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

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 we see now in actual clinical practice are more highly nicotine dependent, which applies to FTQ scores of 7 or greater.

The next study enrolled 206 patients who were enrolled in 1989 and 1990 in a study of sustained-release bupropion; their average FTQ score was 6.65. The next study enrolled 206 patients who were enrolled in 1989 and 1990 in a study of sustained-release bupropion; their average FTQ score was 6.65.

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

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 oxygenation 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 transpulmonary 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 impractical 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.
FDA Committees to Assess LABA Safety in Asthma

BY TERRY RUDD
Elsevier Global Medical News

The safety of long-acting β₂-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, Pulmonary and Critical Care Medicine 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 (formoterol), and Foradil Aerolizer (formoterol). The warning cautions that long-acting β₂-adrenergic agonists (LABAs) may increase the risk of asthma-related deaths. Boehringer Ingelheim, which makes Advair and Serevent, funded the meta-analysis (Ann. Intern. Med. 2008;149:33-42).

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 1,175 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 corticosteroids alone.

The analysis “confirms that treatment with long-acting β₂-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 for meterol and salmeterol taken by asthma patients who also took inhaled corticosteroids, with a particular focus on serious adverse events.


“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 caution.

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

Several Agents Needed to Quit

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.

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 Z Vyvanse, as well as for several other drug companies.

To see a video discussion with Dr. Sachs, visit www.youtube.com and search for “ElseGlobalMedicalNews.”

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In our lifetime, we humans will breathe, on average, over a half billion times. Respiratory disease can turn this vital function into a lifelong challenge. Abbott Respiratory is dedicated to using its proven resources and expertise to advance the science and practice of respiratory care.

Our guiding principle could not be more fundamental: making every breath count.

*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.


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Lung Cancer Diagnoses Decline, Hospitalizations Do Not

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 1997 and 2007, 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 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 1997, ranging from 477,600 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 45 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 persons, vs. 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.

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 payer. 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 6.6% 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 slightly more than three quarters of hospital stays associated with a principal lung cancer admission. The rate of hospitalization for therapeutic radiology or chemotherapy procedures increased 13%—despite a steady decline in the number of Americans diagnosed with the disease during the same period.

In contrast, similar patients who lacked all three of those clinical signs had a 0.3% rate of mechanical ventilation during their hospitalization, said Dr. Andrew F. Shorr, FCCP, who is 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 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, according to Elsevier Global Medical News. Dr. Andrew F. Shorr, FCCP, reported at the annual meeting of the American College of Chest Physicians.

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, who is 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.”

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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 high- and low-risk groups. The three parameters were then tested using the validation cohort, and the results confirmed the initial finding (see table). In contrast, 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 hypercapnic. 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.

Quantifying the Risk of Mechanical Ventilation in COPD Patients

<table>
<thead>
<tr>
<th>Number of assessment measures positive at time of initial hospitalization</th>
<th>Mechanical ventilation rate during hospitalization in the derivation cohort</th>
<th>Mechanical ventilation rate during hospitalization in the validation cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.2%</td>
<td>0.3%</td>
</tr>
<tr>
<td>1</td>
<td>1.2%</td>
<td>1.2%</td>
</tr>
<tr>
<td>2</td>
<td>4.2%</td>
<td>5.5%</td>
</tr>
<tr>
<td>3</td>
<td>10.1%</td>
<td>12.4%</td>
</tr>
</tbody>
</table>

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

Dr. Nicola Ihanan, 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 strongly linked to the risk of death in patients hospitalized for an acute exacerbation of COPD. Nevertheless, 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 the nonusers, Dr. Khemasuwan reported.

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.

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. Guterman, 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 discontinued use at least 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. 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

Azactam is indicated for the treatment of infections caused by aerobic gram-negative microorganisms.

### INSTRUCTIONS AND USAGE

For the treatment of infections caused by aerobic gram-negative microorganisms.

### CONTRAINDICATIONS

Azactam is contraindicated in patients with a history of hypersensitivity to aztreonam, penicillins, cephalosporins, or sulfonamides.

### ADVERSE REACTIONS

A comprehensive list of adverse reactions is available; subsequently, appropriate antibiotic therapy should be continued.

### DOSAGE AND ADMINISTRATION

Concurrent initial therapy with other antimicrobial agents and AZACTAM is recommended before the causative organism(s) is known in seriously ill patients who are also at risk of having an infection due to gram-positive aerobic pathogens.

### Nursing Mothers:

AZACTAM is excreted in human milk. Lactating women should be advised to discontinue AZACTAM before breastfeeding and to resume breastfeeding after concluding therapy.

### Adverse Laboratory Changes:

### Skin and Soft-Tissue Infections:

Infections caused by Enterobacter cloacae, Klebsiella oxytoca, Citrobacter species and Serratia species.

### Superinfection:

The use of antibiotics may promote the overgrowth of nonsusceptible organisms, including Candida species. If superinfection occurs during therapy, appropriate measures should be taken.

### Pregnancy/Preparation Category:

Hepatitis, jaundice

### Special Senses—tinnitus, diplopia, mouth ulcer, altered taste, numb tongue, sneezing, nasal congestion

### Cardiovascular—hypotension, transient ECG changes (ventricular bigeminy and PVC), flushing

### Hypersensitivity—anaphylaxis, angioedema, bronchospasm

### Other—vaginal candidiasis, vaginitis, breast tenderness

### PRECAUTIONS

### Administration:

Azactam is a white to off-white powder for intramuscular injection. The use of alcohol to prepare the injection site should be discouraged.

### Special Considerations:

### Hematologic: Splenomegaly

### Nephrotoxicity and Ototoxicity of Aminoglycoside Antibiotics.

### Imipenem–Cefetanum:

Imipenem–Cefetanum is a combination of two antibiotics, imipenem and cefetanum.

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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 when the first unit of blood was received was 26 days. Eleven patients died, and 57 developed nosocomial infections. Dr. Raquel Nahra said that the analysis showed that patients who received a first unit of blood that was at least 26 days old, the analysis showed that patients who 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 catheter use to as short a time course as necessary, utilizing specific insertion practices for bloodstream catheters, and daily assessment for pulmonary, critical care, and sleep medicine at North Shore–University Hospital in Camden, N.J. Current practice in the United States is to discard blood once it is 42 days old, she noted.

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 17 days in the hospital. Patients had a 2.9-fold 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.

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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.
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 chloride, phenols, nitrosamines, reactive oxygen species, and various pro-carcinogenic polycyclic aromatic hydrocarbons (PAHs). In fact, benzo(a)pyrene, a PAH that plays a prominent role in human cancer, is present in marijuana cigarette. Second, approximately a fourfold amount of the tar from the smoke of marijuana than 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, 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. Fourth, intraperitoneal administration of delta-9-tetrahydrocannabinol (THC), the major psychoactive ingredient in marijuana, to immunocompetent mice implanted with EGFR (epidermal growth factor receptor), and DNA ploidy (a marker of genetic instability), consistent with dysregulated growth and pre-tumor progression. Fourth, intraperitoneal administration of delta-9-tetrahydrocannabinol (THC), the major psychoactive ingredient in marijuana, to immunocompetent mice implanted with EGFR (epidermal growth factor receptor), and DNA ploidy (a marker of genetic instability), consistent with dysregulated growth and pre-tumor progression. 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 or upper airway cancers 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. 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. 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. Three case-control studies that examined cannabis use as a possible risk factor for lung cancer were conducted in North Africa. 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). 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 included 110 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 kif (a powdery preparation from the dried flowers of the female cannabis plant mixed with tobacco), with or without snuff. Results indicated that the combined use of hashsh/kif and snuff was associated with a 6.7-fold greater risk (95% CI, 1.65-26.90) for developing lung cancer, while the risk was much lower for the use of hashsh/kif without snuff (1.4-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 kif includes tobacco, the effect of cannabis independent of tobacco cannot be assessed in this study.

A more recent Tunisian hospital-based case-control study that included 149 incident lung cancer cases and 191 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 and the other in New Zealand, have been published within the past 2 years. The Los Angeles study included, over a 4½-year period, 79 patients with lung cancer 55 years of age and 324 randomly selected control subjects matched for age. All subjects underwent interviewer-administered questionnaires to assess possible risk factors for lung cancer. Relatively few patients (10%) and control subjects (1.3 of 96,818) to 21 (14,322) for tobacco smokers, with pack-year histories ranging from less than one pack a day to 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. All subjects underwent interviewer-administered questionnaires to assess possible risk factors for lung cancer. Relatively few patients (10%) and control subjects (1.3 of 96,818) to 21 (14,322) for tobacco smokers, with pack-year histories ranging from less than one pack a day to two packs a day with a clear dose-response relationship.

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**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, hypothyroidism, 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, dyspnea, 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 FEV1, within minutes (XOPENEX 1.25 mg; day 0, week 0)2
  - From a subset of patients with baseline FEV1 <60% of predicted (n=36)3
  - Over the course of the study, mean time to 15% improvement in FEV1 was 9 minutes (1.25 mg) and 17 minutes (0.63 mg)2
  - In the overall population over the course of the study, the mean time to a 15% increase in FEV1 was 10 minutes (1.25 mg) and 17 minutes (0.63 mg)2
- **Sustained.** >15% improvement up to 8 hours postdose in some patients1
  - Mean duration of effect measured by a >15% increase in FEV1, 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 albuterol1

**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

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*From a randomized, double-blind, parallel-group, 4-week clinical trial of patients aged 12 years or older (n=352) with moderate-to-severe asthma. The primary end point was peak change in FEV1, after 4 weeks. XOPENEX Inhalation Solution was significantly better than placebo (P<.001).*


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

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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, that the negative results of this study are due to the small sample size of the much larger Los Angeles study, that the small sample size of the New Zealand study led to markedly inflating the association of marijuana use and the occurrence of lung cancer.

Limitations of all of the foregoing epidemiologic studies include possible underreporting and invalidity of use in countries where marijuana use is illegal, sampling bias, and failure to control for covariates such as alcohol use, tobacco smoking and other known cancer risk factors.

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

The answer to this question is important not only from a public health perspective and the benefit and harms of medical 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 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.

References


Editor’s Insight

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

**Dr. Donald P. Tashkin, FCCP**
Division of Pulmonary and Critical Care Medicine
David Geffen School of Medicine at UCLA
Los Angeles, CA
N E W S F R O M T H E C O L L E G E

PRESIDENT’S REPORT
The Physician Manpower Debate

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.

Continued on following page
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.

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Tribute, New Leadership at CHEST Foundation

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.

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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 E. 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.
**Critical Care Commentary**

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

D

[... meanwhile, a series of articles has been published in this issue of the Critical Care Commentary section covering topics in 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 on the consistent application of national patient safety goals. The most recent set was published in 2008 (www.joint-commission.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.

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” versus “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.

Investigators Discuss Studies on Anticholinergic Inhalers


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ost 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 β₂-agonist) for those with an FEV1 below 50% predicted. More than 4 billion dollars has been spent on inhalers for COPD — about half that for tiotropium inhalers, which are used by more than 8 million patients. Most pulmonary specialists 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 ipratropium 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 (Anthonissen 2002). Inhaled tiotropium and ipratropium are absorbed and excreted in the urine (Caillard 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 not associated with increased 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 Medicine, 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 the 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, Columbus 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.
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 serving approximately 35,000 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 a option for meeting the IPS standard. Due to AGM’s busy 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;29:297).

A recent study examined the impact of providing 24/7 continuous, rather than on-demand, attending coverage at a single medical ICU that was staffed by residents and fellows at all times (Gajic et al. Crit Care Med 2008;36:346). 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, 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’s or 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 unrecognized 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 Wochenchr 2006;131:2461; Raggi. Minerva Anestesiol 2007; 193) 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 depression, exhaustion, and depression—disenchantment symptoms. Some of the factors contributing to burnout are certainly addressable, but others are parts of the nature of practicing critical care medicine.

Environmental factors, such as shift work, unknown workloads, varying days, 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—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. Endelman, et al.

 Obesity and Persisting Sleep Apea After Adenotonsillectomy in Greek Children. By Dr. M.T. Apostolidou, et al.

 Evaluation of Chronic Influenza in Children. By Dr. S. Asiloy, et al.


 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. Hall, et al.

Recent Advances in Chest Medicine

■ Emerging Pharmaco-therapies for COPD. By Dr. P.J. Barnes, FCCP

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Continued from previous page.
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.”

Some 112 health care workers were nominated this year, making it the most competitive year ever. The nominees ranged from social workers 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.

CYNTHIA FRENCH, NP, MS

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1935 - 2009
Guideline Implementation: Focus for the Future

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 electronic 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 FDA 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 cardipulmonary guidelines and resources.

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

Guideline Implementation: Focus for the Future

Guideline Implementation: Focus for the Future
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 as 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 32 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 inquiries should be submitted to: Eugene Bliecker, 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: ebblecker@wfubmc.edu

Generous compensation and benefits package include health benefits, generous 401k, sign-on and relocation bonus, plus opportunity for Partnership. For more information, contact Lisa Morgan at 888-800-8237 or email CV to lisam@eddocs.com

Multiple ongoing research and clinical programs

Suburban Atlanta

Well-established, busy 11-physician single-specialty Pulmonary practice in suburban Atlanta, Georgia, looking for one or more BC/BE Pulmonary/Critical Care physicians. Sleep certification a plus. Practice includes all aspects of pulmonary medicine, including critical care, sleep medicine, outpatient clinic, pulmonary rehab and clinical research. Practice located at two large acute care hospitals, one being the busiest ER in Georgia, and also near a long term acute care hospital. Competitive salary with bonus potential, generous benefits package and malpractice coverage. Fax CV to: 770-790-1738.

Pulmonary/Critical Care Opportunity

Pulmonary/Critical Care group is seeking an Associate in one of the fastest growing cities in the nation, Las Cruces, New Mexico. Must be board eligible/certified. Competitive first year income guarantee. Excellent marketing and relocation assistance. Strong primary care referral base. Located in charming university community, Las Cruces offers 350 days a year of sunshine, warm weather, and low cost of living. Surrounding mountain and desert landscapes provide for great outdoor recreation activities. Contact Sam Benevento, Director of Physician Recruitment, Memorial Medical Center, by phone: 575-532 7404, or e-mail samyeann.benevento@nmt.net

Pulmonary Critical Care Opportunity

Sutter Medical Group (SMG) is seeking a BE/BC Pulmonary Critical Care physician in Auburn, CA. Good call schedule. Option for hospitalist work if desired.

SMG offers an income guarantee with shareholder track, generous compensation, benefits, and retirement package.

Sutter Auburn Faith Hospital is a medium sized hospital with a 24/7 hospitalist program, open ICU, high resolution CT scan, cardiac cath lab, full nuclear medicine department, bronchoscopy suites and a pulmonary function laboratory. Auburn is centrally located in the Sierra Nevada foothills between Sacramento and Lake Tahoe. Auburn is close to shopping and restaurants, and offers a variety of outdoor activities.

PULMONOLOGY/Critical Care Opportunity

Pulmonology/Critical Care group seeking an Associate in one of the fastest growing cities in the nation, Penobscot Bay. Ideal for outdoor enthusiasts. Family oriented with excellent schools. Immediate availability. Contact Dan Bennett, Director of Operations, Waldo County General Hospital, PO Box 287, Belfast, ME 04915, 207-930-6741. E-mail: dbennett@wcdi.com. Website: www.wcdi.com.

Job ID: 36112

FOR MORE INFORMATION CONTACT:

Abingdon, MD 21009.

Sutter Auburn Faith Hospital, has 95 beds, a 24/7 hospitalist program, open ICU, high resolution CT scan, cardiac cath lab, full nuclear medicine department, bronchoscopy suites and a pulmonary function laboratory. The community of Auburn is nestled in the Sierra Nevada foothills approximately 35 miles northeast of Sacramento. Auburn is known for its family-oriented atmosphere and for its excellent schools. Residents enjoy year-round outdoor recreations such as golfing, hiking, biking, and white water rafting.

Pulmonary Critical Care Opportunity

PULMONARY/Critical Care/SLEEP
LOWELL, MASSACHUSETTS

An exciting opportunity exists for a BC/BE physician to join a successful four-physician pulmonary/critical care sleep/private practice 30 miles north of Boston. Mail CV to Lung Specialists, Att: Sandra Rondeau, 275 Vannum Avenue, Suite 203, Lowell, MA 01854. brondeau@ismru.net

Visit www.ismru.net

PULMONOLOGY/Critical Care Opportunity

Sutter Auburn Faith Hospital, has 95 beds, a 24/7 hospitalist program, open ICU, high resolution CT scan, cardiac cath lab, full nuclear medicine department, bronchoscopy suites and a pulmonary function laboratory.

Auburn is located in charming university community, Las Cruces offers 350 days a year of sunshine, warm weather, and low cost of living. Surrounding mountain and desert landscapes provide for great outdoor recreation activities. Contact Sam Benevento, Director of Physician Recruitment, Memorial Medical Center, by phone: 575-532 7404, or e-mail samyeann.benevento@nmt.net

Seeking Pulmonary/Critical Care specialist to join rapidly growing practice in Austin, TX. Responsibilities include critical care coverage for two community hospitals and one regional referral hospital, as well as outpatient pulmonary and sleep medicine practice. Compensation package includes health benefits, generous 401k, sign-on and relocation bonus, plus opportunity for Partnership. For more information, contact Lisa Morgan at 888-800-8237 or email CV to lisam@eddocs.com

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MARIETTA PULMONARY MEDICINE

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BEAUTIFUL COAST OF MAINE

BC/BE Pulmonologist

Multi-specialty community hospital seeks physician for outpatient, hospital and critical care. Belfast offers beautiful views of Penobscot Bay. Ideal for outdoor enthusiasts. Family oriented with excellent schools. Immediate availability. Contact Dan Bennett, Director of Operations, Waldo County General Hospital, PO Box 287, Belfast, ME 04915, 207-930-6741. E-mail: dbennett@wcdi.com. Website: www.wcdi.com.

Suburban Pittsburgh

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 recom-
mended 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 variabil-
ity 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 Is-
land. In most states, there was no signific-
ants increase in the percentage of children who were fully vaccinated, com-
pared 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 need-
ed to identify knowledge deficits or logis-
tical barriers that might contribute to con-
tinued low influenza vaccination cov-
erage 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 vaccination to all patients during flu season, holding vaccination-only clinics, and using reminder/recall systems, they noted.

FYI

Quality Reporting Portal

A new self-service look-up tool on the Physician Quality Reporting Initiative portal allows eligible professionals to 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 links

Megers several quality improvement resources. Visit the site at www.qualitynet.org/pqri. Eligible professionals can also 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 par-

hhs.gov/PQRI/03_EPrescribingIncentiveProgram.aspx/TopOfPage.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

CSL Behring

Zemaira®

Zema®

Alpha1-Proteinase Inhibitor (Human)

Manufactured by:

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Eden Prairie, MN 55344 USA

US License No. 1767

Contraindications

Zemaira® is contraindicated in individuals with a known hypersensitivity to any of its components.

CONTRAINDICATIONS

Zemaira® is contraindicated in individuals with a history of anaphylaxis or severe systemic response to A

Proteinase Inhibitor (Human). It is also not known whether Zemaira® is safe for use in pregnant women. Zemaira® is administered to a nursing woman.

Zemaira® is excreted in human milk. Because many drugs are excreted in breast milk, a decision should be made whether to discontinue breastfeeding or discontinue the drug.

No. of related adverse events (rates per infusion) 6 (0.005) 5 (0.031)

No. of adverse events regardless of causality (rates per infusion) 298 (0.230) 83 (0.519)

No. of subjects with related adverse events (%) 19% 41.1%

No. of adverse effects regardless of causality (cases per infusion) 19 (0.15) 5 (0.30)

Table 3: Summary of Adverse Events

The frequencies of adverse events per infusion that were mild or moderate in Zemaira® treated subjects, regardless of causality, were: headache (31 events/1,194 infusions, 2.5%), upper respiratory infection (1.6%), urticaria (1.5%), maculopapular rash, herpes zoster (1.0%), rash (1.0%), pruritus (0.9%), bronchospasm (0.9%), arthralgia (0.9%), fever (0.6%), pain (0.6%), back pain (0.5%), cellulitis (0.5%), accidental injury, back pain, chest pain, diarrhea, headache, injection site reaction, intramuscular injection, myalgia, nausea, peripheral edema, phlebitis, pruritus and rash.

Zemaira® is indicated for chronic augmentation and maintenance therapy in individuals with alpha-1 antitrypsin deficiency (A1-PI deficiency) and clinical evidence of emphysema. Zemaira® increases antitrypsin and functional (A1-antitrypsin) serum levels and lung long-acting flow levels of A1-PI.

Zemaira® is a plasma-derived human proteinase inhibitor (A1-PI) that reduces the long-term effects of chronic augmentation and maintenance therapy of individuals with Zemaira® are not available.

Safety and effectiveness in pediatric patients have not been established. Zemaira® is not indicated as therapy for lung disease patients in whom severe congenital A1-PI deficiency has not been established.

SIDE EFFECTS

Zemaira® is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. Because Zemaira® is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent.

The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for evidence of infectious diseases, e.g., hepatitis B and C, and HIV, and by inactivating and/or removing certain viruses during manufacture. (See section for viral reduc-
tion procedures.) Despite these measures, such products may still potentially contain infectious agents which may be transmitted by this product should be reported by the physician or other healthcare provider to CSL Behring

Intracranial injury

Intracranial hemorrhage

Intracranial hematomas

Intracranial abscess

Intracranial infection

Intracranial sepsis

Intracranial suppuration

Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage

Intracranial hematomas

Intracranial abscess

Intracranial infection

Intracranial suppuration

Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage

Intracranial hematomas

Intracranial abscess

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Intracranial fistula

Intracranial necrosis

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Intracranial abscess

Intracranial infection

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Intracranial fistula

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Intracranial hematomas

Intracranial abscess

Intracranial infection

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Intracranial fistula

Intracranial necrosis

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Intracranial hematomas

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Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage

Intracranial hematomas

Intracranial abscess

Intracranial infection

Intracranial suppuration

Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage

Intracranial hematomas

Intracranial abscess

Intracranial infection

Intracranial suppuration

Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage

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Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage

Intracranial hematomas

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Intracranial infection

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Intracranial fistula

Intracranial necrosis

Intracranial hemorrhage
Zemaira® — The next generation in purity for Alpha-1 augmentation therapy

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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 A1-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.