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"Among the 18 fundamental points in the U.S. pandemic plan, there is little mention of bacterial vaccines," said Dr. Keith Klugman.

Pneumonia Vaccine Key For Pandemic Flu Plans

BY KATE JOHNSON
Elsevier Global Medical News

MONTREAL — U.S. plans for an influenza virus pandemic should include a strong recommendation for bacterial pneumonia vaccination, as this measure has been shown to reduce influenza mortality by up to 50%, said Dr. Keith Klugman.

"Among the 18 fundamental points in the U.S. pandemic plan, there is little mention of bacterial vaccines. I believe their role is significant and has not been considered up until now," he said at an international conference on community-acquired pneumonia.

Although the influenza virus alone can be fatal, the risk of death is greater with secondary pneumococcal infection, said Dr. Klugman, professor of infectious diseases and the William H. Foege Chair of Global Health at Emory University, Atlanta.

"The combination of bacterial superinfection and influenza is highly fatal. It's a huge problem, and it's not a small part of influenza mortality and morbidity," he said in an interview.

Evidence that pneumococcal infection played a major role in the 1918 influenza pandemic "is substantial, but seems to have been forgotten," Dr. Klugman recently wrote in a letter to the editor (Science 2007;316:49-50), citing historical evidence of culturable pneumococci in the blood of at least half of the survivors and victims of influenza in two

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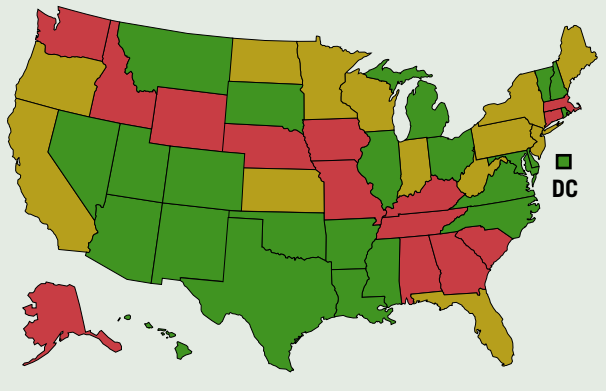
VITAL SIGNS

Medicaid Coverage of Smoking Cessation Treatments



Provides full coverage for smoking cessation to all beneficiaries through Medicaid

Provides partial smoking cessation coverage through Medicaid to all or some beneficiaries

Provides no coverage through Medicaid for smoking cessation

Source: 2003 data, American Cancer Society

Elsevier Global Medical News

FDA Panel Divided On Advair 500/50 For COPD Treatment

Infections, survival data questioned.

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

GAITHERSBURG, MD. — A federal advisory panel last month unanimously agreed that studies of the Advair Diskus 500/50 combination dose of fluticasone propionate and salmeterol inhalation powder for maintenance treatment of chronic obstructive pulmonary disease demonstrated a "clinically meaningful" drop in COPD exacerbations.

But the Food and Drug Administration's Pulmonary-Allergy Drugs Advisory Committee voted 9 to 2 that the data did not provide "substantial convincing evidence" that Advair 500/50 increased survival.

The advisory panel also expressed concern about an increase in respiratory infections and pneumonia in patients who were taking the combination dose, and members questioned the lack of data comparing the 500/50 dose with the 250/50 formulation of Advair.

The panel made no recommendation regarding approval of the 500/50 formulation for COPD. The FDA usually follows the advice of its advisory panels, which is not binding.

Based on the data, "I can't see myself saying to a patient, 'Take this drug—it's going to make you live longer,' " said panelist Dr. Lee Newman, professor in the department of preventive medicine and biometrics, University of Colorado, Denver.

Dr. I. Marc Moss of the University of Colorado, Denver, agreed that the data showed treatment reduced exacerbations. If the drug is approved, however, and if the pneumonia signal turns out to be a real problem, the trade-off would be an increased risk of pneumonia, cautioned Dr. Moss, the Roger Sherman Mitchell professor of medicine in the division of pulmonary sciences and critical care medicine at the

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INSIDE

Smokers Quitting After CABG Gain 3 Years

BY BRUCE JANCIN
Elsevier Global Medical News

NEW ORLEANS — Patients who quit smoking within a year after coronary artery bypass graft surgery prolong their life expectancy by an average of 3 years, Dr. Don Poldermans said at the annual meeting of the American College of Cardiology.

"This [information] is a practical tool for physicians to use. …It may be the ultimate reason for the patient to quit smoking," observed Dr. Poldermans of Erasmus University, Rotterdam, the Netherlands.

It's well accepted that smoking cessation after coronary revascularization or MI reduces mortality risk. Dr. Poldermans presented the first study to quantify this benefit in years of life saved.

He reported on 30-year outcomes for 1,041 consecutive patients who underwent venous CABG at the medical center in 1971-1980. A total of 551 were smokers at the time, of whom 43% quit within the next year.

The 10-year survival was 88% in the smoking cessation group, compared with 77% in the persistent smokers. Survival at 15 and 30 years was 70% and 19%, respectively, in the patients who had quit smoking, compared with 53% and 11% in those who did not.

The average post-CABG life expectancy was 20 years for patients who quit smoking and 17 years for persistent smokers.

Smokers who were younger than 50 years at the time of CABG and who quit smoking within the next year lived an

See **CABG** • *page 3*

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Panel Vote Comes With Caveats

FDA Panel • *from page 1*

University of Colorado.

There are three approved dosage strengths of the combination dry powder formulation marketed as Advair Diskus by GlaxoSmithKline (GSK): 100/50, 250/50, and 500/50, which contain 100 mcg, 250 mcg, and 500 mcg of the fluorinated corticosteroid fluticasone, respectively, each with 50 mcg of salmeterol, a long-acting β-agonist. Only Advair Diskus 250/50 has an approved COPD indication, for maintenance treatment of airflow obstruction in patients with COPD associated with chronic bronchitis. All three doses are approved for asthma.

The panel meeting was held to review GSK's proposed indication for Advair 500/50 as twice-daily maintenance treatment of airflow obstruction in patients with COPD and to increase survival and reduce exacerbations in patients with a forced expiratory volume in 1 second (FEV_1) less than 60% of the predicted value. The manufacturer based the proposal on two randomized, double-blind, controlled studies. The effect of Advair 250/50 on these end points has not been studied, according to the FDA.

In the TORCH (Towards a Revolution in COPD Health) study, a 3-year international study published in February, Advair 500/50 dosed twice daily was compared with the individual components and placebo. The trial included 6,112 COPD patients, ages 40-80 years, with an FEV_1 less than 60%. The same treatment groups were compared with placebo in a 1-year study of 1,465 patients, the TRISTAN (Trial of Inhaled Steroids and Long-Acting β_2-Agonists) study.

In both studies, moderate/severe exacerbations were significantly lower among Advair-treated patients, compared with patients on placebo. In the TORCH study, exacerbations were also significantly lower, compared with the two separate components.

In the TORCH study, all-cause mortality after 3 years (the primary end point) was 2.6% lower in Advair-treated patients than among those on placebo (12.6% vs. 15.2%, respectively). The difference failed to achieve statistical significance, however, with a *P* value of 0.052 (N. Engl. J. Med. 2007;356:775-89). All-cause mortality was comparable in the salmeterol-only arm, at 13.5%.

Among the U.S. patients, who composed 23% of the study enrollees, all-cause mortality among Advair-treated patients was only 1.6% lower than that of patients taking placebo.

In the TORCH study, the rate of pneumonia was 20% among those on Advair and 19% among those on fluticasone, compared with 12% of patients on placebo and 13% of those on salmeterol. The rate of lower respiratory tract infections was 34% among those on Advair and 30% among those on fluticasone, compared with 26% among those on placebo and those on salmeterol.

The panel agreed that the increased rate of respiratory infections and pneumonia was a clear signal and should be studied further. Advisory panel members also took issue with the way pneumonias and exacerbations were defined.

Several panelists recommended that Advair 500/50 be compared with the 250/50 dose, although such a study could take up to 7 years.

Dr. Polly Parsons, FCCP, director of the pulmonary and critical care medicine unit at Fletcher Allen Health Care, Burlington, Vt., said that as a clinician, she would have to choose between Advair 500/50 and 250/50 "without really understanding what to do." The two doses have not been directly compared, she added, and it is not clear if the lower dose works as well as the higher dose. Dr. Parsons also expressed concern about the increase in long-term complications with the higher dose.

GSK officials said the risk of pneumonia is being evaluated in HMO databases in the United States, where Advair 500/50 is occasionally used for COPD, and general practitioner databases in the United Kingdom, where the 500/50 dose is approved for COPD. Final results are expected this summer.

There is no evidence of immunosuppression among patients on this dose of Advair, according to GSK, or evidence of an increase in opportunistic infections. ■

IN THIS ISSUE

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As-Needed Asthma Combo Lowered Steroid Exposure

BY MARY ANN MOON
Elsevier Global Medical News

Symptom-driven "rescue" use of a single inhaler containing beclomethasone plus albuterol was as effective at controlling mild persistent asthma as was regular twice-daily use of inhaled beclomethasone alone in a prospective, randomized study.

As-needed use of the combination inhaler led to significantly lower cumulative exposure to corticosteroids. In addition, "the simple, symptom-driven use of inhaled beclomethasone and albuterol may overcome one of the major problems in the treatment of chronic diseases such as asthma: poor compliance," wrote the study's investigators.

Dr. Alberto Papi, FCCP, of the University of Ferrara (Italy) and his associates compared outcomes with four different inhaler treatments in a 6-month study of 393 adults with mild persistent asthma who were treated at 25 medical centers throughout Europe in 2002-2004. The study was funded by Chiesi Farmaceutici. Dr. Papi has received support from Chiesi Farmaceutici, GlaxoSmithKline, AstraZeneca LP, Boehringer Ingelheim, and Merck Sharp & Dohme.

Participants were randomly assigned to one of four treatment groups: as-needed combination therapy (250 mcg beclomethasone and 100 mcg albuterol in a single inhaler), regular twice daily combination therapy plus albuterol as needed, regular beclomethasone therapy (250 mcg twice daily) and albuterol as needed, or placebo twice daily plus albuterol as needed.

After 6 months of treatment, the morning peak expiratory flow rate—the primary outcome measure—did not differ significantly between the as-needed combination therapy group and the regular twice-daily beclomethasone or regular combination therapy groups (N. Engl. J. Med. 2007;356:2040-52).

The cumulative dose of beclomethasone was significantly lower in the subjects who took as-needed combination therapy (18.5 mg) than in the group receiving regular beclomethasone therapy (77.0 mg) or regular combination therapy (77.1 mg). The number of adverse events did not differ significantly among the treatment groups.

"Our results confirm and extend the conclusions of Boushey et al, who showed that mild persistent asthma is equally controlled by intermittent and regular treatment with inhaled corticosteroids," said Dr. Papi and his associates. ■

CHEST PHYSICIAN

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MRSA Community-Acquired Pneumonia Difficult to Treat

BY KATE JOHNSON
Elsevier Global Medical News

MONTREAL — The high mortality in community-acquired pneumonia caused by methicillin-resistant *Staphylococcus aureus* may be largely due to Panton-Valentine leukocidin toxin, according to Dr. Ian Gould, consultant microbiologist at the University of Aberdeen (Scotland).

Thus, efforts to control the infection should probably focus on the toxin as well as the bacteria, Dr. Gould said at an international conference on community-acquired pneumonia (CAP).

"Switching off toxin production is probably a major issue because it's mainly a toxin-induced disease," he said in an interview at the meeting. "Even if the antibiotics can kill the bug, the toxin's still there and that's what's doing the damage."

Panton-Valentine leukocidin (PVL) toxin is produced mostly by community-acquired, as opposed to hospital-acquired, strains of methicillin-resistant *S. aureus* (MRSA). And the prevalence is increasing, Dr. Gould said.

"Clearly, there have been big changes in the epidemiology of community-acquired MRSA, and now there are quite a few epidemic strains that produce PVL," he said. In fact, according to a recent report from the Centers for Disease Control and Prevention, the majority of reported community-acquired MRSA infections are PVL-producing strains (MMWR 2007;56:325-9).

Although most of these infections involve skin and soft tissue and are "relatively mild," according to Dr. Gould, "more and more commonly, we're seeing very severe respiratory disease associated with community-acquired MRSA PVL strains." In the recent CDC report of 10 cases of MRSA-associated CAP, all isolates were positive for PVL toxin.

"This is an organism that causes severe pneumonia," said Dr. Coleman Rotstein, who also presented at the meeting, which was sponsored by the International Society of Chemotherapy. The key features of CAP caused by MRSA are empyema and necrotizing pneumonia, said Dr. Rotstein, professor of medicine at McMaster University, Hamilton, Ont.

He and other experts at the meeting agreed that treatment options are limited.

"When it comes to treatment, we are standing in the dark, with a case mortality in the published literature of around 75%," Dr. Gould said. "It's kind of like going back to the influenza epidemic after the First World War, when there were no antibiotics."

"For these new MRSA CAP etiologies, the present arsenal of antibiotics is unfortunately insufficient," said Dr. Ethan Rubenstein, who also presented at the meeting.

"Evidently, the β-lactams are useless, and vancomycin is associated with unfavorable clinical results even when used in higher doses," said Dr. Rubenstein, professor and head of infectious diseases at the University of Manitoba, Winnipeg.

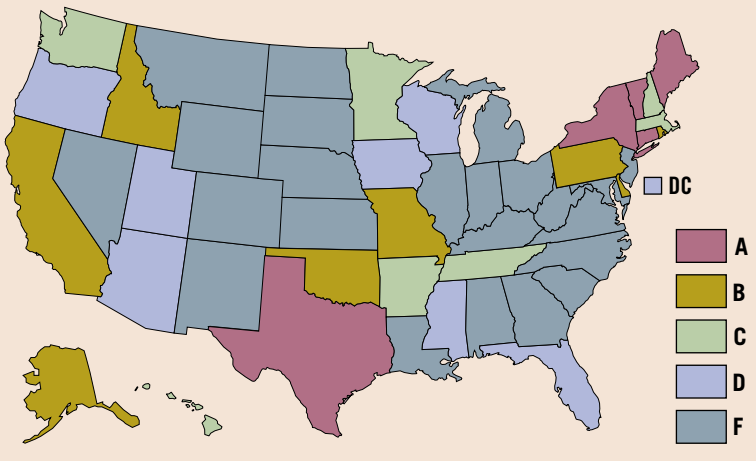
According to Dr. Gould, high-dose clindamycin or linezolid are good options, not only for their antibacterial effects but also because of their potential ability to lower PVL production. "[Intravenous] immunoglobulin is also well recognized as an adjunct, but I don't know if there's much evidence for its effect—although there are PVL antibodies in it," he said. In addition, gentamicin is indicated for patients who are bacteremic.

"We haven't seen the end of this story by any means—this is a highly adaptable, rapidly developing organism—and I am not usually known for my pessimism, but I have to say things are going to get worse here before they get better," Dr. Gould said. ■

Dr. Aymarah Robles, FCCP, comments: *Sobering commentary on the current MRSA epidemic. The changing epidemiology and the role of PVL toxin-producing strains in community-acquired MRSA, including severe CAP, merit clinician awareness. The need for a broader arsenal and the development of new antibiotics is once more painfully apparent.*

DATA WATCH

Laws on Youth Access to Tobacco: Most States Get Failing Grade



Note: Scores based on points given for laws pertaining to minimum age, packaging, clerk intervention, photographic ID requirement, vending machines, free distribution/samples, graduated penalties, random inspections, and statewide enforcement.
Source: 2005 data, American Lung Association

ELSEVIER GLOBAL MEDICAL NEWS

Bacterial Superinfection Lethal

Pneumonia Vaccine • *from page 1*

studies (Br. Med. J. 1919;1:3-5; JAMA 1918;71:1735).

And a randomized, controlled trial by Dr. Klugman and his colleagues has shown that, in children, vaccination against pneumococcal bacteria results in a 31% decrease in pneumonias associated with respiratory viruses (Nat. Med. 2004;10:811-3).

"Because of the vaccine, they are not getting the superinfection that brings them to the hospital," he said at the meeting, which was sponsored by the International Society of Chemotherapy.

The 23-valent pneumococcal polysaccharide vaccine (PPV 23) is currently recommended in adults older than 65 years, but giving the 7-valent pneumococcal conjugate vaccine (PCV 7) to children is more protective against bacterial pneumonia in the adult population, said Dr. Klugman.

Data from the Centers for Disease Control and Prevention show that adult infections with the seven pneumococcal strains covered in the children's vaccine have decreased, while infections from the other 16 strains covered by the adult vaccine have increased. "The burden of disease in adults has been impacted more by giving the conjugate vaccine to children than by giving the 23-valent vaccine to adults," said Dr. Klugman.

This has led some investigators to ask whether adults might benefit by being immunized using the children's conjugate vaccine. (See box.)

In addition, a new study (Lancet 2007;369:1179-86) offers the first evidence that vaccinating children protects adults against all pneumococcal pneumonia, not just bacteremic pneumococcal pneumonia.

Improving pneumococcal vaccine coverage in children could result in major reductions in infection across all ages, he said. "Only about 60% of kids currently get the full four doses of the conjugate vaccine, and it's that fourth dose that induces the full immunity and stops transmission." ■

Dr. Aymarah Robles, FCCP, comments: *This is an excellent reminder of the importance of pneumococcal vaccine. Vaccination of at-risk patients helps to decrease their vulnerability, morbidity, and mortality. Vaccination of children is an important public health goal, because it helps to protect adults from pneumococcal infection.*

Should Adults Get Children's Vaccine?

Is there a role for giving the children's conjugate vaccine to adults?

A recent study suggested that it may not be as simple as that (Vaccine 2007;25:4029-37). Immunogenicity among elderly patients (aged 70-79 years) who were given the children's dose of conjugate vaccine was "nothing to get overly excited about," Dr. Klugman said. "Perhaps the dose designed for a primary response in kids is not enough for adults," he suggested.

And a study presented at the 2006 International Symposium on Pneumococci and Pneumococcal Diseases by Dr. Andrés de Roux of the Universitat Autònoma de Barcelona and colleagues suggested that the administration of the children's conjugate vaccine to elderly patients within 1 year of giving them the polysaccharide vaccine could actually suppress immunity.

"It seems the adult vaccine interferes with the response to the conjugate, which is a concern, because it means we can't simply give the conjugate to people who have previously had the [23-valent vaccine]. There will have to be a strategy, and it seems that certainly the conjugate needs to be given before the 23-valent," Dr. Klugman said.

Dr. Klugman said that in his opinion, a new conjugate vaccine, with coverage of more strains than the current one, will eventually replace the PPV 23 for adults.

Benefits of Smoking Cessation

CABG • *from page 1*

average of 3.5 years longer than did those who kept smoking. Patients aged 50-60 years at surgery who ceased smoking gained an average of 2.8 years, compared with persistent smokers. Those who quit following CABG after age 60 had a 1.7-year greater life expectancy than did those who didn't quit.

Dr. Poldermans said that these are conservative estimates of the life expectancy benefit of smoking cessation, because they derive from the early era of CABG. In the early 1970s, CABG was largely reserved for relatively young, otherwise healthy patients of a sort that cardiac surgeons seldom encounter today. The average age of the study population was 53 years. Diabetes and other comorbid conditions were uncommon. Vein grafts were the rule; the far more durable arterial grafts didn't become the norm until the 1980s. Today's CABG patients are much sicker, older, and higher risk than were those of 30 years ago—and the greater a patient's risk, the greater the benefit of an effective intervention.

After adjustment for potential confounders, smoking cessation remained an independent predictor of lower mortality, conferring a 38% relative risk reduction. That's as good as or better than other secondary prevention measures, he noted. ■

Diesel Exhaust Linked to Myocardial Ischemia in CHD

BY BRUCE JANCIN
Elsevier Global Medical News

NEW ORLEANS — Brief inhalation of dilute diesel exhaust at levels comparable to those encountered curbside along city streets promotes myocardial ischemia in patients with coronary heart disease, Dr. David E. Newby reported at the annual meeting of the American College of Cardiology.

He presented the first-ever study in which patients with known CHD were deliberately exposed to air pollution. The purpose was to pinpoint the mechanisms underlying the well-established epidemiologic association between air pollution and increased cardiovascular morbidity and mortality.

"Not everybody believes that air pollution is linked to cardiovascular disease, particularly pressure groups backed by the automobile industry. So we felt it was very important to show what the mechanisms are," explained Dr. Newby, professor of cardiology at the University of Edinburgh.

He and his coinvestigators in Edinburgh and at Umeå (Sweden) University briefly exposed 20 Swedish patients with prior MI to either dilute diesel exhaust at a concentration of 300 mcg/m^3 or to filtered air during intervals of moderate exercise or rest in a double-blind crossover study conducted in a special chamber.

All patients had stable CHD, having previously undergone coronary revascularization. All were on standard evidence-based medications for secondary prevention.

Exposure to diesel exhaust caused a threefold increase in the magnitude of exercise-induced ST-segment depression: a mean 49 mcV of ST depression, compared with 17 mcV of ST depression while breathing filtered air during exercise.

In addition, blood levels of tissue plasminogen activator—which is a potent endogenous clot dissolver—declined significantly after patients were exposed to diesel exhaust, providing a second specific mechanism to explain the oft-described link between air pollution and the occurrence of cardiovascular events.

Dr. Newby noted that the World Health Organization has estimated that nearly 1 million deaths per year are attributable to inhalation of polluted air.

His study was funded by the British Heart Foundation. ■

Dr. Peter McKeown, FCCP, comments: *This is an interesting and somewhat controversial article regarding the effects of diesel pollution in patients with known (albeit treated) coronary disease.*

Unfortunately, the authors have chosen a specific pollutant—namely, diesel fumes, which contain particulate and chemical residues. They did not elucidate the particular agent causing the effect, nor did they mention whether a relative hypoxemia was associated with the exposure.

Further study along these lines on the effect of different environment pollutants and specific agents is clearly warranted.

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Exposure to diesel exhaust caused an increase in exercise-induced ST-segment depression and a decline in blood levels of tissue plasminogen activator.

Telephone Intervention Curbed Number of ED Asthma Visits

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Introduction of a simple telephone follow-up program has taken a big bite out of asthma-related emergency department visits at one large Midwestern inner-city hospital.

The result has been a strong shift of patients from the overcrowded ED to the asthma clinic, where they receive far more comprehensive, prevention-oriented treatment at less institutional cost, Rita A. Mangold said at the annual meeting of the American College of Chest Physicians.

The program led to a 40% reduction from the historic annual average of about 1,300 adult asthma ED visits.
MS. MANGOLD

The emergency department at Truman Medical Center Hospital Hill in Kansas City, Mo., handles roughly 57,000 patient visits per year, including more than 50% of all asthma-related ED visits for adults in the city. In an effort to curb revolving-door use of the ED for asthma attacks, in 2001 Truman introduced an ED protocol, consistent with national guidelines, involving patient asthma education by a respiratory therapist in the ED and provision of samples of controller medications when indicated. Unfortunately, this didn't put much of a dent in ED asthma visits, explained Ms. Mangold, a nurse asthma specialist at the medical center.

In the spring of 2004, therefore, the hospital launched a program in which the nurse advice-line staff began telephoning all ED adult asthma patients and assisting them in obtaining follow-up care. If they didn't have a primary care physician or were deemed high risk according to national asthma guidelines—meaning they had at least three ED visits for asthma within the past year, an ED visit or hospitalization for asthma in the past month, or two or more asthma-related hospitalizations in the past year—an appointment was made for them at the Truman asthma clinic.

The results have been dramatic: roughly a 40% reduction from the historic average of about 1,300 adult asthma ED visits per year. "This is the first time we've ever been able to achieve this and sustain it," she noted, adding that the effect appears to be snowballing. "We had only 36 ED visits for asthma in August."

Meanwhile, the number of asthma clinic visits has climbed by a corresponding 40%. In the clinic, patients receive a far more thorough evaluation than is possible in the ED. They also gain access to all sorts of ancillary services, such as qualification for Medicaid and enrollment in medication compassionate care programs.

At Truman, an asthma-related ED visit costs about $300. A clinic visit costs considerably less and results in fewer future asthma attacks. The key to avoiding interdepartmental skirmishing is getting top administrators to recognize those benefits.

An audience member said his hospital in Brooklyn, N.Y., tried a telephone follow-up program but found it had limited impact. "Half of the phone numbers didn't work or the patients didn't want to talk to us no matter what, even if they had severe disease. That's a big issue," he added.

Ms. Mangold described such patients as "frequent flyers"—people who make a habit of skipping out on their bills. She makes a point of establishing a rapport with them. "I have their personal phone numbers. They know I'm not calling them for the bill," she said. ■

Some Smokers Can Quit After Brief Counseling

BY BRUCE JANCIN
Elsevier Global Medical News

NEW ORLEANS — Behavioral interventions aimed at smoking cessation showed modest albeit statistically significant efficacy in a new meta-analysis of 51 randomized controlled trials totaling nearly 27,000 smokers, Salvatore Mottillo reported at the annual meeting of the American College of Cardiology.

The behavioral interventions were of four types: brief physician-given advice to quit, typically a one-on-one intervention lasting 30 seconds to a couple of minutes; individual counseling by a therapist or physician in a more in-depth session of at least 20 minutes; group counseling; or proactive telephone counseling in which a nurse or therapist makes multiple phone calls to follow up on the patient's smoking status.

All 51 studies used biochemically validated patient self-reported smoking abstinence at 6 and/or 12 months as an end point.

Control subjects were individuals who felt motivated to quit smoking but received no assistance. Their success rate was about 10%. All four types of behavioral intervention boosted the success rate to about 15%-17%, with no significant difference among them, according to Mr. Mottillo.

"What's interesting is clearly there's not one intervention that stands out as being more effective than the others. It seems as though minimal clinical intervention—that's the brief advice provided by a physician—may be as effective as these more resource-intensive interventions which require a lot more time and a lot more money," said Mr. Mottillo, an undergraduate student at McGill University, Montreal, in an interview.

"The government spends a lot of money on telephone hotlines to help patients quit smoking; that might not be any more helpful to patients than a physician telling someone to quit," he said.

He and his coinvestigators have applied to the Canadian Institutes for Health Research for funding of a head-to-head comparative trial testing that hypothesis, he added.

Nicotine patches and other pharmacotherapies appear to be slightly more effective than are behavioral interventions. In a separate meta-analysis, Mr. Mottillo's coinvestigators found that motivated patients given pharmacotherapeutic help were roughly twice as likely to quit smoking as controls. However, there hasn't been a randomized trial comparing behavioral and pharmacologic interventions, noted Mr. Mottillo. ■

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Panel Backs Plan to Cut Transfusion-Related Lung Injury

A unanimous decision supports the use of predominantly male plasma for transfusions.

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

GAITHERSBURG, MD. — A Food and Drug Administration advisory panel has supported the practice of limiting the use of plasma from female donors to reduce the incidence of transfusion-related acute lung injury in plasma transfusion recipients.

At a meeting of the FDA's Blood Products Advisory Committee in April, the panel agreed in a 13 to 0 vote that the use of predominantly male plasma for transfusions would reduce the incidence of transfusion-related acute lung injury (TRALI), the leading cause of transfusion-related deaths reported to the FDA over the past 3 years.

ALLOTYPIC LEUKOCYTE ANTIBODIES FROM FEMALE DONORS' PLASMA HAVE BEEN ASSOCIATED WITH CASES OF THE SYNDROME IN RECIPIENTS.

TRALI is an acute syndrome characterized by severe shortness of breath within 6 hours of a transfusion, with bilateral pulmonary infiltrates on chest x-ray and arterial oxygenation desaturation but no signs of fluid overload, in the absence of other detectable causes. If recognized early, TRALI is treatable, and symptoms usually resolve within 24-48 hours; however, the reported mortality rate ranges from 10% to 50%, according to the FDA.

TRALI cases have been associated with plasma from female donors, which is thought to be related to the presence of allotypic leukocyte antibodies in donors, stimulated by pregnancy and transfusions. Because donors implicated in cases of TRALI in recipients have often been women who have leukocyte antibodies, reducing the use of such donors has been considered as a strategy for reducing TRALI, according to the FDA. In the United Kingdom, the incidence of TRALI dropped dramatically after 2003, when the National Blood Service decided to use mostly male plasma for transfusions. In the U.S. blood banking community, this approach has been implemented voluntarily or is under consideration.

The panel largely agreed that this approach would not affect the U.S. supply of plasma. However, Dr. Irma Szymanski, professor of pathology, at the University of Massachusetts, Worcester, said that while there is evidence of an association between plasma from female donors and a greater risk of TRALI, plasma from some female donors has not been associated with TRALI cases, and they should not be eliminated from the donor pool. And Dr. Maureen Finnegan, of the department of orthopedic surgery at the University of Texas at Dallas, added that a plasma shortage could occur in the event of a national disaster that presented increased demand.

The panel unanimously agreed that while some preliminary data suggest an association between increased TRALI risk in recipients and the presence of antineutrophil and anti–human leukocyte antigen (HLA) antibodies in donors, it is too early to recommend screening donors for these antibodies. More data are anticipated from ongoing studies, including a National Institutes of Health–sponsored 5-year study on the prevalence of HLA and granulocyte antibodies in blood donors at U.S. blood centers. The study will correlate the presence of HLA class 1 and 2 antibodies in blood donors with certain factors, such as the number of pregnancies and lifetime history of transfusion, in over 5,000 female donors, and in men with and without a history of blood product transfusion.

In another unanimous vote, the panel did not support eliminating the use of plasma from donors with a history of transfusions, because currently there is no evidence that this strategy would reduce the incidence of TRALI.

One of the speakers at the meeting, Dr. Ravi Sarode, director of transfusion medicine at the University of Texas at Dallas, said that there is widespread misuse of plasma in clinical practice and that reducing inappropriate use of plasma would also decrease the incidence of TRALI. For example, protamine is the appropriate treatment for heparin-induced bleeding, but many surgeons continue to prescribe fresh frozen plasma, which may make bleeding worse, he said.

While all blood products that are transfused have been implicated in TRALI, most cases are associated with plasma products, such as fresh frozen plasma.

After a previous meeting of the same panel, the FDA issued a letter to physicians about TRALI in October 2001. Reports of TRALI subsequently increased: 21 deaths were reported between October 2003 and September 2005, and 35 deaths were reported in 2006. Those 35 deaths accounted for 51% of all reported transfusion-related fatalities that year. TRALI-related morbidity is much higher, occurring at a rate of one case per 2,500 to 5,000 transfusions, according to FDA estimates. ■

Common Examples of Plasma Misuse

During a presentation at the FDA meeting on the misuse of plasma in clinical practice, Dr. Sarode cited heparin-induced bleeding as one example.

Protamine is the appropriate treatment for heparin-induced bleeding, but many surgeons continue to prescribe fresh frozen plasma in this setting, which may make bleeding worse, said Dr. Sarode, director of transfusion medicine at the University of Texas at Dallas.

Practicing clinicians and medical students need more education about transfusion medicine and hemostasis, he said. More than 3 million units of plasma are infused annually in the United States, most often before an invasive procedure or to correct an abnormal coagulation test result. But presurgical hemostasis assessments are performed primarily by labs, "rather than by good clinical history about bleeding," he said.

He cited one study of 80 patients with elevated international normalized ratio (INR) who received fresh frozen platelets (FFP) for prophylaxis (41%) or bleeding (59%). Two-thirds of those patients received two to four units, and 25% received more than four units. But in 89% of these cases, treatment failed to correct prothrombin time (PT) to within 3 seconds above the normal range (Am. J. Gastro. 2003; 98:1391).

He said that plasma therapy is often misused to correct mild to moderate abnormal PT/INR, without bleeding, and as a volume expander. But published data provide no evidence-based guidance for use of FFP or platelet transfusions before procedures in patients with mild to moderate coagulation test abnormalities, he said.

In the United States, the number of units of FFP used per 1,000 population is at 13.9, which is almost twice as high as some other countries, such as the United Kingdom, where it is 6.4 units per 1,000 population.

Blood banks in hospitals should practice transfusion medicine "rather than function simply as dispensing units," which is the case for almost all hospitals in this country, Dr. Sarode said.

At Parkland Memorial Hospital in Dallas, which has a very active transfusion medicine practice, plasma use has dropped by 60% since 2001, while the number of admissions and trauma cases has remained the same.

Lung Transplant Patients Often Fail to Share End-of-Life Wishes

BY BRUCE K. DIXON
Elsevier Global Medical News

SALT LAKE CITY — Cystic fibrosis patients seeking lung transplants are less likely to share end-of-life decisions with their physicians than are those not on a transplant list, according to data presented at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

The poster study also revealed an association between awaiting lung transplantation and greater use of life-sustaining treatments, according to Dr. Elisabeth Potts Dellon and her colleagues at the University of North Carolina at Chapel Hill.

Dr. Dellon and her colleagues reviewed the medical records of consecutive cystic fibrosis patients who died during treatment at the university between 1994 and 2004. Of 38 decedents, 20 had received or were awaiting lung transplants, whereas 18 were not referred for transplant or declined the option, said Dr. Dellon, a fellow in pediatric pulmonology.

Of those who had documented advance directives, transplant patients more often asked to be designated a "full code" status (100% vs. 29%). Later, when death was imminent, most patients had a do-not-resuscitate order, but transplant patients were less likely to participate in this decision (15% vs. 61%).

INITIATE CONVERSATIONS ABOUT LUNG TRANSPLANT EARLY IN THE DISEASE, WHEN PATIENTS CAN MAKE GOOD DECISIONS.

Transplant patients also were more likely than nontransplant patients to die in the intensive care unit (85% vs. 50%), and to be intubated until shortly before death (80% vs. 36%).

Differences were clinically and statistically significant despite the small number of patients who experienced cystic fibrosis as their terminal illness, the authors wrote.

The data suggest that end-stage cystic fibrosis patients and their physicians are not discussing important decisions about end-of-life care to an appropriate degree, Dr. Dellon said in an interview.

"Patients awaiting a lung transplant are unlikely to have a discussion about what they would do in the event that it became clear that they were going to die, because they're hanging on to hope of a successful transplant and extended survival," she said, adding that physicians taking care of cystic fibrosis patients should initiate conversations with patients and family members.

"And they should do so as early in the disease as possible, when patients can make good decisions about what they would like to accomplish, what kind of treatment they want, where they would like to die, and whom they want present," Dr. Dellon said.

Communication about patient wishes also is hampered by insufficient documentation of patient-physician conversations, she said. ■

Biologic Markers Can Help Limit Antibiotic Overuse

A procalcitonin assay approved in Europe has been used to track the progression of bacterial pneumonia.

BY KATE JOHNSON
Elsevier Global Medical News

MONTREAL — In community-acquired pneumonia, overuse of broad-spectrum antibiotics can be curbed with the help of biologic markers such as procalcitonin, according to Dr. Jean Chastre of the Hôpital de la Pitié-Salpêtrière, Paris.

Blood levels of procalcitonin (PCT) rise in patients with bacterial infections but remain fairly low in those with viral infections, and PCT levels decrease as the bacterial infection subsides. Measuring PCT levels thus aids decisions about whether to prescribe antibiotics, what type to prescribe, and for how long, he said at an international conference on community-acquired pneumonia (CAP).

"We use antibiotics for too long for too many patients, and in doing so are favoring the emergence of resistant strains," Dr. Chastre explained in an interview at the meeting, which was sponsored by the International Society of Chemotherapy.

"The more antibiotics we use, the more resistance we are going to see," Dr. Jean-Claude Pechère agreed in an interview. In his presentation, he outlined a 2004 study in which PCT-guided therapy for lower respiratory tract infections significantly reduced antibiotic use, compared with standard care (Lancet 2004;363:600-7). "With these biomarkers, we suddenly realized we could cut antibiotic consumption almost in half. In Europe, we are speaking of millions of patients," said Dr. Pechère, a professor of medicine at the University of Geneva.

Although a PCT assay is approved in Europe, it is still not widely available. And it is even less available in North America, said Dr. Thomas File, FCCP, a professor of internal medicine and head of infectious diseases at Northeastern Ohio Universities, Rootstown. "There are a few places where they have it available in the [emergency department], but in most places it takes several hours to get the result back—maybe even a day," Dr. File said in an interview. "We need a lot more studies looking at its applicability at the point of service."

Because initiation of antibiotic therapy is recommended within hours of a diagnosis of bacterial CAP, a PCT assay may not be practical for guiding initial treatment decisions, he said. "I think it's probably going to be more helpful in making decisions about duration of therapy, or changing therapy."

For example, antibiotics can be stopped if the PCT results suggest that bacterial infection is unlikely, explained Dr. Chastre, who has received research funding and is a speaker for Brahms Diagnostics LLC, which makes a PCT assay. Or, therapy could be shortened if serial PCT measurements suggest a rapid response. "It's probably possible, even in severe pulmonary infection, to shorten the duration of antibiotics to 5 or 7 days if the PCT is decreasing very rapidly," Dr. Chastre said.

'WE SUDDENLY REALIZED WE COULD CUT ANTIBIOTIC CONSUMPTION ALMOST IN HALF. IN EUROPE, WE ARE SPEAKING OF MILLIONS OF PATIENTS.'

European guidelines recommend that empiric therapy for bacterial CAP should provide coverage against the most common pathogen (*Streptococcus pneumoniae*) but not atypical pathogens, whereas North American experts favor a wider spectrum of coverage that includes the atypicals. PCT-guided therapy could allow European physicians to continue with less complete initial coverage by identifying the nonresponders who need expanded therapy, Dr. Pechère said.

In the future, it may even be possible to use PCT levels to distinguish typical from atypical CAP pathogens, he added, citing one study that noted lower levels in hospitalized CAP patients infected with typical—compared with atypical—bacteria (Infection 2000;28:68-73). However, a more recent study concluded that PCT levels were not predictive of type of pathogen (Clin. Microbiol. Infect. 2007;13:153-61).

Dr. Chastre emphasized that, in evaluating the severity and progression of pneumonia, PCT levels should always be considered together with other clinical parameters. "This marker is not 100% sensitive in some patients because some people, even with very severe disease, can have low levels," he said, citing his own study showing low PCT levels in some patients with ventilator-associated pneumonia (Am. J. Respir. Crit. Care Med. 2005;171:48-53).

The reverse can also be true, with high levels of PCT seen in nonseptic conditions such as trauma, cardiogenic shock, and heat stroke, among others, he said. ■

Some Pulmonary Sarcoidosis Resolves Without Treatment

BY SHARON WORCESTER
Elsevier Global Medical News

DESTIN, FLA. — Treatment is not necessary in all patients with pulmonary sarcoidosis, Dr. Marc Judson, FCCP, said at the annual Rheumatology on the Beach.

More than two-thirds of patients with this form of sarcoidosis, which accounts for the vast majority of cases, will spontaneously remit. Thus the side effects of corticosteroids, the most common form of treatment for these patients, often are not worth the limited benefits seen with treatment, said Dr. Judson, professor of medicine at the Medical University of South Carolina, Charleston.

There is some retrospective evidence that corticosteroid treatment promotes relapse. In one study, more than 70% of patients who received treatment relapsed, compared with less than 10% who received no treatment, according to Dr. Judson.

He recommends using a decision analysis based on prognostic factors and the degree of pulmonary function in patients with pulmonary sarcoidosis. With this approach, asymptomatic patients are left untreated, and those with mild pulmonary dysfunction and minimal functional limitation are observed without treatment. These patients are likely to experience spontaneous remission.

Patients with an excellent prognosis (see box) are also observed, but palliative care can be attempted when necessary.

In patients who have mild to moderate pulmonary dysfunction and mild to moderate functional limitation, treatment and observation for deterioration are both acceptable options, but Dr. Judson recommends observation initially, with treatment for any deterioration, and a steroid trial if no improvement is seen within 3 to 6 months.

Prednisone at 20-40 mg per day (he noted that he has had good success with 20 mg) for 2-6 weeks is recommended in those who do undergo treatment. Following the initial 2-6 week dosing regimen, the dose is tapered over 1-3 months to a maintenance dose, which is used for 3-9 months. The patient is then tapered off the drug over 1-3 months, followed by an observation period and a second trial of this approach in those who relapse.

Other treatment options include methotrexate, pentoxifylline, chloroquine, azathioprine, and infliximab. Methotrexate is the most studied of these drugs and appears to have some benefit; conversely, azathioprine appears to have the least benefit, he said.

Recent data on infliximab are, however, promising. Dr. Judson and his colleagues found that the overall change from baseline was 2.5% predicted forced vital capacity at 24 weeks in 93 patients treated with either 3 or 5 mg/kg of infliximab. The percentage may sound small, but the change was statistically significant, he noted.

Dr. Judson disclosed that he has received research grants from Centocor, the maker of infliximab. ■

When to Treat Pulmonary Sarcoidosis With Corticosteroids

Disease Severity	Treatment
Asymptomatic patient	No treatment
Mild pulmonary dysfunction/minimal functional limitation	Observation/no treatment
Patients with excellent prognosis (such as those with erythema nodosum, early-stage disease)	Observation/treatment as warranted
Mild to moderate pulmonary dysfunction or functional limitation	Treatment or observation for deterioration. Treat in the event of deterioration or if no improvement is seen in 3-6 months.
Severe pulmonary dysfunction or functional limitation	Treat

Source: Dr. Judson

Dr. Joseph Barney comments: *In patients with pulmonary sarcoidosis and dyspnea, exercise oximetry is an important component of the initial evaluation. Pulse oximetry is noninvasive, widely available, and can detect abnormalities in gas exchange prior to pulmonary function testing. Reduction in forced vital capacity and desaturation during a 6-minute walk test are strong indications for immunosuppressive therapy and further evaluation of the lung parenchyma with high-resolution chest tomography.*

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Literature Reviews Prognosticators For Sarcoidosis

Data suggest that most patients with sarcoidosis will experience spontaneous remission with or without treatment, while up to a third of patients will develop chronic disease.

A review of the literature suggests there are several factors that can help predict a good prognosis (likelihood of remission) or a poor one (likelihood of chronic disease development).

Stage I vs. stage II-III disease as determined by chest x-ray and the presence of erythema nodosum appear to be predictive of a good prognosis, Dr. Judson said.

The following factors predict poor prognosis: black race, extrathoracic disease, aged 40 years or older, splenic involvement, lupus pernio, disease duration more than 3 years, forced vital capacity less than 1.5 L, and stage IV disease/aspergilloma on chest x-ray, with the latter two factors also being risk factors for death from sarcoidosis.

However, death from the disease occurs rarely (in 3%-5% of patients); most will die with their disease, as opposed to from their disease, Dr. Judson said, adding that in most patients, sarcoidosis is present for 5-25 years prior to death.

Bone Mineral Density Lower in Children With Cystic Fibrosis

BY JONATHAN GARDNER
Elsevier Global Medical News

In a French study, children and adolescents with cystic fibrosis showed early signs of defective bone mineralization that were independent of either nutritional status or disease severity.

Cystic fibrosis (CF) has already been linked to low bone mineral density (BMD) in adults, but researchers in the current study found that children with CF had lower BMD scores than did others their age without the disease, suggesting that adult bone disease may originate in youth.

"We recommend that all children with CF undergo assessment of BMD and body composition early in life to make it possible to target those who need preventive treatment," wrote the researchers, led by Dr. Isabelle Sermet-Gaudelus of the Service de Pédiatrie Générale at Necker-Enfants Malades Hospital, Paris (Am. J. Respir. Crit. Care Med. 2007;175:951-7).

The investigators used dual-energy x-ray absorptiometry to study 114 children and adolescents aged 2-18 years recruited at the hospital. Their BMD and other physical characteristics were compared with 317 healthy children and adolescents matched for sex, puberty status, and height-adjusted age.

Mean lumbar spine BMD *z* scores in the CF patients were -0.96 in the 25 children younger than age 6, -0.91 in the 53 children aged 6-10, and -1.4 in the 36 children aged 11-18. Results were adjusted for such factors as the small size of the patients for their age and late onset of puberty.

CF lung disease was minimal and nutritional status was good in 41 patients with a mean age of 9, but their mean lumbar spine *z* score was -0.5. Univariate analysis revealed that the *z* score in this group was not correlated with body composition or CF disease severity.

The researchers found a significantly higher risk of low BMD in children with a low percentage of fat free mass (FFM). A total of 60% of normal-weight CF patients had FFM *z* scores below -2. "This hidden loss has been previously reported in adults with CF. Our data demonstrate that this can also occur early in childhood, even in children with a normal nutritional status," the authors wrote. ■

White Blood Cells May Not Be Best Infection Marker in RSV

An abnormal white blood cell count is not a useful marker for predicting concurrent serious bacterial infection in infants and young children hospitalized with respiratory syncytial virus lower respiratory tract infection, results from a large single-center study demonstrated.

The finding is important because "although there is a practice guideline for treatment of infants and young children aged 0-36 months with fever without a source (Pediatrics 1993;92:1-12), there is no guideline that specifically addresses the treatment of febrile infants and young children with clinical evidence of viral infection," Dr. Kevin Purcell and Dr. Jaime Fergie said.

The researchers studied the records of 1,920 infants and young children admitted to Driscoll Children's Hospital in Corpus Christi, Tex., with respiratory syncytial virus (RSV) lower respiratory tract infections between July 1, 2000 and June 30, 2005 (Pediatr. Infect. Dis. J. 2007;26:311-5).

They collected information on temperature, complete blood count with manual differential, and bacterial culture results. They defined fever as a temperature of 100.4° F or higher before admission. The WBC count was considered abnormal if it was lower than 5,000/mcL of blood or if it was 15,000/mcL or more.

The median age of the 1,920 patients was 142 days, and 672 had a complete WBC count and bacterial culture.

Overall, only 34 of the 672 patients (5.1%) had a positive bacterial culture. The probability of a WBC less than 5,000/mcL and a level between 15,000 and 29,999/mcL being associated with a concurrent serious bacterial infection ranged from 0% to 5.7%. This was no different from the rate of a normal WBC in febrile and afebrile patients, which ranged from 3.9% to 4.7%. However, they noted that patients with a WBC of 30,000/mcL or greater were about six times as likely to have a concurrent serious bacterial infection as those with lower levels.

"On the basis of these results, applying the practice guideline for treatment of infants and young children aged 0-36 months with fever without a source to patients with RSV lower respiratory tract infection is of no use in predicting the presence of a concurrent serious bacterial infection," the researchers concluded.

—Doug Brunk

Pertussis Booster Protects Adolescents Beyond 5 Years

BY MARY ANN MOON
Elsevier Global Medical News

The acellular pertussis booster vaccine provides immunity that persists beyond 5 years in adolescents, and it likely will do the same in adults, reported Dr. Kati Edelman of Turku (Finland) University Hospital and her associates.

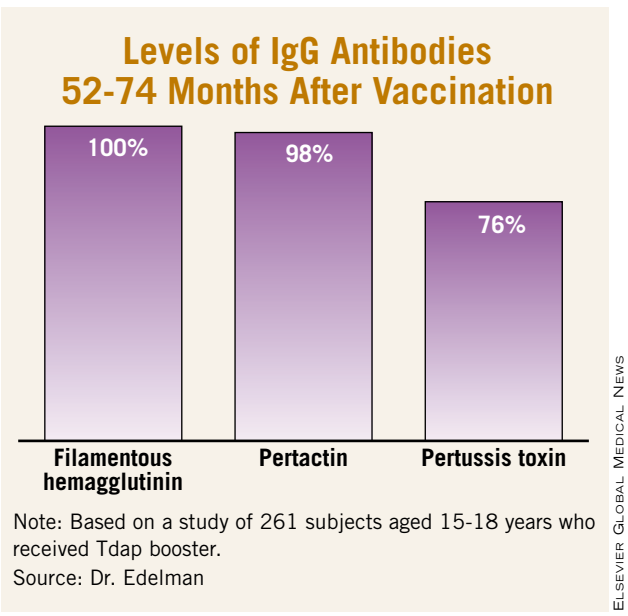
In what they described as the first long-term study that assessed both cell-mediated and humoral immunity conferred by the pertussis booster, the researchers found that both types of immunity persisted for 5 years or more in subjects who had received the booster between the ages of 11 and 13 years. This result indicates that the interval between routine booster immunizations can be extended beyond 5 years, they said (Clin. Infect. Dis. 2007;44:1271-7).

In an editorial comment accompanying this report, Dr. James D. Cherry of the University of California, Los Angeles, wrote that an immunization program of boosters every 10 years for adolescents and adults would curtail the spread of pertussis in the general population, which would in turn spare infants, who are the most vulnerable to the infection.

"It is time for those who care for adults to learn from pediatrics that universal immunization works and, if implemented, would do much to control the spread of pertussis in the United States," he noted.

There are as many as 3.3 million cases of pertussis in adolescents and adults in the United States every year. Most of these cases are not recognized as pertussis and are misdiagnosed as bronchitis or upper respiratory infection.

"It should also be noted that the rates of reported pertussis are 40- to 160-fold less common than actual illness rates, and that asymptomatic infections are 4-22 times more common than symptomatic infections" in these age groups. Symptomatic adolescents and adults are the major source of exposure for infants, Dr. Cherry said (Clin. Infect. Dis. 2007;44:1278-9).



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In their study, Dr. Edelman and her associates followed 296 subjects aged 15-18 years who had received a pertussis booster 52-74 months previously, then narrowed the group down to 261 who had received the Tdap (Boostrix, GlaxoSmithKline Biologicals) booster. All had been immunized against pertussis as babies. For comparison, 38 subjects who had not received the booster also were studied.

A total of 79% of the adolescents who received the booster showed persistent cell-mediated immunity to any of the three pertussis antigens. The duration of humoral immunity was comparable to that achieved with primary pertussis immunization. All subjects showed detectable filamentous hemagglutinin IgG, 98% had detectable pertactin IgG, and 76% had detectable pertussis toxin IgG. IgG antibodies declined somewhat over time but remained significantly elevated, compared with prebooster levels.

It was notable that among subjects who lost pertussis toxin antigen IgG, nearly half had retained cell-mediated immunity to pertussis toxin, which may well have continued to protect them against the infection, Dr. Edelman and her associates said.

Both antibody levels and pertussis-specific cell-mediated immunity levels were higher in subjects who received the booster than in controls.

GlaxoSmithKline Biologicals provided materials for the study, and two researchers have been employed by the company. Dr. Edelman reported no conflicts of interest. Dr. Cherry reported conflicts of interest with GlaxoSmithKline and Sanofi Pasteur. ■

Dr. Susan Harding, FCCP, comments: *This article has implications beyond the pediatric population. In 2005, Tdap (tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis) vaccine was licensed in the United States for use in people aged 11-64 years. The Advisory Committee on Immunization Practices recommended Tdap for all adolescents and adults in place of the tetanus-diphtheria booster. We now have the opportunity to reduce the morbidity of pertussis in adults by vaccinating adults with Tdap; so add Tdap to your influenza/pneumococcal vaccine checklist.*

Inadequate Number of Asthmatic Children Vaccinated for Flu

BY DIANA MAHONEY
Elsevier Global Medical News

Less than one-third of children with asthma between the ages of 2 and 17 years received the influenza vaccine during the 2004-2005 influenza season, according to the first national estimate of influenza vaccine coverage in children with asthma by the Centers for Disease Control and Prevention.

While this rate is approximately three times higher than that reported for nonasthmatic children, the "inadequate" numbers indicate "that opportunities for vaccination during health care provider visits likely are being missed," according to Susan M. Brim of the CDC's National Center for Environmental Health and her colleagues (MMWR, 2007 March 9; 56:193-6).

IN THE 12 MONTHS PRECEDING THE SURVEY, VACCINE COVERAGE FOR ASTHMATIC CHILDREN WAS RELATED TO THE NUMBER OF HEALTH CARE VISITS.

With data from the 2005 National Health Interview Survey (NHIS)—a cross-sectional, household interview survey in the United States—the CDC investigators analyzed influenza vaccine coverage rates for the 5,124 youth aged 2-17 years represented in the database and determined that 29% of children with current asthma had received the influenza vaccine for the September 2004–February 2005 influenza season, compared with 10.3% of their nonasthmatic peers.

Of the children with current asthma, vaccine coverage was highest—at 32.9%—in the 2- to 4-year-old age group, compared with 28% in both the 5- to 12-year-old and 13- to 17-year-old age categories.

Children who had experienced an asthma attack or episode within the 12 months prior to the survey (35.9% of those with asthma) were more likely to have been vaccinated than children with current asthma but no past-year history of an asthmatic episode (20%). Children aged 5-12 years with current asthma and no past year history of an asthmatic episode had the lowest vaccination coverage rate, at 16.4%, in the asthma group, the authors reported.

When the data were analyzed on the basis of the number of health care visits per child during the 12 months preceding the survey, influenza vaccine coverage among children with asthma was directly related to the number of visits.

"Approximately 10.8% of children with current asthma who had one health care visit in the preceding year were vaccinated, whereas 42.0% of children with [10 or more] visits were vaccinated," Ms. Brim and her associates wrote.

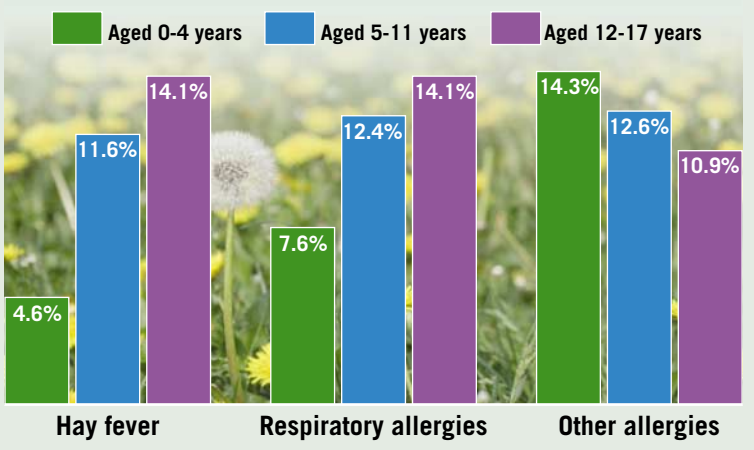
Because the 2005 NHIS was the first to include questions on influenza vaccination in the child portion of the survey, "the results of this analysis cannot be compared with previous years," according to the authors.

"Analysis of NHIS data from 2006 and future years will allow determination of trends in national influenza vaccination coverage in children with asthma," they wrote.

Such monitoring is essential for the design of public health strategies for increasing influenza vaccination coverage that targets all children with asthma, particularly those with the lowest coverage rates, the authors stressed. Continued monitoring also will be necessary to determine whether and to what extent changes, such as the 2006 revision to Advisory Committee on Immunization Practices (ACIP) influenza vaccination recommendations to include all children between the ages of 6 and 59 months, will impact actual coverage rates, they noted.

Possible recall bias, the potential for misclassification of responses resulting from inaccurate reporting of vaccination dates, and the absence of information regarding whether vaccinated children 9 years old or younger received the second dose of the vaccine as recommended by the ACIP are among the study's limitations, said Ms. Brim and her associates. ■

DATA WATCH



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Pulmonary Perspectives

Outcomes for COPD Therapy

A focus on clinical trial end points such as FEV_1 is potentially of limited value to many patients.

Of the multiple challenges facing the clinician practicing pulmonary medicine, two can be particularly vexing with regard to interpreting and applying the clinical trial literature: first, how does one take data obtained in dozens, if not hundreds, of patients and apply these data to the management of an individual patient (*ie*, does the study fit this patient?), and second, how does one counsel the patient with regard to benefits that might be reasonably expected from the addition of a new therapy to his or her management plan, *ie*, is the outcome meaningful to this patient?

The issue of whether the study fits the patient can be particularly difficult in a disease like COPD. To demonstrate significant findings with regard to a primary outcome variable like FEV_1, clinical investigators typically enroll a relatively homogeneous population of participants with the goal of minimizing clinical or physiologic heterogeneity that can dilute a treatment effect. However, trials that exclude COPD patients who manifest bronchodilator responsiveness, as an example, may not necessarily provide data of optimum relevance to this sizeable subpopulation of COPD patients.

THE INTERPRETATION OF THE TORCH MORTALITY FINDINGS REMAINS SUBJECT TO THE JUDGMENT OF THE CLINICIAN, WHO MUST FOCUS ON THE OUTCOMES MOST RELEVANT TO THE INDIVIDUAL PATIENT.

A separate but related issue is encountered when a clinical trial exquisitely characterizes participants using biomarkers, such as induced sputum, to characterize airway inflammation, toward the goal of being able to more carefully predict which patient responds to which therapy and why. This practice, prevalent in academic clinical trials, is somewhat of a double-edged sword: it can provide data necessary to move the personalization of therapy forward, but it might use data available only in a tertiary-care referral center to do so. When the majority of patients with prevalent diseases like COPD are cared for in primary care settings, this lack of "translatability" to the busy practice environment becomes problematic.

We as clinicians are left to make our best guess as to how the data from any given study apply to any individual patient. For this reason, we have to take a somewhat empiric longitudinal approach to treatment, trying something, seeing if it worked, and then altering the approach based not on randomized, placebo-controlled, parallel-arm clinical trial data, but on "n of 1" clinical trial data obtained from the individual patient in whom we are trying to optimize therapy.

Again, the second question of particular importance to patients is, "Is the outcome meaningful to this patient?" Regulatory agencies typically require pharmaceutical companies to design trials around quantitative outcomes such as FEV_1, outcomes whose performance in clinical trials is thought to be relatively well understood and whose change is thought to reflect important effects on underlying pathophysiologic processes, such as airway inflammation or bronchoconstriction.

However, a focus on FEV_1 alone is potentially of limited value to many patients: first, a majority of patients do not experience symptoms until the FEV_1 becomes substantially reduced, perhaps to levels as low as 50% of predicted normal; and second, the FEV_1 is not what is paramount in the mind of the patient who is substantially impaired by a disease like COPD—what is important to this patient is feeling better, being able to participate fully in life, and having a sense of hope that a specific treatment is going to improve the quality of his or her life. While improving lung function may achieve these goals in some patients, there is clearly a dissociation in the clinical trial literature between improvements in lung function and improvement in these other meaningful clinical outcomes.

The literature investigating the effect of inhaled corticosteroids (ICS) in COPD is one example of this conundrum. International guidelines recommend the addition of ICS to inhaled bronchodilators for the treatment of COPD in patients with an FEV_1 <50% of predicted who experience exacerbations at least once per year. A primary data set of large, placebo-controlled trials evaluating change in FEV_1 in response to ICS for 12 months or longer as the primary outcome suggests that these agents have minimal impact on the rate of decline in lung function in COPD over the long term, findings that have been underscored by multiple post hoc and other meta-analyses.

However, many of these same "negative" studies reported beneficial effects of ICS on patient-centered outcomes, such as exacerbation frequency, symptoms, quality of life, and other measures of health status. These outcomes are arguably more meaningful to individual patients than is the FEV_1 per se, and the fact that ICS improve many of these outcomes has been used to justify their wide-scale use in COPD. However, these findings relate to secondary outcome variables that often have demonstrated large relative but small absolute improvements, leaving residual uncertainty as to just how much benefit an individual patient may experience, as well as how quickly that benefit might be observed.

The recently published TORCH (Toward a Revolution in COPD Health) trial (*N Engl J Med* 2007; 356:775) is likely to refocus the discussion of clinically relevant outcomes in COPD clinical trials. This important study involving 6,000 patients with COPD tested whether mortality (an outcome that is easily defined and incontrovertible and one that both patients and physicians can agree is meaningful) would be reduced compared with placebo by treatment with combination ICS and long-acting inhaled beta-agonist therapy for 3 years. An important issue for US physicians is that one of the treatment medications (placebo; fluticasone, 500 mcg twice daily; salmeterol, 50 mcg twice daily; or the combination of fluticasone 500 mcg and salmeterol 50 mcg twice daily) was dosed above the currently approved level for COPD (fluticasone 250 mcg twice daily).

The investigators used a broad definition of COPD, enrolling subjects between 40 and 80 years of age with a 10 pack-year history of cigarette smoking, airflow limitation as reflected by an FEV_1/FVC ratio of <0.7, and an FEV_1 percent predicted of <60%, with bronchodilator responsiveness of <10%. Follow-up was virtually complete with vital status obtained on all but one study participant. An independent clinical end point committee adjudicated the cause of death in each case.

TORCH demonstrated a hazard ratio for death in the combination therapy arm vs placebo of 0.825, with a 95% confidence interval of 0.681 to 1.002 (p=0.052). The reduced hazard ratio for death suggests a benefit. However, the p value of 0.052 exceeds the commonly applied statistically significant threshold of 0.05. Complicating this issue is a public statement by the FDA that for approval of a drug for an end point like mortality based on the results of a single study, a much more robust statistical mortality benefit (perhaps a p value <0.01) would have been expected. However, there was a clear beneficial effect of the higher dose of the ICS/long-acting inhaled beta-agonist combination therapy on improvements in health status and exacerbation frequency, important outcomes that are also likely to be perceived as beneficial by patients.

TORCH leaves us with uncertainty of the performance of mortality as an end point in COPD clinical trials. On the one hand, it is difficult to justify altering generally accepted assessments of whether the null hypothesis has been rejected simply because the p value is "close" to 0.05. On the other, the end point under consideration is mortality, one which we would very much like to influence in a disease like COPD. Furthermore, the biologically plausible mechanism by which combination therapy with ICS and a long-acting inhaled beta-agonist might actually affect mortality in COPD is unclear. Until we know more about the factors that govern mortality in COPD and the mechanisms by which various therapies might alter these factors, the interpretation of the TORCH mortality findings and application thereof remains subject to the judgment of the clinician, focusing on the outcomes most relevant to the individual patient. ■

Dr. E. Rand Sutherland, MPH, FCCP
National Jewish Medical and Research Center
Denver, CO

DR. GENE L. COLICE, FCCP
Editor,
Pulmonary Perspectives

Editor's Insight

Dr. Sutherland raises provocative and clinically relevant questions. How should the practicing clinician use the results of the TORCH study in treating patients with COPD?

One difficult issue is fairly balancing the safety concerns found with the doses of fluticasone used in this study (500 mcg twice per day) against both the efficacy obtained and the safety profile for the dose of fluticasone (250 mcg twice per day) currently approved in the United States for the treatment of COPD.

Clinically important side effects were seen with fluticasone treatment in the TORCH study (*eg*, greater incidence of pneumonia, oropharyngeal candidiasis, and dysphonia with fluticasone treatment and evidence of systemic effect through suppression of cortisol production). Without a lower-dose fluticasone comparison treatment arm, it is difficult to know whether the benefit obtained with the higher dose is balanced by the possible risks.

Another difficult issue is understanding why combined ICS and long-acting inhaled beta-agonist therapy would reduce mortality in COPD. Preliminary work had suggested that the anti-inflammatory effect of fluticasone might reduce a "systemic inflammatory process occurring in COPD." This hypothesis does not seem likely, given the observation that the fluticasone treatment arm had a numerically greater number of deaths than the placebo arm.

Understanding more fully the biologic mechanisms of mortality in COPD is, as Dr. Sutherland presciently points out, a critical next step.

—Editor

AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

PRESIDENT'S REPORT

Ultrasonography Performed by Intensivists

Nobody could question the value of ultrasonography in the noninvasive diagnosis of diseases of the chest, abdomen, and veins. Yet, there are few among us who practice critical care medicine who have not had the experience of pleading with a radiologist to bring an ultrasound device to the ICU *stat* to diagnose a deep venous thrombosis or hydronephrosis or a cardiologist to do a stat echo to see if a patient in shock has cardiac tamponade. The alternative is to take an unstable patient on the "adventure" of going to another part of the hospital for a study.

BY DR. MARK J. ROSEN, FCCP

In other parts of the world, including Germany and Japan, internists in training receive hands-on education in many aspects of ultrasonography. Our colleagues in emergency medicine are far ahead of us intensivists; many use limited and goal-directed sonography routinely in diagnosis and as a valuable adjunct to performing invasive procedures. With an ultrasound device in hand, they can immediately and reliably answer questions like, "Does this patient have pericardial tamponade? Or a pneumothorax?" or "Where is the internal jugular vein?"

Ultrasonography is now so integral to the current practice of first-rate emergency medicine that many training programs offer formal 1-year fellowships in emergency medicine ultrasonography.

Ultrasonography is an almost-perfect noninvasive tool. It is about as dangerous as a stethoscope and much more useful a lot of the time. It can also be done repeatedly and inexpensively, without the need to move unstable people around the hospital. It can also be done in the middle of the night, again and again, by the same physician who will interpret and use the results of the test.

So why have intensivists not demanded to receive proper training in ultrasonography for their critically ill patients?

One reason is reluctance to take on a turf battle with radiologists or cardiologists, who too often reserve the mantle of proficiency for themselves, and whose professional societies have published training guidelines that exclude other specialties from establishing their expertise. Remember that using that reasoning, pulmonary physicians would still not perform flexible bronchoscopy, and, perhaps, right heart catheterization would still be the exclusive domain of cardiologists.

Another obstacle to ultrasonography as a standard part of the intensivists' arsenal is the lack of options for proper training. The ACCP has already taken steps to provide needed training for our members in this exciting field, and we are planning to expand our programs rapidly to meet future demand. Starting with a few sessions and a postgraduate course that included experts from around the world, as well as a limited hands-on program in the Simulation Center at CHEST 2006, ACCP has taken a leading role in advancing use of ultrasonography by our members. Under the leadership of Dr. Paul H. Mayo, FCCP; Ed Dellert, Vice President of Educational Resources, and Viva Siddall, Assistant VP of Educational Resources, the ACCP gave a 3-day hands-on course on "Ultrasonography: Competence in the ICU." Because all attendees would be given intensive hands-on training, we could accommodate only 150 people, and we reached capacity within a few days of announcing the program. Participants' level of experience ranged from fellows still in training to clinicians in practice for 10 or 20 years. Using 16 machines with an instructor at each station teaching four or five people at a time, attendees were immersed in sonographic imaging of the thorax, abdomen, blood vessels, and heart.

I had the privilege of attending to help with the logistics, but I got recruited to be a shirtless "subject" in a hands-on session on vascular imaging. Ten members of the College were tasked with locating my internal jugular and subclavian veins, and they were all ultimately successful and ready to apply their skills at home.

The next steps are to provide more training opportunities at CHEST 2007 and future programs on basic and advanced ultrasonography in critical care.

The need to make ultrasonography part of an intensivist's repertoire is real. As a professional society, it is the ACCP's responsibility to provide the proper training to become proficient, the tools to allow those trained to be credentialed at their hospitals, and the support to fight the local turf battles if and when they arise. Our members are asking us for it, but our patients will receive the real benefits. ■

EDUCATION INSIGHTS

Quality Improvement in Maintenance of Certification

BY SANDRA ZELMAN LEWIS, PHD
ACCP Research Specialist
AND ED DELLERT, RN, MBA
ACCP VP of Educational Resources

The Quality Improvement Committee (QIC) endeavors to offer ACCP members information and tools to facilitate QI efforts and help to improve patient care.

In partial fulfillment of this goal, the QIC invites ACCP members to a special session at CHEST 2007 titled: **"Maintenance of Certification Made Ridiculously Simple: Tips and Tools for Completing the Practice Performance Requirement."**

If you are engaged in Maintenance of Certification, you might be confused about the requirements or have questions about whether QI projects in which you are already engaged will meet those requirements.

This session will review the fundamental principles of individualized practice improvement by reviewing a project developed by the ACCP Quality Improvement Committee on Quality Care in COPD.

The National Quality Forum–endorsed performance measures in COPD will be reviewed, and tools for collecting, reporting, and responding to the information will be provided.

Upon completion of the session, participants will be able to complete a QI project in their own practice easily and efficiently and will be provided with a means of reporting this to the ABIM to meet the requirements for maintenance of certification.

COL Lisa K. Moores, MC, USA, FCCP, Vice Chair of the QIC, will chair this session. Additional faculty include Dr. Michael H. Baumann, FCCP, Chair of the QIC, and QIC members Dr. Bruce M. Fleegler, FCCP, and Dr. William S. Krimsky.

Plan to attend this session on Monday, October 22, 2007, from 4:15 PM to 5:45 PM. ■

Chicago: Sink Your Teeth In

When it comes to dining, Chicago has it all – and then some. The city's mainstays are known to include deep-dish pizza and Chicago red hots, but there is so much more from which to choose. Chicago's cuisine knows no limits!

With such a vast array of options, dinner recommendations can be tricky, but here are few ideas sure to appease any appetite.

Stick with the classics and go where the locals go. For a quick bite in Chicago, grab a beef at Al's #1, a burger at Billy Goat's, or a Chicago hot dog at Portillo's. If a fine steak is what you fancy, try Ruth's Chris, Gibson's, or Tavern on Rush.

For a romantic dinner for two, visit the Signature Room on the 95th floor of the Hancock building, Fulton's on the River, or Seasons at the Four Seasons Hotel. And then, of course, there's pizza. Lou Malnati's, Pizzeria Uno, Gino's East, Piece…the list goes on and on.

But that's not nearly all. Thanks to the city's diverse neighborhoods, Chicago offers a plethora of ethnic restaurants.

If you yearn for a great gyro, head to Greektown.

Or if Cantonese is what you crave, make your way to Chinatown.

For authentic Italian, where else but Little Italy?

There are also great Polish, Mexican, Mediterranean, French, Thai, Indian, German, Ethiopian, and even Burmese eateries scattered about town.

With variety such as this, you're taste buds are sure to be catered to. Whether you desire aristocratic entrees or family-style fare, you're guaranteed to find it here, which is why Chicago is our kind of a town and the perfect place for CHEST 2007!

For more information about Chicago, visit www.choosechicago.com/default.html.

Watch www.chestnet.org/CHEST for details about CHEST 2007. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

NETWORKS

Shorter Course TB Therapy and the COURAGE Trial

Allied Health

The NetWork has had the opportunity and privilege to serve on the steering committee of the Critical Care Institute (CCI) for the ACCP for the last 4 years. This appointment expires in October 2007.

Being a member of the CCI has been a great opportunity for the Allied Health NetWork membership to participate in one of two exciting institutes that are supported by the College.

There were three NetWork highlights approved for CHEST 2007: Environmental Emergencies: Wilderness Medicine; Pulmonary Rehabilitation Paradigm Shift: Beyond COPD; and COPD Awareness: Learn More Breathe Better, An NHLBI Campaign (Organized by Dr. Loren Greenway, FCCP, Dr. Brian Carlin, FCCP, and members of the NIH steering committee for COPD awareness).

Under the direction of Craig Megargee, a Pennsylvania member of our Allied Health NetWork, a NetWork subcommittee is being organized to help market the NetWork to potential members of the allied health profession.

Chest Infections

The TB Trials Consortium
Searching for Shorter Course Therapy

The Tuberculosis Trials Consortium (TBTC) is a Centers for Disease Control and Prevention–sponsored collaboration of North American and international investigators for clinical tuberculosis (TB) research.

This effort began in the early 1990s to continue the long history of clinical trials that were previously conducted by the United States Public Health Service, ending with Study 21, which established 2 months of isoniazid (H), rifampin (R), and pyrazinamide (Z) (HRZ) plus 4 months of HR as standard TB treatment in the 1980s.

The first TBTC trial, Study 22, studied the long-acting rifamycin, rifapentine, given once weekly with isoniazid during the last 4 months of treatment. Briefly, rifapentine was good for patients with "a little bit" of TB: noncavitary, smear-negative cases, without HIV coinfection (*Lancet* 2002; 360:528).

The latest trials have studied the use of moxifloxacin (M) substituting for ethambutol (E) in Study 27 and for isoniazid (H) in Study 28 during the first 8 weeks of treatment in smear-positive TB cases.

In a murine model, moxifloxacin is very active against TB both singly and in combination with standard drugs. Moxifloxacin has a long half-life of 12 hours, a low minimum inhibitory concentration (MIC) against TB, and the highest peak concentration to MIC ratio of the available quinolones. Its early bactericidal activity is similar to isoniazid, but moxifloxacin may have better activity against slow-growing "persister" organisms, raising the possibility that its use might enable shorter course 4-month treatments for TB. The combination MRZ is more active against TB than HRZ in the mouse model (*Am J Respir Crit Care Med* 2004; 169:421).

Study 27, comparing moxifloxacin against ethambutol (HRZM vs HRZE) showed that culture conversion to negative at 8 weeks was not enhanced by moxifloxacin, but at earlier time points, there was a trend toward conversion sooner (*Am J Respir Crit Care Med* 2006; 174:331).

Study 28 (Evaluation of a Moxifloxacin-Based, Isoniazid-Sparing Regimen for Tuberculosis Treatment) compared MRZE vs HRZE during the first 8 weeks of therapy, also with an endpoint of culture conversion to negative. This study just completed enrollment in February 2007, with analysis pending.

A study evaluating the concomitant use of moxifloxacin and rifapentine (both having long half-lives) given with Z plus E is being planned. Hopefully, these novel approaches will lead to TB treatment regimens of 4 months' or shorter duration.

For more information on the TBTC, go to www.cdc.gov/nchstp/tb/tbtc.

Dr. Thomas E. Walsh, FCCP
Chest Infections
Steering Committee Member

Clinical Pulmonary Medicine

New Therapeutic Strategies Emerging for COPD

COPD has long been a therapeutic stepchild, with COPD patients using "hand-me-down" therapies and therapeutic strategies developed for asthmatics. There may be light at the end of the tunnel for COPD patients, as new research illustrates successful outcomes for specific therapies.

Use of the long-acting anticholinergic agent, tiotropium, has been shown to improve outcomes in COPD patients. In placebo-controlled studies, tiotropium improves spirometric indices, reduces the use of short-acting beta-agonists, and improves quality of life measurements (*Chest* 2004; 126:1946). Tiotropium improves exercise tolerance, in part, by reducing the hyperinflation that occurs with exercise (*Chest* 2005; 128:1168).

Addition of the long-acting beta-agonist, formoterol, to tiotropium, leads to further improvement in airflow obstruction, hyperinflation, and the uses of short-acting beta-agonists (*Chest* 2006; 129:509).

Current studies suggest that the regular use of tiotropium may retard the progressive loss of lung function seen in COPD patients, even after they quit smoking; the UPLIFT trial is underway in an attempt to address this issue.

The success of inhaled corticosteroids in treating and controlling asthma has been extrapolated by many practitioners to patients with COPD.

The TORCH study (*N Engl J Med* 2007; 356:775) randomized patients to four arms: placebo, inhaled fluticasone, inhaled salmeterol, and an inhaled combination of fluticasone and salmeterol. Results show that no treatment group had a significant improvement in mortality compared with placebo, the identified primary outcome measurement for this study.

Combination therapy was associated with improved spirometric indices and health-related quality of life. There was a suggestion that the use of inhaled fluticasone might be associated with an increase in the incidence of pneumonia in the fluticasone and combination arms of the trial.

These results suggest that the use of inhaled corticosteroids in patients with COPD requires prudence and forethought.

One novel therapy receiving attention is the use of retinoids to treat COPD. Animal models suggest that retinoid use may lead to augmentation of lung reparative processes and, thus, ameliorate the severity of emphysema in persons with smoking-related lung disease.

The FORTE trial demonstrated no definite clinical benefit from the administration of all-trans retinoic acid in two different doses when compared with placebo (*Chest* 2006; 130:1334). However, there are currently ongoing trials evaluating more selective retinoic acid derivatives in order to investigate this concept further.

Many new therapies are on the horizon for patients with COPD. For pulmonary practitioners, the therapeutic nihilism of the past regarding COPD patients promises to be replaced by evidence-based effective treatment strategies.

Dr. Daniel R. Ouelette, FCCP
Clinical Pulmonary Medicine
Steering Committee Member

Cardiovascular Medicine and Surgery

The "COURAGE" Trial: A Paradigm Shift in the Treatment of Patients With Stable Angina Pectoris?

To great fanfare, the results of the COURAGE trial were presented at the 56th Annual Scientific Session of the American College of Cardiology, with nearly simultaneous publication in the *New England Journal of Medicine*. The study compared patients with stable CAD, receiving percutaneous coronary intervention (PCI) plus optimal medical therapy vs optimal medical therapy alone. The study hypothesis was that PCI-based therapy would be superior in reducing the risk of subsequent cardiovascular events.

Primary end point of the study was death from any cause and nonfatal myocardial infarction (MI). Secondary outcomes included a composite of death, MI, stroke, and hospitalization for unstable angina.

The results showed neither benefit in survival or prevention of nonfatal MI nor any difference in the secondary end points, leading to the succinct summary in the accompanying NEJM editorial, "PCI should not play a major role as part of secondary prevention."

This study could change the landscape of treatment for patients with stable coronary artery disease substantially. Since approximately 85% of all PCI procedures are performed electively, a substantial reduction in coronary stent procedures (more than one million in 2004) may occur.

The response from industry was swift.

On the day of presentation, Cordis Cardiology distributed a "Dear Colleague" letter by Dr. D. Kandzari, the Chief Medical Officer, emphasizing the study limitations, particularly the fact that only 3% of the PCI group received drug-eluting stents (DES). Though DES reduce the need for revascularization, they have not

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AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

Community Outreach Event at CHEST 2007

Plans are well underway for the CHEST 2007 CHEST Foundation and ACCP Industry Advisory Council Community Outreach Event at CHEST 2007.

This annual event will be held on Monday, October 22. It will begin with a training session from 8:00 AM to 9:00 AM and continue with ACCP member volunteers and Ambassadors Group volunteers boarding a bus to Kinzie Elementary School in Chicago.

The Lung Lessons™ program, developed by The CHEST Foundation, will be presented to 125 fifth and sixth grade students.

Kinzie Elementary School has an enrollment of 710 students and is a member of the Math/Science Midway Cluster. Its vision is to create a positive learning environment in which students are motivated to strive for excellence and take an active and responsible role in their education, so they will become contributing members of society.

Consider volunteering for this popular educational activity.

You can indicate your interest by checking the Special Events section on your CHEST 2007 registration form, or sending an e-mail to Sue Ciezadlo at sciezadlo@chestnet.org. ■

8th Grader Donates to Foundation

Healthy lungs are of particular interest to Jared Scharf, an 8th grader from Hastings-on-Hudson, NY. He is a trumpeter, a long-distance runner, and his grandfather suffers from pulmonary fibrosis. Knowing firsthand the devastation this disease causes, Jared wanted to make a difference. And last year, he got his chance.

Jared Scharf donated to help fight pulmonary fibrosis.

While becoming a Bar Mitzvah in 2006, Jared participated in the Mitzvah of Tzedakah or statement of charity. As an expression of his philanthropic spirit, Jared donated a portion of his gift money to The CHEST Foundation.

"I would like to help ease others' pain from pulmonary fibrosis and the emotional pain of people who are related to someone with pulmonary fibrosis," Jared wrote in his Tzedakah statement. Jared learned of The Foundation through his aunt, Dr. Stephanie Levine, FCCP, who is a member of The CHEST Foundation Board of Trustees and Chair of The CHEST Foundation Awards Committee. Jared's support and charitable donation were given with the hope of helping find a treatment to stop or slow the advancement of lung disease.

You can support the work of The CHEST Foundation also and learn more about its efforts in helping your patients live and breathe easier. Make a donation today at www.chestfoundation.org. ■

We're in the News

BY JENNIFER STAWARZ
ACCP Senior Manager, Public Relations

Throughout the spring, the ACCP and the journal *CHEST* have welcomed a constant stream of media coverage.

Journal studies combined with special initiatives related to public affairs and the ACCP Institutes have led to more than 600 print, broadcast, and Internet news stories in the last 3 months.

Listed below are just a few of the top-tier media outlets that have featured news stories about the ACCP or *CHEST*.

CHEST

In April, a study showing how statins can help reduce death related to pneumonia and influenza was featured in several news outlets including: *Los Angeles Times*, *Globe and Mail*, Reuters, ABC News, CNN, and Bloomberg.

Additional studies from the February, March, and April issues appeared in *USA Today Magazine*, *Child*, *American Family Physician*, *AARC Times*, *Geriatrics*, *JAMA*, National Public Radio, and MSNBC.

Cough Guidelines

In March, the Associated Press quoted the ACCP cough guidelines in its story related to the FDA's decision to revisit the use of cold/cough medicines in children.

As a result, the ACCP was mentioned in numerous print and Internet media outlets, including *New York Times*, *Chicago Tribune*, and the *Baltimore Sun*.

Workforce Legislation

The *Patient-Focused Critical Care Enhancement Act* was introduced in the US Senate by Senators Durbin and Crapo on February 28. As part of the Critical Care Workforce Partnership, the ACCP developed a joint press release to promote the new critical care workforce bill to the media.

Overall, media outreach resulted in critical care workforce stories in *Investors Business Daily*, CNN, and Yahoo! News. In addition, the March issue of *ADVANCE for Managers of Respiratory Care* featured a front-page story about the workforce shortage.

ACCP Sleep Institute

The ACCP Sleep Institute survey was designed to gather the perspective of clinicians about women's sleep issues and complement the consumer-focused National Sleep Foundation 2007 Sleep in America Poll, which sought to look at the sleep patterns of adult women.

The ACCP Sleep Institute survey found that the majority of ACCP members are knowledgeable about women's sleep issues and are actively managing their patients' sleep problems.

A press release regarding the findings of the survey was drafted and released in early March to coincide with National Sleep Awareness Week. As a result of media outreach, news stories about the ACCP Sleep Institute survey appeared in *Sleep Review*, *Health Care Weekly*, Medical News Today online, and United Press International. ■

Chadwick Medal Awarded to Dr. Irwin

At the 62nd annual meeting of the Massachusetts Thoracic Society, held on April 4, 2007, Dr. Richard S. Irwin, FCCP, was presented with the society's highest honor, the Henry D. Chadwick Medal. The medal was presented by Dr. Mark Madison for the Massachusetts Thoracic Society. It is awarded for outstanding and meritorious contributions to the field of pulmonary medicine.

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been shown to reduce MI and death, suggesting the central message of COURAGE may not change.

The PCI group in the COURAGE trial did experience, initially, an improved resolution of anginal symptoms, but at 5 years, the angina-free percentage was the same for both treatment groups. Several points merit consideration.

COURAGE was very "selective"; only 9% of patients screened were enrolled, raising the possibility that results are not easily extrapolated to a wider patient group.

The study comprised mostly middle-aged white men (85% of the study population; mean age 61.5 years). Patients with significant systolic dysfunction (EF = 30%), recent revascularization and recurrence of symptoms, non-Caucasian ethnic groups, and female gender may not have the same outcome.

The COURAGE cohort also was exceptionally well cared for medically, the level of risk factor control and adherence is unusual. Can similar outcomes be observed in a less stringent medical therapy group?

The COURAGE trial is an important step toward challenging the cardiologist regarding the prevailing "fix-it now" mentality in patients with diagnosed, yet stable, coronary artery disease.

The fact that more than 25% of eligible patients did not participate because of either physician or patient refusal to consent suggests a bias toward PCI-based therapy. ■

Dr. Thomas R. Behrenbeck, PhD, FCCP
Vice Chair, Cardiovascular Medicine and Surgery NetWork

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

Get Acquainted With … THE NATIONAL SLEEP FOUNDATION

To promote healthy sleep, the National Sleep Foundation (NSF) organizes a variety of national public education and advocacy campaigns throughout the year.

For the last 10 years, NSF has launched National Sleep Awareness Week™ (NSAW) in early spring—the week prior to daylight savings time.

This year, NSF is adding several new initiatives to its program roster: the National Sleep Awareness Roundtable, an advocacy campaign to secure funding for sleep programs at the CDC, and the development of Drowsy Driving Prevention Week™.

▶ **NSAW:** NSAW arrived early this year and featured:
—A scientific workshop on women and sleep.
—A press conference to release the findings of the 2007 NSF *Sleep in America* poll.
—NSF's 7th Annual "Night of a Thousand Dreams" Gala celebrated achievements in the field of sleep and provided an opportunity for NSF to raise funds for its education, research, and advocacy programs. The ACCP was presented with this year's NSF Organization Leadership Award.

▶ **Community Sleep Awareness Partners™:** During the week, over 800 sleep centers and hospitals (many with ACCP members) executed local events across the country to raise awareness of sleep issues.

▶ **National Sleep Awareness Roundtable (NSART):** Initiated by NSF, NSART is a national partnership of governmental, professional, voluntary, and other organizations. NSF is pleased that ACCP is a founding member of NSART (www.NSART.org).

NSF and NSART seek funding for CDC sleep programs to expand data collection and surveillance activities on sleep, create education and awareness materials for the public and health care professionals, and establish fellowship opportunities.

Visit www.sleepfoundation.org/advocacy or contact John Rancourt in NSF's Government Affairs department at jrancourt@sleepfoundation.org to learn how you can help.

▶ **Drowsy Driving Prevention Week:** To generate national public awareness concerning the dangers of drowsy driving among the most vulnerable of groups—teens and college-aged drivers—NSF will kick off the first ever Drowsy Driving Prevention Week on November 5, 2007.

Partnerships Are Key to NSF Methods

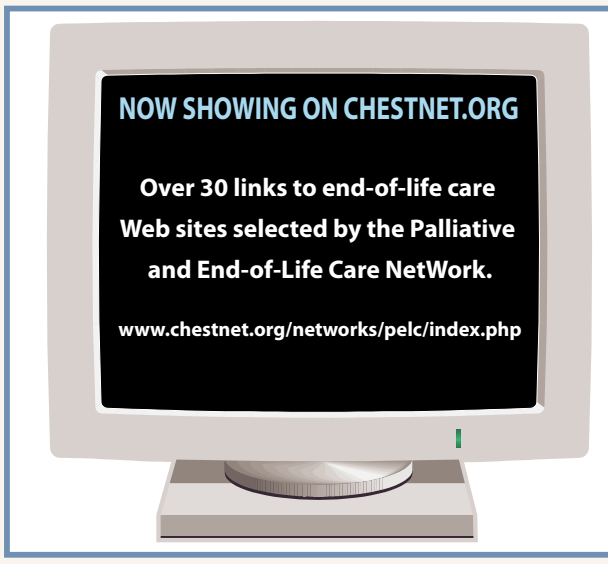
The NSF makes forming partnerships a priority. In this regard, NSF has welcomed positive working relationships with ACCP and its Sleep Institute and welcomes the input and involvement in sleep advocacy and raising sleep awareness by all ACCP members.

For more information about any of our initiatives, visit our Web site, www.sleepfoundation.org, or contact us at nsf@sleepfoundation.org. ■

ACCP Product of the Month: Kicking Back the Covers—Webcast

View the newest virtual symposium Webcast, "Kicking Back the Covers on Restless Legs Syndrome (RLS): Increasing the Understanding of Diagnosis and Treatment," with audio tracks and faculty presentations from our CHEST 2006 satellite symposia. This Webcast will provide the latest information related to RLS, including a comprehensive discussion of diagnostic techniques, disease characterization, comorbid conditions, and treatment strategies.

To view the virtual satellite symposium Webcast, visit the ACCP online education site at www.chestnet.org/education/online/index.php, and click on the Webcast link. ■



Practice Management PQRI FAQ

What is PQRI?

Physician Quality Reporting Initiative (PQRI) is the latest initiative from Centers for Medicare and Medicaid Services (CMS). PQRI establishes a financial incentive for physicians to participate in a voluntary quality-reporting program, on a designated set of quality measures. A list of these measures is available on www.cms.hhs.gov/pqri.

What is the reporting period and the financial incentive?

The reporting period is July 1 through December 31, 2007. The submission deadline for claims to be eligible for up to 1.5% financial incentive bonus on all Medicare claims paid is February 29, 2008. No registration is required to participate. Analysis is performed at the individual provider level, thus, the National Provider Identifier (NPI) is required to process the proposed 1.5% lump-sum bonus payment. Quality performance measures will be reported as CPT Category II codes placed on a paper CMS-1500 claim form or electronic 837-P claims submission.

What does the 80% threshold mean?

At least three performance measures must be reported for at least 80% of the cases in which a measure was reportable, between July 1 and December 31, 2007. Therefore, if you plan to participate, it is important to begin on July 1. ACCP encourages practice administrators to speak with their software vendors to evaluate their ability to participate in this new program on July 1.

Who is eligible to participate in PQRI?

Physician and nonphysician providers.

Why is it important?

Look at this as a trial period. Quality reporting is not going away and may have greater significance in 2008. The August 2007 Medicare Physician Fee Schedule rule should provide more information on what CMS anticipates for performance quality reporting in 2008. We know they will suggest practices developing electronic medical records (EMR). ■

Diane Krier-Morrow, MBA, MPH, CCS-P

What is an example of a relevant pulmonary measure?

COPD
3023F Spirometry results documented and reviewed
3027F Spirometry test results demonstrate $FEV_1/FVC = 70\%$ or patient does not have COPD symptoms
4025F Inhaled bronchodilator prescribed AND 3025F Spirometry test results demonstrate $FEV_1/FVC < 70\%$ with COPD symptoms (*eg*, dyspnea, cough/sputum, wheezing)

Modifiers for use with performance measures

1P Documentation of medical reason(s) for not documenting and reviewing spirometry results
2P Documentation of patient reason(s) for not documenting and reviewing spirometry results
3P Documentation of system reason(s) for not documenting and reviewing spirometry results
8P Spirometry reasonably not documented and reviewed, reason not otherwise specified

What are the ways to successfully report PQRI?

Dr. Adam reviews and documents spirometry results on COPD patient Ms. Eve (3023F), OR Dr. Adam documents that spirometry is contraindicated because Ms. Eve is on a ventilator and reports (3023F-1P) OR Dr. Adam did not document anything about spirometry and reports (3023F-8P).

What else do I need to understand about reporting quality performance measures?

Submitted charge field cannot be left blank. Submitted line-item charge should be $0.00. If billing software does not accept a zero line-item charge, a small amount can be substituted, *eg*, $0.01.

The patient cannot be charged for reported quality measures.

Medicare contractors will be reporting line-item denials on all performance measures on the Medicare Summary Notice (MSN).

For additional information, contact our coding and reimbursement consultant, Diane Krier-Morrow, MBA, MPH, CCS-P at dkriermorr@aol.com or (847) 677-9464.

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Palliative Care in the ICU

Palliative care in the ICU? At first blush, the idea seems almost incongruous. Critical care is often associated with high technology used aggressively to treat life-threatening conditions in an attempt to preserve and prolong life.

In contradistinction, palliative care is often thought of as an approach used to treat symptoms and to relieve suffering. Aren't these incompatible?

Actually, there is a growing consensus that palliative care is very compatible with the care of critically ill patients. One of the primary goals of palliative care—the relief of suffering—is a secondary goal of critical care.

Conversely, a secondary goal of palliative care is to preserve life, consistent with the wishes of the patient and family. So, the two approaches are consistent and complementary (Byock I. *Crit Care Med* 2006; 34[suppl]:S302).

Moreover, about 20% of patients admitted to an ICU die in the hospital, making palliative and end-of-life care in the ICU even more of an imperative (Angus DC, et al. *Crit Care Med* 2004;32:638).

These views have been examined recently by the Palliative Care in the ICU Workgroup, sponsored by the Robert Wood Johnson Foundation.

Critical Care Institute
American College of Chest Physicians

This workgroup was composed of leaders in critical care from the United States and Canada and focused on practical approaches to integrate palliative care in our daily ICU experiences. Several pilot projects were developed and supported in this effort.

The experience at one regional medical center will help illustrate some of the ways these pilot programs found to establish palliative care approaches in the ICU.

Located in Allentown, PA, Lehigh Valley Hospital and Health Network is a 700-bed community-based, regional medical center with a 28-bed medical/surgical ICU. Although several network demonstration projects had been undertaken, no palliative care services had been established for inpatient care.

The goal was to integrate palliative care principles by creating a culture and processes that support a model in which patients' preferences and quality of life values are directly incorporated into the interdisciplinary care plan.

The culture emphasized a patient/family-centered process that provided the relief of physical suffering arising and the suffering arising from emotional, social, and spiritual sources.

Using the domains of ICU palliative care set forth by the Palliative Care in the ICU Workgroup to guide interventions, the focus was on practical, simple ways to integrate these palliative care principles without the need for specialized palliative care services (see Table in Clark EB, et al. *Crit Care Med* 2003; 31:2255).

The association of palliative care with end-of-life care (at times being synonymous) clouded the perception of palliative care. Understanding this misperception helped to form the content and focus for education of the medical and nursing staff.

A 6-h in-service was implemented for all ICU nurses. The curriculum included the overview/definition of palliative care, pain management and adjunctive therapy, spirituality vs religiosity, and ethical principles. In addition, these "core" palliative care principles were incorporated into annual competency training for the nurses to sustain and build on the learning process.

Educating physicians was challenging. Having a physician champion in the ICU was paramount to success. The medical and surgical house staff was the easier group to "capture," requiring lectures during their ICU rotation that included communication skills around delivering bad news and holding a family meeting.

In addition, pastoral care assisted in monthly didactic sessions (usually held in conjunction with the morbidity/mortality conference) to examine issues surrounding "moral distress," patient/family spiritual needs during a life crisis, and concerns regarding our own mortality. Medical grand rounds were used as a forum to review palliative care principles, and an annual regional symposium was offered.

However, the most successful education forum was the development of computer-assisted physician order entry order sets that standardized the approach to patient care around key palliative care interventions, including withdrawal of mechanical ventilation, agitation/sedation, and bowel regimens.

When using these order sets, the physician was educated with the rationale and evidence for each intervention.

Although appearing transparent, making clinical process change can be challenging. For example, something as simple as "opening" ICU visiting hours can be met with resistance, usually from staff with unwarranted concerns.

It was imperative to have a nurse-led committee explore the issues of open visitation. Using peer-reviewed literature, a subgroup of ICU nurses created flexible visiting hours that met both the needs of the patient/family and the nurses' concerns around patient confidentiality and open access.

In light of the true interdisciplinary nature of the ICU, nursing empowerment was embraced as a tool to improve the nurses' self-value and promote sustainability of the palliative medicine integration. Nurses were encouraged to participate in physician-facilitated rounds in which their input was valued, particularly in regard to patient safety, family psychosocial issues, and treatment plan.

Their professionalism was reinforced by the development of nurse-driven protocols, such as glucose/insulin therapy, electrolyte replacement, and agitation-sedation protocols.

As members of the ICU team, the nurses began to feel more integrated and valued in the treatment plan for their patients. In addition, they felt more confident when discussing diagnosis, treatment, and prognosis with the family.

These interventions, as well as others, changed the culture of the ICU. Increased discussion of symptoms, family knowledge/concerns, and attendance of the bedside nurse during rounds showed a palpable improvement in documentation around goals of care and symptom assessment and management.

Demonstrated by the Critical Care

Continued on following page

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

ACCP WORLDWIDE: 70th Anniversary Venezuelan Meeting

Held from April 19 to 20 in Barcelona, Venezuela, the Venezuelan Society of Pulmonology and Thoracic Surgery's course attracted over 600 participants—pulmonologists, cardiovascular and thoracic surgeons, internal medicine specialists, and some respiratory therapists.

Faculty included several US and international ACCP Fellows who presented at this ACCP-endorsed course.

Dr. Carlos Ibarra-Perez, FCCP, Vice Chair of the ACCP Council of International Regents and Governors, stated that (the meeting) "was a scientific success; the meeting rooms were always full, and the quality of the presentations was superb. The ACCP should be congratulated for sponsoring such high quality meetings."

Dr. Jose L. Martinez-Pino, FCCP, and Dr. Jose O. Isea-Dubuc, FCCP, ACCP International Regent and Governor for Venezuela, respectively, organized the course.

Dr. Carlos Rojas, President of the Venezuelan Society of Pulmonology and Thoracic Surgery, was one of the organizers also. ■

Continued from previous page

Family Satisfaction Survey, families felt better supported around the domains of communication and comfort. Just as important was a demonstrated decrease in ICU length of stay for those patients in which a family meeting was held within 48 hours of admission.

This experience illustrates many of the basic principles both of the barriers to establishing a successful palliative care program in an ICU and the approaches to overcome those barriers.

In summary, in part because so many patients die in the ICU or shortly after transfer from an ICU, it is now becoming widely accepted that palliative care plans and processes should be incorporated into the care of all ICU patients. This is true even of those patients not expected to die because the goals of critical care and palliative care are complementary and mutually compatible.

While establishing programs adhering to recognized quality measures can be challenging, the experience of a growing number of centers, such as Lehigh Valley Hospital, demonstrate the feasibility and desirability of establishing such programs. ■

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Domains of Palliative Care and Interventions

Domain 1: Patient and Family-Centered Decision Making
24- to 48-h meeting with family to discuss diagnosis, treatment options, and estimated prognosis
–Identify spokesperson
–Sharing care plan on a daily basis
–Status of advance directive and DNR orders
–Meet with family at change of care or prognosis

Domain 2: Communication Within the Team and Patients/Families
–Interdisciplinary care planning (forms and checklist), including clinical, ethical, and spiritual input
–Meet in appropriate setting
–Record general content of family meetings with use of form

Domain 3: Continuity of Care
–Nurse transfer form (used on transfer and discharge)

Domain 4: Emotional and Practical Support for Patients/Families
–Distribute written materials in the waiting room that describe critical care and palliative care services
–Arrange for social support for those dying alone
–Partner with network's hospice program for bereavement services
–Strengthen family relations and communication
–Open visitation
–ICU waiting room ambassador program

Domain 5: Symptom Management and Comfort Care
–"Comprehensive comfort care"
–Comfort care order form
–Use quantitative assessment scale for pain and symptom management
–Best practice for withdrawing aggressive interventions, including mechanical ventilation
–Standardizing symptom management
–Development of ICU protocols and guidelines for neuromuscular blockade, agitation/sedation, and bowel regimen

Domain 6: Spiritual Support for Patients/Families
–Assess and document spiritual needs by a pastoral care provider within 72 hours of admission
–Pastoral care provider as part of the interdisciplinary team that rounds daily
–Respond in appropriate manner

This Month in *CHEST*: Editor's Picks

BY DR. RICHARD S. IRWIN, FCCP
Editor in Chief, CHEST

▶ **Detection of Epidermal Growth Factor Receptor Mutation in Transbronchial Needle Aspirates of Non-small Cell Lung Cancer.** *By Dr. A. Horiike, et al*

▶ **The Incidence of Recognized Heparin-Induced Thrombocytopenia in a Large Tertiary Care, Teaching Hospital.** *By Dr. M. A. Smythe, FCCP, et al*

▶ **Predictors of Survival in COPD Patients With Chronic Hypercapnic Respiratory Failure Receiving Noninvasive Home Ventilation.** *By Dr. S. Budweiser, et al*

▶ **Obesity Hypoventilation Syndrome: Hypoxemia During Continuous Positive Airway Pressure.** *By Dr. D. Banerjee, et al*

▶ **Quality, Size, and Composition of Pediatric Endobronchial Biopsies in Cystic Fibrosis.** *By Dr. N. Regamey, et al*

▶ **Medical Therapy for Pulmonary Arterial Hypertension: Updated ACCP Evidence-Based Clinical Practice Guidelines.** *By Dr. D. B. Badesch, FCCP, et al*

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AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

Standards for Establishing and Sustaining Healthy Work Environments: Effective Decision Making

BY KEVIN D. REED, MSN, RN, CNA-BC, CPHQ

In 2001, the American Association of Critical-Care Nurses made a commitment to actively promote the creation of healthy work environments that support and foster excellence in patient care wherever acute and critical care nurses practice. As a result, the AACN Standards for Establishing and Sustaining Healthy Work Environments was published.

The six standards align with the core competencies for health professionals as outlined by the Institute of Medicine. Each of the standards is considered essential, and all interact in a dynamic way to promote clinical excellence and optimal patient outcomes.

The Effective Decision Making standard affirms that nurses must be valued and committed partners in making policy, directing and evaluating clinical care, and leading organizational operations. As the single constant professional presence with hospitalized patients, nurses are in the unique position to gather and interpret data into meaningful information to assist physicians in diagnosis and treatment.

In addition, evidence suggests that physicians and administrators tend to perceive patient safety as primarily a nursing responsibility.

Involvement of nurses in decision making has been associated with positive patient outcomes, including mortality, pain management, and a higher perceived quality of care.

Nonetheless, nurses' participation in various patient safety processes has been quite limited. A majority feel powerless to change things they dislike in their work environment.

Included in the standards are critical elements that outline the structures, processes, programs, and behaviors that are required for the standards to be achieved.

These elements serve as a roadmap for successful implementation of the standards. Moreover, they reaffirm that safe and respectful environments are imperative.

There are seven critical elements for the successful implementation of effective decision making:

- The health-care organization provides team members with support for and access to ongoing education and development programs focusing on strategies that ensure collaborative decision making. Program content includes mutual goal-setting, negotiation, facilitation, conflict management, systems thinking, and performance improvement.
- The health-care organization clearly articulates organizational values, and team members incorporate these values when making decisions.
- The health-care organization has operational structures in place that ensure the perspectives of patients and their families are incorporated into every decision affecting patient care.
- Team members share accountability for effective decision making by acquiring necessary skills, mastering relevant content, assessing situations accurately, sharing fact-based information, communicating professional opinions clearly, and inquiring actively.
- The health-care organization establishes systems, such as structured forums involving all departments and health-care disciplines, to facilitate data-driven decisions.
- The health-care organization establishes deliberate decision-making processes that ensure respect for the rights of every individual, incorporate all key perspectives, and designate clear accountability.
- The health-care organization has fair and effective processes in place at all levels to objectively evaluate the results of decisions, including delayed decisions and indecision.

To obtain a copy of the Standards, visit www.aacn.org. ■

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Dr. Devereaux Named 'Best Mom'

Dr. Asha Devereaux, FCCP, was a guest on the Morning Show for NBC on April 27, where she was honored as one of "San Diego's 50 Best Moms."

Dr. Devereaux's daughter, Sabrina, submitted an essay for the best mom contest and described her mom as her "super hero."

Sabrina's essay was in the top 50 out of 3,600 essays submitted. She wrote in her winning essay, "My mother could have been rich and famous … an award-winning doctor … but she chose to have my brother and me."

"When Hurricane Katrina hit, she was deeply hurt by the devastation it had caused to the lively city she used to live in. She took a plane to New Orleans and helped bring the city out of its horrible state. Our community was proud of her, but no one was as proud of her as me." ■

ACCP

Mobility Protocol Leads to Earlier Discharge From ICU

Survivors' length of hospital stays were 14.9 days in the protocol group and 17.2 days in the control group.

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

ORLANDO — The use of a low-impact mobility protocol in the intensive care unit could help reduce hospital length of stay for patients with acute respiratory failure requiring mechanical ventilation, according to Dr. Peter Morris, FCCP, and colleagues at Wake Forest University in Winston-Salem, N.C.

In a study of 330 patients who were admitted to the ICU, researchers found that the use of a standardized protocol administered by an ICU mobility team was safe and resulted in shorter stays in the hospital.

The study included adult patients with acute respiratory failure on mechanical ventilation who had been admitted to the medical ICU. Patients were excluded if they had significant cognitive impairment, inability to walk, or hospitalization in the last 30 days.

The study was unblinded and patients were assigned to either the control or the protocol group based on whether the mobility team was present in their ICU. A triage nurse independent of the study assigned patients to one of seven ICUs based on bed availability, Dr. Morris said at the annual congress of the Society of Critical Care Medicine.

The protocol was designed from nursing and physical therapy policies and procedures already in place in the hospital. However, patients in the protocol group had their care coordinated by an independent mobility team, which included two nursing assistants, a critical care nurse, and a physical therapist. The protocol began on the first day of admission to the ICU and continued 7 days a week until the patient was moved to a regular bed.

Patients in the protocol arm could receive four levels of mobility interventions. Generally, upon admission to the ICU, patients were unconscious and considered level 1. They received passive range of motion delivered three times a day by a nursing assistant. Once patients gained consciousness, they were considered level 2 and continued to receive passive range of motion, and were also eligible to receive care from a physical therapist. The minimum goal was to have people sit up in bed twice a day, Dr. Morris said.

Level 3 of the protocol involved an attempt at sitting on the edge of the bed. If patients were strong enough, they could progress to level 4 of the protocol, which involved getting out of bed and moving to a chair. The team defined getting out of bed as meaning that the patient's foot had to touch the floor.

During the 24 months of the study, 330 patients were enrolled in the project, with 165 patients assigned to the protocol group and 165 to the control group. There were no differences in diagnoses at the time of admission, and there were no statistically significant differences in gender, age, body mass index, and Apache II scores.

There were 20 deaths in the protocol group and 30 deaths in the control group, but the difference was not statistically significant, Dr. Morris said.

The primary end point of the study was hospital length of stay. The hospital length of stay among survivors was 14.9 days in the protocol group and 17.2 days in the control group, a result that reached statistical significance. After adjusting for severity of illness and other factors, the researchers found a similar reduction in length of stay, with an average of 11.2 days among patients in the protocol group, compared with 14.5 days for patients in the control group.

Patients in the protocol group also spent significantly more time with a physical therapist than did patients receiving usual care in the ICU. Of patients in the protocol group, 82% received at least one physical therapy session, compared with about 55% in the control arm.

The number of days to the first time out of bed was 5 days on average among patients in the protocol group, compared with 11 days in the usual care control group. In addition, about one-fifth of the protocol group patients were able to achieve standing at the bedside while still orally intubated, Dr. Morris said.

In terms of safety of the intervention, there were no deaths during any of the mobility sessions, no extubations, and no CPR administration. The most frequent reason cited for ending a session early was a decrease in oxygen saturation, Dr. Morris said.

Limitations of the study included the fact that it was unblinded and nonrandomized, and researchers did not perform functional measurements at discharge from the ICU or the hospital, he said. ■

Micafungin Rivals Liposomal Amphotericin B

The drugs were equally effective against Candida *infection; micafungin led to fewer adverse events.*

BY JONATHAN GARDNER
Elsevier Global Medical News

Micafungin was as effective as liposomal amphotericin B as a first-line treatment of candidemia and invasive candidosis and caused fewer adverse events in a randomized phase III trial published April 26.

A total of 531 patients with a confirmed *Candida* infection at baseline were randomized to receive a median daily dose of either 100 mg of micafungin or 3 mg/kg body weight of liposomal amphotericin B. Of the 392 patients who received at least five doses of a study drug, 89.6% in the micafungin group and 89.5% in the amphotericin B group were successfully treated, defined as both a clinical and a mycological response at the end of treatment, investigators reported online in the Lancet.

Notably, when all 531 patients were considered, four types of adverse events were significantly less common in the micafungin group during treatment and through 12 weeks of follow-up: back pain (0.4% vs. 4.5%), increased blood creatinine (1.9% vs. 6.4%), rigors (0.8% vs. 6.4%), and infusion-related reactions (17% vs. 29%).

Renal adverse events caused physicians to end treatment for eight patients in the liposomal amphotericin B group, compared with one patient in the micafungin group (Lancet 2007 April 26 [Epub DOI: 10.1016/S0140-6736(07)60605-9]).

Hepatic events caused seven patients in the micafungin group to end treatment, compared with three in the liposomal amphotericin B group. One case in each group was considered serious.

"Our results establish micafungin as a treatment option for first-line therapy of candidaemia and invasive candidosis," wrote Ernst-Rüdiger Kuse of the Klinik für Viszeral und Transplantationschirurgie, Hannover, Germany, and associates.

"Our data also show that micafungin has a better safety profile than does liposomal amphotericin B in terms of renal function, infusion-related events, and electrolyte disturbances," they wrote.

The study was sponsored by the maker of micafungin, Astellas Pharma GmbH, which has also paid lecture or consulting fees to five of the study coauthors.

The researchers enrolled 537 patients in Australia, Brazil, Europe, India, North America, South Africa, and Thailand.

In the per-protocol population—those patients with a confirmed *candida* infection who took at least five doses of the study medication—the successful treatment rate was 89.6% for micafungin (181 of 202) and 89.5% for liposomal amphotericin B (170 of 190). Median duration of drug use was 15 days in both groups.

In the intention-to-treat population—the 531 patients who received at least one dose of a drug—18% in the micafungin group and 17% in the liposomal amphotericin B group died during the treatment phase.

These findings were consistent regardless of *Candida* species and of prognostic factors such as neutropenic status and catheter status.

If the 12-week follow-up period is included, 40% of patients in each treatment group died. The fungal infection was considered to have contributed to the cause of death for 13% of the micafungin patients and 9% (25) of the liposomal amphotericin B patients.

For those patients with candidemia in the per-protocol population, there were similar success rates between treatment groups: 90.6% (154 of 170) with micafungin and 90.8% (148 of 163) with liposomal amphotericin B. For those with invasive candidemia, success rates were 84% (27 of 32 cases) with micafungin and 82% (22 of 27) with liposomal amphotericin B.

Persistence rates at the end of therapy also were similar: 9% (18) in the micafungin group and 9% (16) in the liposomal amphotericin B group, on a per-protocol basis. ■

Sepsis Protocol Helps Blunt Adverse Effect of BMI

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

ORLANDO — The use of a standardized therapeutic approach for treating patients with severe sepsis may help to mitigate the increased mortality associated with a high body mass index, according to research presented at the annual congress of the Society of Critical Care Medicine.

Dr. Puneet S. Garcha and his colleagues at Drexel University, Philadelphia, performed a retrospective study of 62 patients with severe sepsis who were treated under a standardized therapeutic sepsis guideline based on early goal-directed therapy.

PATIENTS WITH A BODY MASS INDEX OF 30 KG/M² OR GREATER HAD A 28-DAY MORTALITY RATE SIMILAR TO PATIENTS WITH A LOWER BMI.

All of the patients studied were admitted to a tertiary care unit's medical intensive care unit over a 15-month period between December 2004 and March 2006.

The results of the study showed that patients who had a body mass index (BMI) value of 30 kg/m^2 or greater had a 28-day mortality rate similar to that of patients who had a lower BMI value, Dr. Garcha and his colleagues wrote in a study presented as a poster at the meeting.

The researchers compared 41 patients who had a BMI value of 29.9 or less to 21 patients with a BMI value of 30 or greater.

Patients in both groups had similar mean Acute Physiology and Chronic Health Evaluation (APACHE II) scores (25.8 in the lower BMI group, compared with 25.3 in the higher BMI group). In addition, the time to achievement of resuscitation goals and time from onset of severe sepsis to antibiotic administration was similar in both groups.

Outcomes that were analyzed by the researchers were 28-day mortality, number of days on a ventilator, days spent in the intensive care unit, and days in the hospital, in an effort to determine the impact of higher BMI values. None of the factors was found to be statistically significant.

The 28-day mortality among patients with a BMI of 29.9 or less was 32.7%, compared with 34% among the cohort that had a BMI of 30 or greater.

While higher BMI was not associated with an increase in 28-day mortality, the researchers did observe a trend in the data indicating increased resource use in that group.

For example, patients in the higher BMI group seemed to spend a greater number of days in the hospital. Among survivors, those with a BMI of 29.9 or less spent 48 days in the hospital on average, compared with 59 days on average among survivors in the higher BMI group. The difference in number of days in the hospital approached statistical significance ($P = 0.06$).

Long-term follow-up will be necessary to determine whether the mortality benefit observed at 28 days continues over time despite the morbidity and risk of complications seen in higher BMI patients, the researchers wrote. ■

Adrenal Insufficiency May Predict Death in Sepsis Patients With ARDS

BARCELONA — The rate of relative adrenal insufficiency is very high in patients with severe sepsis and acute respiratory distress syndrome, and is a good predictor of mortality in this group, Dr. Hu Qiu said at the annual congress of the European Society of Intensive Care Medicine.

His prospective observational study included 155 such patients, all of whom received a corticotrophin stimulation test upon developing their respiratory distress. The patients' mean age was 63 years, and the mean APACHE II score was 20.

Adrenal insufficiency was identified in 68 patients (43%). Overall mortality was quite high, with 86 patients (54%) dying by day 28.

However, adrenal insufficiency was significantly more common among those who died (54 patients, 63%) than among those who survived (14 patients, 20%). Mortality at day 28 was higher in the group with an adrenal insufficiency (76.5% vs. 38%). Patients who died were also older than those who survived (66 years vs. 60 years) and had higher mean APACHE II scores (22 vs. 18).

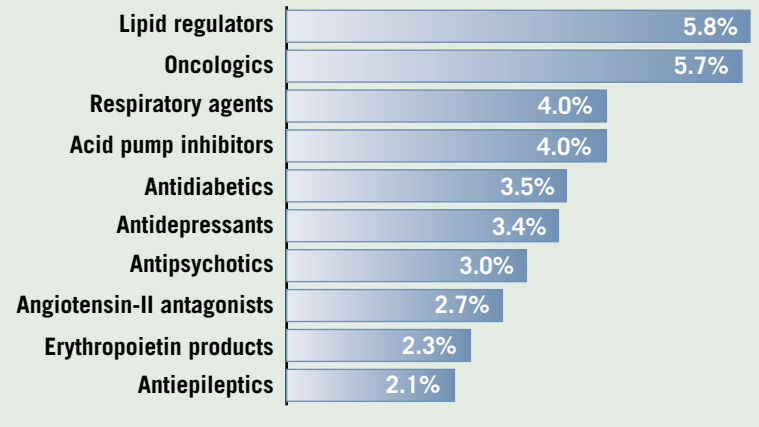
As an independent predictor of death, adrenal insufficiency had a sensitivity of 75% and a specificity of 62%, said Dr. Qiu of the Nanjing Zhong-Da Hospital, Nanjing, China.

—Michele G. Sullivan

Dr. Curtis Sessler, FCCP, comments: *Adrenal insufficiency is increasingly recognized as a common condition among critically ill patients, and one associated with increased risk of death. Proposed diagnostic criteria for AI differ among experts, however, and standardization would be helpful. In contrast to other independent risk factors for death, AI can be treated with corticosteroid therapy, so establishing the diagnosis is crucial.*

DATA WATCH

Top 10 Therapy Classes by Percentage of Global Sales



Source: 2006 data, IMS Health Inc.

ELSEVIER GLOBAL MEDICAL NEWS

Lung Transplants Succeed in Older, Selected Patients

BY MITCHEL L. ZOLER
Elsevier Global Medical News

WASHINGTON — Patients who are age 65 or older can successfully undergo lung transplantation, based on an experience with 48 patients treated at a single center.

"Our results suggest that a select group of older patients can safely undergo lung transplant with acceptable outcomes," Dr. Sam Bastani said at the annual meeting of the American Association of Thoracic Surgery. The older patients generally lacked other comorbidities, they usually received a single lung, and they often received a lung from a nonstandard donor, said Dr. Bastani, a surgeon at the University of California, Los Angeles.

The report showed "superlative" results for the operative and perioperative morbidity and mortality in patients who were 65 or older, commented Dr. John C. Wain, FCCP, a thoracic surgeon at Massachusetts General Hospital in Boston.

Although consensus guidelines specify an upper age limit of 65 for patients receiving a single lung and 60 for patients getting a bilateral lung transplant, surgeons at UCLA stopped using age as an absolute contraindication in 1999. They reviewed their experience during March 2000-September 2006, during which 48 patients age 65 or older received lung transplants. The characteristics and outcomes of these patients were compared with a group of patients younger than 65 who received one or two transplanted lungs at UCLA during the same period. The younger patients were selected for this analysis by matching them with the older patients based on diagnosis, date of transplant, and their lung allocation score.

A series of relative contraindications were applied to the older patients that could exclude them from receiving a transplant: a body mass index of less than 18 kg/m^2 or greater than 30 kg/m^2, obstructive coronary artery disease, peripheral or cerebral vascular disease, renal insufficiency based on a creatinine clearance rate of less than 50 mL/min, or debilitation.

Debilitation was a subjective criterion that gave the UCLA surgeons the flexibility to deny a transplant to any older patient who was judged as being too ill to undergo transplant surgery.

The average age of the older patients was 66 years, ranging from 65 to 72. The matched, younger patients averaged 58 years old, with a range of 33-64. The average lung allocation score was about 39 for both groups.

Immunosuppression was performed using an interleukin-2 receptor blocker in 67% of the older patients and 24% of younger patients. A more standard immunosuppression regimen of rabbit antithymocyte globulin, a polyclonal mix of antibodies, was used on the remaining 33% of older patients and 76% of younger patients.

Nonstandard donor lungs were used in 46% of the older patients, compared with 28% of younger patients. Among the patients who received nonstandard lungs, 61% of the older patients received a lung from a donor who was older than 55, compared with 29% of younger patients.

Single lungs were transplanted into 76% of the older patients (with the other 24% getting a bilateral transplant) and into 16% of the younger patients. Although single-lung transplants were more common among the older patients, the UCLA team did not use any firm age cutoff for determining who could get a bilateral transplant. "What this study really compared was single-lung transplants in older patients to double-lung transplants in younger patients," Dr. Wain said.

Survival rates were similar in the two groups. During the first 30 days after transplantation, more than 95% of patients survived in both groups. During the first year after transplant, the survival rate was about 80% in the older patients and about 91% in younger patients, a difference that was not statistically significant.

The most common cause of death during the first year was bacterial infection, which was responsible for 75% of the fatalities in older patients and 67% of deaths in younger patients. The survival rate to 3 years after surgery was about 70% in both age groups. ■

Dr. Keith Wille, FCCP, comments: *Most transplant centers generally recognize older age (65 years for single lung transplant or 60 years for bilateral lung transplant, respectively) to be a relative contraindication to lung transplantation, as registry data suggest less optimal survival rates with advancing age. In these patients, the benefits and risks of transplantation must be carefully weighed, with consideration of all other comorbidities and contraindications. Appropriate recipient selection, regardless of age, remains essential for optimal long-term outcomes.*

Lung Infections Linked to Mortality in Ped Transplants

BY ROBERT FINN
Elsevier Global Medical News

SAN FRANCISCO — Children who contract pulmonary infections in the year after receiving a lung transplant are 70% more likely to die than are those with no such infections, Dr. Lara A. Danziger-Isakov reported in a poster presentation at the American Transplant Congress.

Clinicians should consider prophylaxis in children judged to be at risk, concluded Dr. Danziger-Isakov, of the Cleveland Clinic, and her colleagues.

The multicenter, retrospective cohort analysis involved 555 patients at 12 centers, all of whom had data collected from the time of transplant until death, retransplantation, or 365 days after transplantation. During that time, 92 (17%) of those children contracted 99 pulmonary fungal infections, and 12 died.

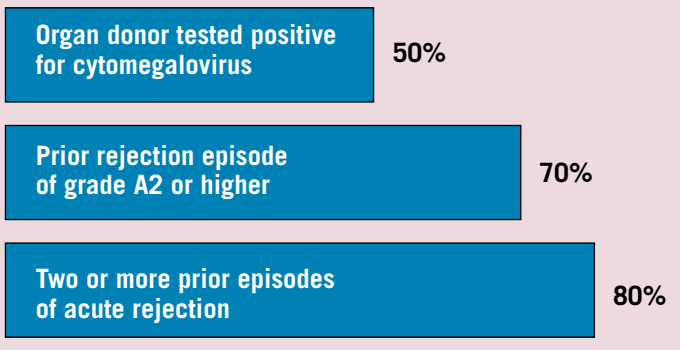
The fungal infections occurred throughout the posttransplant year, with a mean of 78 days and a median of 26 days post transplant. Children with infections were significantly older than those without (15.2 years versus 12.6 years), and were significantly more likely to have pretransplant colonization.

Candida and *Aspergillus* species were the most common organisms recovered from the infected children; 23% of the children with *Aspergillus* and the 7% of the children with *Candida* died.

In a multivariate analysis that controlled for a number of possible confounders, the investigators found that having two or more prior episodes of acute rejection increased the chance of developing an infection by 80%. Other risk factors were being 15 years old or older, an immunosuppressive regimen including tacrolimus, and a prior rejection episode of grade A2 or higher.

But cystic fibrosis, induction therapy, and the type of transplant were not associated with fungal infections, noted the investigators at the meeting, which was cosponsored by the American Society of Transplant Surgeons and the American Society of Transplantation. ■

Percentage of Increase in Risk for Fungal Infection After Lung Transplant



Note: Based on a retrospective cohort analysis of 555 pediatric patients.
Source: Dr. Danziger-Isakov

ELSEVIER GLOBAL MEDICAL NEWS

Embolization of Localized PAVMs Improved Respiration

BY SHERRY BOSCHERT
Elsevier Global Medical News

SEATTLE — Three-year average follow-up on 42 adults who underwent embolization of localized pulmonary arteriovenous malformations showed that the treatment significantly improved respiration and prevented paradoxical emboli, Dr. Jean-Pierre Pelage said at the annual meeting of the Society for Interventional Radiology.

Pulmonary arteriovenous malformations (PAVMs) are rare communications between branches of pulmonary arteries and pulmonary veins through small aneurysms that cause respiratory problems and impair the filtering function of the lungs. Diagnosis usually follows paradoxical emboli—transient ischemic attacks (TIAs); strokes, or brain abscesses.

In the current series, 99 PAVMs were embolized in 47 procedures using 530 coils. The patients had a mean partial pressure of alveolar carbon dioxide ($PACO_2$) of 76 mm Hg before embolization, which improved to 92 mm Hg after treatment and remained stable, said Dr. Pelage of Hôpital Ambroise Paré in Paris, and his associates.

Dyspnea in 22 patients (53%) at presentation disappeared after treatment in all but 5 patients.

Among a subset of 24 patients evaluated by CT imaging after treatment, 20 (83%) showed complete retraction of the PAVMs, which is the criterion of successful embolization, he said. Of 52 PAVMs in these patients, 48 (92%) successfully were occluded by embolization.

At total of 12 patients (29%) originally were diagnosed with PAVMs after paradoxical emboli, and 3 patients had failed previous embolizations. After the embolizations in the current series, two patients (5%) presented with new paradoxical emboli related to a central recanalization through the coils. One was retreated successfully with embolization; the other refused to have another procedure.

Most patients presented with multiple PAVMs, mainly in the lower lobes. Most lesions had simple rather than complex architecture. The average diameter of the feeding artery was 6 mm, "rather large," Dr. Pelage said.

After treatment, two patients had small or large PAVMs with feeding arteries measuring 3 mm each. Embolization is indicated for primary or secondary prevention of paradoxical emboli in patients who have PAVMs with feeding arteries larger than 3 mm. Embolization also may be considered for patients with respiratory symptoms due to PAVMs, especially multiple or large PAVMs, he said.

Four PAVMs that remained patent after the current embolizations had complex architecture with multiple feeder arteries.

At the time of embolization, three patients developed mild hemoptysis due to trauma to the artery.

Short-term complications of treatment included fever and pulmonary infarction in about 10% of patients. One patient with a huge feeding artery of a single PAVM developed a massive pleural effusion requiring drainage, which was successful. ■

Sleep Apnea Undiagnosed in Many Surgical Patients

Screening followed by testing revealed that an estimated 14% of patients had sleep apnea.

BY SHERRY BOSCHERT
Elsevier Global Medical News

CHICAGO — Obstructive sleep apnea in surgical patients mostly goes undiagnosed and may put them at risk for postoperative respiratory arrest, Dr. Kevin J. Finkel said in a poster presentation at the annual meeting of the American Society of Anesthesiologists.

An investigation of 2,867 adults undergoing surgery at Barnes-Jewish Hospital, St. Louis, suggests that 14% had undiagnosed obstructive sleep apnea, and that OSA affected a total of 21% of surgical patients, said Dr. Finkel, clinical research coordinator in the anesthesiology department, Washington University, St. Louis, Mo.

Patients completed a screening questionnaire during their preoperative medical evaluation.

A total of 182 patients reported having been diagnosed with OSA sometime in the past, and 516 patients who reported no prior diagnosis of OSA scored at high risk for the condition on the screening questionnaire.

Patients in the latter group were asked to wear a headset device (the ARES Unicorder) during sleep to assess the severity of sleep apnea by recording the number of abnormal breathing events per hour of sleep.

Of 215 high-risk patients who successfully used the device during sleep, 80% were diagnosed with OSA.

If that 80% rate applied to all 516 patients who screened positive for high risk on the questionnaire (including those without successful device readings), 413 (14% of all surgical patients) had undiagnosed OSA. Combining those 413 patients with the 182 patients who reported a prior diagnosis of sleep apnea gives an overall incidence of 21%, Dr. Finkel and his associates said.

The device readings also showed that the rate of abnormal breathing events during sleep increased significantly among patients with moderate or worse sleep apnea when in a supine position, compared with sleeping on their sides. After surgery, it is common for patients to be placed in a supine position.

"If you know that your patients are at risk for sleep apnea, try to not position them on their backs. That potentially could save lives," Dr. Finkel said. He has no association with the company that makes the Unicorder.

In a separate poster presentation at the meeting, Dr. Frances Chung said that surgeons or anesthesiologists should refer patients with difficult endotracheal intubation for evaluation of OSA after recovery from surgery.

She and her associates referred 83 patients who were difficult to intubate. Of the 32 who agreed to undergo overnight polysomnography, 65% were diagnosed with OSA, reported Dr. Chung of the University of Toronto.

Difficult intubation was defined as needing two or more attempts for successful endotracheal intubation, or as grade 3 or 4 according to Cormack and Lehane direct laryngoscopic view.

ABNORMAL BREATHING EVENTS INCREASED WHEN PATIENTS WITH MODERATE SLEEP APNEA WERE IN A SUPINE POSITION RATHER THAN ON THEIR SIDES.

Dr. Chung's findings support the results of a previous retrospective study that found sleep apnea in 53% of 15 patients with difficult intubations.

She and associates are developing a simplified four-question tool that might make it easier for surgeons or anesthesiologists to screen for OSA. Patients are asked to answer "yes" or "no" to the following set of questions:

- Do you snore loudly (loud enough to be heard through closed doors)?
- Do you often feel tired, fatigued, or sleepy during daytime?
- Do you have high blood pressure?
- Has anyone noticed that you stop breathing during your sleep?

In a pilot study, Dr. Chung and her colleagues compared three screening methods for sleep apnea: the Obstructive Sleep Apnea Questionnaire, the Berlin Questionnaire, and the American Society of Anesthesiologists checklist for obstructive sleep apnea.

The researchers administered these three tools to 34 patients before admission for surgery. Patients also underwent polysomnography, the gold standard for the diagnosis of sleep apnea.

Results showed that the four-item Obstructive Sleep Apnea Questionnaire had a positive predictive value of 67% and a negative predictive value of 12%, compared with polysomnography.

The more complex nine-item Berlin Questionnaire, which has been validated on primary care (but not surgical) patients, had a positive predictive value of 81% and a negative predictive value of 38%.

The Berlin Questionnaire "is quite complicated for an anesthesiologist or surgeon" to use, Dr. Chung said.

The American Society of Anesthesiologists (ASA) checklist for obstructive sleep apnea had a positive predictive value of 72% and a negative predictive value of 19%.

The ASA checklist has not been validated as a screening tool, and "we think it's probably not so user friendly" in the surgical setting, she added.

The study is ongoing and will enroll 240 patients to reach the sample size for validation of the new questionnaire. ■

Untreated Sleep Disorders May Prolong PTSD in Some Patients

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SCOTTSDALE, ARIZ. — Untreated sleep-disordered breathing may perpetuate posttraumatic stress disorder over a period of weeks, months, and even years, Dr. Lois E. Krahn proposed at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

"Patients have a lot of sleep complaints. They have trouble falling asleep. They have nightmares, and one very interesting finding of late is they also have a fairly high rate of obstructive sleep apnea," said Dr. Krahn, chair of the department of psychiatry and psychology at the Mayo Clinic in Scottsdale, Ariz.

In one posttraumatic stress disorder (PTSD) study cited by Dr. Krahn, subjective sleep disturbance was described as "a hallmark of PTSD" in elderly war veterans (Biol. Psychiatry 2000;47:520-5). Even though patients with untreated obstructive sleep apnea and sleep movement disorders were not included in the sample, the investigators reported finding many cases in patients who were screened for the study.

Dr. Krahn posited that obstructive sleep apnea may predispose some patients to wake up in the middle of the night.

"So that may be a feature that causes this condition [PTSD] to be perpetuated," she said.

In an interview at the meeting, Dr. Krahn suggested ordering polysomnography when PTSD patients do not show improvement with therapy. They may continue to relive their trauma at night, she said.

"Their sleep wasn't terrific before this traumatic event. Now they've got nightmares. With the combination, they have a more chronic disorder."

Many psychiatric disorders overlap with sleep disorders, and the two can be difficult to distinguish, Dr. Krahn said. She suggested asking new sleep patients whether they are sleepy or fatigued during the day.

OBSTRUCTIVE SLEEP APNEA MAY PREDISPOSE SOME PATIENTS TO WAKE IN THE MIDDLE OF THE NIGHT, WHICH MAY CAUSE PTSD TO BE PERPETUATED.

Patients who present only with daytime sleepiness are more likely to have a sleep disorder, according to Dr. Krahn. If the main complaint is fatigue or exhaustion, the differential diagnosis expands to a wide range of psychiatric and medical disorders.

Two key tools for evaluating patients with sleep complaints, she suggested, are the Epworth Sleepiness Scale and the clinical interview. Patients with obstructive sleep apnea or narcolepsy tend to score high on the Epworth scale, whereas patients whose main complaint is fatigue score low.

The clinical interview helps the physician tease out factors in daily life that might influence sleep.

As an example, she cited a nursing home resident who was forced to go to bed from 7 p.m. to 7 a.m. The man took naps during the day because he was depressed.

Depression and sleep disorders are often comorbid, Dr. Krahn said. As many as 20% of insomnia patients are depressed, and 90% of patients hospitalized for depression also have disrupted sleep.

"If you have someone come to you with sleepiness, it's important to ask about their mood," she said, suggesting simple questions such as, "Are you sad? Are you blue? Are you able to pursue your interests?"

She also recommended asking about mood if patients present with sleepiness in winter.

"There is no seasonal hypersomnia," Dr. Krahn said, suggesting that such patients might be suffering from seasonal affective disorder.

Similarly, Dr. Krahn noted that patients with panic disorder can have attacks during the day and at night. If the interview reveals that attacks occur only at night, suspect sleep apnea.

People with bipolar and psychotic disorders sometimes seek help from a sleep clinic rather than a psychiatrist, according to Dr. Krahn. Lacking insight into their disorders, these patients focus on insomnia as a symptom they want fixed.

To tease out bipolar disorder, Dr. Krahn suggested asking patients the following question: "Have you had periods of your life where you have not needed to sleep—where you have not had more than 3 hours of sleep and you still had enough energy to function or even quite a bit of energy?"

"That is a pretty specific scenario for mania," she said, warning that bipolar patients often resist their diagnosis. "It is more socially acceptable to have insomnia than to have bipolar disorder," she noted.

Psychotic disorders are often associated with insomnia, she said. In addition, Dr. Krahn noted that many patients gain weight on the newer atypical antipsychotic drugs. The increase in weight that is associated with taking these drugs puts them at increased risk of obstructive sleep apnea.

Educating these patients about continuous positive airway pressure therapy can be a challenge, she warned, describing a patient who was afraid of inhaling a poison gas. ■

Does Apnea Impair Your Patients' Ability to Drive?

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SCOTTSDALE, ARIZ. — Evidence-based medicine provides no easy answers for a physician who must decide whether or not to report an obstructive sleep apnea patient to the state department of motor vehicles, according to Dr. Brian A. Boehlecke, FCCP.

Numerous studies have failed to identify a method for determining which individuals with obstructive sleep apnea are more likely to have motor vehicle accidents, he said at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

"There is no correlation between symptoms and objective measures of vigilance or performance," said Dr. Boehlecke, a professor of medicine at the University of North Carolina in Chapel Hill, reviewing one of many studies with similar findings.

People with the disorder are more likely to be in a motor vehicle accident, he said, but the overall risk is low. In one report, patients had more crashes than did a control group during a 3-year period (odds ratio 2.6). Some had two and three crashes, but most did not have any accidents, and no physiologic markers predicted which patients were at greater risk (Am. J. Respir. Crit. Care Med. 1998;158:18-22).

In study after study, objective measures such as scores on the Epworth Sleepiness Scale, Karolinska Sleepiness Scale, respiratory disturbance index, and the apnea-hypopnea index did not predict reaction time or driving performance, he said.

In a recent trial, 20 obstructive sleep apnea patients and 40 controls took a battery of tests, including a driving simulator (Eur. Respir. J. 2005;25:75-80). Dr. Boehlecke said that almost all the apnea patients had some impairment of vigilance or attention, but no one test predicted ability to remain awake and stay attentive.

Effectiveness of measures to counteract night drowsiness also is highly variable, according to Dr. Boehlecke.

He referred physicians treating sleep apnea patients to recommendations of the American Thoracic Society (Am. J. Respir. Crit. Care Med. 1994;150:1463-73) and a statement on commercial drivers from a Joint Task Force of the American College of Chest Physicians, the American College of Occupational and Environmental Medicine, and the National Sleep Foundation (Chest 2006;130:902-5).

The thoracic society calls on physicians to know the applicable laws in their state, to give high-risk drivers a warning of risk, and to report high-risk drivers who insist on driving before being treated for obstructive sleep apnea or who fail to comply with treatment.

Dr. Boehlecke noted that the joint statement gives an apnea-hypopnea index of less than 5 with continuous positive airway pressure at initial tritration, or an index of no more than 10 depending on clinical findings, as objective measures for when commercial drivers should be allowed to return to work. He questioned whether the thresholds were realistic given the inconclusive literature. It also calls for evaluation of compliance with treatment.

In the absence of an easy method for predicting when a patient poses a danger, he urged physicians to rely on their clinical judgment.

In North Carolina, he said, the law does not require him to report obstructive sleep apnea patients who pose a risk. Nonetheless, he reported a school bus driver suspected of having the disorder. Her license was suspended while he confirmed the diagnosis, and it was reinstated after she started treatment.

"You've got to live with yourself, and do what you think is right," Dr. Boehlecke said.

"Don't be afraid to use your clinical judgment because nothing is a strong predictor of risk." ■

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Snoring in Children Linked to Poor School Performance

BY ROBERT FINN
Elsevier Global Medical News

RANCHO MIRAGE, CALIF. — Third graders who do not have obstructive sleep apnea but are habitual snorers have much higher odds of having behavioral and academic problems than children who never snore, according to a poster presented at a conference on sleep disorders in infancy and childhood.

Children who snored were 2.8 times as likely to have hyperactive behavior, 9.5 times more likely to experience daytime tiredness, and 7.4 times more likely to fall asleep at school, compared with children who never snored, Dr. Michael S. Urschitz of University Hospital of Tübingen (Germany), and his colleagues reported at the meeting sponsored by the Annenberg Center for Health Sciences.

In addition, children who snored were 4.1 times more likely to exhibit concentration deficits, 2.2 times more likely to perform poorly in mathematics, and 2.9 times more likely to perform poorly in science.

The behavioral outcomes were adjusted for gender and age, and the academic outcomes were additionally adjusted for maternal education, paternal education, and class membership.

The group was selected from 1,144 children attending primary schools in Hanover, Germany. In all, 410 never snored and 114 snored habitually, based on their parent's responses to a questionnaire.

Ambulatory sleep studies were obtained in 90 of the snorers, 76 of whom had an apnea-hypopnea index of less than 0.8 an hour and were judged to be nonapneic. These 76 children were compared to the 410 nonsnorers.

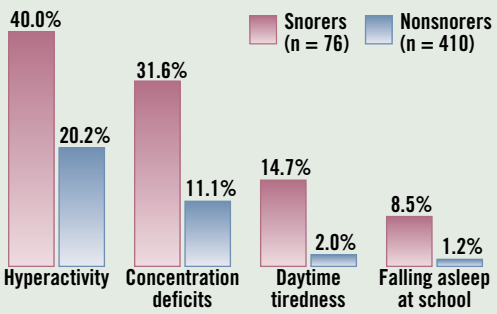
The 25-item questionnaire included questions related to hyperactivity, inattention, and tiredness. The researchers used report cards to judge each child's academic performance in mathematics, science, spelling, reading, and handwriting.

The investigators suggested that the children's deficits might be related to an increased susceptibility to sleep fragmentation.

Current guidelines, including those of the American Academy of Pediatrics, suggest that primary snoring in children is benign. The investigators described the need for further studies on this issue as "urgent" and suggested that the guidelines might need to be re-evaluated. ■

Dr. Susan Harding, FCCP, comments: *This well-designed study supports the notion that children who snore and have an apnea-hypopnea index of less than 1 an hour are more likely to have excessive daytime sleepiness and hyperactivity. Treatment intervention studies would solidify this association.*

Nonapneic Habitual Snoring May Affect Behaviors



Source: Dr. Urschitz

ELSEVIER GLOBAL MEDICAL NEWS

Many Allergic Rhinitis Patients Lack Adequate Amount of Sleep

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — During the winter months, people with allergic rhinitis report more sleep problems than does the general population, Dr. Eli Meltzer reported during a poster session at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

The finding underscores the importance of asking patients with allergic rhinitis how their symptoms are affecting their sleep quantity and quality.

"If you don't get adequate sleep, we know people are cognitively impaired and often psychosocially impaired," Dr. Meltzer, an allergist who practices in San Diego, said in an interview.

In a study funded by GlaxoSmithKline, Dr. Meltzer and his associates mailed a 27-item survey to 6,476 people nationwide between December 2005 and February 2006 who had completed a screening questionnaire during May and June of 2004 that was intended to target people with symptoms of allergic rhinitis. The purpose of the follow-up survey was to provide a longitudinal assessment of disease and to capture seasonal variation in disease burden.

Respondents used the Medical Outcomes Study Sleep Scale to rate their sleep. This instrument measures quality and quantity of sleep on two scales that range from 0 to 100: a sleep adequacy scale and a sleep problems index scale. Higher scores on the sleep adequacy scale correspond to more adequate amounts of sleep, while higher scores on the sleep problems index scale correspond to poorer sleep quality. Mean general population norms for the scales are 60.5 and 26.9, respectively.

Complete data were available on 5,371 of the survey respondents. Of these, 1,788 (33%) reported experiencing symptoms consistent with seasonal or perennial allergic rhinitis during the past 4 weeks that were not related to a cold or to the flu, such as runny nose/sniffling, sneezing, and itchy nose, congested nose, and postnasal drainage.

The allergic rhinitis sufferers' mean scores on the sleep adequacy scale and the sleep problems index scales were 51.1 and 35.3, respectively. In addition, more than 65% of the allergic rhinitis sufferers reported problems falling asleep or falling back to sleep upon awakening, and fewer than half indicated that they get enough sleep or feel rested upon awakening.

"That's a staggering amount," said Dr. Meltzer, who also is a professor of pediatrics at the University of California, San Diego.

He disclosed that he has received research grants and honoraria from GlaxoSmithKline. ■

Provigil Maker Cited for 'Fatigue' Promotion

The Food and Drug Administration has sent a warning letter to the manufacturer of modafinil about promoting the drug for the treatment of fatigue associated with some neurologic and psychiatric disorders for which the drug is not approved.

Modafinil, marketed as Provigil by Cephalon, is approved for improving wakefulness in people with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS), and shift work sleep disorder (SWSD). It is also approved for people with OSAHS as an adjunct to standard treatment for the underlying obstruction.

But a warning letter sent by the FDA to Cephalon, dated Feb. 27, said that as part of a presentation made on behalf of the company at a meeting of the Maryland Department of Health and Hygiene's Pharmacy and Therapeutics Committee in August 2006, a handout was provided on the use of modafinil in the medical and psychiatric population. The handout was "false and misleading," because it "states or suggests that Provigil is safe and effective in the treatment of various disorders associated with fatigue, sleepiness, or inattentiveness, when in fact, Provigil is not indicated for fatigue at all and is indicated only for specific groups of patients with excessive sleepiness," according to the FDA letter.

As requested by the FDA, Cephalon submitted a response to the letter. The response said that the company takes its regulatory responsibility seriously and that the company has "worked diligently to develop procedures and policies to ensure that our products are lawfully promoted."

—Elizabeth Mechcatie

Plan to Pay for Performance Looks Likely After 2008

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

SAN DIEGO — Within the next few years, Medicare is likely to move from a system of pay for reporting to pay for performance, Jeff Flick, a regional administrator for the Centers for Medicare and Medicaid Services, said at the annual meeting of the American College of Physicians.

Mr. Flick, who is based in San Francisco, predicted that Congress is likely to approve funds to continue the Medicare Physician Quality Reporting Initiative (PQRI) in 2008.

However, in future years the program is likely to convert to a pay-for-performance system, he said, which could be similar to the system being developed for hospital value-based purchasing.

CMS IS CURRENTLY RECEIVING DATA ON HOSPITAL, HOME HEALTH, AND NURSING HOME QUALITY, BUT NOT ON PHYSICIANS.

"I believe we're not going to move away from this," he said.

PQRI is a voluntary program that will let physicians earn a bonus of up to 1.5% of their total allowed Medicare charges during the last 6 months of 2007 for reporting on certain quality measures.

Congress authorized the establishment of the 6-month pay-for-reporting program last December as part of the Tax Relief and Health Care Act of 2006. Changes to PQRI—and actual implementation of a pay-for-performance system—would require additional legislation from Congress.

Officials at the Centers for Medicare and Medicaid Services have selected 74 quality measures that can be used by physicians across specialties. If four or more measures apply, physicians must report on at least three measures for at least 80% of cases in which the measure was reportable.

If no more than three measures apply, each measure must be reported for at least 80% of the cases in which a measure was reportable, according to CMS.

ACP has estimated that the typical internist will be able to earn about $1,500 for reporting over the 6-month period. But the amount earned will depend on the case mix of the practice, said Robert Doherty, senior vice president for governmental affairs and public policy at ACP.

"If you look at this program, it's one that can teach us a lot for the future. It's not the answer," Mr. Doherty said. "But if you do participate, you'll learn a lot about the program."

ACP officials would rather see a "weighted" performance payment that would take into consideration the impact and the additional work related to measures for chronic diseases, he said.

But physicians who choose to participate in the program will have a chance to learn about the quality of care they are providing and to get ready for pay for performance, Mr. Flick said.

Physicians will also be sending the message to Congress that they are not afraid of quality, he said.

What is fundamentally driving the program is the need to move toward value, he said. CMS is currently receiving data on hospital, home health, and nursing home quality, but not on physicians.

"We need data. We need to begin to understand information on quality of care," Mr. Flick said. ■

Bioterrorism DVD

The Agency for Healthcare Research and Quality has released a DVD titled "Cross Training Respiratory Extenders for Medical Emergencies (Project XTREME)" to train nonspecialist health care professionals to provide basic respiratory care and ventilator management to adult patients in any mass casualty event. A free copy of the DVD and a CD-ROM containing a related report can be ordered by calling 800-358-9295 or e-mailing ahrqpubs@ahrq.hhs.gov. ■

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Zemaira® is indicated for chronic augmentation and maintenance therapy for adults with alpha$_1$-proteinase inhibitor (A_1-PI) deficiency and emphysema.

Clinical data demonstrating the long-term effects of chronic augmentation therapy with Zemaira® are not available.

As with other Alpha-1 therapies, Zemaira® may not be appropriate for the following adult individuals as they may experience severe reactions, including anaphylaxis: individuals with a known hypersensitivity and/or history of anaphylaxis or severe systemic reaction to A_1-PI products or their components and individuals with selective IgA deficiencies who have known antibodies against IgA.

In clinical studies, the following treatment-related adverse events were reported in 1% of subjects: asthenia, injection-site pain, dizziness, headache, paresthesia, and pruritus.

Zemaira® is derived from human plasma. As with all plasma-derived products, the risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

For more information, call **1-866-ZEMAIRA (1-866-936-2472),** or visit **www.Zemaira.com.**

Zemaira®
alpha$_1$-proteinase inhibitor (Human)
Unmatched purity. Uncompromised care.

Please see brief summary of full prescribing information on following page.

* Shelf life purity specification is ≥90%

† In a retrospective analysis in the pivotal clinical trial, Zemaira® patients were three times less likely to experience exacerbations of their COPD than Prolastin® patients

‡ No clinically significant differences were detected between the treatment groups

§ Based on recommended dosage as stated in the product package inserts of 60 mg/kg body weight at the infusion rate of 0.08 mL/kg/min