**Top Stories**

**Intervention Cut Central Catheter Infections by 66%**

By Mary Ann Moon

A “simple and inexpensive” intervention to reduce ICU infections related to central catheter lines decreased the infection rate by 66% in 107 hospitals throughout Michigan, according to a new study.

The overall median rate of central-catheter-related bloodstream infections per 1,000 catheter-days was held to zero throughout 18 months of follow-up, reported Dr. Peter Pronovost of Johns Hopkins University, Baltimore, and his associates.

“Important reductions in morbidity and health care costs could be achieved if the intervention could be introduced successfully nationwide or worldwide.”

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**FDA Panel Votes To Strip Ketek of Two Indications**

**Chronic bronchitis exacerbations mixed.**

By Alicia Ault

Silver Spring, Md. — The antibiotic Ketek (telithromycin) is neither safe nor effective for treating acute exacerbation of chronic bronchitis or acute sinusitis, according to a Food and Drug Administration advisory committee that recommended that the agency remove those indications from the drug’s approved labeling.

The panel—a joint meeting of the FDA’s Anti-Infective Drugs and Drug Safety and Risk Management Advisory committees—concluded that although Ketek has been marketed since 2004, safety concerns argue against using the drug in two conditions that generally resolve on their own.

The panel voted 16-1 that Ketek should retain its approval for treating mild to moderate community-acquired pneumonia, but as a second- or third-line therapy. Ketek’s maker, Sanofi-Aventis, also presented data suggesting that the drug may be effective against multidrug-resistant Streptococcus pneumoniae, which was persuasive to the committee.

“If this is a drug that we need, but this is not something I’d reach for, and this is something I’d discourage people from using,” said Dr. Margo Smith, a panelist from the Washington Hospital Center.

If the FDA follows the panel’s advice, as it normally does, the agency would determine how to educate physicians on the revised uses. Sanofi-Aventis agreed that it would create a medication guide for consumers. FDA and Sanofi-Aventis would work out the content of the black box warning, which is likely to touch on the potential for liver toxicity, visual disturbances, loss...

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**Study: Ambrisentan Effective in PAH**

By Bruce Jancin

Salt Lake City — The investigational endothelin receptor antagonist ambrisentan appears to provide a more favorable risk/benefit ratio than current therapies do for pulmonary arterial hypertension, Dr. Lewis J. Rubin, FCCP, said at the annual meeting of the American College of Chest Physicians.

Results of the phase III randomized double-blind ARIES-I trial demonstrate that ambrisentan has good efficacy as once-daily oral therapy. What sets it apart from other effective endothelin receptor antagonists is that it displayed no liver toxicity in ARIES-I. No subjects developed liver function test abnormalities over 12 weeks, noted Dr. Rubin, professor of medicine at the University of California, San Diego.

Ambrisentan’s manufacturer, Gilead Sciences, last month submitted the drug for approval by the Food and Drug Administration for once-daily treatment of pulmonary arterial hypertension.

Ambrisentan is a high affinity propanoic acid-class endothelin receptor type A-selective agent with no interactions with warfarin or sildenafil.

Two oral twice-daily sulfonamide-class agents, bosentan (the endothelin receptor antagonist now on the market) and sitaxsentan (now under FDA review), are both associated with dose-dependent increases...
Panel Debates Ketek Safety

Ketek • from page 1

Ketek was under scrutiny during most of 2006. Senator Chuck Grassley (R-Iowa) has alleged that the drug was approved on the basis of a fraudulent trial, known as study 3014. On the eve of the 2-day FDA panel meeting, Sen. Grassley released a letter to — of his Finance Committee’s investigation into the Ketek approval. He alleged that FDA managers failed to notify the Anti-Infective Drugs Advisory Committee when it met in 2003 that the agency had concerns about study 3014’s integrity.

The panel recommended approval at that time, based in part on study 3014. The agency later held a closed-door meeting with the panel to discuss problems with study 3014, but Sen. Grassley alleges that the committee members still were not given a complete story.

In making the original approval decision, the agency determined that it could toss out tainted data from study 3014 and instead rely on postmarketing data collected on about 4 million patient exposures in Europe, said Dr. Janice Soreth, director of the FDA’s division of anti-infective and ophthalmology products, at the December meeting.

Several speakers at the FDA meeting, including a reviewer recently departed from the Ketek team, had heard of the controversy re emerging during the poll. The agency’s reliance on postmarketing data instead of a prospective safety study for approval.

But the advisory panel did not seem as concerned. The older postmarketing safety information—combined with updated surveillance reports from Europe and postmarketing data collected in the United States since Ketek’s introduction—was presented at length.

FDA staffers disagreed on the incidence of side effects, as did the FDA and Sanofi-Aventis. Sanofi estimated that at date, the reporting rate in Europe for serious hepatic reactions is 4 to 10 per million courses of therapy. According to the FDA, from 2004 to 2006 there were 12 cases of acute liver failure among 5 million U.S. prescriptions, for a reporting rate of 23/10 million prescriptions. By comparison, the antibiotic trovafloxacin (trovafloxacin) had a rate of 98 per 10 million in its first year on the market. The drug was subsequently recalled.

The FDA asked several experts from the Drug-Induced Liver Injury Network to take a closer look at 53 reports of hepatic toxicity associated with Ketek use. The network is a cooperative funded by the National Institute of Diabetes, Digestive, and Kidney Disorders.

One of those experts, Dr. William Lee, director of the clinical center for liver diseases at the University of Texas at Dallas, said that of the 53 patients, 44 were hospitalized, and there were five deaths and two liver transplants. The cases had similar clinical features, including rapid onset, prominent liver joint, aches, and right upper quadrant pain.

Dr. Lee said he believed that 28 of the 53 were very likely or probably caused by Ketek, 17 were possibly related, and 8 had insufficient data to make a ruling. He said the hospitalization rate was probably 1 in 10,000 for liver toxicity and 1 in $10,000 for acute liver failure. Ketek’s profile would be worse if it were a chronic medication, he said. “The severity may be limited simply because the drug exposure is quite short,” Dr. Lee said.

Sanofi maintained that the hepatotoxicity was similar to that of other antibiotics. The panel was split on whether Ketek was an outlier.

Committee members were more concerned about exacerbations of myasthenia gravis, a neurological condition affecting 35,000-70,000 Americans. But many individuals aren’t aware they have the condition and might unwittingly take Ketek. The drug’s label already includes a warning against use in affected patients, but that has not stopped such use.

The FDA’s review found 33 reports of exacerbations of myasthenia gravis since 2004. Of those, seven were life threatening and two required ventilation or intubation.

There were 71 cases of vision disorders and 23 cases of disturbances in consciousness with serious outcomes. In one case, an 18-year-old passed out while driving and struck and killed a pedestrian.

Sanofi-Aventis stuck to its data showing that Ketek was no different from other drugs in the class. “Overall, we believe that the safety risks with telithromycin appear to be similar to widely prescribed antibiotics,” said Dr. Bruno Leroy, head of the company’s internal medicines.

Some FDA staffers were not convinced. “Ketek stands out among the drugs in the class.” Overall, we believe that the safety risks with telithromycin appear to be similar to widely prescribed antibiotics,” said Dr. Bruno Leroy, head of the company’s internal medicines.

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Some FDA staffer
Think of COPD as a Multisystem Disease

COPD takes its heaviest extrapulmonary toll on the cardiovascular, muscular, and skeletal systems.

BY BRUCE JANCIN
Elsevier Global Medical News

When Defining COPD in the Elderly, It May Be Best to Go With the GOLD

SALT LAKE CITY — It’s high time to recognize that chronic obstructive pulmonary disease is a multisystem disorder extending well beyond the lungs, Dr. Stanley B. Fiel, FCCP, said at a satellite symposium held in conjunction with the annual meeting of the American College of Chest Physicians.

Chronic obstructive pulmonary disease (COPD) is best viewed as a systemic inflammatory disorder, not merely an inflammatory disorder of the respiratory tract. The extrapulmonary systems where COPD takes its heaviest toll are the cardiovascular, muscular, and skeletal.

Even among patients with severe COPD, only about one-quarter of deaths are due to COPD. Among those with moderate COPD, it’s closer to 5%. The predominant cause of mortality in COPD patients is atherosclerotic cardiovascular disease, added Dr. Fiel, chairman of medicine at Morristown (N.J.) Memorial Hospital. He has served as a consultant to Altana Pharma, which sponsored the symposium.

Cardiovascular Risk

Major contributions to understanding the association between COPD and cardiovascular risk have been provided by Dr. Don D. Sin, FCCP, of the University of British Columbia, Vancouver, and his coinvestigators. They showed in an analysis of 1,861 participants in the first National Health and Nutrition Examination Survey Epidemiologic Followup Study that a reduced forced expiratory volume in 1 second (FEV1) is a risk factor for cardiovascular hospitalization or mortality independent of smoking history, Framingham risk score, and other potential confounders. Individuals in the lowest FEV1 quintile had a 5.6-fold increased risk of fatal ischemic heart disease, compared with those in the top quintile. That was true even across a relatively narrow range of FEV1, declines, from a mean of 109% to 88% of predicted (Chest 2003;127:1952-9). As part of the same report, the Canadian investigators conducted a meta-analysis of 12 large published cohort studies that looked at cardiovascular mortality based on FEV1, in nearly 84,000 subjects.

Some of the worst FEV1 quintile had an adjusted 75% increased risk of cardiovascular mortality, compared with those in the best quintile.

“So why don’t primary care physicians do more routine measuring of FEV1? It’s a good question, since we know that just as blood pressure is an independent risk factor for cardiovascular mortality, so does serum albumin, in patients regardless of whether they smoke or don’t smoke,” Dr. Fiel said.

One major difference between high blood pressure and low FEV1, as cardiovascular risk factors, however, is that as yet there are no prospective data demonstrating how to intervene effectively in COPD patients to reduce their cardiovascular risk. He conceded. Investigative interest in potential targets for preventive therapy is focused on the elevated levels of fibrinogen, neutrophils, platelets, and C-reactive protein that characterize COPD patients. Inflammatory cytokines are also upregulated in COPD patients, a proinflammatory state similar to that present in rheumatoid arthritis.

Using the GOLD criteria might result in overdiagnosis of mild COPD in the elderly. In response to this argument, the latest American Thoracic Society/European Respiratory Society guidelines for interpreting spirometry, published in 2005, recommend adopting the age-adjusted LLN to classify obstruction on spirometry. But this has a problem: It is based on a meta-analysis of cross-sectional data. And cross-sectional data do not provide any information about longitudinal outcomes—which is what really matters, Dr. Mannino said. To elevate the debate by introducing outcomes data, he and his coinvestigators turned to the National Institutes of Health-sponsored prospective epidemiologic Cardiovascular Health Study. He reported on 4,965 study participants through age 64 years who were examined between baseline spirometry and up to 11 years of follow-up. Twelve percent were current smokers, and 42% were former smokers; 95% were white, and 57% were women. The population of interest in this analysis was the 1,134 subjects whose baseline FEV1/FVC was less than 0.70 but above the LLN.

Death occurred in 32.6% of the 4,965 subjects during follow-up, and 38.8% had one or more COPD-related hospitalizations. The subgroup whose FEV1/FVC fell between 0.70 and the LLN had an adjusted highly significant 30% increased risk of mortality and a 2.6-fold risk of COPD-related hospitalization during follow-up, compared with asymptomatic subjects with normal lung function.

“If these people were characterized using the LLN, they would all be counted as normal—and they’re clearly not normal,” Dr. Mannino noted, adding that intervention would likely help these patients.

The group whose FEV1/FVC was less than 0.70 but above the LLN had a 30% increased risk of mortality. DR. MANNINO

The overarching goal of Healthy People 2010 is to reduce health disparities in the U.S. population, and I think you’ll agree that we have a health disparity here with respect to smoking groups,” said Dr. Lee of the epidemiology and public health department at the University of Miami.

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COPD patients with an FEV1 less than 50% of predicted, corresponding to Gold stage 3 or 4 disease. Among patients with COPD and an FEV1 greater than 50% of predicted, osteoporosis or osteopenia was present in 69% (Am J Respir Crit Care Med 2004;170:1286-93).

Other studies have shown that the bone density abnormalities in COPD can’t be explained simply by being a consequence of prolonged use of corticosteroids. Such abnormalities are present in most steroid-naive patients with advanced COPD.

Skeletal Muscle Atrophy

Loss of fat-free mass in patients with COPD is common and is associated with reduced endurance, poor quality of life, and decreased exercise ability. Dutch investigators recently reported that the prevalence of abnormal body composition—defined by low mass index and/or low fat-free mass index—was 43% among women and 21% in men in a cohort of 389 outliers with moderate to severe COPD (Respir Med 2006;100:1349-55).

The intermediary between systemic inflammation and cachexia in COPD is thought to be the nuclear transcription factor kappa beta, Dr. Fiel said.

Drivers of COPD

BY BRUCE JANCIN
Elsevier Global Medical News

WASHINGTON — Significantly fewer white-collar workers than blue-collar workers are smokers, according to National Health Interview Survey data from more than 140,000 respondents.

Pooled smoking data from 1997 to 2004 showed the highest reported rates among blue-collar construction workers (39%) and the lowest reported rates among health professionals (5%), said David J. Lee, Ph.D., who presented the findings at a conference on tobacco control sponsored by the American Cancer Society.

“The overarching goal of Healthy People 2010 is to reduce health disparities in the U.S. population, and I think you’ll agree that we have a health disparity here with respect to smoking groups,” said Dr. Lee of the epidemiology and public health department at the University of Miami.

Dr. Lee cited his study of 8-year smoking trends by occupational category based on NHIS data in which the 20 occupations with the highest smoking rates (all greater than 40%) included blue-collar jobs, and included bartenders, waiters, main- tenance workers, truck drivers, and carpenters (J Occup Environ Med. 2004;46:538-48).

“We saw some evidence of a smoking decline [among rooers who topped the list with a 58% smoking rate], but it was not statistically significant,” he said. But office-based physicians found that the occupations with the lowest smoking rates were classified as white-collar jobs, and ranged from 15% among airline pilots to 4% among cler- gy and physicians.

Despite evidence of declining smoking rates in some blue-collar professions, the findings suggest that blue-collar workers need more attention from their employers and health professionals if they are going to stop smoking.

Workplace health and safety programs offer excellent opportunities to encourage smokers to quit, especially those who rarely see a physician in the clinic, Dr. Lee said. But office-based physicians who ask their blue-collar patients about smoking and assist those who want to quit are effective in reducing the occupational disparities, he emphasized.

—Heidi Splete
Studies Support Safety of Long-Acting β-Agonists

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Reassurance about the cardiovascular safety of long-acting β₂-agonists in patients with chronic obstructive pulmonary disease was provided by two large studies presented at the annual meeting of the American College of Chest Physicians.

Sarika S. Ogale presented a nested case-control study involving 104,459 predomi-
nantly elderly male patients with newly diagnosed COPD in the national Department of Veterans Affairs database. During an average follow-up of 1.5 years and a maximum of 3.8 years, 6,954 of the patients were hospitalized for acute coronary syndrome, heart failure, or cardiac arrhythmia. Heart failure was the primary admitting diagnosis in nearly 3,100 patients, with the remainder being split roughly equally between ACS and arrhythmia. The control group consisted of 34,770 VA pa-
tients matched for age and du-
ration of COPD.

After adjusting for COPD severity as re-
lected in the number of exacerbations in the year prior to the event, use of other medications, cardiovascular risk factor pro-iles, and other factors, the cardiovascular event rate in COPD patients who had ever used long-acting β-agonists (LABAs) proved to be virtually identical to that in never users, according to Ms. Ogale, a graduate student in the pharmaceutical medicine graduate program at the Uni-
versity of Washington, Seattle.

She and her coworkers also broke down the data by comparing cardiovascular event rates in patients who had used LABAs for up to 4 months with those in pa-
tients who had a greater than 4-month his-
tory of cumulative exposure to LABAs. They chose 4 months as the cutoff be-
cause that was the median duration of us-
age in the study. Once again, event rates were virtually identical in the group with less or no LABA exposure and the group with longer duration of LABA usage.

The investigators next plan to reanalyze the data looking at all-cause mortality. They also want to see if the results vary by racial group.

Short-acting β-agonists such as albuterol have been associ-
ated with an increased risk of cardiovascular events in ob-
servational studies. LABAs were linked to increased mor-
tality in a study of American anesthetics in the Salmeterol Multicenter Asthma Research Trial (SMART), whose find-
ings have come under heavy criticism. But the cardiovas-
cular safety of LABAs in the COPD population has previ-
ously been looked at mainly in studies too short in duration to be conclusive.

In a separate presentation, Dr. Bartolome R. Celli, FCCP, said there was no hint of increased mortality in the same arm of the landmark Towards a Revolution in COPD Health (TORCH) study. In fact, there was a nonsignificant trend for greater survival in the salmeterol arm than in the fluticasone arm of the 3-year double-blind trial in which 6,112 COPD patients were randomized to twice-daily salmeterol, fluticasone, placebo, or the salmeterol/fluticasone combination known as Seretide in the United States as Advair and in Eu-
rope as Serevent, according to Dr. Celli, professor of medicine at Tufts University, Boston.

Drug’s Liver Effects Limited

Ambrisentan • from page 1

in liver function abnormalities that can force treatment discon-
tinuation.

The ARIES-1 trial involved 202 patients with pulmonary ar-
terial hypertension (PAH), who were randomized to 12 weeks of double-blind placebo or once-
daily ambrisentan at 5 mg or 10 mg.

Recently two-thirds of patients had idiopathic pulmonary ar-
terial hypertension. Most others had pulmonary arterial hypertension associated with connective tissue disease.

Most subjects had moderate disease; 58% of patients were World Health Organization class II, 32% were class III, and 10% were class IV.

The study patients’ mean base-
line 6-minute walk distance was

341 m, which is indicative of moderate impairment.

The primary study end point was change in 6-minute walk dis-
tance over 12 weeks. It increased by 43.6 m with 10 mg of am-
brisentan and 24.8 m with 5 mg and it decreased by 7.8 m on placebo, suggesting a possible dose-response effect.

The edema is an endothelin receptor–class effect.

It is typically mild and rea-
sonably well managed with low-dose diuretics without need for dose adjustment of the anti-PAH drug, Dr. Rubin said.

During a mean ex-
tended follow-up of 1.4 years and a maxi-

Drug’s Liver Effects Limited

Ambrisentan • from page 1

Dr. Thomas Behrenbeck, FCCP, comments: Ambucidant is a new representative of the endothelin receptor antagonist class, one of the three major mechanistic pathways known to be affected in patients with pulmonary arterial hypertension.

This study is encouraging, as the drug does seem to cause liver function abnormalities, which have limited treatment with the other drugs of the class.

It remains to be seen if am-
brisentan will have a beneficial ef-
fect on the long-term outcome of these patients.

The laboratory-defined cutoff for pneumococcal resistance to erythro-
mycin is 16 mg/mL. Some researchers, however, have advocated the 16 mg/mL cutoff value as more likely to result in breakthrough bacteremia, Dr. Grant explained.

Comparison of isolates from all three patient groups found that breakthrough bacteremia occurred at a broad range of MIC values above 1 mg/mL, not just at the higher levels of resistance, Dr. Grant said.

Among patients with MIC values of 1 mg/mL or greater, the distribution of MICs did not differ significantly between groups.

An MIC of 16 mg/mL or greater was observed in 39% of the group who failed macrolide therapy and in 6% of patients who developed bacteremia after recent macrolide therapy or not taking antibiotics.

Dr. Susan Harding, FCCP, comments: We need to recognize potential treatment failures because of macrolide resistance, especially in patients who have recently used macrolides.

By Sherry Boschert
Elsevier Global Medical News

San Francisco — Drug resistance was a common cause of treatment fail-
ure in 26 patients with community-ac-
quired pneumonia who developed bacteremia while being treated with macrolide antibiotics. Dr. Gavin Bayan Grant said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Of the 26 patients who developed bac-
teriaemia while on erythromycin, clarith-
romycin, or azithromycin therapy, 21 (81%) had resistant organisms, com-
pared with 15 (44%) of 34 patients who developed bacteremia after one month of one of the macrolides (defined as 16-90 days before the bacteremia diagnosis) and 14% of 721 patients who had not been taking any antibiotics and de-
veloped bacteremia.

Macrolide antibiotics are standard therapy for outpatients treatment of pneumonia, and evidence that signifi-
cant macrolide resistance occurs has been inconclusive, said Dr. Grant of the Centers for Disease Control and Pre-
vention, Atlanta.

After controlling for patient age, im-
munosuppression, chronic comorbidi-
ties, and residence in a long-term care facility, patients failing macrolide thera-
py were 5 times more likely to have resistant organisms, compared with pa-
tients who developed bacteremia after recent macrolide use, and 26 times more likely to have resistance than patients with bacteremia who had not been tak-
ing antibiotics.

The study also found that clinicians who define macrolide resistance using a cutoff of a minimum inhibitory con-
centration (MIC) of at least 16 mcg/mL will miss a significant percentage of the treatment failures.

“Failures often occur at macrolide MICs less than 16 mcg/mL,” Dr. Grant said.

Dr. Grant is a consultant to Myogen Inc., the company that sponsored the ARIES-1 clinical trial.

Gilead Sciences acquired Myo-
gen in November 2006, and will market ambrisentan in the Unit-
ed States. GlaxoSmithKline will market ambrisentan outside the United States.

The incidence of liver function test abnormalities in the ARIES-1 phase III trial was zero.

Dr. Rubin is a consultant to Myogen Inc., the company that sponsored the ARIES-1 clinical trial.

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brisentan will have a beneficial ef-
fect on the long-term outcome of these patients.
Home Nebulizer Misuse Cited in Asthma Deaths

By Bruce Jancin
Elsevier Global Medical News

SALT LAKE CITY — Misuse of home nebulizers appears to be an important factor in many asthma deaths in children and young adults, Dr. Amit Gupta said at the annual meeting of the American College of Chest Physicians.

His retrospective study of all 86 asthma deaths in 2- to 34-year-olds in Michigan in 2002-2004 concluded that many involved individuals had a home nebulizer but weren’t using it in accordance with the NIH-National Asthma Education and Prevention Program guidelines.

“The widespread prescription and use of home nebulizers in asthma may lead to an overreliance on bronchodilators and underuse of steroids. This may lead to subsequent delay in seeking medical care during an acute exacerbation, or to poor chronic control of asthma, which may eventually lead to a poor outcome,” said Dr. Gupta of Michigan State University, East Lansing.

The study focused on 86 asthma deaths in Michigan; 48 of these deaths involved 19- to 34-year-olds. Of the 38 pediatric deaths, all but 1 occurred in children at least 5 years old.

A panel of experts reviewed medical records for 1 year before death as well as death certificate data and the results of next-of-kin interviews obtained in 61 cases.

Surprisingly, 35% of adult fatalities occurred in people with moderate persistent asthma. Dr. Gupta noted.

National Asthma Education and Prevention Program guidelines recommend limiting the use of home nebulizers to acute asthma exacerbations that are monitored with a peak flow meter (PFM). Patients whose symptoms and peak flow readings don’t improve after a single use are supposed to seek immediate medical attention. And all patients prescribed a home nebulizer are supposed to have a written asthma action plan to guide them in the event of an acute exacerbation or emergency.

The Michigan investigators found that 52 patients had a home nebulizer, but only 9 had a written asthma action plan—and none used it to monitor their disease. Sixteen percent of children and more than 30% of adults with a nebulizer used it regularly, with frequencies ranging from once per week to six times daily.

Study findings revealed that 38 patients had a PFM, including 29 with a home nebulizer. More than half of children with a PFM used it regularly; none of the adults did. Nineteen individuals used their home nebulizer prior to their fatal asthma attack; only 9 of the 19 did so in conjunction with use of a PFM.

All 52 patients who had a home nebulizer met national guidelines criteria for the use of chronic corticosteroids as asthma control medication, but inhaled or oral steroids were prescribed in only two-thirds of those patients. Moreover, only 11 of 52 were using steroids as prescribed, continued Dr. Gupta.

The next-of-kin interviews as well as patient behavior suggested home nebulizers had provided the deceased with a false sense of security during acute exacerbations. Moreover, the rapid symptomatic relief obtained with use of the nebulizer led many patients to use nebulized bronchodilators frequently, resulting in poor chronic control of their respiratory disease—exactly the sort of vicious circle that the national guidelines were designed to prevent.

“Asthma morbidity and mortality in the United States remain ‘unacceptably high,’” he said. An estimated 4,000 people die each year from asthma. The disease results in 7.5 million preventable sick days annually. In Michigan alone, there are roughly 10,000 hospitalizations for asthma each year.

He proposed several interventions to improve home nebulizer safety: dispensing the devices only together with a PFM and a written asthma action plan; pharmacist notification to physicians regarding frequent bronchodilator refills; and better patient and physician education about home asthma management.

One pediatrician in the audience observed, “When home nebulizers are prescribed by ER docs and other physicians who don’t appreciate enlightened asthma management, you plug the nebulizer in and you unplug the physician from the equation.”
Ringer’s May Be Safer Than Starch Solutions in Sepsis

BY MICHELE G. SULLIVAN

Barcelona — Hydroxyethyl starch solutions can’t be recommended for fluid resuscitation in patients with severe sepsis or septic shock, or in those at risk of renal problems, researchers said at the annual congress of the European Society for Intensive Care Medicine.

The starch solutions are associated with higher rates of acute renal failure and increased 90-day mortality in these patients, especially in those who receive more than the highest recommended dosage of 22 mL/kg of body weight, said Dr. Frank M. Brunckhorst of the Friedrich Schiller University of Jena (Germany).

Dr. Brunckhorst, who also manages the German Sepsis Society, reported the interim results of the Influence of Colloid vs. Crystalloid Volume Resuscitation in Patients with Severe Sepsis and Septic Shock (VISEP) study. VISEP, a phase III trial, randomized patients to volume replacement with either 10% hydroxyethyl starch (HES) 200/0.5 solution (10% Hemohes) or Ringer’s lactate solution.

The study was powered for 1,200 patients, but it was suspended after the first interim analysis of 600 showed trends of increased renal failure and mortality in the HES group, Dr. Brunckhorst said.

All patients in the study had either severe sepsis or septic shock; their mean age was 64 years. The mean Acute Physiology and Chronic Health Evaluation II score was 20, and the mean Simplified Acute Physiology Score (version II) was 53.

Hemodynamic stabilization occurred significantly faster in the HES group. Mortality at 28 days was slightly but not significantly higher in the HES group, compared with the Ringer’s lactate group (27% vs. 24%), a trend repeated for 90-day mortality (41% HES vs. 34% Ringer’s lactate). There were no significant differences in the Sequential Organ Failure Assessment scores overall. However, the coagulation and renal subscores were significantly higher in the HES group, Dr. Brunckhorst said.

In addition, almost twice as many HES as Ringer’s patients needed hemodialysis during their treatment (31% vs. 19%), with a total of 650 days of dialysis in the HES group and 312 days in the Ringer’s group. Acute renal failure rates were also higher in the HES group (35% vs. 23%).

The highest recommended dosage of HES (22 mL/kg) was exceeded in 99 patients. A subanalysis of this group identified a dose-dependent mortality increase at 90 days: 75% of those who exceeded the dosage and 49% of those who did not died. “This was highly statistically significant,” Dr. Brunckhorst said.

No previous study identified increased mortality with high HES doses, he said—probably because the observation period was too short. “All the other studies had a follow-up of only a few days. This was a phenomenon observed only after 3 weeks.”

In 2003, when the VISEP study began, 10% HES was the lightest molecular weight and most rapidly degrading colloidal fluid replacement solution available, said Dr. Konrad Reinhart, a coinvestigator of the VISEP trial. Since then, lighter solutions have come to market. But he said that no studies have demonstrated enough treatment superiority to convince him to use any colloidal solution instead of Ringer’s.

“Several case reports have demonstrated harm.”

Dr. Reinhart is also not convinced that any starch solutions can be recommended in sepsis patients, he said. There are many case reports of pruritic dermatitis associated with starch deposits in the dermis. Autopsy reports have also shown starch deposits in kidneys and liver that persisted for more than 10 years after HES treatment, said Dr. Reinhart, director of the department of anesthesiology and intensive care medicine at the University Hospital of the Friedrich Schiller University of Jena.

“The starch solutions are associated with higher rates of acute renal failure and increased 90-day mortality.”

Dr. Reinhart is also not convinced that acute renal failure is the only factor involved in the increased risk of death in HES patients. “Several case reports have looked at foamy macrophage syndrome in these patients,” he said (Ann. Int. Med. 2002;137:1013-4).

He said his institution has restricted the use of starch solutions. “We have stopped using them in our unit, and I won’t use them at all in sepsis patients,” Dr. Reinhart said. “No data have ever demonstrated a beneficial effect (over Ringer’s), but a lot have demonstrated harm.”
By Bruce Wilson
Elsevier Global Medical News

Philadelphia — Postoperative radiation therapy and chemotherapy for patients with non-small cell lung cancer that has spread to the mediastinal lymph nodes allowed them to survive longer than patients who did not receive radiation, according to a study presented at the annual meeting of the American Society for Thoracic Radiology and Oncology.

In addition, a subanalysis of the ANITA (Adjuvant Navelbine International Trialists Association) trial showed that in the absence of adjuvant chemotherapy, postoperative radiation therapy (PORT) improved 5 year survival in patients with node positive disease, but was harmful to N1 and N0 patients.

With adjuvant chemotherapy, PORT improved survival in N2 patients but was harmful to N1 and N0 patients.

The multinational ANITA 1 trial enrolled 840 patients with stage IB-IV non–small cell lung cancer and randomly assigned them to observation (433 patients) or a chemotherapy and radiation therapy (PORT) arm (407 patients). All patients had been cleared patients who went on to thoracotomy and the other refusing surgery.

“Radiation was neither mandatory nor randomized but only recommended by protocol in patients with node-positive disease,” said lead author Dr. Jean-Yves Douillard, professor of medical oncology at Rene Descartes University of Nantes, France.

A total of 232 patients with node-positive disease received PORT. 144 patients (31%) in the observation arm, and 88 (22%) in the chemotherapy arm.

In the intention-to-treat (ITT) analysis, patients who received chemotherapy survived a median of 65.7 months, compared with 43.7 months for the observation arm, a significant difference (Lancet Oncol. 2006;7:719-27).

Overall survival at 5 years with chemotherapy improved by 8.6%, an improvement that was maintained at 7 years (5.8%). When examined by stage, the authors found no difference in survival between the arms in stage I patients. However, stage II patients treated with chemotherapy had a nonsignificant 12.6% survival advantage at 5 years.

A univariate analysis of the ITT population showed that all patients who received PORT had a distinct, significant survival advantage.

The subanalysis of patients who received chemotherapy showed an overall 5-year survival of 51 months in the chemotherapy arm and 43 months in the observation arm. However, when broken down by nodal status, patients with N1 disease who received chemotherapy plus PORT had lower median survival rates than those who received chemotherapy alone (46.4 months vs. 96.3 months, respectively).

Conversely, N1 patients who received PORT plus chemotherapy did better than those who had no chemotherapy or PORT (50.2 months vs. 25.9 months).

On the other hand, patients with N2 disease received benefit with additional PORT, with or without chemotherapy. Patients who received chemotherapy plus PORT survived longer than those who received chemotherapy alone (47.4 months vs. 23.8 months, respectively), whereas those who received PORT alone received no benefit and those who received no treatment (22.7 months vs. 12.7 months).

Douillard stressed that the results are a demonstration of the major importance of PORT and should be interpreted with caution. They will be tested in a randomized trial being planned.

These findings are in line with those of other studies in which radiation appears to be of benefit for patients with N2 disease, but not for patients with N1 or N0 disease. Dr. Benjamin Movsas wrote in an accompanying editorial (J Clin Oncol. 2006;24:2998-3006). “In this study, there was absolutely no increased risk for patients with N2 disease, and it was the patients with the least to gain—N0 and N1 patients—who had the most to lose,” said Dr. Movsas, chairman of the department of radiation at the Henry Ford Health System, Detroit.

An important component of the ANITA 1 trial was the sequence of PORT after adjuvant chemotherapy. An earlier trial demonstrated no survival advantage by combining chemotherapy and radiation therapy postoperatively (N Engl J Med. 2000;343:1217-22). Movsas said this suggests that using chemotherapy to achieve an overall survival benefit, followed by radiotherapy for local recurrence and disease-free survival benefits.

“This is the sequential strategy that was used in the ANITA trial for patients that received both chemotherapy and radiation,” he said. The results suggest that as systemic control and overall survival improve, the importance of local control increases.

Until the results of the randomized trial are in, Dr. Movsas recommended that patients with N2 disease be given the option of PORT after adjuvant chemotherapy, because the benefits in terms of local control and disease-free survival outweigh the risks.

By Jane Salodof McNeill
Elsevier Global Medical News

Stockholm — Transcervical extended mediastinal lymphadenectomy, a new technique for staging non–small cell lung cancer patients, proved superior to standard cervical mediastinoscopy in a clinical trial presented at a meeting of the European Association for Cardio-Thoracic Surgery.

Dr. Jaroslav Kuzdzal reported that transcervical extended mediastinal lymphadenectomy (TEMLA) found positive nodes in 7 of 8 patients with non–small cell lung cancer (NSCLC) who had mediastinal metastases subsequently detected in 13 patients who underwent thoracotomy after TEMLA staged them as node negative. The remaining patient cleared by TEMLA was unfit for surgery.

In contrast, cervical mediastinoscopy found positive nodes in 3 of 20 patients and missed positive nodes that were subsequently detected in 5 of 15 cleared patients who went on to thoracotomy. Two other patients deemed node negative by mediastinoscopy did not undergo thoracotomy, one being unfit for surgery and the other refusing surgery.

“Radiation was neither mandatory nor randomized but only recommended by protocol in patients with node-positive disease,” said lead author Dr. Jean-Yves Douillard, professor of medical oncology at Rene Descartes University of Nantes, France. A total of 232 patients with node-positive disease received PORT. 144 patients (31%) in the observation arm, and 88 (22%) in the chemotherapy arm.

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Until the results of the randomized trial are in, Dr. Movsas recommended that patients with N2 disease be given the option of PORT after adjuvant chemotherapy, because the benefits in terms of local control and disease-free survival outweigh the risks.

Dr. Kuzdzal, a thoracic surgeon at the Pulmonary Hospital in Zakopane, Poland, and his Polish colleagues concluded that TEMLA’s sensitivity and predictive value were both 100%. They calculated a sensitivity rate of 66.7% and a negative predictive value of 37.5% for cervical mediastinoscopy.

Based on these results, the investigators stopped the randomized controlled trial, which had been scheduled to enroll 100 non–small cell lung cancer (NSCLC) patients. Dr. Kuzdzal said the hospital also has abandoned cervical mediastinoscopy because it missed metastases in 25% of patients in the mediastinoscopy arm of the trial.

“TEMLA is the standard technique for staging all potentially at-risk patients [at the hospital],” he said in a plenary address at the meeting, which was held by the European Society of Thoracic Surgeons.

Dr. Kuzdzal’s coauthors included TEMLA’s creator, Dr.Marcin Zielinski, the head of the department of thoracic surgery in Zakopane. They published a description of the technique last year (Eur. J Chest Physiol.2006;3:1217-22). TEMLA is more effective because it is more thorough than cervical mediastinoscopy.

Dr. Kuzdzal said they found neither more impairment nor more unfit patients with TEMLA.

The TEMLA procedure does not produce greater changes in lung ventilation nor gas diffusion across the alveolar-capillary membrane, compared to standard mediastinoscopy, he said in a separate presentation on pulmonary function.

Ultimately, the investigators are hoping that longer follow-up will reveal better survival in more than 220 patients so far staged with TEMLA. “We know this technique is superior to other techniques in terms of staging, but we also think it might have also a curative impact,” Dr. Kuzdzal said.

By Robert Cerfolio, FCCP
Comments: Although transcervical extended mediastinal lymphadenectomy is a promising technique, the risk of the procedure may be too high in inexperienced hands. Since the vast majority of lung cancer surgery is performed by surgeons who have “low volume experience,” and because more than 50% of mediastinoscopies yield no lymph nodes, the emphasis should be on training surgeons on this procedure can be used to biopsy lymph nodes that have been targeted by integrated PET/CT.

New Staging Technique Beat the Standard in NSCLC Trial

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Reflux May Trigger Cough in Some Asthmatic Children

BY DAMIAN MCNAMARA
Elsevier Global Medical News

Orlando — Reflux prompted coughing for more than a third of pediatric patients with asthma in a study, suggesting both acid and nonacid reflux can be important triggers for some patients.

Multiple studies suggest an association between often-undetected gastroesophageal reflux and asthma symptoms in adults; data in children are fewer.

However, treatment of reflux with a proton pump inhibitor (PPI) did not improve asthma symptoms in two large adult studies or one prospective pediatric study.

“We know [an association between asthma and reflux is a long and ongoing saga, but we didn’t know which was causative],” Dr. Devendra Mehta said in an interview during a poster presentation at the annual meeting of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

Use of pH monitoring alone—which detects only acid reflux—was a limitation of previous studies, he said. Impedance monitoring improves detection by including nonacid reflux episodes.

“With newer technology, we can now see the stomach contents coming up and time it with the cough,” said Dr. Mehta, a gastroenterologist at the Nemours Children’s Clinic in Orlando.

Dr. Mehta and his colleagues assessed reflux in 87 children with asthma using combination pH and multichannel impedance monitoring. The mean age of the study participants was 7 years (range, 6 months to 18 years), and 49 were male. The researchers excluded candidates who were taking acid-suppression medications, and then studied 59 remaining patients.

A total of 38% of cough episodes occurred within 2 minutes of reflux, in about the same proportion after acid, weak acid, and nonacid reflux.

The cough episodes did not vary significantly by patient age or asthma severity. “We are zeroing in on this population where reflux is causing an important part of the illness,” Dr. Mehta said.

“The next phase will be treatment of these children with combined therapy to see if we can help their asthma or keep it from getting worse,” he said.

Dr. Mehta suggested a combination trial of a PPI and a motility agent for patients whose asthma does not improve with other therapies, to detect any concomitant reflux.

“We want to start out with younger kids to prevent them from a long course of lung problems,” Dr. Mehta said.

Gastroesophageal reflux may trigger asthma symptoms by first causing microaspiration, which then leads to edema, inflammation, and bronchial hyperreactivity. Dr. Colin Rudolph said during another presentation at the meeting.

Evidence supports reflux as a potential contributor to severe, persistent asthma, said Dr. Rudolph, a pediatrician at the gastroenterology clinic of Children’s Hospital of Wisconsin, in Milwaukee.

“Evidence does not support a reflux prescription in all patients with persistent asthma who fail conventional therapies,” Dr. Rudolph said.

He cited two double-blind, placebo-controlled studies that assessed PPI treatment of reflux in adults with asthma.


“So a trial of PPI therapy should be considered reasonable in patients with [gastroesophageal reflux] symptoms and moderate to severe asthma,” Dr. Rudolph said, “but efficacy may only be expected in patients who have nocturnal asthma symptoms.”

In another study of adults treated with lansoprazole, there was no significant improvement in symptoms of asthma or pulmonary function (Chest. 2005;128:1128-35).

Only one set of researchers assessed treatment of reflux in pediatric patients with asthma in a prospective, randomized fashion. Dr. Rudolph said.

In that study, although omeprazole failed to improve the symptoms of asthma or lung function among a group of 38 children, the researchers “found that the PPI improved quality of life for the treatment group” (Arch. Dis. Child. 2005;90:956-60).
The ACCP’s mission is to promote the prevention and treatment of disease through leadership, education, research, and communication, and working with like-minded organizations is critical to supporting that mission. Among our most gratifying accomplishments in the last few years has been developing close collaborative relationships with other professional organizations, such as the strong and coordinated advocacy effort to influence public policy on the critical care workforce shortage by ACCP, the American Association of Critical-Care Nurses (AACN), American Thoracic Society (ATS), and Society of Critical Care Medicine (SCCM).

Training pathways and requirements for certification in pulmonary, critical care, and sleep medicine are also of great importance to our members, our profession, and the general public. The ACCP has forged strong partnerships with other organizations to shape how our profession evolves in response to rapid changes in educational methodology, informatics, and the drive to improve and document quality of care.

The ACCP now has several areas of collaboration with the American Board of Internal Medicine (ABIM), the US board that sets the standards and certifies the knowledge, skills, and attitudes of physicians who practice in internal medicine and its subspecialties. Through its Certification and Maintenance of Certification (MOC) programs, successful candidates are awarded or maintain “board-certified” status. This demonstrates to the public that they have successfully completed a rigorous educational and evaluation process designed to assess the knowledge, experience, and skills required to provide high-quality patient care. In addition, MOC programs foster lifelong learning and a commitment to improving clinical practice.

To its great credit, ABIM elicits input enthusiastically from professional societies about the content and processes of certification, and the ACCP is committed to all of these activities. The College has participated in every ABIM Liaison Committee for Recertification meeting, offering ABIM views on the appropriate requirements for MOC, along with providing source material to ABIM for pulmonary and critical care clinicians to fulfill these requirements with a Performance Improvement Module in asthma care. ABIM requires completion of self-evaluation modules to demonstrate medical knowledge and encourage learning, and ACCP was the first organization to offer ABIM module-based sessions at its annual meeting and board review courses; they have been a standard feature of these courses since 2002. We are developing online modules based on ACCP-SEEK that will allow candidates to complete 20 “learning” points for pulmonary and critical care medicine, respectively. These may be used instead of the traditional ABIM Self-Evaluation Process (SEP) modules.

The ABIM recently changed the “official” status of Critical Care Medicine by recognizing it as a subspecialty rather than an “added qualification.” Physicians with certificates in critical care medicine and geriatric medicine are no longer required to maintain their certificate in internal medicine to participate in the MOC program, although they are encouraged to do so.

To further define the field of critical care, ABIM charged a “critical care stakeholders” group to advise them on specifying the competencies of subspecialists in pulmonary and critical care medicine. In this exciting new effort, representatives of ACCP, ATS, SCCM, and the Association of Pulmonary and Critical Care Program Directors are now charting the future of subspecialty training by defining the domains of knowledge and the ways to demonstrate competency required to be certified as a subspecialist.

This collaboration among societies is surely the most constructive and effective way to have a positive impact on our profession. It should also be important for each of us as people: if not now, then all of us, our families and our friends will be patients, and we will all eventually have a critical illness.

We now have the opportunity to work with our colleagues to influence what we expect our own doctors to know and how we expect them to act. We have to do it right, and working with our colleagues, I am confident that we will.
CHEST Physician • January 2007

NEWS FROM THE COLLEGE

Chest Infections

BY DR. KELLY WOOD, FCCP

MRSA infections in the ICU pose significant challenges to pulmonary and critical care physicans. A significant rise in community-acquired MRSA is being reported. These include reports from neonatal intensive care units (Pediatr Infect Dis J 2006; 25:557; Pediatr Infect Dis J 2005; 24:1122) and cases of soft tissue infections (N Engl J Med 2005; 352:1445). Efforts must be made to minimize the selection and spread of these genetically distinct organisms in our ICUs. The indiscriminate use and overuse of antibiotics in the care of agricultural and domesticated animals must be examined in conjunction with similar practices in humans in order to understand all potential facets of this problem.

Most emerging infectious diseases in the world are zoonotic. From 1996 to 2004, 21% of 10,490 reports of animal diseases from 191 countries submitted to the Program for Monitoring Emerging Diseases (ProMED) concerned humans affected by zoonotic disease (J Am Vet Med Assoc 2006; 229:1090). Due to the use of antibiotics to treat animals, agricultural animals have long been known to be a source of resistant bacteria. A Dutch study demonstrated transmission of MRSA between an animal and human (pig and pig farmer), between family members (pig farmers and their families), and between a nurse and patient in the hospital (Emerg Infect Dis [serial]. 2005 Dec [date cited]. Available at: www.cdc.gov/ncidod/EID/vol11no12/05-0428.htm. Medical and veterinary personnel should appreciate that animals can carry MRSA, and transmission between humans and domestic animals, although not common, can occur. Cats may serve as reservoirs for MRSA infections in humans (Am J Vet Res 2006; 67:1421; J Sm Anim Prac 2 004; 45:591). MRSA has also caused infections in dogs (Vet Rec 1999;

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Continued from previous page

“CHEST is above all a clinical journal, with a very important educational mission,” said Dr. Irwin. “The recent editorial changes illustrate the goal of improving the quality of research, scholarly works, and educational offerings published in CHEST.”

Recent international initiatives and technological advances have helped make CHEST accessible to more readers across the globe. CHEST has a print circulation of 20,450, reaching more than 100 countries, which is the highest of any medical journal in the respiratory, critical care, and sleep fields.

In its quest to expand medical knowledge beyond the English-speaking world, the ACCP publishes CHEST editions in Spanish, Italian, Turkish, and Chinese, and it also publishes an English edition in India; there are currently almost 38,000 recipients of these international editions.

For more information about the journal CHEST, please visit the journal Web site at www.chestjournal.org.

The survey was commissioned by The Walchli Tauber Group, Inc., advertising representatives for CHEST, and fielded by The Mataiali Group, Inc. To ensure a high quality study, readership was measured on a totally unaided basis, and the sponsorship of the study was not disclosed to respondents.
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MRSA has resulted in a significant number of new disease cases, the current state of antimicrobial resistance demands collaborative research between medical and veterinary personnel in order to control resistance and prevent transmission. In 2006, we saw the establishment of the Centers for Disease Control and Prevention (CDC) as a World Organization for Animal Health (OIE) Collaborating Center for Emerging and Reemerging Zoonoses. This served as an initiative by health and animal organizations to respond to emerging zoonotic diseases that potentially impact human health. A forum was established to examine the epidemiology of pathogens and diseases shared by humans and animals, as well as the effects of agricultural practices on humans (www.cdc.gov/ncidod/EID/vol12no12/06-1281.htm).

Allied Health
The Allied Health NetWork provides allied health professionals a method of communicating with all members of the ACCP. The membership of the

Continued on following page
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NetWork includes respiratory care practitioners, physician assistants, nurses, physical therapists, and pharmacists, as well as physicians.

The Airways, Allied Health, Respiratory Care, and Home Care NetWorks recently coordinated efforts and developed patient instructions for the use of inhaled aerosol devices. These step-by-step instructions provide patients and physicians information on usage and cleaning for most delivery devices available today. These are available for download at www.chestnet.org/patients/guides/aerosolDevices.php

The NetWork specializes in providing resources and information for patients, caregivers, and healthcare providers. In addition to the resource on inhaled aerosol devices, the NetWork's patient care guidelines cover a wide range of topics, including asthma, COPD, and chronic obstructive pulmonary disease. These guidelines are designed to help patients understand their condition, manage their symptoms, and work with their healthcare provider to achieve optimal outcomes.

The NetWork also offers educational resources for healthcare providers, including a variety of webinars, podcasts, and articles on the latest research and treatment options. These resources are intended to help providers stay up-to-date on best practices and improve the quality of care they deliver.

In conclusion, the NetWork is an organization that is dedicated to improving the lives of patients with respiratory conditions by providing valuable resources and support through its patient care guidelines and educational programs for healthcare providers. By working together, the NetWork aims to help patients achieve their treatment goals and live healthier, more productive lives.
The ACCP-CCI, under the stewardship of Chair Dr. Curt Sessler, FCCP, and an active presence in the world of critical care medicine, as we seek to serve both our members and their patients.

We are pleased to announce that Dr. Gene L. Colice, FCCP is the new Editor of Pulmonary Perspectives. Dr. Colice is Professor of Medicine at The George Washington University School of Medicine in Washington, DC. He is also Director of Pulmonary, Critical Care, and Respiratory Services at Washington Hospital Center in Washington, DC. Dr. Colice currently is a member of the ACCP Bylaws and Quality Improvement Committees, Vice-Chair for the ACCP Diagnostics and Management of Lung Cancer Steering Committee, and member of the ACCP SEEK writing committee for pulmonology. As Editor of Pulmonary Perspectives, Dr. Colice plans to "offer a forum for provocative opinions about items of current interest to the pulmonary community, not only those generated in the ACCP, but from any member of the ACCP."
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Practice Management Update

The ACCP needs your help. Have you had a desire to actively be involved in national coding and reimbursement issues? Are you interested in becoming an active member of the ACCP Practice Management Committee? Are you interested in the business side of medical practice? Are you detail oriented? Do you have e-mail and can you work with e-mailed attachments?

Then, the ACCP has a voluntary position that will suit your interests. The College has advisors and alternate advisors participating in the American Medical Association’s CPT and RUC processes. As part of this responsibility, you would participate in the monthly ACCP Practice Management Committee conference call.

Requirements: ACCP and AMA memberships, and a desire to participate in national processes that affect the CPT codes you use and your future Medicare reimbursement.

Apply for this position by e-mailing Marla Brichta at the address mbrichta@chestnet.org, with a short biographical sketch of your background to include: name, e-mail address, telephone number, specialty, and practice concentration. State any expertise that you have related to coding and reimbursement issues.

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Why Did the Chicken Cross the Road?

By Ed Dellert, RN, MBA
Vice President, Educational Resources

Because it was there,” correct? This age-old question has been contemplated for generations. Plato thought it was done for the greater good. Aristotle thought it was in the nature of chickens to cross roads. Captain James T. Kirk thought it was to boldly go where no chicken has gone before. What if, however, we were to replace this question with, “Why did the physician cross the road?” In today’s health care regulatory environment, with the need to measure “physician competency,” it seems that it might be an appropriate question to ask.

September 5, 2006: The Accreditation Council for Continuing Medical Education (ACCFME) released the latest update to the guidelines for providers of continuing medical education (CME). The focus upon the updated criteria is highlighted in the following three areas that state CME must:

1. Contribute to patient safety and practice improvement
2. Be based upon valid content
3. Be independent of commercial interests

These three areas are to be incorporated throughout the year into individual physician educational activities by the CME curriculum provider. The outcome of these learning experiences should demonstrate how the collective curriculum impacts the CME provider’s educational mission. Specifically, providers must begin to assess how educational experiences are facilitating physician learning and enabling a means to assess physician performance, competence, and clinical impact upon patient outcomes.

October 10, 2006: A letter came from the office of the ACCME stating that the updated criteria are designed to align the goals of the CME providers with the goals of CME learners (ie, physicians). In today’s environment of health care, both parties are being asked to assess their abilities and demonstrate change and improvement. Medical education is being driven by professional practice gaps of physician learners, and needs are being expressed in terms of knowledge, competence, and/or performance changes, as it impacts upon professional practice. Success will be based upon “data.” Dr. James Thompson, President and CEO of the Federation of State Medical Boards of the United States, stated the following as it relates to the release of ACCME’s updated criteria:

“The new accreditation elements will prove to be valuable in the national initiatives to assure competence of physicians. This level of activity is just what has been needed to place the continuing medical education community at the forefront of improving quality in the practice of medicine.”

Implementation of the updated criteria is to begin November 2008, with demonstration of 100% compliance by 2012. (See figure.)

November 16, 2006: The US Council of Medical Specialty Societies (CMSMS) hosts a 1-day summit discussing the use of physician’s self-assessment programs. Two Canadian researchers, Dr. David A. Davis, of the University of Toronto, and Dr. Kevin Eva, of the program for Educational Research and Development at McMaster University, highlighted their findings during their most recent research.

Dr. Davis highlighted his most recent article in the Journal of the American Medical Association, with the following findings:

1. CME credit, relicensure (revalidation), and recertification are linked to the abilities of physicians to assess their own needs and select learning activities to meet those needs.

2. In a literature search of comparisons between self and external assessment, 14 of 20 studies demonstrated little, no, or an inverse relationship, 7 demonstrated a positive association.

3. A number of studies found the worst accuracy in self-assessment among those who were the least skilled.

Conclusion: The preponderance of evidence suggests that physicians have a limited ability to accurately self-assess.

For more information on Dr. Davis’s article, go to the following URL: http://jama.amaassn.org/cgi/content/full/296/9/1094.

Dr. Eva concluded similar findings in an article he described from the October 2005 supplement in Academic Medicine. He indicated the following:

1. The archetype of the self-regulating professional will reflect regularly on practice and self-assessment gaps, seek to redress these, and incorporate new knowledge and skills in practice.

2. All but the very highest performers tend to overestimate their ability.

3. Those most in need of improvement are least likely to know.

Conclusion: A critical premise (self-assessment) underpinning the concept of self-regulation is unsustainable.

For more information on Dr. Eva’s article, go to the Academic Medicine home page and search for the archive editions under the October 2005 supplement, entitled “Self-Assessment in the Health Professions: A Reformulation and Research Agenda” at www.academichmedicine.org.

Dr. Robert Galbraith, Director of the Center for Innovation of the National Board of Medical Examiners (United States), discussed the development of practice or work profiles for individual physicians, linking these to multiple-choice questions to test knowledge competency, and, in turn, adding external assessment in the forms of comparison to practice norms and mentoring. These steps, he suggested, could assist physicians in demonstrating learning and performance improvement.

Highlights of the discussion also indicated that the US Federation of State Medical Boards is seeking to move from a mandatory credit-hour basis in most states to measurement of the ongoing competence of a physician. Many countries still have no relicensure requirements in place.

December 3, 2006: In physics, “theory” is when you know how it works, but it still doesn’t. “Practice” is when it works, but you don’t know why. I think what has happened is that theory and practice have joined forces together, where nothing works, and no one knows why? The ACCP, however, is looking for tools in which the theory is how adults best learn. The practice is how best to teach adults and capture that learning process to determine knowledge competency and correlate it to individual clinical practice.

This entire discussion is not new news to the ACCP Continuing Education Committee. This has been discussed over the past few years and has evoked many ideas on how the ACCP can best serve to meet these future demands of its constituency.

In 2007, these discussions will now lead to the implementation of a new Continuing Medical Education learning curriculum, and we hope it will transform teaching and learning in chest medicine.

Our hope is to encourage ACCP membership participation by educating everyone about the need—and how that need will be met by participating in this new learning structure. This article is just the beginning of that educational process. So, why will you cross the road? Or will you?

As always, feel free to contact me for questions or comments on this article, at edellert@chestnet.org.
Creating Healthy Work Environments: Introduction

The AACN and the ACCP are committed to safe, quality care.

BY DENISE C. THORNYBY, MS, RN, CNAA; AND DR. CURTIS N. SESSLER, FCCP

Critically ill patients are our most vulnerable patients in health care and require the full contribution and skill of competent and caring physicians and nurses.

For decades, both professions have focused on the acquisition of knowledge and skills required for excellent patient care. Less attention has been traditionally placed on the “soft” skills of communication, collaboration, and creating work cultures that support effective teamwork.

There is a growing body of evidence pointing to links between effective nurse-physician collaboration and improved outcomes (including reduced mortality rates) for patients, the adequacy of nurse staffing and patient outcomes, and the quality of the work environment with clinical performance.

The Institute of Medicine (IOM), in Crossing the Quality Chasm: A New Health System for the Twenty-First Century, calls for a revolution in the way in which we communicate with each other, anticipate and modify patients’ risk, and evaluate our effectiveness.

The leaders of the American Association of Critical-Care Nurses (AACN) and the American College of Chest Physicians (ACCP), who have a long history of collaboration and support on important issues in critical care, have committed to promote healthy work environments that foster safe, quality care. In 2005, ACCP established six evidence-based, relationship-centered standards to cultivate healthy work and care environments:

- Skilled communication
- True collaboration
- Effective decision-making
- Appropriate staffing
- Meaningful recognition
- Authentic leadership

These standards involve fundamental concepts in the way individuals on the health-care team relate and interact with one another. Promotion of these standards is crucial to ensure patient safety, decrease medical errors, improve delivery of care, and increase the retention of staff by decreasing conflict, stress, and moral distress among members of the health-care team.

The critical elements of the standards may be found on the AACN Web site at www.aacn.org/HWE.

As physicians and nursing leaders in the care of the critically ill, it is imperative for us to consider strategic actions to transform the culture and work environment within our units and hospitals. How can you personally make an impact in your ICU and more broadly throughout your health-care system?

Changing long-held biases and ingrained behaviors is challenging work that requires true collaboration among those who are leading the charge. Familiarize yourself with the AACN standards and consider the implementation strategies identified by authors of the article, One Year after the AACN Standards: Where we are now? Additionally, articles in this and subsequent issues of CHEST Physician by physician and nurse leaders will provide valuable insight and personal experience for successful implementation of each of the individual standards.

We must all strive to establish and sustain healthy work environments—our patients’ health and our professional well-being depend upon it.

Watch for future articles in CHEST Physician on the Healthy Work and Care Environments initiative.

References
3. American Association of Critical-Care Nurses (AACN). AACN standards for establishing and sustaining healthy work environments. Also Viers, CA. AACN, 2005

Ms. Thornoby is Director, Education & Professional Development, Virginia Commonwealth University Health System, Richmond, VA.

Dr. Sessler is an Orhan Muren Professor of Medicine, Virginia Commonwealth University Health System, and Medical Director of Critical Care, Medical College of Virginia Hospitals, Richmond, VA.

CheST Physician Welcomes New Editorial Advisory Board Members

CHEST Physician is pleased to introduce our readers to the newest members of our editorial advisory board.

Dr. Doreen Addrizzo-Harris, FCCP (not pictured) is Associate Professor of Medicine at NYU School of Medicine. Dr. Addrizzo-Harris is an ACCP Governor for New York City and presently serves on the Health and Science Policy Committee and the Government Relations Committee.

Dr. Stephen A. Geraci, FCCP, is Professor and Vice-Chair, Department of Internal Medicine, University of Mississippi School of Medicine, and Chief of the Medical Service, G.V. (Sonny) Montgomery VA Medical Center, Jackson, MS. Dr. Geraci is Chair of the ACCP Cardiovascular Medicine and Surgery NetWork and serves on the CHEST 2007 Scientific Program Committee.

Dr. Stephen M. Pastores, FCCP, is Associate Attending Physician and Director of the Critical Care Medicine Fellowship program at Memorial Sloan-Kettering Cancer Center in New York, NY, and Associate Professor of Medicine and Anesthesiology at Weill Medical College of Cornell University. Dr. Pastores is a member of the Association of Pulmonary and Critical Care Medicine Program Directors and the steering committee of the ACCP Cardiovascular Medicine and Surgery NetWork.
CHEST 2006 WRAP-UP

CHEST 2006—A Meeting of Minds, Mountains, and Moments

BY PAM GOORSKY
Assistant Vice President, Editorial Resources

They arrived in Salt Lake City—thousands of physicians and their teams, their colleagues, and their families. They arrived from more than 60 countries. They arrived to lecture, to listen, and to learn. And they arrived with great expectations of an educational event that would provide new knowledge that could be applied immediately in their practices here in the United States and around the globe.

CHEST 2006 met and exceeded those expectations, offering 6 days packed with education, simulation, collaboration, and just plain fun. With more than 200 educational opportunities, ranging from mini-satellites to literature reviews to a ballroom-filled keynote session, CHEST 2006 provided a nonstop, unmatched educational venue. Having 30 curriculum categories from which to choose, attendees enjoyed the advantages of the multidisciplinary nature of CHEST. The ACCP NetWorks offered 26 open meetings, so attendees could choose one or more to enjoy special presentations geared to particular interests.

Collaborative meetings with national and international organizations allowed ACCP leaders to share and discuss mutual goals with others of similar interests. A record-breaking number of exhibits furnished important information on new pharmaceuticals, equipment, and technologies. Numerous ACCP and CHEST Foundation honors and awards graced the Convocation ceremony and the Wednesday evening awards reception.

And what would a CHEST meeting be without The CHEST Foundation’s Making a Difference Dinner? Or the opening reception? Or a night of special reunions to meet and greet friends and colleagues? These traditional events and many more were met with enthusiasm and wonderful crowds.

Join us for CHEST 2007 in Chicago, and once again experience the ACCP heritage of educational excellence.

By the way, More than 450 research posters were presented at CHEST 2006.

ACCP “LEARN” Scholarship Researching the Educational Impact of Medical Education

The ACCP Continuing Education Committee has launched a groundbreaking scholarship program to award and promote research efforts in continuing medical education (CME) to better understand how education designs impact physicians and clinical outcomes.

Up to $15,000 will be awarded to support one 2-year study that:

• Impacts the future development of clinically relevant medical education initiatives within the ACCP.
• Identifies and advances the best delivery of medical education.

Applicants must:

• Be an ACCP member.
• Submit proposals to study learning outcomes of ACCP educational activities and measure the effect on physician knowledge and health-care delivery.
• Complete an online application for this award by January 10, 2007.

Learn more and apply at www.chestnet.org/education/scholarship.

Call for abstracts

ABSTRACT SUBMISSION DEADLINE:
MONDAY, APRIL 30, 2007

Be part of the CHEST 2007 program by submitting an abstract of your original investigative work for presentation during the meeting.

• Gain international exposure. Your work will be presented to an international audience and published in a CHEST supplement.
• Receive feedback from the clinicians likely to use your data in their practices. Health-care professionals in chest and critical care medicine will review and comment on your work.
• Participate with the ACCP in efforts to fight chest diseases. By presenting your findings, you join the ACCP in its mission to advance the prevention and treatment of chest diseases through research and education.
• Compete for ACCP Investigative awards. Monetary awards are granted by The CHEST Foundation to investigators whose work is judged to be outstanding by the reviewers.

Abstract submission to CHEST 2007 is FREE. Domestic and international submissions are encouraged. Abstracts will be graded individually on scientific merit and originality. Abstract submission begins early March. Submit online at www.chestnet.org by clicking on the Abstracts and Case Reports Submission link when available. For questions, call (800) 343-2227 or (847) 498-1400.
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Honors Bestowed at The CHEST Foundation Dinner

Mr. Paul Shaffer, Musical Director of the Late Show with David Letterman, was presented with a Special Humanitarian Award at the Making a Difference Awards Dinner celebration in Salt Lake City, UT, during CHEST 2006. In a special awards ceremony, Dr. Diane E. Stover, FCCP, immediate past Chair of The CHEST Foundation’s Board of Trustees, presented her good friend, Paul Shaffer, with The CHEST Foundation’s Special Humanitarian Award.

This award acknowledges the outstanding pro bono service Mr. Shaffer has provided The CHEST Foundation. He has twice donated his time and talent to serve as emcee at the Making a Difference Awards Dinner, first in Seattle, WA, in 2004, and again this past year in Salt Lake City. In another display of generosity, Mr. Shaffer lent his talent and celebrity status to The Foundation when he agreed to appear in and narrate The CHEST Foundation’s 10th Anniversary Commemorative video, which was debuted at the Making a Difference Awards Dinner in Salt Lake City.

In every instance, Mr. Shaffer’s involvement has brought about a great deal of joy, excitement, and interest for The Foundation. The CHEST Foundation is forever grateful to Mr. Shaffer for his generosity and commitment.

The CHEST Foundation also paid tribute to outgoing Chair and longtime member, Diane E. Stover, MD, FCCP.

Mr. Paul Shaffer bestowed to her a gift of thanks and directed everyone’s attention to a special video that highlighted Dr. Stover’s years of dedication and involvement with The CHEST Foundation.

Dr. Stover has played an integral role in The CHEST Foundation since its creation a decade ago, first by becoming a Board of Trustees member in 1998. She was elected President of the Board of Trustees in 2002 and served for 2 years in that capacity until becoming Chair in 2004. As a leader of The Foundation during its formative years, Dr. Stover’s desire to advance The Foundation was communicated through the three themes she put forth: face, focus, and fundraising. During her tenure, Dr. Stover fostered awareness and growth in the areas of focus central to The CHEST Foundation. She challenged The Foundation’s Development and Marketing Committees to expand the donor base, while educating members and strategic partners on the many educational programs and resources available through The CHEST Foundation. She demonstrated her commitment to The Foundation’s Clinical Research Awards program by assisting in its expansion through development of strategic partnerships with patient advocacy groups, as well as serving as an annual reviewer for the LUNGevity Foundation/CHEST Cancer Foundation Award in Lung Cancer Research.

Dr. Stover’s passion and work to bring about a tobacco-free world was the impetus that provided The Foundation with the tobacco prevention program and many of the antitobacco products that are currently available to ACCP members and their patients. In 1999, Dr. Stover, serving as the Chair of the Task Force on Women & Girls, Tobacco, & Lung Cancer, directed the Task Force in creating the first tobacco prevention speakers’ kit, which has just been updated and released as a fourth edition, titled “Make the Choice: Tobacco or Health?” The new speakers’ kit has already been distributed to classrooms throughout Illinois. Additionally, the speakers’ kits have inspired other ACCP members to translate and adapt them for use in Asia, France, and the Indian subcontinent.

The ACCP and The CHEST Foundation leadership and staff congratulate Dr. Diane Stover on her many contributions to The Foundation and her impressive legacy of leadership.

View The CHEST Foundation’s 10th Anniversary Commemorative video at www.chestfoundation.org.
Second Dopamine Agonist Approved for Restless Legs

BY ELIZABETH MECHCATIE
Eisai Syntelis Medical News

While misdiagnosis of restless legs syndrome remains common, the Food and Drug Administration has increased the agents available to treat this movement disorder by approving the dopamine agonist pramipexole for moderate to severe cases.

Pramipexole is the second drug and the second dopamine agonist to be approved for this condition. The first was ropinirole (Requip), another dopamine agonist approved last year for restless legs syndrome (RLS), which affects as many as 3% of the population. Dopamine agonists had been considered first-line treatments for moderate to severe RLS by expert consensus panels before they were approved, according to Dr. John Winkelman, medical director of the Sleep Health Center at Brigham and Women’s Hospital, and Harvard Medical School, Boston.

While it will take more time for recognition of RLS to improve, “the good news is that the treatments are so effective and generally so well tolerated, it is gratifying to treat,” and response to treatment is typically rapid, Dr. Winkelman said. It is “the usual patient who doesn’t have some response to one of the dopamine agonists,” he added. Both pramipexole, marketed as Mirapex by Boehringer Ingelheim, and ropinirole, marketed as Requip, have been available for almost 10 years, since they were approved for Parkinson’s disease. Dr. Winkelman is a consultant to Boehringer Ingelheim and to ropinirole manufacturer GlaxoSmithKline, as well as other companies that manufacture products for insomnia and other sleep disorders.

Pramipexole was significantly more effective than placebo in four randomized, double-blind, 3- to 12-week studies of about 1,000 patients with moderate to severe RLS, which evaluated the effect of treatment on a scale based on patient-reported symptoms and a Clinical Global Impressions scale.

Dr. Winkelman was the lead author of one study of 344 patients, published in September, which found that at 12 weeks, those on three fixed doses of pramipexole improved significantly more from baseline than those on placebo in a scale that represented patient rating of symptom severity, which covers effects on sleep and next day functioning. In addition, 70%-75% of patients on the three doses of pramipexole studied were rated as ‘very much improved’ or ‘much improved’ on a clinician rating scale, compared with 51% of those on placebo, a significant difference (Neurology 2006;67:1034-9). A strong placebo effect was seen on both of these primary end points, which he noted was true for disorders where people are asked how they are doing.

Side effects were generally mild, with no serious adverse events. Nausea was the main side effect that was more common in patients on the drug (19% vs. almost 9%), but was mild and reversible.

Because this was a forced titration study, where patients are titrated up to the preassigned dose, even if they responded to a lower dose, side effects may have been more common than if doses were individualized, he said. Interestingly, a benefit of the low dose of 0.125 mg over placebo was seen at 1 week, he pointed out.

RLS becomes more prevalent as people age, with the typical age of onset in the 40s and 50s. The symptoms and effects of the disorder are not well recognized, he said, noting that RLS interferes with a person’s daytime functioning and ability to fall asleep and stay asleep. People with moderate to severe RLS have symptoms at least three times a week.

The indications section of the revised label for pramipexole lists diagnostic criteria for RLS, including an urge to move the legs that is “usually accompanied or caused by uncomfortable and unpleasant leg sensations,” symptoms that begin or worsen during periods of inactivity, such as lying or sitting, and symptoms that are partially or totally relieved by movement such as walking or stretching.

Why a dopamine agonist works in restless legs syndrome is not entirely clear, he said. Dopamine is potentially involved in sensorimotor integration, and RLS is considered a sensorimotor disorder.

The dopamine agonist doses used for RLS are much lower than doses used to treat Parkinson’s. The FDA-recommended starting dose is 0.125 mg taken once daily 2-3 hours before bedtime. If necessary, the dose can be increased every 4-7 days to 0.25 mg daily, and, if necessary, to 0.5 mg daily after another 4-7 days. The revised label says that there is no evidence that a 0.75 mg daily dose provides any more benefit than the 0.5 mg dose.

Mayo Clinic Study: Evaluate Sleep Apnea As Part of Preventive Cardiology

CHICAGO — Obstructive sleep apnea is associated with subclinical coronary artery disease independent of the traditional cardiovascular risk factors, Dr. Dan Sorajja reported at the annual scientific sessions of the American Heart Association.

Moreover, the severity of subclinical coronary artery disease as reflected by the extent of coronary artery calcium (CAC) on electron beam CT increases with obstructive sleep apnea severity. For this reason, the presence and severity of obstructive sleep apnea ought to be incorporated into coronary artery disease risk stratification and preventive cardiological efforts, according to Dr. Sorajja of the Mayo Clinic, Rochester, Minn.

He reported on 202 consecutive patients with no history of coronary artery disease who underwent electron beam CT within 3 years of polysomnography at the Mayo Clinic. They were a median of 50 years old, with a mean body mass index of 33 kg/m2. More than half were hypertensive and 44% had hypertension.

CAC was present in 67% of patients and in 31% without obstructive sleep apnea. And apnea, in turn, was present in 76% of those with CAC. The mean CAC score was 144 Agatston units in those with obstructive sleep apnea and 26 Agatston units in those without.

In a multivariate analysis, the adjusted odds ratio for CAC increased in stepwise fashion with each increasing quartile of obstructive sleep apnea severity as determined by the apnea-hypopnea index (AHI). The prevalence of coronary artery disease was 2.1-fold greater in patients in the second obstructive sleep apnea severity quartile, with an AHI of 5-13, than in those in the lowest quartile. The CAC prevalence was 4.3-fold greater among patients in the third quartile, with an AHI of 14-32, than in the first. And in individuals in the top quartile, where the mean AHI was 63, the prevalence of CAC was 33.3-fold greater than in the first quartile.

The chief limitation of a cross-sectional study such as this one is the potential for selection bias, he conceded.

Obstructive sleep apnea is a common medical condition. The prevalence of significant obstructive sleep apnea symptoms has been estimated at 4%-9% among middle-aged adults. The condition has previously been shown to be a cause of hypertension. It is also associated with an increased risk of MI and with elevated rates of several important risk factors for coronary artery disease, including dyslipidemia, diabetes, and obesity, Dr. Sorajja noted.

—Bruce Jancin
Health Plan Feedback to Doctors Improved Asthma Care

BY JANE SALODOFF MacNeil
Elisvier Global Medical News

San Francisco — What health plans tell physicians can make a difference in the quality of care their patients receive, according to a report on asthma care published January 2007 in CHEST PHYSICIAN. In particular, providers who received feedback and notification of their patients’ control status were more effective in prescribing medication for their patients than those who did not receive such information.

The first feedback was about how the provider compared to other physicians with respect to quality-of-care benchmarks. The other was provider notification of patients’ asthma status and asthma-related hospitalization or an asthma-related emergency room visit, both of which were provided by the health plan.

Two types of communication significantly increased the proportion of children with severe asthma who filled their controller prescriptions. Dr. William O. Cooper, chief medical officer at the American Pediatric Society, Society for Pediatric Research, Ambulatory Pediatric Association, and American Academy of Pediatrics, chaired the meeting, which was sponsored by the American Pediatric Society, Society for Pediatric Research, Ambulatory Pediatric Association, and American Academy of Pediatrics.

The retrospective cohort study reviewed records from 2000 to 2002 for 3,058 children in Washington state. In this population, only 77.4% of children filled their controller prescriptions, the health plan reported at the annual meeting of the Pediatric Academic Societies.

The effects of feedback and notification were most pronounced for children with uncontrolled asthma, as defined by having at least one of three or more beta agonists prescribed in the 6 months prior to their entering the study. Feedback to doctors who already were caring for children with severe asthma who did not receive feedback or notification increased the proportion treated to 81.6% with notification and 82.1% with feedback. When feedback and notification were both used, 85.5% filled their controllers (odds ratio 1.7, compared with children in plans that provided neither).

The mean number of days that controllers were filled also increased from 144 with no communication to 181 with feedback and notification. On average, children in plans with feedback and notification filled their controllers for 225 days.

Children in plans with feedback filled their controllers for 17.6 days more on average than children in plans with no feedback. If the plans had one component, either feedback or notification, then the benefit averaged 10.3 more days of filled controllers.

Notification, by itself, resulted in more than 200 days that controllers were filled on average, the most of any option as a population as a whole. The effects of feedback and notification were most pronounced for children with both components filled, as defined by having at least one of three or more beta agonists prescribed in the 6 months prior to their entering the study. Feedback to doctors who already were caring for children with severe asthma who did not receive feedback or notification increased the proportion treated to 81.6% with notification and 82.1% with feedback. When feedback and notification were both used, 85.5% filled their controllers (odds ratio 1.7, compared with children in plans that provided neither).

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In North American clinical trials of MAXIPIME at a dose of 0.5 to 2 g IV q12h, the most common adverse events were local reactions (3%), including phlebitis (1.3%), pain and/or inflammation (0.6%); rash (1.1%). Pseudomembranous colitis has been reported with nearly all antibacterial agents, including MAXIPIME, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to administration of antibacterial agents.

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Please see brief summary of prescribing information on adjacent page.