninvasive positive-pressure ventilation (NPPV) in patients with acute respiratory failure secondary to acute exacerbation of COPD.

The outcomes of interest were ventilatory function, symptoms related to ventilatory function, general functional or health status, mortality, and health services utilization. The findings related to clinical assessment of patients with acute exacerbation of COPD include the following:

- Patients with acute exacerbations of COPD have high rates of abnormalities on chest roentgenograph, particularly when compared with patients with asthma in whom low rates of abnormalities are found.
- Comorbid conditions that often complicate assessment of acute exacerbation of COPD—congestive heart failure and pneumonia—are significant but inexact predictors of two abnormalities on chest radiograph—pulmonary edema and infiltrate.
- Prevalence of deep venous thrombosis among patients hospitalized for acute exacerbations of COPD is high in some studies; however, few data are available to quantify the risk for pulmonary embolus among patients with acute exacerbation of COPD with or without known deep venous thrombosis.

Among the findings related to the prognosis of patients with acute exacerbation of COPD are the following:

- While several factors are associated with worsening clinical condition in patients with acute exacerbation of COPD, no model accurately predicts clinical outcomes; therefore, ongoing monitoring is needed for many patients.
- Among patients with acute exacerbation of COPD selected for outpatient treatment, relapse rates were between 11% and 17% at 48 hours and between 23% and 32% at 2 weeks. Hospitalization at index visit ranged from 24.2% to 71% among patients presenting to the emergency department.
- The history of individual patients was consistently identified as predictive of relapse, as was baseline pulmonary function, measured by forced expiratory volume in 1 second (FEV_1) or forced vital capacity. Data that describe acute respiratory physiology predicted relapse, as did data that describe treatments used in the emergency department and clinical response.

Other findings include the following:

- Trials of antibiotic treatment of patients with acute exacerbations of COPD show evidence of improvement in pulmonary function and suggest that patients with greater evidence of bacterial infection and greater severe illness benefit more from antibiotics; however, this has not been conclusively demonstrated.
- Inhaled ipratropium bromide and beta2-agonists were shown to have similar effects; however, neither class demonstrated conclusive evidence of benefit in placebo or other no-treatment control trials. Most trials were too small to demonstrate a clinically important benefit.
- Several trials provided evidence that a course of systemic corticosteroids provides benefit in patients hospitalized with acute exacerbation of COPD. The risk of treatment failure was reduced by 10%, and FEV_1 showed an improvement averaging about 0.1 L in the first hours to days of treatment.
- Studies show no benefit from the mucolytic drugs studied (ambroxol, bromhexine, domiodol, potassium iodide, and S-carboxymethyl-cysteine) in improving ventilatory function in acute exacerbation of COPD. Some studies reported subjective improvement in symptoms associated with decreasing sputum viscosity.

Findings related to the use of NPPV are the following:

- NPPV is an effective alternative to mechanical ventilation by endotracheal intubation for some patients with acute respiratory failure secondary to acute exacerbation of COPD.
- Selection of mask interface and/or ventilator mode can be important to patient tolerance, and thus to the efficacy of the intervention. Each mask and ventilation mode comes with its own set of morbidities. The pressure-support ventilation and continuous or bi-level positive airway pressure modes of ventilation appear to be best tolerated and most effective for correcting hypercarbia. Assist control ventilation mode with NPPV is generally poorly tolerated unless volume and rate are adjusted to the individual patient.

A limited number of prepublication copies of this report are available free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295.

From the FDA

FDA approves health claim for vitamin B

The Food and Drug Administration agreed to permit a health claim to appear on labels of dietary supplements that contain a combination of folic acid and vitamins B_6 and B_{12} touting the ability of vitamin B to reduce the risk of vascular disease. The agency had

approved a longer, less-specific claim in November; however, the dietary supplement industry objected to the version.

The approved claim reads, "As part of a well-balanced diet that is low in saturated fat and cholesterol, folic acid, vitamin B_6, and vitamin B_{12} may reduce the risk of vascular disease." It is to be followed by an FDA statement that includes "...evidence to support the claim is inconclusive." As the new claim has been approved, legal action taken on behalf of dietary supplement manufacturers to have the claim cleared will be dismissed.

FDA finds allergens unlisted in ingredients

The Food and Drug Administration found that 25% of food manufacturers in a study include—but do not list—ingredients that can cause potentially fatal allergic reactions, putting people with food allergies who depend on labels at risk. Further, 47% of the manufacturers did not test their products for label and content congruity.

The study of 85 cookie, candy, and ice cream manufacturers was undertaken because of an increase in the recall of foods due to unlisted allergens. Allergy-inducing raw ingredients (for example, nuts) were unintentionally added to products as a result of being prepared alongside other products.

Seven million people in the United States suffer from food allergies.

FDA approves inhalation solution for bronchospasm

The Food and Drug Administration approved ipratropium bromide and albuterol sulfate (DuoNeb Inhalation Solution) for patients with bronchospasm associated with chronic obstructive pulmonary disease who require more than one bronchodilator. The premeasured combination of solutions in a one unit-dose vial facilitates faster treatment time and reduces risk of cross-contamination.

Trial results involving 863 people indicate that the combination of ipratropium bromide and albuterol sulfate improves bronchodilation over albuterol sulfate alone (24%) and ipratropium bromide alone (37%).

Side effects include chest pain, pharyngitis, diarrhea, nausea, bronchitis, and leg cramps. Albuterol sulfate can have a significant cardiovascular effect, significant hypokalemia, and paradoxial bronchospasm.

FDA approves methotrexate

The Food and Drug Administration approved new dosage strengths of methotrexate (Trexall) tablets—5 mg, 7.5 mg, 10 mg, and 15 mg—for patients with severe psoriasis, adult rheumatoid arthritis, and certain neoplastic diseases. The antimetabolite had only been available as 2.5-mg tablets. Physicians may now prescribe higher dosage strengths using scored tablets.

FDA approves pantoprazole intravenous formulation for patients with gastroesophageal reflux disease

The Food and Drug Administration approved pantoprazole (Protonix IV) intravenous formulation for short-term treatment of patients with gastroesophageal reflux disease who cannot take pantoprazole sodium orally. Until now, physicians had used intravenous H2-antagonists to treat these patients.

The safety and efficacy of pantoprazole IV for injection as an initial treatment have not been demonstrated. The most common reported adverse events associated with the intravenous formulation are abdominal pain, chest pain, rash, and pruritus.

More than 40% of adults in the United States have gastroesophageal reflux disease.

From the CDC

Chemical exposure report provides new tool for tracking

The Centers for Disease Control and Prevention released the first National Report on Human Exposure to Environmental Chemicals. Whereas chemical exposure had been estimated by measuring air, water, and soil samples, measurements in this study were taken directly from human blood and urine samples. The report will be used as a base measurement of chemical levels to determine trends in exposure. It does not include information on health risks associated with exposure.

The report measures population exposure to 27 environmental chemicals, including metals (for example, lead, mercury, cadmium), pesticide metabolites, phthalate metabolites, and cotinine, a nicotine metabolite.

Scientists measured cotinine (a breakdown product of nicotine after it enters the body), which indicates the amount of exposure a person has had to tobacco, and found a 75% decline in serum cotinine levels for nonsmokers—a reduction in exposure since 1991. Tobacco smoke remains a major public health issue, however, as more than half of American teenagers are exposed to the carcinogen.

Another finding is that blood lead levels continue to decline among children overall; however, children who live in environments at high risk for lead exposure remain a public health concern.

Scientists will continue to measure the 27 original substances and will add other substances to future reports.

Surgeon general report targets smoking in women and girls

As lung cancer accounted for 25% of all female cancer deaths in 2000 (up from 3% in 1950), the US surgeon general has issued a 675-page report, "Women and Smoking," prepared by officials at the Centers for Disease Control and Prevention. Since 1980, three million women have died prematurely because of smoking, and lung cancer claims 27,000 more women's lives each year than breast cancer.

In 2000, 30% of high school senior girls reported smoking in the past month. In response, Health and Human Services representatives plan to develop strategies to educate teenagers about smoking and to curb tobacco marketing aimed at this group, as 80% of smokers begin smoking as teenagers. The report also states that women who do not attend college after high school are most likely to smoke and less likely to quit.

Smoking—the leading cause of cancer death in women and of preventable death for both men and women—claims more than 40,000 lives a year and can shorten a woman's life by 14 years.

The report and a summary can be found

at *www.surgeongeneral.gov/library*. The chapter that relates the effects of tobacco to states of disease, "Health Consequences of Tobacco Use Among Women," will be of special interest to health professionals.

From the NIH

Immunotoxin-based treatment benefits patients with hairy cell leukemia

Of 16 patients with chemotherapy-resistant hairy cell leukemia who received a new immunotoxin-based drug, 11 had complete remissions during an ongoing Phase 1 trial conducted by the National Cancer Institute, National Institutes of Health. The high response rate—remissions of 18 months with few major side effects—have researchers optimistic about the drug's use for patients with other cancers because a significant benefit was seen in patients with chronic lymphocytic leukemia treated with BL22.

BL22 is a recombinant immunotoxin designed to link cell-killing toxins to antibodies that guide the toxin to the cancer cell. The drug is created by cloning portions of antibodies to portions of a toxin excreted by bacteria. Stem cells appear to replace normal B cells lost in short-term treatment. It appears that BL22 cleans the body of malignant circulating cells but may also remove malignant stem cells.

The most serious side effect of BL22 is a decrease in platelet and red blood cell counts, which suggests clotting in the kidney. Patients who had kidney failure associated with treatment recovered and had complete remissions.

Other protein found in development of B cells

An inhibitory enzyme called TIMP-1 appears to activate expression of IL-10 in normal B cells and B-cell non-Hodgkin's lymphoma, according to scientists at the National Cancer Institute, National Institutes of Health. This finding may have implications for previous trial results that indicate IL-10 is associated with maturation of B lymphocytes, as TIMP-1 was present in cells and serum in the studies. Further, high TIMP-1 levels were found in high-grade B-cell lymphoma and were nearly absent in low-grade cancers.

For B lymphocytes to secrete antibodies, they must first differentiate and mature. IL-10 was reported to bes the signaling protein essential for maturation; however, TIMP-1 has also been shown to signal cells to grow. In this study, scientists performed trials with Burkitt's lymphoma cell lines and found that all of the cell lines that expressed TIMP-1 also expressed IL-10, but in those lacking TIMP-1, no IL-10 was produced. Further, the expression of IL-10 was proportional to the level of TIMP-1 in the cell. ◆