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At only about 21% coverage, "we still have a long way to go" to vaccinate children aged 6-23 months, said Dr. Anthony Fiore.

Flu Vaccination Rates Too Low in Young Kids

BY SHARON WORCESTER
Elsevier Global Medical News

ATLANTA — Influenza vaccination rates remain low among children aged 6-23 months, despite a recommendation made 3 years ago by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices that children younger than age 2 years be vaccinated.

At the committee's autumn meeting, Dr. Anthony Fiore reported that the latest data show complete coverage of only about 21% in this age group.

"We still have a long way to go," explained Dr. Fiore of the CDC.

The findings, which are from the 2007 National Immunization Survey and which are based on the 2006-2007 influenza season, were published recently in Morbidity and Mortality Weekly Report.

Data emerging from the 2007-2008 season appear similar to those from 2006-2007, Dr. Fiore noted.

Because children younger than age 2 years are at the greatest risk for influenza-related hospitalizations, ACIP in 2002 encouraged vaccination of this population, and in 2004 strengthened their stand by recommending vaccination.

According to the MMWR report, 32% of children aged 6-23 months received one or more doses of vaccine during the

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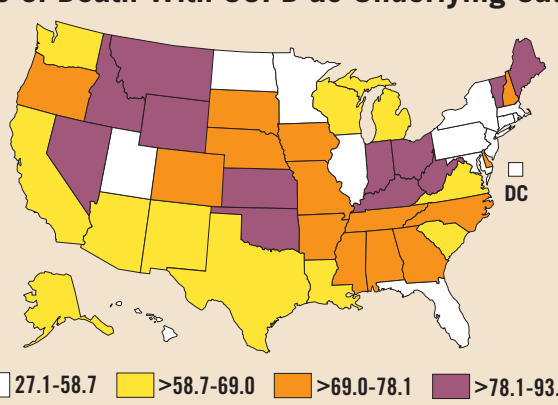
VITAL SIGNS

Rate of Death With COPD as Underlying Cause



Note: Deaths per 100,000 population in 2005, among adults at least 25 years old.
Source: MMWR 2008;57:1229-32

Elsevier Global Medical News

Smokers' Nicotine Dependence Rises, Complicates Quitting

Most patients now highly dependent.

BY MITCHEL L. ZOLER
Elsevier Global Medical News

PHILADELPHIA — American smokers have, on average, become significantly more nicotine dependent since 1989—which means that more aggressive interventions are needed to help them quit.

That's because most of the smokers who could more easily quit have already done so. "The low-hanging fruit has been plucked; the less-addicted smokers are out of the pool. We're left with people who are more dependent," Dr. David P.L. Sachs said at the annual meeting of the American College of Chest Physicians.

"The vast majority of patients we see now in actual clinical practice are more highly nicotine dependent," said Dr. Sachs, director of the Palo Alto (Calif.) Center for Pulmonary Disease Prevention. Dr. Sachs documented this shift by comparing the average level of nicotine dependence in patients who participated in three smoking-cessation studies that he collaborated on during 1989-2006.

In all three studies, nicotine dependence at baseline was quantified with the Fagerström Tolerance Questionnaire (FTQ), a brief, self-report survey that measures nicotine dependence on a scale of 0-10, with 10 being the highest level of dependence.

Among 220 U.S. smokers enrolled in 1989 and 1990 in a study of a nicotine patch, the average FTQ score was 6.65. The next study enrolled 206 patients in 1994 in a study of sustained-release bupropion; their average FTQ score was 7.02, significantly higher than in the prior study. This average also fell into the category of "high" nicotine dependence, which applies to FTQ scores of 7 or greater.

The third study group cited by Dr. Sachs included 204 patients who were enrolled in 2005-2006 to assess an individualized treatment regimen. These people

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INSIDE

Strategy Boosted Oxygenation in ALI

BY MICHELE G. SULLIVAN
Elsevier Global Medical News

An individualized ventilation strategy based on transpulmonary pressure estimated by esophageal pressure significantly improved oxygen saturation in patients with acute lung injury, and was associated with a trend toward improved survival, a randomized trial has found.

Because the ventilation was adjusted to meet each patient's estimated transpleural pressure, it achieved optimal oxygenation while avoiding the problems associated with underinflation or overdistention, study investigators reported.

"The improvements [in lung function] were achieved without elevating transpulmonary pressure at the end inspiration above the physiologic range," wrote Dr. Daniel Talmor, FCCP, of Beth Israel Deaconess Medical Center, Boston, and his colleagues (N. Engl. J. Med. 2008; 359:2095-104).

However, the use of esophageal pressure to estimate transpulmonary pressure is rife with possibilities for error, according to Dr. Gordon Bernard, FCCP, who wrote an accompanying editorial. "Estimating pleural pressure this way is imprecise and may be inaccurate," he said in an interview. "If there was an easy, accurate way to measure pleural pressure, then we would have been titrating ventilation to it a long time ago."

The study comprised 61 patients (average age, 53 years) with acute lung injury or acute respiratory distress syndrome.

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FDA Committees to Assess LABA Safety in Asthma

BY TERRY RUDD
Elsevier Global Medical News

The safety of long-acting β_2-adrenergic agonists for asthma treatment will take center stage this month at a joint meeting of three Food and Drug Administration advisory committees.

The FDA's Pulmonary-Allergy Drugs Committee, Drug Safety and Risk Management Committee, and Pediatric Advisory Committee are slated to meet Dec. 10-11 to discuss the risks and benefits of the long-acting bronchodilators in adults and children with asthma.

In 2006, the FDA issued a black box warning for Advair Diskus (fluticasone propionate with salmeterol), Serevent Diskus (salmeterol), and Foradil Aerolizer (formoterol). The warning cautions that long-acting β_2-adrenergic agonists (LABAs) may increase the risk of asthma-related death, and should be reserved for use in patients who aren't "adequately controlled on other asthma-controller medications," or in those for whom disease severity "clearly warrants" treatment with two maintenance therapies.

The black box warning came in the wake of the Salmeterol Multicenter Asthma Research Trial (SMART), which pointed to an increased incidence of asthma-related deaths among patients taking salmeterol (Chest 2006;129:15-26).

However, two large meta-analyses published in 2008 found potentially positive trends in the safety of LABAs in asthma.

The first meta-analysis included 66 GlaxoSmithKline trials involving 20,966 patients who received either inhaled corticosteroids plus salmeterol or inhaled corticosteroids alone. Six of the trials involved a total of 1,575 children (aged 4-17 years). GlaxoSmithKline, which makes Advair and Serevent, funded the meta-analysis (Ann. Intern. Med. 2008;149:33-42).

The analysis suggested that adding salmeterol to inhaled corticosteroids did not increase the risk of asthma-related hospitalization, compared with inhaled corticosteroids alone, the investigators said. There were 35 asthma-related hospitalizations among patients using corticosteroid plus salmeterol, compared with 34 among those receiving inhaled corticosteroid alone.

The analysis "confirms that treatment with long-acting β-agonists and inhaled corticosteroids, compared with inhaled corticosteroids alone, decreases risk for some severe exacerbations but may not alter the risk for asthma-related hospitalization, intubation, or death," the investigators said.

In the second review, researchers examined the safety of the LABAs formoterol and salmeterol taken by asthma patients who also took inhaled corticosteroids, with a particular focus on serious adverse events.

Their meta-analysis included 62 randomized, controlled trials culled from a search of MEDLINE, EMBASE, ACPJC, and Cochrane databases, and involved 29,401 patients (Am. J. Respir. Crit. Care Med. 2008;178:1009-16).

The reviewers found no statistically significant differences in asthma-related hospitalizations and asthma-related serious adverse events between groups taking LABAs and inhaled corticosteroids and groups using inhaled corticosteroid only.

Furthermore, "our results show that the absolute increase in LABA-associated deaths or intubations from asthma in populations, such as those participating in these trials, is small, if it exists at all (three deaths and two nonfatal intubations in 15,710 patients receiving LABA)," the investigators wrote.

"We have not, however, excluded the possibility of a relative increase in deaths in patients receiving LABA who are also using [inhaled corticosteroids], a possible increase that may be important at a population level or to individual patients," they cautioned.

Lead author Dr. Roman Jaeschke disclosed receiving lecture honoraria from AstraZeneca, Merck Sharp & Dohme, Boehringer Ingelheim GmbH, and GlaxoSmithKline. ■

Several Agents Needed to Quit

Dependence • *from page 1*

had an average FTQ score of 7.44, a significant jump above the 1994 average.

Looked at a different way, the percentage of patients rated as highly nicotine dependent, with an FTQ score of 7 or higher, was 56% in 1989-1990, 66% in 1994, and 73% in 2005-2006.

The consequence of this trend is that physicians should expect a challenge with most patients whom they try to help quit smoking, Dr. Sachs said. He suggested that physicians start by measuring the FTQ score for each prospective quitter.

If the smoker is highly dependent, with an FTQ score of 9 or 10, then the physician will need to prescribe several agents to help the patient quit. "The higher the FTQ score, the more withdrawal symptoms and the less effective is treatment," he said. "If you try to use over-the-counter treatments, it won't be effective."

For a highly dependent person, three or more standard, OTC nicotine patches worn simultaneously will probably be necessary. The patients also will need to have an additional nicotine source for times of stress, such as nicotine gum, nasal spray, inhaler, or lozenges. In addition, highly dependent patients will likely need treatment with sustained- or extended-release bupropion (Zyban). Another effective smoking-cessation drug is varenicline (Chantix).

The key to treating high dependence is individualizing treatment and finding a regimen that consistently controls a patient's urge to smoke, he explained. Once the patient quits, the next step is sticking with the regimen, and then cautiously tapering it down over time.

Although some patients can eventually come off drug treatment entirely, others may require some type of maintenance treatment indefinitely, Dr. Sachs added.

Dr. Sachs has received research grants from, has been a consultant to, and has been a speaker for, Pfizer, which markets Chantix, and GlaxoSmithKline, which markets Zyban, as well as for several other drug companies.

To see a video discussion with Dr. Sachs, visit www.youtube.com and search for "ElsGlobalMedicalNews." ■

Dr. Philip Marcus, FCCP, comments: *We have been taught to ask about smoking, and if our patient smokes, discuss smoking cessation. Now, we need to recognize that the intensity of the addiction is also important and will help to determine the appropriate intervention. It should not take much time to incorporate this scale into our daily activities.*

IN THIS ISSUE

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CHEST PHYSICIAN

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*Estimated breaths for a person of 83 years. †Estimated breaths for a person of 81 years. ‡Estimated breaths for a person of average life span.

Note: Calculations are adapted from Brain JD. Control of breathing. The Merck Manual Online Medical Library Web site. http://www.merck.com/mmhe/sec04/ch038/ch038e.html#sec04-ch038-ch038e-17. Accessed August 13, 2008; and Heron MP, Hoyert DL, Xu J, Scott C, Tejada-Vera B; for the Division of Vital Statistics. Deaths: preliminary data for 2006. *Natl Vital Stat Rep*. 2008;56(16):1-52.

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Lung Cancer Diagnoses Decline, Hospitalizations Do Not

BY DIANA MAHONEY
Elsevier Global Medical News

Fewer Americans are being diagnosed with lung cancer, yet more are being hospitalized for it.

The federal government's Agency for Healthcare Research and Quality has released new data showing that the number of hospital admissions associated with a principal diagnosis of lung cancer remained stable between 1995 and 2006, and the number of hospitalizations with lung cancer as a secondary diagnosis increased 15%—despite a steady decline in the number of Americans diagnosed with the disease during the same period.

The discrepancy can be attributed in large part to the fact that patients with lung cancer are living longer thanks to therapeutic advances and are receiving more in-hospital treatments, including surgery and chemotherapy, according to the agency's News and Numbers report released Nov. 12 (www.ahrq.gov/news/nn/nn111208.htm).

With data from the 2006 Nationwide Inpatient sample database, a statistical analysis of hospital stays for lung cancer showed that of the 535,700 hospitalizations citing a lung cancer diagnosis in 2006, 149,900 were principally for lung cancer and 386,000 were for hospital stays in which lung cancer was a secondary diagnosis.

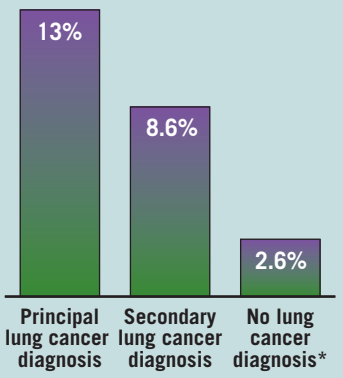
"Overall, the total number of lung cancer–related hospitalizations has increased 10% since 1995, ranging from 475,600 stays in 1999 to a high of 542,200 stays in 2005," according to the report.

About 63% of hospitalized lung cancer patients in 2006 were 65 years or older, and only 2.4% occurred in patients younger than 44 years. When patients younger than 45 years were hospitalized, twice as many stays involved a secondary diagnosis of lung cancer, "potentially indicating follow-up hospitalizations for sequelae of lung cancer," the authors wrote.

Men were hospitalized for lung cancer overall more often than women, and men older than 65 years had the highest rates of hospitalization for all lung cancer patients. Women between 18 and 44 years had a slightly higher rate of hospitalization, at 4.7 stays per 100,000 population, than men in the same age group, at 4.1 stays per 100,000.

The highest rate of hospitalizations with lung cancer as a primary diagnosis was observed in the South, with 89 admissions per 100,000 persons, vs. approximately 30, 55, and 34 per 100,000, respectively, in the Northeast, Midwest, and West. In contrast, the highest rate of lung cancer stays overall was observed in the Northeast, with 178 stays per 100,000 persons, vs. 137, 109, and 81 in the Midwest, South, and West, respectively.

In-Hospital Death Rates



*Rate for nonmaternal, nonneonatal hospitalization.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

An analysis of lung cancer hospitalizations by primary payer showed that Medicare was the most common payer both for principal and secondary stays, and private insurance was the second most common. Uninsured patients accounted for 3.6% of principal lung cancer admissions and 1.8% of secondary admissions, both of which are less than the 5.8% average rate of uninsured nonmaternal, non-neonatal hospitalizations, the authors stated.

The rate of in-hospital deaths associated with lung cancer hospitalization in 2006 was 13% of those associated with a principal lung cancer diagnosis, and 8.6% of those associated with a secondary diagnosis—both of which are substantially higher than the 2.6% observed for the average nonmaternal, non-neonatal hospitalization.

An evaluation of common procedures associated with lung cancer–related hospitalizations showed that cancer (lung cancer, other cancer, secondary malignancies) or some type of maintenance therapy (radiology, chemotherapy) accounted for approximately 40% of all hospital stays. Respiratory diagnoses—such as pneumonia, chronic obstructive pulmonary disease, respiratory failure, and pulmonary heart disease, among others—were also common reasons for lung cancer–associated hospital stays, the authors wrote.

When procedures were performed during lung cancer stays, the four most common among patients hospitalized primarily for lung cancer were diagnostic bronchoscopy and biopsy of the bronchus (49%); lobectomy or pneumonectomy (31%); incision of pleura, thoracentesis, chest drainage (16%); and blood transfusion (11%).

The four most common procedures when lung cancer was the secondary diagnosis were blood transfusion (15%); respiratory intubation and mechanical ventilation (10%); incision of pleura, thoracentesis, chest drainage (9%); and diagnostic bronchoscopy and biopsy of the bronchus (8%).

Additional procedures that were common to all hospitalizations included therapeutic radiology, cancer chemotherapy, and upper gastrointestinal endoscopies and biopsies, according to the authors. ■

Three Measures May Predict Need for Ventilation in COPD

BY MITCHEL L. ZOLER
Elsevier Global Medical News

PHILADELPHIA — Three easily obtained clinical measures can predict who will probably need mechanical ventilation among newly hospitalized patients with an acute exacerbation of chronic obstructive pulmonary disease, based on an analysis of data from almost 100,000 patients.

Patients presenting to an emergency department with an acute exacerbation of chronic obstructive pulmonary disease (COPD) with a BUN level of greater than 25 mg/dL, altered mental status, and a pulse of more than 109 beats/minute had about an 11% rate of mechanical ventilation during their index hospitalization, Dr. Andrew F. Shorr, FCCP, reported at the annual meeting of the American College of Chest Physicians.

All three are simple measures that don't require blood gas measurements or invasive testing.
DR. SHORR, FCCP

In contrast, similar patients who lacked all three of those clinical signs had a 0.3% rate of mechanical ventilation later during their hospitalization, said Dr. Shorr, associate director for pulmonary and critical care medicine at the Washington (D.C.) Hospital Center.

Determining a patient's risk for needing mechanical ventilation early during hospitalization is important, he said in an interview, because "if you know there is a high risk, you can arrange closer monitoring and an earlier start to ventilatory support. That's better than waiting until the patient is so sick that intubation is tenuous."

Also, "you don't want to put a patient [who has a high risk for needing mechanical ventilation] in an unmonitored room," he added. "With identification of high risk, you can put them in higher-level care while they declare themselves by getting better or worse."

Dr. Shorr and his associates reviewed 98,036 patients who were admitted to any of 191 U.S. hospitals for acute exacerbation of COPD during 2004-2006. The sample was randomized into a derivation cohort and a validation cohort. The researchers then took the derivation cohort and used classification and regression tree analysis to assess demographic, clinical, and hospital characteristics to find parameters that best distinguished patients who required mechanical ventilation from those who did not.

That analysis showed that three parameters worked well together to segregate patients into low- and high-risk groups. The three parameters were then tested using the validation cohort, and the results confirmed the initial finding (see table). In both cohorts, the three parameters accounted for slightly more than three quarters of the risk for mechanical ventilation.

"These three markers don't have anything to do with the lungs," Dr. Shorr noted. "Our hypothesis is that they are simple markers for end-stage organ dysfunction." A BUN level of greater than 25 mg/dL is a marker for volume depletion. Altered mental status is a marker for a patient who is hypoxic or hypercarbic. And a pulse rate of more than 109 beats/minute is a marker for shock, hypoxia, or acidosis.

All three are simple measures that don't require blood gas measurements or invasive testing, and they can be assessed with little interobserver variability.

At last year's annual meeting of the American College of Chest Physicians, Dr. Shorr and his associates reported that the same three measures could help predict the risk of death in patients hospitalized for an acute exacerbation of COPD. Patients who met all three criteria had a mortality rate of nearly 14%, compared with a rate of less than 1% among patients who met none of the three criteria. ■

Quantifying the Risk of Mechanical Ventilation In COPD Patients

Number of assessment measures positive at time of initial hospitalization	Mechanical ventilation rate during hospitalization in the derivation cohort	Mechanical ventilation rate during hospitalization in the validation cohort
0	0.3%	0.3%
1	1.2%	1.2%
2	5.4%	5.5%
3	10.1%	12.4%

Note: The three measures assessed for this analysis were BUN level > 25 mg/dL; altered mental status; pulse rate > 109 beats/minute.
Source: Dr. Shorr

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Dr. Nicola Hanania, FCCP, comments: *This study identifies factors that predict the need for mechanical ventilation in patients with COPD exacerbation. Of interest, none of these factors is related to the respiratory mechanics or the clinical presentation of these patients, which include respiratory muscle fatigue, hypercapnia, and hypoxemia, and which are usually deranged in this population. Therefore, even though this study sheds new light on predictors that may help clinicians when assessing patients with COPD exacerbation, these predictors should only be used in the context of the clinical presentation of the patient and his/her initial response to therapy.*

Statins Curbed VTE in Patients With Solid Organ Tumors

BY MITCHEL L. ZOLER
Elsevier Global Medical News

PHILADELPHIA — Statin treatment was linked with a significantly reduced risk for venous thromboembolism in a case-control, observational study of 740 patients with solid organ tumors at one center.

Use of statins during the weeks prior to hospitalization for a solid tumor was linked with a 67% reduction in VTE risk, compared with cancer patients who had never used a statin or had discontinued use at least 2 months before their hospitalization.

The study was reported by Dr. Danai Khemasuwan at the annual meeting of the American College of Chest Physicians.

The results came from an analysis that controlled for several possible confounding factors, reported Dr. Khemasuwan, an internist at Albert Einstein Medical Center in Philadelphia.

The incidence of VTE among statin users was 8%, compared with 21% in nonusers.
DR. KHEMASUWAN

Treatment within the prior 2 months was considered current because results from prior studies had reported that the effect of statins on lowering serum levels of C-reactive protein persists for 2 months, he said.

"It's fascinating that the effects of statins may extend to the venous circulation," commented Dr. David D. Gutterman, a professor of medicine at the Medical College of Wisconsin in Milwaukee. "Statins improve endothelial function [in arteries] and it may be that the same improvement occurs on the venous side."

Statins may also reduce VTE risk by its effect on lipids, by its anti-inflammatory effect, or by an antithrombotic effect, said Dr. Khemasuwan. "Most data on statins are on the lipid-lowering effect and effects on the arterial circulation. I thought, what about the venous circulation?"

The study reviewed 740 consecutive patients who were admitted to Albert Einstein Medical Center during October 2004–September 2007 with a diagnosis of cancer of the breast, lung, colon, prostate, stomach, esophagus, pancreas, ovary, kidney, or brain. The study excluded patients who had been treated with an anticoagulant prior to hospitalization. Their average age was 65 years, 52% were women, and 76% were African American.

Current or recent statin use was identified in 194 patients (26%); 546 patients (74%) had never been treated with a statin or had stopped treatment more than 2 months before their hospitalization. This analysis did not subdivide patients by the type of statin they took or the dosage. The most common statins used were atorvastatin (Lipitor), rosuvastatin (Crestor), and simvastatin (Zocor).

During hospitalization, VTE occurred in 132 patients (18%). The incidence among statin users was 8%, compared with 21% in nonusers. In a multivariate analysis that controlled for smoking status, documented metastatic disease, current chemotherapy, immobilization, and treatment with aspirin, patients who were current or recent statin users had a 0.33 relative risk for VTE, compared with the nonusers, Dr. Khemasuwan reported.

The study did not receive any commercial support, and Dr. Khemasuwan had no financial disclosures.

To see a video disussion with Dr. Khemasuwan about his findings, go to www.youtube.com and search for "ElsGlobalMedicalNews." ■

Dr. Keith Wille, FCCP, comments: *The findings reported by Dr. Khemasuwan and colleagues are intriguing and add to a growing body of literature suggesting a beneficial role for statins in the prevention of VTE. Although prior studies are conflicting, there is some evidence that high D-dimer levels, which have been associated with recurrent VTE, can be lowered by statin therapy (J. Thromb. Haemost. 2004;2:718-25). Furthermore, retrospective studies (Arch. Intern. Med. 2001;161:1405-10; Fundam. Clin. Pharmacol. 2004;18:477-82) and one prospective trial (Ann. Intern. Med. 2000;132:689-96) offer indirect evidence that statins may protect against VTE occurrence. At present, no study has directly addressed whether or not statins prevent VTE in a randomized, prospective manner; so, the above studies should be interpreted with caution. However, Dr. Khemasuwan's results do highlight the need for prospective statin trials in patients with high VTE risk to answer this important clinical question.*

Method May Have Pitfalls

Oxygenation • *from page 1*

Their mean APACHE (Acute Physiology and Chronic Health Evaluation) II score was 27, and they had a median of two failed organs. Although the study was slated to enroll 200 patients, it was stopped at 61 after proving its primary end point of a clinically critical difference in oxygen saturation between the two groups (PaO_2:FIO_2 80 mm Hg higher in experimental patients than control patients at 72 hours).

All patients underwent esophageal pressure measurement before they were randomized. An esophageal balloon catheter was passed into the stomach and then withdrawn into the esophagus to a depth of 40 cm from the incisors, to record esophageal pressure during mechanical ventilation. For one-third of the patients, it was not possible to pass the balloon into the stomach; cardiac artifact confirmed placement in the esophagus.

These initial measurements guided ventilator settings for patients who were randomized to esophageal pressure guidance. Tidal volume was set at 6 mL/kg of predicted body weight. Positive end-expiratory pressure (PEEP) was set to achieve a transpulmonary pressure of 0-10 cm of water, according to a sliding scale based on partial pressure of arterial oxygen and the fraction of inspired oxygen (PaO_2:FIO_2).

Control patients were ventilated with a low tidal volume strategy of 6 mL/kg of predicted body weight, with PEEP based on the value of PaO_2:FIO_2. Oxygenation measurements were taken at 5 minutes after ventilator initiation and again at 24, 48, and 72 hours.

Significant between-group differences in PaO_2:FIO_2 favoring the experimental group occurred at 24 hours. By 72 hours, PaO_2:FIO_2 improved by 131 mm Hg in the esophageal-pressure group and by 49 mm Hg in the control group, a significant difference. Respiratory system compliance improved in both groups, but was significantly higher in the esophageal pressure group (45 vs. 35 mL/cm of water at 72 hours).

PEEP differences were apparent on the first day of therapy. By 24 hours, the between-group difference in PEEP was 8 cm of water; at 72 hours, mean PEEP in the esophageal pressure group was 17 cm, compared with 10 cm of water in the control group, a highly significant difference.

At all time points from 24 hours forward, mean transpulmonary end-expiratory pressure was above 0 in the esophageal-pressure group, but remained negative in the control group.

Clinical outcomes were classified as secondary in this study. There were no significant differences between the groups in ventilator-free days or lengths of ICU stay. By day 28, 17 of the 61 patients had died. Unadjusted mortality was lower in the experimental group, but not significantly so (17% vs. 39%). After adjustment for the initial APACHE II score, however, the difference in 28-day mortality became significant: Patients in the experimental group were 54% less likely to have died.

At 180 days, the mortality rate between groups did not differ significantly, although after adjustment for initial APACHE II scores, those in the experimental group were 49% less likely to have died than those in the control group.

Dr. Talmor and his coinvestigators admitted that the assessment of transpulmonary pressure via esophageal pressure is a tricky business. "There is currently mistrust of the use of esophageal pressure measurements in supine, critically ill patients, largely because of possible artifacts associated with body position and lung pathological conditions," they wrote.

Dr. Bernard, a pulmonary and critical care medicine specialist at Vanderbilt University Medical Center, Nashville, Tenn., agreed. "Although the concept of using transpulmonary pressure is straightforward and physiologically sound, using esophageal pressure as a surrogate for pleural pressure needs a lot more study before we can use it clinically."

His editorial pointed out some potential problems (N. Engl. J. Med. 2008;359:2166-8). "Many assumptions must be made in order to accept that pressure in the esophagus dynamically and accurately reflects pleural pressure. For instance, we must assume that the balloon pressure reflects the esophageal pressure, that the transmural pressure in the esophagus is 0 cm of water, [and] that the esophagus is not compressed by intrathoracic structures such as the heart."

Finally, Dr. Bernard said in the interview, improved oxygenation doesn't necessarily translate into improved clinical outcomes.

In the ALVEOLI (Assessment of Low Tidal Volume and Elevated End-Expiratory Volume to Obviate Lung Injury) trial, "oxygen status was greatly improved, but there was no improvement in survival. You can always improve oxygenation by giving higher PEEP, but that doesn't necessarily mean your clinical outcomes are going to be better," he said. ■

Older Transfused Blood May Boost Infection Rate

BY MITCHEL L. ZOLER
Elsevier Global Medical News

PHILADELPHIA — For a transfusion, fresher blood is better.

Patients who received a first unit of packed red blood cells that had been stored for at least 26 days following donation were twice as likely to develop a nosocomial infection as patients who received more recently donated blood, Dr. Raquel Nahra said at the annual meeting of the American College of Chest Physicians.

But the practical implication of the finding is not to simply discard old blood sooner. "From our results, it's clear that the younger the blood the less the risk of infection, but it's hard to say we should just use fresher blood for all patients. We can't just discard blood that is older than 26 days," said Dr. Nahra, an infectious diseases physician at Cooper University Hospital in Camden, N.J. Current practice in the United States is to discard blood once it is 42 days old, she noted.

Patients had a 2.9-fold risk of infection when they received any unit that was at least 29 days old.
DR. NAHRA

An alternative response is to limit blood transfusions to those that are absolutely necessary, thereby relieving pressure on the banked blood supply. "If a more restrictive transfusion strategy were applied, it would skew the blood supply to a younger age," said Dr. David R, Gerber, FCCP, associate director of the ICU at Cooper University Hospital and senior investigator for the study.

Standard practice at most U.S. hospitals has moved to a more restrictive transfusion approach in recent years, commented Dr. Mark J. Rosen, FCCP, chief of the divisions of pulmonary, critical care, and sleep medicine at North Shore–University Hospital and Long Island Jewish Medical Center in New Hyde Park, N.Y. "We used to transfuse everyone to a hemoglobin of 10 g/dL. Now, if a patient has a hemoglobin of 7 g/dL or higher and is doing okay and does not have coronary disease or another reason to get better oxygen delivery, we generally don't transfuse," he said.

The study by Dr. Nahra, Dr. Gerber, and their associates reviewed 421 patients who received one or more units of packed red blood cells at Cooper University Hospital from July 2003 to September 2006. The median age of the patients was 66 years, and they spent a median of 5 days in the ICU and a median of 17 days in the hospital. The analysis looked at the age of the oldest unit of blood they received, the age of the first unit of blood, and the total number of units they received.

The average age of the blood they received was 26 days. Eleven patients died, and 57 developed nosocomial infections.

In addition to showing a doubled risk of infection when the first unit of blood was at least 26 days old, the analysis showed that patients had a 2.9-fold risk of infection when they received any unit that was at least 29 days old. Both of those were statistically significant associations, Dr. Nahra reported.

The analysis failed to find any significant link between the age of blood transfused and the rate of death or length of stay in the hospital or ICU. Patients who received five or more units of packed red cells were significantly more likely to develop at least one nosocomial infection, compared with patients who received less blood.

Red cells stored for more than 2 weeks begin to release increased amounts of proinflammatory cytokines, which may underlie an increased susceptibility to infection, Dr. Nahra said. ■

Dr. Vera de Palo, FCCP, comments:
Hospital quality groups are implementing strategies to reduce the risk of nosocomial infection, thus making hospital care safer for patients. Improving hand hygiene, limiting urinary and bloodstream catheter use to as short a time course as necessary, utilizing specific insertion practices for bloodstream catheters, and daily assessment for extubation from mechanical ventilation are just a few of the quality improvement actions that have been adopted. The study by Dr. Nahra, Dr. Gerber, and their associates focuses on another important variable that confers risk for the development of nosocomial infection. Until further study advances practices that can help reduce this risk, the best approach seems to be the adoption of a transfusion-conservative approach in patients who do not have coronary disease or another reason for increasing oxygen delivery.

Pulmonary Perspectives

Does Regular Marijuana Smoking Lead to Pulmonary Disease? Part 2: Marijuana Smoking and Lung Cancer

Although observations suggest a link between the two, research to date has not revealed a clear association.

Evidence for a Link Between Marijuana Use and Lung Cancer

There are five observations that suggest a link between marijuana smoking and the development of lung cancer. First, marijuana smoke contains several of the same carcinogens and cocarcinogens as tobacco smoke, including vinyl chlorides, phenols, nitrosamines, reactive oxygen species, and various pro-carcinogenic polycyclic aromatic hydrocarbons (PAHs). In fact, benzo[α]pyrene, a PAH that plays a prominent role in human cancer, is present in marijuana tar at a higher concentration than in tobacco tar.

Second, approximately a fourfold amount of the tar from the smoke of marijuana than that from the same quantity of tobacco is deposited in the respiratory tract due to differences in the manner in which marijuana and tobacco are smoked,[1] thus magnifying the level of exposure to carcinogens from each marijuana cigarette.

Third, bronchial biopsy specimens from heavy, regular smokers of marijuana only have shown widespread histopathologic alterations (including squamous metaplasia and nuclear atypia) that have been associated with the subsequent development of bronchogenic carcinoma in tobacco smokers.[2] At the same time, immunohistochemical studies performed on these biopsy samples have shown overexpression of Ki-67 (a nuclear proliferation marker), EGFR (epidermal growth factor receptor), and DNA ploidy (a marker of genetic instability), consistent with dysregulated growth and pre-tumor progression.[3]

Fourth, intraperitoneal administration of delta^9-tetrahydrocannabinol (THC), the major psychoactive ingredient in marijuana, to immunocompetent mice implanted with non–small cell lung cancer cell lines led to acceleration in lung tumor growth compared with mice given vehicle alone.[4] Tissue assays from the tumors and spleens resected from THC-treated mice showed overproduction of immunosuppressive cytokines (IL-10 and TGF-β) and underproduction of immunostimulatory cytokines (IL-2 and INF-γ) compared with control mice, suggesting THC-induced suppression of protective immune responses to tumor growth. The latter suggestion is supported by findings that the THC -induced acceleration of lung tumor growth was blocked by pretreatment with monoclonal antibodies against IL-10 and TGF-β. Moreover, the augmentation of tumor cell growth by THC was also blocked by coadministration of a selective antagonist against CB2 receptors (which are expressed primarily on immune cells). Therefore, THC accelerates tumor growth *in vivo* by a cytokine-dependent and CB2 receptor-mediated mechanism that impairs the development of antitumor immunity.

CASE-CONTROL STUDIES HAVE YIELDED INCONSISTENT FINDINGS CONCERNING THE ASSOCIATION BETWEEN HEAVY MARIJUANA USE AND THE OCCURRENCE OF LUNG CANCER.

Fifth, that marijuana may be a risk factor for respiratory cancer is further suggested by several small case series that reported an unusually high proportion of marijuana use among young individuals (< 45 years old) in whom lung cancer[5] or upper airway cancers[6-9] were diagnosed, compared to the prevalence of marijuana use in similarly aged individuals in the general population.

Evidence Against a Link Between Marijuana Use and Lung Cancer

In contrast to the findings already noted regarding the augmentation of lung cancer growth by THC in a murine model that was attributable to THC-related suppression of the host's protective immune response against tumor growth, several investigators have demonstrated an antitumoral effect of THC and other cannabinoids on a variety of malignancies in both cell culture systems and animal models.[10,11] Such antitumoral effects have been attributed to the antiproliferative, preapoptotic, and antiangiogenic properties of cannabinoids.

► Epidemiologic Studies

Despite the apparent association between marijuana use and respiratory cancer suggested by case series, such series do not provide strong evidence of a causal association, since they are uncontrolled, indicating the need for well-designed epidemiologic studies. Several controlled epidemiologic studies have addressed this question with conflicting results, as described below.

Retrospective analysis of data from a large cohort of 65,000 subscribers to a Northern California health maintenance organization failed to find an elevated risk for tobacco-related malignancy, including lung and upper airway cancer, among ever or current marijuana smokers (MS), after adjustment for tobacco smoking.[12] Weaknesses of this study included the relatively young age of the participants at the end of follow-up and inclusion of relatively few long-term or heavy MS.[12]

Three case-control studies that examined cannabis use as a possible risk factor for lung cancer were conducted in North Africa.[13-15]

A Tunisian study, including 110 patients with lung cancer and 110 control subjects, reported a markedly elevated odds ratio (OR) for ever use of cannabis (OR=8.2, 95% CI, 1.3-15.5).[13] However, this study did not control for the confounding influence of concomitant use of tobacco, which is commonly mixed with cannabis.

A second lung cancer case-control study from Northern Morocco that included 118 patients with cancer and 235 control subjects assessed the association between lung cancer and the use of hashish (the oily resin derived from the *Cannabis sativa* plant) and kiff (a powdery preparation from the dried flowers of the female cannabis plant mixed with tobacco), with or without snuff.[14] Results indicated that the combined use of hashish/kiff and snuff was associated with a 6.67-fold greater risk (95% CI, 1.65-26.90) for developing lung cancer, while the risk was much lower for the use of hashish/kiff without snuff (1.93-fold [95% CI, 0.57-6.58]) and lower still for the use of snuff only (OR=1.06 [95% CI, 0.33-3.47]). However, since kiff includes tobacco, the effect of cannabis independent of tobacco cannot be assessed in this study.

A more recent Tunisian hospital-based case-control study[15] that included 149 incident lung cancer cases and 188 control cases revealed an odds ratio for the past use of marijuana and lung cancer of 4.1 (95% CI, 0.9-9.0) after apparent adjustment for age, tobacco use, and occupational exposure. However, because of the traditional practice in this society of mixing tobacco with marijuana before smoking, it was not possible for the authors to fully adjust for the confounding effect of tobacco.

Two well-designed case-control studies that were prospectively planned to estimate the effects of marijuana use on lung cancer, one in Los Angeles[16] and the other in New Zealand,[17] have been published within the past 2 years.

The Los Angeles study included, over a 5-year period, 611 patients with lung cancer 65 years of age and 1,040 control subjects matched on age, gender, and residential neighborhood.[16] All subjects underwent a detailed face-to-face interview eliciting a detailed lifetime history of drug use (including tobacco), as well as relevant information concerning occupational and environmental exposures, diet, family history of cancer, and socioeconomic characteristics that could potentially influence the occurrence of cancer. A comparable proportion of the patients and control subjects were either former MS (43.8% and 42.3%, respectively) or current MS (6.7% and 11.4%, respectively). Also, over 10% of both patients and control subjects had reported having used marijuana relatively heavily (at least 10 joint-years). Using logistic regression adjusting for potentially confounding covariates (age, gender, race, education, tobacco history, etc), the ORs for the association between marijuana use and lung cancer were below 1.0 in every category of marijuana use, including users from 10 to 60 joint-years, indicating a null association and no trend toward a dose-response relationship. By contrast, the adjusted ORs for the association between tobacco and marijuana use ranged from 1.3 (0.96,1.8) to 21 (14,32) for tobacco smokers, with pack-year histories ranging from less than one pack a day to over two packs a day with a clear dose-response relationship.

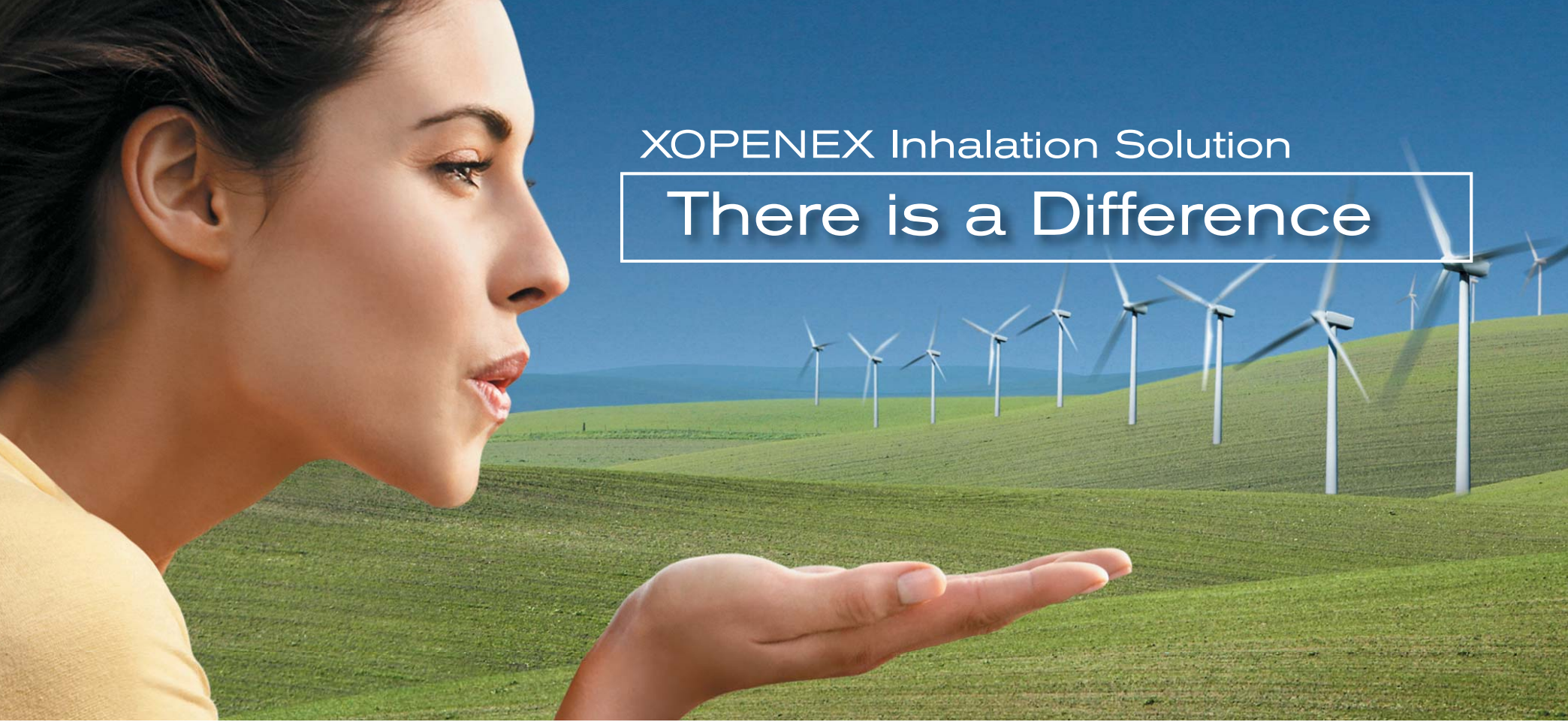
The New Zealand study identified, over a 4½-year period, 79 patients with lung cancer 55 years of age and 324 randomly selected control subjects matched for age.[17] All subjects underwent interviewer-administered questionnaires to assess possible risk factors for lung cancer. Relatively few patients (n=6) and control subjects (n=14) were included in the highest (*ie*, the third) tertile of marijuana use (>10.5 joint-years). Multivariate logistic regression was used to estimate the association of lung cancer risk with marijuana smoking, adjusting for relevant variables.

The results indicated no significant association of marijuana smoking overall with lung cancer (relative risk [RR] 1.2 [95% CI, 0.5-2.6]). The RR was 0.3 (95% CI, 0.1-1.3) in the 1st tertile, 0.9 (95% CI, 0.3-2.9) in the 2nd tertile, and 5.7 (95% CI, 1.5-21.6) in the 3rd tertile of marijuana use. When joint-years of use were fitted as a continuous variable, a significant increasing risk of 8% with each joint-year of use was found (RR 1.08 [95% CI, 1.02-1.18]). The authors concluded that long-term marijuana use increases the risk of lung cancer in young adults.

Limitations of this study include the fact that it is a small study (only 79 cases) and that only 14 patients and 4 of the 324 control subjects (1.2%) smoked marijuana heavily in their lifetime (>10.5 joint-years), in contrast to the Los Angeles study in which 115 out of the 1,016 control subjects

Continued on page 10

Dr. Gene L. Colice, FCCP
Editor, *Pulmonary Perspectives*



Indication

XOPENEX® (levalbuterol HCl) Inhalation Solution is indicated for the treatment or prevention of bronchospasm in adults, adolescents, and children 6 years of age and older with reversible obstructive airway disease.

Important Safety Information

Patients receiving the highest dose of XOPENEX Inhalation Solution should be monitored closely for adverse effects, and the risk of such effects should be balanced against the potential for improved efficacy. XOPENEX Inhalation Solution is contraindicated in patients with a history of hypersensitivity to levalbuterol hydrochloride or levalbuterol tartrate, respectively, racemic albuterol, or any component of the drug product. XOPENEX Inhalation Solution and other β-agonists can produce paradoxical bronchospasm, which may be life threatening: see the accompanying Prescribing Information regarding potential drug interaction with β-blockers, diuretics, digoxin, or MAOI and tricyclic antidepressants. If additional adrenergic drugs, including other short-acting sympathomimetic bronchodilators or epinephrine, are to be administered by any route, they should be used with caution to avoid deleterious cardiovascular effects. Due to the cardiovascular side effects associated with β-agonists, caution is generally recommended for patients with cardiovascular disorders (especially coronary insufficiency, cardiac arrhythmias, and hypertension), diabetes, hyperthyroidism, or convulsive disorders.

In patients aged 6 to 11 years, the most common adverse events (occurring in ≥2% of patients receiving XOPENEX Inhalation Solution at either 0.31 mg or 0.63 mg and more frequently than patients receiving placebo) were headache, rhinitis, pharyngitis, asthma, fever, viral infection, rash, accidental injury, diarrhea, asthenia, lymphadenopathy, and urticaria.

In patients 12 years and older, the most common adverse events (occurring in ≥2% of patients receiving XOPENEX Inhalation Solution at either 0.63 mg or 1.25 mg and more frequently than patients receiving placebo) were viral infection, rhinitis, nervousness, tremor, flu syndrome, sinusitis, accidental injury, anxiety, cough increased, pain, tachycardia, turbinate edema, migraine, dizziness, dyspepsia, and leg cramps.

Relief From the Start,
When Your Patients Need It Most

- **Proven.** XOPENEX Inhalation Solution (0.63 mg) response was clinically comparable to racemic albuterol sulfate (2.5 mg)[1]
- **Rapid.** 44% mean improvement from baseline FEV_1 within minutes (XOPENEX 1.25 mg; day 0, week 0)*[2]
  - From a subset of patients with baseline FEV_1 <60% of predicted (n=36)[2]
    - Over the course of the study, mean time to 15% improvement in FEV_1 was 9 minutes (1.25 mg) and 17 minutes (0.63 mg)[3]
  - In the overall population over the course of the study, the mean time to a 15% increase in FEV_1 was 10 minutes (1.25 mg) and 17 minutes (0.63 mg)[1]
- **Sustained.** >15% improvement up to 8 hours postdose in some patients[1]
  - Mean duration of effect measured by a >15% increase in FEV_1 was approximately 5 hours (0.63 mg) and 6 hours (1.25 mg)

Proven Safety Profile

- Incidence of nervousness and tremor was low and comparable to placebo (0.63-mg dose)[2]
- The 1.25-mg dose of XOPENEX Inhalation Solution produced a slightly higher rate of systemic β-adrenergic adverse events than the 2.5-mg dose of racemic albuterol[1]

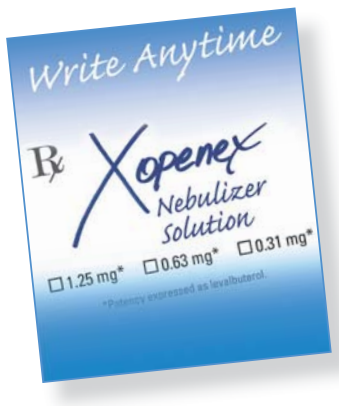
Be Sure to Write XOPENEX Inhalation Solution
For Your Patients to Get XOPENEX Inhalation Solution

Prepare for the Season
For Samples of XOPENEX, Ask Your Sepracor Representative

*From a randomized, double-blind, parallel-group, 4-week clinical trial of patients aged 12 years or older (n=362) with moderate-to-severe asthma. The primary end point was peak change in FEV_1 after 4 weeks. XOPENEX Inhalation Solution was significantly better than placebo ($P < .001$).

References: 1. XOPENEX Inhalation Solution (prescribing information). Marlborough, MA: Sepracor Inc; 2007. **2.** Nelson HS, Bensch G, Pleskow WW, et al. Improved bronchodilation with levalbuterol compared with racemic albuterol in patients with asthma. *J Allergy Clin Immunol.* 1998;102(6, pt 1):943-952. **3.** Data on file. CSR 051-024. Sepracor Inc, Marlborough, MA.

Please see Brief Summary of complete Prescribing Information on following page.



Xopenex®
(levalbuterol HCl) Inhalation Solution
0.31 mg, 0.63 mg and 1.25 mg[x]
[x]Potency expressed as levalbuterol.

Efficacy and Safety—in the Same Breath

Continued from page 8

(11.3%) reported >10 joint-years of marijuana use. It seems highly likely, therefore, particularly in view of the negative results of the much larger Los Angeles study, that the small sample size of the New Zealand study led to markedly inflated estimates of the association of marijuana use with lung cancer.

Limitations of all of the foregoing epidemiologic studies include possible underreporting in countries where marijuana use is illegal, sampling bias, and failure to capture heavy or long-term marijuana users in the study population.

Further well-designed, large-scale epidemiologic studies that include a detailed assessment of marijuana exposure (frequency, duration, and amount used) and that adjust adequately for tobacco smoking and other known risk factors are required to more definitively answer the question whether smoking of marijuana is or is not associated with an increased risk of respiratory cancer.

The answer to this question is important for weighing the benefits and risks of medicinal marijuana use and clarifying the public health message regarding marijuana use.

Summary

Prospectively designed population-based case-control studies have yielded inconsistent findings concerning the association between heavy marijuana use and the occurrence of lung cancer. Given the increasing impact that lung cancer is having on world health, it is clear that well-designed studies are required to resolve these questions. ■

Dr. Donald P. Tashkin, FCCP
Professor of Medicine
Division of Pulmonary and Critical Care Medicine
David Geffen School of Medicine at UCLA
Los Angeles, CA

Editor's Insight

Dr Tashkin raises a provocative and clinically relevant concern by discussing literature I do not regularly review about lung cancer and marijuana smoking.

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NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

PRESIDENT'S REPORT

The Physician Manpower Debate

BY DR. JAMES A. L. MATHERS, JR., FCCP

In addition to its leadership in medical education, the College has had an active advocacy program. This program, initially focused on tobacco control, has expanded to address patient care issues, such as access to appropriate oxygen therapy, pulmonary rehabilitation, and sleep therapy. The College has also highlighted our concern about a workforce shortage in the face of increasing demand.

Within the health-care policy debate, a controversy is building over the relevance of physician manpower.

Many physician societies endorse the concept that there is an inadequate number of physicians to meet current demand and project an increasing gap between demand and supply as the population ages and expands. The American College of Physicians and the American College of Chest Physicians have both promoted legislation in the 110th Congress to address the predicted shortfall.

On the other hand, recent published reports suggest that not only do we have an adequate overall supply but that an increased number of physicians or a higher level of training does not produce better access or better outcomes.

In the June 2008 issue of the *Annals of Internal Medicine,* a report maintains that critical care delivered by trained intensivists does not lead to better outcomes compared with general internists. In an article published in the April 17, 2008, *New England Journal of Medicine*, the authors stated: "As we see it, increasing the number of physicians will make our health-care system worse, not better."

In 1992, the highly respected advisors to federal policy makers, the Council on Graduate Medical Education (COGME), released a report foreseeing an excess number of physicians, particularly those with advanced medical training. Their expressed opinion was that further increases in the relative number of physicians with specialty training would hinder federal efforts to contain costs. In 1994, COGME released its follow-up report with specific recommendations for federal legislation.

In 1996, six major medical organizations contributed to an American Association of Medical Colleges (AAMC) consensus statement that agreed with COGME's concerns.

Some of the COGME recommendations were incorporated into the Balanced Budget Act of 1997. This act limited the total number of full-time resident positions to those in existence on December 31, 1996. Furthermore, provisions were included to encourage a voluntary reduction in resident positions through the use of incentive payments to hospitals. If all of COGME's recommendations had been adopted and their goals attained, the nation would currently be producing 25% fewer physicians annually.

In its report released in 2005, COGME reversed the positions taken in 1992 and 1994 and recommended an increase of 3,000 medical school graduates by 2015. In 2006, the AAMC also reversed its position and has now recommended a substantial increase in medical school enrollment.

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NEWS FROM THE COLLEGE

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The COMPACCS study, produced through a partnership of ACCP, SCCM, and ATS, and published in 2000, is well known to our membership. The findings were supported by a 2006 Health Resources and Services Administration report to Congress. Resulting legislation has been actively promoted by our Health Affairs Division. This legislation will expire at the end of the 110th Congress.

There have been remarkable advances in medical knowledge and technology since I graduated from medical school. Patients are living longer with more medical problems through access to a technological menu that includes some expensive items. When statistical comparisons are made using current data and relating it to data of previous decades, it appears that this detail is often overlooked.

Adherence to both rigid statistical analysis and imperfect outcome evaluations overlooks important realities of clinical practice. The current clinical practice environment does not encourage physician commitment to dealing with difficult medical problems.

My experience suggests that we have a substantial shortage of physicians willing to take responsibility for the care of patients with advanced disease and complex medical or surgical problems.

While the debate intensifies, my group practice, unable to find an adequate number of additional physicians, has adapted to the annual increase in demands for our services by the addition of physician extenders, an ICU telemedicine program, postponing retirement, and a close relationship with the hospitalist teams at each of our hospitals.

It remains difficult for me to understand how advisors to health policy makers at the federal level arrived at the conclusion that increased physician training leads to a decrease in the quality and efficiency of medical care.

An analysis based on a framework of statistics completely misses the dynamics of a community practice. ■

CHEST 2008 Abstracts Bring Nationwide Media Attention

The American College of Chest Physicians welcomed nationwide media coverage surrounding the scientific abstracts presented at CHEST 2008 in Philadelphia.

Abstracts generating the most media interest were related to a variety of consumer-focused topics, including the use of statins as a preventive therapy for blood clots; how stored blood may be linked to infection; and how the U.S. nicotine addiction rate is at a 15-year high.

These abstracts and many others resulted in hundreds of print, broadcast, and online stories around the world.

On a local level, the ACCP also benefited from the Philadelphia Phillies race to become Major League Baseball World Series Champions. The *Philadelphia Inquirer* newspaper mentioned the ACCP annual meeting in two stories related to the World Series and the many visitors to Philadelphia.

Although media coverage for the annual meeting is expected to continue throughout the year, preliminary results show that the ACCP and CHEST 2008 were mentioned in numerous top-tier media outlets, including:

- *USA Today*
- *Wall Street Journal*
- *New York Times*
- *Chicago Tribune*
- *Los Angeles Times*
- *Washington Post*
- *U.S. News and World Report*
- MSNBC

And over 200 preliminary television broadcast stories in such top markets as New York; Chicago; Los Angeles; Washington; Boston; and Philadelphia have been noted. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

Tribute, New Leadership at CHEST Foundation

CHEST Foundation Tribute for Dr. Forrest M. Bird a Great Success!

The CHEST Foundation celebrated the outstanding career and innovation of Forrest M. Bird, M.D., Ph.D., Sc.D., with a special tribute held during the 10th Annual Making a Difference Awards Dinner on Saturday, October 25, 2008, in Philadelphia. This fall, The CHEST Foundation established the Forrest M. Bird, M.D., Ph.D., Sc.D. Endowment in Mechanical Ventilation to honor Dr. Bird and his work in the area of mechanical ventilation. This endowment ensures that advances in education, research, and treatment of respiratory disease will have the support needed for continued advancements in this area of chest medicine.

Donations to the endowment are being accepted and can be made online at The Foundation Web site, www.chestfoundation.org. Contact Teri Ruiz at truiz@chestnet.org or at (847) 498-8308.

New Leadership for The CHEST Foundation

At CHEST 2008, The CHEST Foundation ushered in a new era of leadership. The term of Dr. D. Robert McCaffree, Master FCCP, as Chair ended, and the Board of Trustees thanked Dr. McCaffree for 10 years of leadership, commitment, and humanitarian efforts on behalf of The Foundation. Dr. McCaffree will continue his Board service in the role of Assistant Treasurer.

Dr. Robert G. Johnson, FCCP, became Chair of The CHEST Foundation for a 2-year term, and Dr. John C. Alexander, Jr., FCCP, assumed the role of President, also for a 2-year term. Dr. Gerard A. Silvestri, FCCP, will serve for the next 2 years in the position of Treasurer.

The CHEST Foundation thanked four Board members who rotated off in 2008: Dr. Asha V. Devereaux, FCCP; Dr. LeRoy M. Graham, FCCP; Dr. Anne E. O'Donnell, FCCP; and Dr. Mark J. Rosen, FCCP.

The CHEST Foundation Board also welcomed four newly nominated members to the Board: Dr. Paula J. Anderson, FCCP; Robert F. Barnett III; Dr. Janet R. Maurer, FCCP; and Dr. Wickii Vigneswaran, FCCP.

The CHEST Foundation is continually strengthened by the work of its Board members, past and present.

The CHEST Foundation's Annual Year-End Appeal Well Underway

The CHEST Foundation kicked off the annual 2008 year-end appeal during CHEST 2008 with an exciting matching gift fund and multiple challenges made by Foundation leadership. Your year-end contribution to a CHEST Foundation endowment fund or annual gift fund will support the important Foundation work throughout the year.

The CHEST Foundation shares your concerns about improving patient care and fostering clinical research. Your support enables The Foundation to continue quality programs to improve patient care and lung health. Support these ongoing and new initiatives through a tax-deductible contribution to The CHEST Foundation before year-end.

Donate online today by visiting www.chestfoundation.org, or by contacting Teri Ruiz at truiz@chestnet.org or (847) 498-8308. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Burnout and Stress in the ICU: Can They Be Prevented?

During the last year, a series of articles has been published in this Critical Care Commentary section covering topics from safety in critical care, delivering quality in critical care, moral distress in critical care, and optimal staffing in critical care. This article will offer a brief review and discuss burnout and stress prevention.

The pressure to deliver quantifiably safer critical care has increased over the last decade. In 1999, the Institute of Medicine published its seminal article, "To Err is Human: Building a Safer Health System," in which it was reported that 44,000 to 98,000 patients die per year from preventable errors. In 2001, the Agency for Healthcare Research and Quality (AHRQ) reported that over 770,000 patients were subject to preventable adverse events yearly. In 2002, The Joint Commission for Accreditation of Healthcare Organizations (JCAHO) (now called The Joint Commission) implemented its first set of national patient safety goals. The most recent set was published in 2008 (www.jointcommission.org).

Quantifying the delivery of quality care is a priority without clear measures. The Institute for Healthcare Improvement is in the midst of a "5 million lives" campaign that champions efforts to protect patients from medical harm through education and changes to care delivery process. Most of these efforts are focused on care provided in the high-risk ICU environment and are centered on the consistent application of widely accepted guidelines. This has been shown to be most readily attained in ICUs with engaged medical direction and a team approach to governance.

Critical Care Institute
American College of Chest Physicians

Historically, there are three different delivery models in critical care: the open ICU, the mixed ICU, and the closed ICU. A recent review of the provision of intensivist services has designated models as "low intensity" vs "high intensity." The open ICU, which is the traditional delivery system, has the primary attending physician deciding all aspects of the patient's care, with or without an intensivist in the role of consultant. This "low-intensity" model exists in two-thirds of the hospitals around the United States. About 500,000 people in the United States die per year in the ICU, and intensivists do not manage 360,000 of these patients. In the "high-intensity" models (mixed and closed), an intensivist provides all (closed) or some (mixed) of the critical care portion in collaboration (comanagement) with the primary attending physician. These models are seen in only one-third of US hospitals. It is estimated that 54,000 lives could be saved annually, just by changing from a "low-intensity" model to a "high-intensity" model.

The increasing demand for critical care and its providers is not solely a consequence of the perceived advantages of the high-intensity model of care. A major factor driving this demand is the aging of the American population (HRSA Report 2006. www.chestnet.org/practice/gr/hrsa.php). By 2020, the population older

Continued on following page

Investigators Discuss Studies on Anticholinergic Inhalers

Reprinted from the Tuesday, October 28, 2008, edition of the CHEST 2008 Daily News.

Most clinical practice guidelines for COPD currently recommend the daily use of either an anticholinergic inhaler or combo inhaler (high-dose inhaled corticosteroid plus long-acting $ß_2$-agonist) for those with an FEV_1 below 50% predicted. More than $5 billion has been spent on inhalers for COPD — about half that for tiotropium inhalers, which are used by more than 8 million patients. Most pulmonologists only think of dry mouth and urinary retention as bothersome side effects of inhaled anticholinergics; however, large studies published in 2008 reported a significantly increased risk of cardiovascular death.

These reports have prompted the manufacturers, distributors, and promoters of ipratropium and tiotropium to release the preliminary results from the UPLIFT study. Investigators discussed these results at Tuesday's session, "Are Heart Attacks a Side Effect of Anticholinergic Inhalers?" [during CHEST 2008 in Philadelphia]. Session faculty agreed not to discuss, summarize, or compare either the efficacy of various medications for any stage of COPD or the diagnosis and staging of COPD.

Speakers

▶ **Dr. Paul L. Enright,** Professor of Medicine at the University of Arizona in Tucson, discussed results from the Lung Health Study. "Research shows that inhaled tiotropium is absorbed," said Dr. Enright. He noted that sudden death and hospitalizations for malignant arrhythmias and heart attacks were significantly more common in participants randomized to inhaled ipratropium for 5 years (Anthonisen 2002). Inhaled tiotropium and ipratropium are absorbed and excreted in the urine (Caillaud 2007, Kesten 2006, Gross 1988), producing cardiovascular side effects similar to those seen when antimuscarinic drugs are given orally to patients with overactive bladder syndrome (Andersson 2007, Olshansky 2008). These studies suggest a mechanism for the adverse events seen in the Lung Health Study.

▶ **Dr. Donald P. Tashkin, FCCP,** Professor of Medicine, University of California Los Angeles, reported on the results from Boehringer's UPLIFT study. During 4 years of treatment, tiotropium was not associated with increased risk for all-cause mortality, increased risk for cardiovascular mortality, or increased risk for mortality associated with stroke or myocardial infarction (Tashkin 2008), consistent with the pooled results from previous Boehringer studies (Kesten 2006). "With regard to safety as seen in UPLIFT, treatment with tiotropium was associated with reduced mortality," said Dr. Tashkin. "There was evidence for reduced cardiac morbidity, including myocardial infarction. There was no evidence of any increased risk of stroke. And there was reduced lower respiratory morbidity, in particular, a decreased risk for respiratory failure."

▶ **Dr. Todd A. Lee,** with Hines VA Hospital in Hines, IL, and Northwestern University's Feinberg School of Medicine, presented results from the National Veterans Affairs Database. Among nearly 12,000 patients with newly diagnosed COPD who died during a 5-year follow-up period and for which cause of death was ascertained, the cause of death was respiratory for 2,405 patients and cardiovascular disease for 3,159 patients (Lee 2008). After adjusting for markers of COPD severity and cardiovascular disease, the use of ipratropium was significantly associated with increased CVD mortality, consistent with results from other large observational studies (Ringbaek 2003, Macie 2008). "The results of this study raise important questions about the safety of ipratropium in treating COPD," said Dr. Lee. "Better understanding of the risks involved with these medications can help clinicians and patients make more informed decisions as to whether risks outweigh the benefits."

▶ **Dr. Curt D. Furberg,** Professor of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC, presented a systematic review and meta-analysis of 12 high-quality, randomized controlled trials (RCTs) of tiotropium efficacy and 5 RCTs of ipratropium efficacy that reported cardiovascular adverse events (Singh 2008). Both of these inhaled anticholinergic drugs increased the risk of myocardial infarction, stroke, and cardiovascular death, but the risk of stroke was not statistically significant. The "number needed to harm" (via CVD death) was estimated at 40 per year for patients with COPD who were prescribed an inhaled anticholinergic.

"There are major flaws and limitations in sponsor's meta-analyses and in UPLIFT," said Dr. Furberg. "Safety data were either not disclosed or were incompletely reported. Safety data should always be fully presented in a timely manner, even if it is unfavorable to the sponsor."

▶ **Dr. R. Graham Barr,** Departments of Medicine and Epidemiology, Columbia University Medical Center, New York, NY, discussed how to compare conflicting study results. "The possible explanations for the conflicting results that we are seeing include study design differences, patient differences, outcome assessment, drug differences, different hypotheses, and even chance," Dr. Barr said. He added, "Anticholinergics have predictable beneficial and adverse effects. Risk-benefit decisions are best informed by RCT data. So, further objective evaluation of the safety of anticholinergics in RCTs is necessary."

Summary

The speakers agreed that risk factors for CVD, such as smoking and hypertension, are common in COPD patients at all stages, and smoking cessation is the only treatment proven to slow the progression of COPD in all stages and reduce the risk of death from CVD. Decisions regarding changes in the use of tiotropium and ipratropium in COPD patients should take into consideration the individual's degree of symptomatic improvement, preexisting comorbidities, patient comfort level, and potential benefits as weighed against possible increases in risk. ■

Additional information on this topic is available at www.chestnet.org/networks/airway_disorders/copd.php.

NEWS FROM THE COLLEGE

Continued from previous page

than 65 years will increase by 50%, and by 2030, it is estimated to increase by 100%. This elderly population uses a disproportionate share of critical care resources. In the United States, approximately 4 to 6 million people are admitted to an ICU each year, and there are about 6,000 ICUs across the country caring for approximately 55,000 people per day. Critical care accounts for about 10% of all hospital beds, with an annual budget of about $180 billion, or 0.7% of the gross domestic product. About 18 million bed-days are used annually by critical care, and patients older than 65 years use more than 50%. As a result of aging alone, the demand for intensivists would rise by 38% if all other factors remained the same.

The Leapfrog Group promulgated a set of four practices to improve the quality of inpatient care, one of which is the Leapfrog ICU physician staffing (IPS) standard (www.leapfroggroup.org). To meet the IPS standard, the ICU must be managed by an intensivist, and an intensivist must be present during daytime hours and must provide care exclusively in the ICU.

Many centers are exploring the use of telemedicine, especially at night, to increase the availability of intensivist services. While the start-up costs can be high, remotely linked intensivist services have been shown to improve outcomes in some settings (Breslow et al. *Crit Care Med* 2004;32:31). Whether these findings can be generalized is still unclear, and the relative merits of this approach, as opposed to other staffing methods, are unknown. In the 2006 Leapfrog survey, over 80% of the hospitals surveyed provided some financial support for intensivists, and 25% of those hospitals meeting the IPS standard provided full support for intensivists (Pronovost et al. *Crit Care Med* 2007;35:2256).

In academic centers, house staff coverage of ICUs is an option for meeting the IPS standard. Due to ACGME duty hour and curricular demands, and a reduction in the number of house staff in many centers, the supply of available house staff is decreasing, while the demand for ICU coverage is increasing. Acute care nurse practitioners (ACNPs) or physician assistants (PAs), as physician extenders, can provide first-line ICU care in off-hours at a lower cost than intensivist coverage. In 1997, fewer than 10% of ICUs employed ACNPs or PAs (Brilli et al. *Crit Care Med* 2001;29:2007).

A recent study examined the impact of providing 24/7 continuous, rather than on-demand, attending coverage in a single medical ICU that was staffed by residents and fellows at all times (Gajic et al. *Crit Care Med* 2008;36:36). Continuous, attending physician coverage was associated with a small, statistically insignificant reduction in readmission to the ICU with improved patient satisfaction and a modest increase in adherence to recommended processes of care (to which there was already very high adherence). There were no changes seen in length of stay or mortality. The marginal benefit of continuous intensivist coverage requires additional study in different settings and with various models of care.

Factors other than staff numbers, staff orientation (intensivist teams, etc), and staff schedules play a significant role in the present and future of critical care. As we wrestle with the definition and measurement of quality critical care, we generally do not look at the human factors involved. Our quality measurements focus on things and processes (including mortality figures) but do not usually focus on the burden on the patient, his or her family, and the care-giving staff. A growing body of literature, mostly in nursing, has started to look at the factors and consequences of "moral distress" on the staff and the patients. "Moral distress" is a multifactorial process where the caregivers, knowing what they believe is right, cannot accomplish their goal; or, for other social, moral, legal, or ethical concerns, are forced to act in ways that actually make things worse (*ie*, prolonging suffering or not doing enough). This perceived conflict is cited as a primary reason for nurses who leave nursing. Conversely, physicians denied this as a cause. This difference between physicians and nurses is significant. Nurses, as the predominant bedside caregivers, might focus on palliative care to end suffering, whereas physicians may not want to give up too quickly, no matter how bleak the outcome seems (Hamric et al. *Crit Care Med* 2007;35:422). These unresolved issues, if unchecked, may lead to feelings of futility, apathy, anger, and burnout.

Burnout and mental fatigue remain a growing and yet underrecognized problem in critical care. Given the demands of the ICU, and the fact that "perfect" outcomes are impossible to always achieve, mounting pressures are inevitable. As we continue to demand measurable perfection in an imperfect system, we add to these burdens and accelerate the very problems we are trying to avoid.

A number of European studies (Kinzl et al. *Deutsch Med Wochenschr* 2006;131:2461; Raggio. *Minerva Anestesiol* 2007;195) specifically looking at burnout in ICUs reveal that approximately 25% of ICU physicians are at significant risk for burnout or are already there, with another 20% not far behind. Male and female doctors responded to these pressures differently and manifested different symptoms spanning the burnout "spectrum." Using multiple psychometric tests, predominantly the Maslach Burnout Inventory, these authors describe the different symptoms manifested. Men tended to demonstrate depersonalization, aggressive-anger, and extreme rationalization. Women showed introspection–withdrawal, emotional exhaustion, and depression-disheartenment symptoms.

Some of the factors contributing to burnout are certainly addressable, but others are part of the nature of practicing critical care medicine. Environmental factors, such as shift work, unknown workloads, varying demands, and even ambient temperatures and noise contribute to stress.

Factors that can decrease stress and burnout are multidisciplinary rounds, daily goal sheets, conflict resolution, defined medical and nursing leadership, adequate staffing, and use of practice protocols. A collaborative approach to care and goal-setting has also been shown to be correlated with reduced dissatisfaction and stress. However, the perceptions of the success of collaboration can differ among groups —with physicians perceiving that collaboration is successful more frequently than nurses (Hamric et al. *Crit Care Med* 2007;35:422).

As the world of critical care continues to evolve, it remains a daunting task to simultaneously provide quality care, safety, and adequate staffing; decrease burnout and moral distress; and meet some seemingly arbitrary process or quality measures. More definitive measures and clearer collaboration are required for the practice of critical care to continue to grow and evolve. ■

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This Month in *CHEST*: Editor's Picks

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

▶ **Mannose-Binding Lectin Genotypes in Susceptibility to Community-Acquired Pneumonia.** *By Dr. H. Endeman, et al.*
▶ **Obesity and Persisting Sleep Apnea After Adenotonsillectomy in Greek Children.** *By Dr. M.T. Apostolidou, et al.*
▶ **Evaluation of Chronic Cough in Children.** *By Dr. S. Asilsoy, et al.*
▶ **The Asthma-Mental Health Nexus in a Population-Based Sample of the United States.** *By Dr. T. H. Chun, et al.*

Transparency in Health Care
▶ **Perspectives on Continuing Education in the Health Professions: Improving Health Care Through Lifelong Learning.** *By Dr. D. C. Leach; and Dr. S. W. Fletcher.*
G/W Editorial: How Many Unjustifiable Lectures Are Worth $2.4 Billion? *By Dr. W. F. Dunn, FCCP; and Dr. E. Armstrong.*

Global Medicine
▶ **Changing Global Epidemiology of Pulmonary Manifestations of HIV/AIDS.** *By Dr. M. W. Hull, et al.*

Recent Advances in Chest Medicine
▶ **Emerging Pharmacotherapies for COPD.** *By Dr. P. J. Barnes, FCCP*

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AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

CHEST Assistant Editor Receives Prestigious Award

Cynthia French, NP, MS, a nurse practitioner at UMass Memorial Medical Center, is the winner of the prestigious Schwartz Center Compassionate Caregiver Award, given by the Boston-based Kenneth B. Schwartz Center.

The award was presented to Ms. French at the Schwartz Center's annual dinner on November 12 at the Boston Convention and Exhibition Center.

Now in its 10th year, the Schwartz Center Compassionate Caregiver Award recognizes the caregiver in Massachusetts who best personifies the mission of the Schwartz Center to "advance compassionate health care in which caregivers, patients, and their families relate to one another in a way that provides hope to the patient, support to caregivers, and sustenance to the healing process."

CYNTHIA FRENCH, NP, MS

Some 112 health care workers were nominated this year, making it the most competitive year ever.

The nominees ranged from social workers to physicians to nurses. AstraZeneca, a leading pharmaceutical company, has sponsored the award for the past 4 years.

Cindy works as a nurse practitioner in UMass Memorial's Lung and Allergy Center, is the program facilitator for critical care operations, and is the assistant editor of the journal *CHEST*. She has made a career out of recognizing patient needs that are not being met, then working with kindred spirits to create change.

For example, when it became clear that more could be done to improve the quality of life for patients with lung disease, Cindy, along with her long-time collaborator Dr. Richard Irwin, FCCP, and several colleagues, created a pulmonary rehabilitation program, at a time when these programs were few and far between.

And again, when she and Dr. Irwin realized that their pulmonary patients with amyotrophic lateral sclerosis (ALS) were having trouble managing multiple appointments at different locations, they created a virtual ALS center, offering multidisciplinary ALS care in one location.

The College congratulates Cindy on this well-deserved honor and wishes her future success in her endeavors to assist those struggling with lung disease and progressive neurodegenerative illness. ■

NEWS FROM THE COLLEGE

Guideline Implementation: Focus for the Future

BY SANDRA ZELMAN LEWIS, PH.D.
Assistant Vice President, Health and Science Policy & Quality Improvement

This is part 2 of a 2-part series on implementation of guidelines.

The American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines are developed using a rigorous methodology (*CHEST* 2007; 132:1015-1024), taking about 3 years from topic selection to publication. Although ACCP strives to reduce the time and costs involved in developing guidelines, we lack the data to demonstrate how recommendations are implemented into clinical practice.

In 2006, the ACCP requested to review sample tools (*eg,* order sets, electronic reminders, or checklists) from ACCP members, the ACCP Governors, and NetWorks. The intent was to examine how our guidelines were being transformed into useful products to facilitate clinical decision-making at the local level. However, little information was gleaned from these initial efforts.

ACCP also presents our guidelines in an executive summary format entitled, "Clinical Resources," which include quick reference guides, patient education guides, and slide sets. Some have algorithms, checklists, and other decision-support tools, and all include PDA downloads of the quick reference guides. However, these resources alone appear to have little impact on the clinical and educational needs of our members.

Last month's segment of this series covered the challenges and best practices for effective implementation, namely a multifaceted approach consisting of four core properties: (1) local leadership at all levels by respected opinion leaders; (2) a supportive culture and/or incentives for change; (3) development of effective teams; and (4) greater use of information technology (including the Internet). The Health and Science Policy (HSP) Committee proposes utilization of all four elements in future initiatives.

The ACCP is also considering other approaches that should be more effective in improving knowledge uptake and practice change. The Veteran's Administration (VA) is interested in a cooperative quality improvement project based on ACCP guideline recommendations. Although the details are still to be finalized, it will likely make use of the VA's comprehensive and standardized electronic medical record system. The pilot program will test clinical effectiveness through process and outcome assessments.

ACCP Governors were receptive to a proposal that they, as respected local thought leaders, coordinate a series of programs at their own hospitals and others in their region. The educational content would be based on the HSP guideline slide sets and other clinical resources. It is hoped that the first of these programs will be organized in 2009.

In the future, HSP guidelines may look quite different. There will be more user-friendly formats and more tools built into the final documents. Recommendations will be highly searchable by keywords and, possibly, by diagnosis and procedure codes. Online versions will include hotlinks to the following resources:

- The guideline algorithms
- The relevant guideline text
- References
- Original research articles
- PubMed and other such databases
- National Guidelines Clearinghouse
- Guidelines International Network
- FDA alerts
- Endorsed performance measures

The ultimate implementation tools will, of course, be performance measures. If measures are based on the guidelines, and if incentives are significant, hospitals and health care providers will seek the recommendations and tools to guide their treatment decisions. The ACCP wants to be their resource for evidence-based cardiopulmonary guidelines and resources.

We would like to hear other ideas from you. Please contact me at slewis@chestnet.org. ■

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PROFESSIONAL OPPORTUNITIES

Pulmonary/Critical Care Faculty Position
Wake Forest University School of Medicine

The Section on Pulmonary, Critical Care, Allergy and Immunologic Diseases is seeking two BC/BE physicians at the Assistant/Associate Professor level. The principal clinical and teaching focus of these positions will be Critical Care. For candidates interested in a significant research component, opportunity for protected time will be encouraged to support the development of independent and integrated research activities. Currently, the section is an ARDS Network study site and has over 3.3 million in NIH funding, and consists of 22 faculty members (MDs and PhDs). The Section at Wake Forest will continue significant expansion as the result of multiple ongoing research and clinical programs. Winston-Salem and the surrounding Piedmont region of NC provide a unique opportunity for faculty to enjoy work, family and outdoor activities. All inquires should be submitted to: Eugene Bleecker, MD, Chief, Division of Pulmonary, Critical Care, Allergy and Immunologic Diseases, Wake Forest University School of Medicine, Medical Center Blvd., Winston-Salem, NC 27157. E-mail: ebleeck@wfubmc.edu
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Pulmonary Critical Care Opportunity
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Steps Needed to Boost Vaccination

Too Low • *from page 1*

2006-2007 flu season, and only 21% were fully vaccinated.

Two doses given 4 weeks apart are recommended in children younger than age 9 years who are being vaccinated for the first time (MMWR 2008;57:1039-43).

Of note, there was substantial variability in vaccination coverage among states, according to the survey results.

For example, only about 9% of children were fully vaccinated in Mississippi, and nearly 48% were vaccinated in Rhode Island. In most states, there was no significant increase in the percentage of children who were fully vaccinated, compared with the previous flu season.

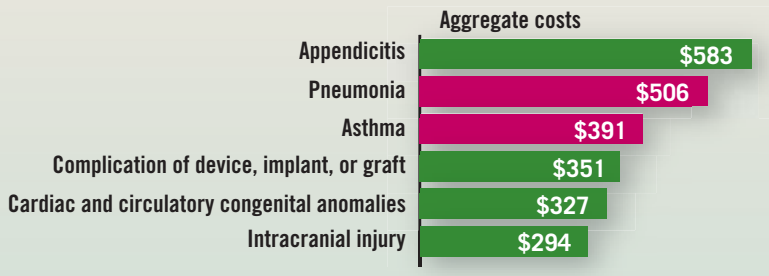
"The findings underscore the need to increase interest in and access to influenza vaccination for more children in the United States. Further study is needed to identify knowledge deficits or logistical barriers that might contribute to continued low influenza vaccination coverage among young children," the article states.

In addition, the authors state in an editorial note that health care providers can help improve vaccination coverage among young children by routinely informing parents about "the substantial burden of influenza illness among young children and about the benefits and safety of preventing influenza with vaccination."

Proven strategies for reducing missed opportunities for vaccination also include having standing orders to offer vaccine to all patients throughout the flu season, holding vaccination-only clinics, and using reminder/recall systems, they noted. ■

DATA WATCH

Most Expensive Hospital Diagnoses for Children
(in millions of dollars)



Note: Based on 2006 data for the Nationwide Inpatient Sample.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

FYI

Quality Reporting Portal

A new self-service look-up tool on the Physician Quality Reporting Initiative portal allows eligible professionals at the Tax Identification Number level to see if their 2007 PQRI Feedback Report is available. If it is, they can register for an account to view the report. The site also has links to several quality improvement resources. Visit the site at www.qualitynet.org/pqri. Eligible professionals also can learn if their feedback report is available by calling the QualityNet Help Desk at 866-288-8912.

E-Prescribing Incentive Web Site

The Centers for Medicare and Medicaid Services has a new E-Prescribing Incentive Program section page. The page has links to a fact sheet as well as to related information on the Physician Quality Reporting Initiative. Eligible professionals do not need to participate in PQRI to participate in the E-Prescribing Incentive Program. Visit the page atwww.cms.hhs.gov/PQRI/03_EPrescribingIncentiveProgram.asp#TopOfPage.

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References: 1. Prolastin® Alpha$_1$-Proteinase Inhibitor (Human), Full Prescribing Information, January 2005. **2.** Aralast™ Alpha$_1$-Proteinase Inhibitor (Human), Full Prescribing Information, August 2005. **3.** Data on file, CSL Behring LLC.

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