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COURTESY DR. PATRICK J. OFFNER

Ventilator bundles must be revised and made more relevant to trauma/surgical ICU patients, Dr. Patrick J. Offner said.

Ventilator Bundles Face Trauma ICU Challenges

BY BRUCE JANCIN
Elsevier Global Medical News

COLORADO SPRINGS — Implementation of a widely advocated bundle of evidence-based practices aimed at reducing ventilator-associated pneumonia had the desired effect in a busy medical ICU but not in the same hospital's level I trauma/surgical ICU, Dr. Patrick J. Offner reported at the annual meeting of the Western Surgical Association.

"I think ventilator-associated pneumonia prevention is an important goal in our patients. However, the ventilator bundle as implemented by us was ineffective in reducing the ventilator-associated pneumonia rate in our trauma ICU," observed Dr. Offner of St. Anthony Central Hospital, Denver.

The explanation for the disparate outcomes is unclear. Compliance with all four elements of the ventilator bundle—elevation of the head of the bed to an angle of 30-45 degrees, daily interruption of sedation to assess readiness for extubation, deep venous thrombosis prophylaxis, and prophylaxis against peptic ulcer disease—was about 85% in both the medical and surgical ICUs in this prospective study, Dr. Offner said.

One thing is clear, however: If implementation of standardized ventilator bundles is going to be incorporated in pay-for-performance, as seems highly likely,

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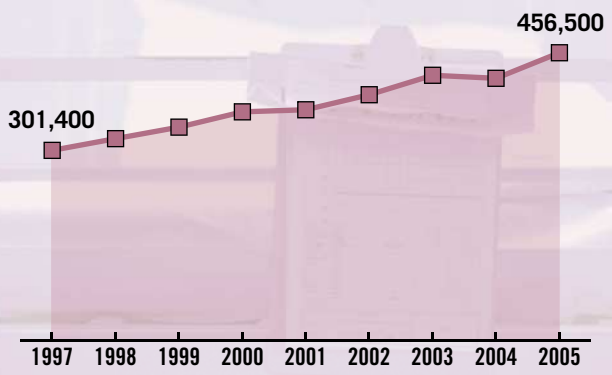
VITAL SIGNS

Number of Hospital Stays Increased 50% With a Diagnosis of Pulmonary Hypertension*



* Includes ICD-9-CM codes for cases of primary pulmonary hypertension, kyphoscoliotic heart disease, and chronic pulmonary heart disease.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

In Setback, Studies Nix Three Therapies For Severe Sepsis

Hydrocortisone, intensive insulin failed.

BY MARY ANN MOON
Elsevier Global Medical News

Three treatments for septic shock or severe sepsis proved nonbeneficial or actively harmful, researchers reported in separate studies in the New England Journal of Medicine.

Hydrocortisone failed to improve survival or accelerate the reversal of septic shock in a study of 499 patients treated at 52 ICUs in Israel and Europe. In addition, both intensive insulin therapy and fluid resuscitation using pentastarch were so harmful that both treatments were halted, in a study of 537 patients in 18 ICUs in Germany.

In the first report, Dr. Charles L. Sprung, FCCP, of Hadassah Hebrew University, Jerusalem, and his associates in the Corticosteroid Therapy of Septic Shock (CORTICUS) study assessed low-dose ("physiologic") hydrocortisone or a placebo infusion, paying particular attention to the 254 subjects (51%) who were predicted to be particularly responsive based on their responsiveness to a pretreatment corticotropin stimulation test.

Current recommendations that call for this treatment for septic shock (and for pretreatment corticotropin testing) are based primarily on results of a single study involving fewer than 500 patients. The efficacy of both low-dose hydrocortisone therapy and of corticotropin testing is still in question, even though both practices are becoming widespread, Dr. Sprung and his associates noted.

In their study, low-dose hydrocortisone did not improve mortality at 1 month, regardless of patients' pretest results. One-month mortality was 39% with hydrocortisone and 36% with placebo, a nonsignificant difference.

Similarly, the proportion of patients who achieved reversal of shock also did not differ

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INSIDE

Urban Kids' Asthma Unexpectedly Unstable

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

A study of inner-city, preschool-age children with asthma found marked fluctuations in the degree of asthma control within 3 months, suggesting that frequent evaluations of asthma control in this population may be warranted, investigators reported.

"We know asthma is an unstable disease, but we underestimated just how unpredictably it could behave over time, especially in inner-city kids," the study's lead author, Dr. Hemant P. Sharma, noted in a statement issued by Johns Hopkins University, Baltimore, where he is a pediatric allergist.

The 6-month study of 150 predominantly black children aged 2-6 years (mean age 4.4 years) with asthma living in Baltimore evaluated their long-term controller medication use and their use of asthma-related health care at baseline, and at 3 and 6 months. At baseline, the children were classified into National Asthma Education and Prevention Program control categories for asthma: mild intermittent (37%), mild persistent (17%), moderate persistent (21%), and severe persistent (25%).

Only 39% of the children in the study reported long-term use of controller medication (inhaled corticosteroids, cromolyn and nedocromil, oral leukotriene modifiers, long-acting β-agonists, and oral theophylline), wrote Dr. Sharma and his associates.

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Sepsis Results Disappoint

Three Therapies • *from page 1*

significantly between hydrocortisone (80%) and placebo (74%). However, reversal of shock tended to occur more quickly in patients who received active treatment.

It appeared that any benefit that may have derived from hydrocortisone therapy was offset by an increased incidence of infection, including new episodes of sepsis or septic shock, and of hyperglycemia and hypernatremia, the investigators said (N. Engl. J. Med. 2008;358:111-24).

Their results showed that neither hydrocortisone therapy nor corticotropin pretesting can be recommended for patients with septic shock, the researchers added.

In the second report, Dr. Frank M. Brunkhorst of Friedrich Schiller University, Jena, Germany, and his associates compared intensive insulin therapy against conventional insulin therapy in patients with severe sepsis or septic shock. They also compared fluid resuscitation using hydroxyethyl starch (HES) against conventional lactate solution in the same patients. The study was sponsored by B. Braun, Novo Nordisk, and HemoCue.

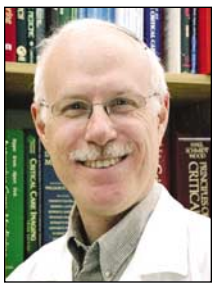
The portion of the study comparing insulin treatments was terminated early when an interim analysis showed that intensive insulin therapy induced an excess of severe hypoglycemic events. Hypoglycemia developed in 12% of subjects on intensive insulin therapy, compared with 2% of those on conventional insulin therapy. Hypoglycemic events more often were classified as life threatening and more often required prolonged hospitalization in the intensive-therapy group.

Mortality was not significantly different between those patients receiving intensive insulin (25% at 28 days and 40% at 90 days) and those patients receiving conventional insulin (26% at 28 days and 35% at 90 days).

The fluid resuscitation portion of the study was terminated early when an interim analysis showed a higher rate of renal failure with HES (35%, compared with 23% with standard lactate) and a trend toward higher 90-day mortality, Dr. Brunkhorst and his associates said. The investigators also noted that they "observed marked adverse effects of HES therapy on kidney function, coagulation, transfusion requirements, and survival" (N. Engl. J. Med. 2008;358:125-39).

Taken together with the results of previous studies of intensive insulin therapy, these findings show that the treatment "has no measurable, consistent benefit in critically ill patients in a medical ICU, regardless of whether patients have severe sepsis, and that such therapy increases the risk of hypoglycemic episodes," Dr. Brunkhorst and his associates said.

Their findings also clearly demonstrate that fluid resuscitation with the pentastarch HES is harmful in patients with severe sepsis and should be avoided, the investigators added. ■



Neither hydrocortisone therapy nor corticotropin pretesting can be recommended.
DR. SPRUNG

Dr. Stephen Pastores, FCCP, comments: *The use of corticosteroids for severe sepsis and septic shock has remained a controversial issue for decades. The investigators of the CORTICUS study have to be commended for conducting the largest multicenter randomized trial of corticosteroids in patients with septic shock.*

Although shock was reversed more rapidly in patients receiving low dose or "physiologic" hydrocortisone, this did not result in reduced mortality. The study also concluded that corticotropin stimulation testing could not identify which septic patients would benefit from corticosteroids. It is important to note that this trial was stopped after only 500 of the planned 800 patients had been recruited, because of slow recruitment, termination of funding, and time expiry of the trial drug. In addition, methodological differences (e.g., severity of illness, time window for study entry, and use of fludrocortisone) between this trial and the earlier seminal study by Annane et al. may explain the disparate outcome results.

Until further and larger trials are conducted, clinicians should avoid using corticosteroids for the routine management of patients with septic shock.

The recently published guidelines from the Surviving Sepsis Campaign recommend that "stress-dose corticosteroid therapy be given only in septic shock after blood pressure is identified to be poorly responsive to fluid and vasopressor therapy (2C)."

The lack of efficacy and significant safety concerns (hypoglycemia, renal failure, coagulopathy) of the VISEP trial regarding intensive insulin therapy and the use of 10% hydroxyethyl starch (HES) also suggest that tight glycemic control (80-110 mg/dL) may not be appropriate for severely ill septic patients, and that HES should be avoided for initial fluid resuscitation.

Correction

The photo caption in "Asthma Survey Casts Doubt on Hygiene Hypothesis" (November 2007, p. 23) incorrectly identified the nebulizer being used by a child as an "inhaler." CHEST PHYSICIAN regrets the error.

IN THIS ISSUE

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Smoke Tied to Worse Lung Function in CF

People with cystic fibrosis who are exposed to secondhand smoke have significantly worse lung function than do those who are not exposed, according to researchers.

The mean reduction in lung function linked to secondhand smoke corresponds to a drop of 8.2% in predicted forced expiratory volume in the first second of expiration (FEV_1). The reduction is 18.6% in patients with a certain high-risk gene variant, wrote Dr. J. Michael Collaco and colleagues at Johns Hopkins University, Baltimore (JAMA 2008;299:417-24).

The reduction in lung function in the high-risk patients is roughly what would be expected after 7.3 years of disease progression. Thus a 17-year-old white male with the gene variant who was exposed to secondhand smoke would have the lung function of a 24-year-old male with the same genotype who was not exposed.

The study involved 812 twins or sibling pairs with cystic fibrosis, mean age 19 years, none of whom was a current or past smoker. Of those, 23.2% were exposed to secondhand smoke in the home, and 16.5% were exposed by maternal smoking during pregnancy.

The study was supported by the National Heart, Lung, and Blood Institute; the Cystic Fibrosis Foundation; and the Flight Attendant Medical Research Institute. The investigators stated that they had no other financial conflicts to disclose.

—Robert Finn

CHEST PHYSICIAN

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Study Links Respiratory Infections With MI, Stroke

BY JONATHAN GARDNER
Elsevier Global Medical News

Myocardial infarction patients were more than twice as likely as controls—and stroke patients were nearly twice as likely—to have suffered a respiratory infection in the week preceding their attack, according to a large case-control study published online in European Heart Journal.

Researchers said the association shown in their study of British National Health Service patients helps explain why the incidence of myocardial infarctions and strokes rises during the winter, when colds and influenza are more common.

Compared with controls, myocardial infarction (MI) and stroke patients were more likely to have had a respiratory infection within 7 days of the event (adjusted odds ratio 2.1 for MIs, 1.92 for stroke), the researchers found.

The association declined over time: at 29-91 days (OR 1.16 and 1.09, respectively) and at 92-365 days (OR 1.08 for both).

The authors said their research demonstrates that further research is necessary to identify the potential physiologic mechanisms in respiratory infections that can trigger an arterial event and possible treatments that could avert them.

"It may therefore be that aborting or preventing attacks of influenza will reduce vascular events, and there are some studies suggesting that this is so, although the evidence is still not conclusive," wrote the researchers, led by Tim Clayton of the medical statistics unit at the London School of Hygiene & Tropical Medicine.

"Since there may be a large number of vascular deaths attributable to respiratory infection, over and above those directly attributable to respiratory disease, the benefits of reducing respiratory infection, particularly during the winter months, could be substantial," the investigators added.

The researchers compared cases of MIs and strokes with an equal number of controls contained in the IMS Disease Analyzer Mediplus, a primary care database with 2 million patients enrolled with 500 general practitioners.

They identified first-time MIs and strokes based on hospital coding and matched them with controls based on year of birth, gender, practice, calendar time, cardiovascular risks, and other factors.

In total, the researchers found 8.4% of 11,155 MI patients and 9.3% of 9,208 stroke patients had suffered a respiratory infection in the preceding year, compared with 6.6% of MI controls and 8% of stroke controls.

Of the MI patients, 2% had a respiratory tract infection in the month before their attack, compared with 0.9% of MI controls, researchers found. Of stroke patients, 1.8% had a respiratory tract infection in the preceding month, compared with 1% of controls, according to the researchers.

The researchers also identified an association between urinary tract infection in the preceding month and stroke (adjusted OR 2.67) but not for myocardial infarction.

The researchers acknowledge that as a case-control study, the controls may not be fully comparable with the stroke and MI patients, and that there may have been some inaccuracy in the recording of respiratory infections. ■

Dr. Mark Metersky, FCCP, comments: *This study provides further evidence of a link between viral respiratory infections and subsequent acute cardiovascular and cerebrovascular events. Inflammation induced by these infections seems to promote thrombosis. The mechanism by which influenza vaccination reduces hospitalization for cardiac diagnoses may be related to this phenomenon.*

CMS Details Quality Of Care Initiative

The Centers for Medicare and Medicaid has released "The Hospital-Acquired Conditions in Acute Inpatient Prospective Payment System Hospitals Fact Sheet" and "The Present on Admission Indicator Reporting by Acute Inpatient Prospective Payment System Hospitals Fact Sheet." These products describe the quality of care initiative, a list of affected and exempt hospitals, and other important information. They are available at www.cms.hhs.gov/HospitalAcqCond/07_EducationalResources.asp. ■

Rivaroxaban Beat Enoxaparin for DVT, PE Prevention

BY FRAN LOWRY
Elsevier Global Medical News

ATLANTA — Rivaroxaban, an investigational oral anticoagulant, is significantly more effective than subcutaneous enoxaparin—the current standard of care—in warding off deep vein thrombosis and pulmonary embolism in patients who have undergone total hip replacement, a phase III study has shown.

Patients who were randomized to rivaroxaban had a 1.1% rate of any DVT, PE, or death, compared with 3.7% for patients on enoxaparin, for a relative risk reduction in total venous thromboembolism of 70%, Dr. Bengt I. Eriksson said at the annual meeting of the American Society of Hematology.

Because rivaroxaban can be given orally and does not require the same intensive monitoring as do the low-molecular-weight heparins, "it promises to be a real boon to orthopedic surgeons and other clinicians who want to protect their patients against this common but significant complication of prolonged surgery," Dr. Eriksson of Göteborg (Sweden) University and Sahlgrenska University Hospital/Ostra, Göteborg, told reporters at a press conference at the meeting.

Rivaroxaban, in joint development by Johnson & Johnson Pharmaceutical Research & Development LLC and Bayer HealthCare AG, is a direct factor Xa inhibitor anticoagulant with predictable pharmacokinetics and pharmacodynamics.

In addition to its high oral bioavailability, it has a rapid onset of action and a low potential for drug-drug interactions, Dr. Eriksson said.

In the RECORD 1 (Regulation of Coagulation in Orthopedic Surgery to Prevent DVT and PE) trial, 3,153 patients were randomized to rivaroxaban (10 mg) beginning 6-8 hours after surgery and then once a day thereafter, or to subcutaneous enoxaparin (40 mg) once daily beginning the evening before surgery and resuming 6-8 hours after surgery, for 5 weeks after total hip replacement surgery.

In addition to the significantly superior result in preventing any DVT, PE, or mortality, rivaroxaban also reduced rates of major venous thromboembolism, compared with enoxaparin (0.2% vs. 2%).

The rates of bleeding were similar with the two drugs, Dr. Eriksson said.

'It was … a big surprise that we actually obtained superiority with rivaroxaban.'
DR. ERIKSSON

"It's very important to know whether rivaroxaban would be associated with a higher risk of developing bleeding complications, and our primary safety end point was major bleeding. The rate for enoxaparin was 0.09% and the rate for rivaroxaban was 0.27%. This was not a statistically significant difference, with a *P* value of 0.22," he said.

The RECORD 1 investigators also convened a panel of cardiologists to assess potential cardiotoxicity, and hepatologists to assess hepatotoxicity, "hot topics with the new oral anticoagulants," but no such toxicities were found, Dr. Eriksson said.

"These results to me personally are very convincing. It was also a big surprise that we actually obtained superiority with rivaroxaban. In fact, it was quite astonishing to see such a difference. I am an orthopedic surgeon, and I know that low-molecular-weight heparin is quite effective, but to see even better results with this oral agent is very encouraging," Dr. Eriksson added.

Dr. Eriksson disclosed that he acts as a consultant for and receives research funding from Bayer HealthCare AG. ■

Dr. Keith M. Wille, FCCP, comments:
Most clinical trials evaluating the oral direct factor Xa inhibitors for VTE prevention have thus far utilized patients undergoing orthopedic procedures. Although hepatotoxicity plagued the first agent in this drug class, newer agents have largely managed to avoid this side effect.

While the role of the oral Xa inhibitors when caring for the medical patient is presently less defined, ongoing trials in acute coronary syndromes, stroke prevention in atrial fibrillation, and DVT treatment should help to address such questions.

Expert Discusses Top Research Articles in COPD

Studies strongly indicate that spirometric detection of COPD increases smoking cessation rates.

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — Recent studies are starting to suggest that identifying chronic obstructive pulmonary disease by spirometry and telling patients of the diagnosis might increase the likelihood of smoking cessation, Dr. Sidney S. Braman, FCCP, said.

A prospective, randomized study of 410 Swedish smokers that combined annual spirometry, brief smoking cessation advice from a nurse, and a letter from the physician to those patients who had COPD showed that smokers given a diagnosis of COPD stopped smoking significantly more often than did those with normal lung function. The 6-month, 1-year, and 3-year cessation rates were 29%, 28%, and 25%, respectively, among patients who were told they had COPD, compared with 5%, 6%, and 9% in those patients without COPD (Scand. J. Prim. Health Care 2006;24:133-9).

The study was highlighted by Dr. Braman as one of the top five COPD articles of 2007 during one of the perennially popular literature-review sessions at the annual meeting of the American College of Chest Physicians. (Dr. Braman included studies from late 2006.)

The research adds fuel to the controversy over routine use of spirometry for case finding in adults with exposure to risk factors such as cigarette smoking, or for those with persistent respiratory symptoms. This controversy exists, in part, because no randomized clinical trial has previously demonstrated that early detection of COPD changes the course of disease or increases the rate of smoking cessation, said Dr. Braman, professor of medicine at Brown University, Providence, R.I., and past president of the ACCP.

In 2005, the task force of the Agency for Healthcare Research and Quality conducted a systematic review of the evidence and concluded that it did not justify recommending spirometry as a routine tool in the practice of primary care. The question was put to the AHRQ by a task force of the American Thoracic Society, the ACCP, and the American Academy of Pediatrics.

Dr. Braman acknowledged that the results of the Swedish study may be limited to patients with mild COPD, because 85% of participants with COPD had mild disease. But he also cited a Polish study of 4,494 current smokers with a history of at least 10 pack-years of smoking that showed an improvement in validated smoking cessation rates of 16.3% in patients who were told they had COPD, compared with 12% in those with normal spirometry (Thorax 2006;61:869-73).

"Hopefully, this and other future studies will provide the needed research that will lead to a widely accepted recommendation for screening spirometry for high-risk patients in the primary care setting," he said.

COPD and PE

Also on the list was a study that tackled the issue of diagnosing acute pulmonary embolism (PE) in patients with COPD—a task that is often difficult, especially during an acute exacerbation of COPD when symptoms of the two conditions may be indistinguishable.

In a study of 123 consecutive patients admitted to the emergency department with a COPD exacerbation, the diagnosis of PE using a standardized diagnostic algorithm was 6% in the 48 patients who had a clinical suspicion of PE by the ED physician and only 1.3% in the remaining 75 patients not suspected (Thorax 2007;62:121-5).

"This study showed that the prevalence of suspected pulmonary embolism in patients presenting with a COPD exacerbation is very low, and that routine investigation for PE in this group is not warranted," Dr. Braman said.

Dr. Braman cautioned that a high clinical suspicion for PE should be maintained when there is no suspicion of infection, either viral or bacterial, in patients with a COPD exacerbation, especially those who require hospitalization.

SMOKERS GIVEN A DIAGNOSIS OF COPD HAD HIGHER CESSATION RATES AT 6 MONTHS, 1 YEAR, AND 3 YEARS THAN DID THOSE WITH NORMAL LUNG FUNCTION.

He cited a French study in which PE was reported in 49 of 197 patients (25%) admitted to the hospital for a severe COPD exacerbation of unknown origin (Ann. Intern. Med. 2006;144:390-6). Patients were excluded from the study if they had a potential infection and therefore symptoms of increased sputum, purulent sputum, recent upper respiratory infection, or consolidation on the chest roentgen-ogram. They also required hospital admission to be entered into the study.

TORCH Trial

Not surprisingly, the widely reported Towards a Revolution in COPD Health (TORCH) trial made the list (N. Engl. J. Med. 2007;356:775-89). In many people's minds, this randomized, double-blind trial of 6,112 patients with COPD was a negative study, because mortality rates for salmeterol or fluticasone propionate monotherapies did not differ significantly from placebo, Dr. Braman said. However, he suggested that a review of the secondary end points is encouraging.

Compared with placebo, combination therapy with salmeterol 50 mcg plus fluticasone 500 mcg twice daily significantly reduced the annual rate of exacerbations from 1.13 to 0.85 and significantly improved health status and spirometric values.

Over the 3-year study period, there also were no significant ocular or bone side effects in this elderly group of COPD patients, although the probability of having pneumonia as an adverse event was higher among those patients receiving corticosteroids.

Rounding out the list of top five COPD articles of 2007 were two other investigations: a large cohort study of 1,302 individuals with airway obstruction that indicates serum C-reactive protein is a strong and independent predictor of future COPD hospitalization and death (Am. J. Respir. Crit. Care Med. 2007;175:250-5), and a study of 176 consecutive patients with various pulmonary diseases, including COPD, that suggests circulating brain natriuretic peptide levels can be used as a prognostic marker and screening tool for significant pulmonary hypertension in chronic lung disease (Am. J. Respir. Crit. Care Med. 2006;173:744-50).

"We may be testing CRP and BNP more in our patients," Dr. Braman said.

Dr. Braman disclosed that he has received research funding from GlaxoSmithKline and Spiration, and he has been a speaker and consultant for Nycomed, GlaxoSmithKline, Pfizer, and Boehringer Ingelheim. ■

Cancer Patients Miss Routine Flu, Pneumonia Vaccinations

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

LOS ANGELES — Physicians cannot assume cancer patients are receiving influenza or pneumonia vaccinations while in the care of oncology specialists.

When surveyed at the University of Pennsylvania in Philadelphia, a third of radiotherapy patients aged 50 years and older reported they never had an annual flu shot. Among those aged 65 years and older, 30% said they never were vaccinated against pneumococcal pneumonia.

National guidelines call for vaccination of persons in these age groups. Moreover, by dint of their cancers and the treatments they were receiving, the patients surveyed were susceptible to life-threatening infections.

Yet many said they did not know about the vaccines, they did not need them, or the vaccinations were not recommended by a physician.

Such patients are falling into a gray zone, according to Dr. Neha Vapiwala, who presented results of the 214-person survey in a poster at the annual meeting of the American Society for Therapeutic Radiation and Oncology. Cancer patients see multiple physicians, none of whom is taking responsibility for routine prevention and maintenance measures, she said.

Although primary care physicians were more likely to recommend vaccinations than oncologists were, they did not do so routinely, according to the subgroup of patients who were vaccinated. Only 7% said that a cancer specialist discussed vaccinations with them; 44% cited conversations with their primary care physicians.

"If there is ever a question about that cancer patient sitting in your office—a question about which routine health maintenance and prevention measures should or shouldn't be recommended—pick up the phone, send that e-mail message, communicate with the oncologist," Dr. Vapiwala urged primary care physicians during a press briefing at the meeting.

Clearer mandates are needed on vaccinations for cancer patients and for "which physician is responsible for what," she said.

"Until that happens, we have patients now every single day in our clinic where assumptions are being made that specialist X is taking care of this item and primary care physician Y is taking care of that."

Although the study relied on patient responses, Dr. Vapiwala, a radiation oncologist at the university, said anecdotal experience supports the finding that vaccinations are being overlooked by oncologists.

Cancer patients see multiple physicians, none of whom is taking responsibility for routine prevention.
DR. VAPIWALA

"We only have to survey the 12 physicians in our department to find the overwhelming majority are guilty. I include myself in that group," she said.

Patients with a wide range of cancers were surveyed in outpatient clinics at the University of Pennsylvania. An unusually high proportion, 98%, completed usable questionnaires. Overall, 28% of the patients surveyed reported having received one or two doses of the pneumococcal vaccine. More than half, 58%, said they had yearly flu shots. The median age of the patients in the survey was 56 years.

The investigators reported no difference among cancer types or treatment regimens with respect to inadequate vaccinations. "There is no reason to believe any of these patients—being in an outpatient setting—had any condition that would prevent them from receiving their vaccines," Dr. Vapiwala noted.

Asked whether using electronic health records to prompt oncologists might be a solution, she said that would be of limited help in tracking which patients need the flu shots.

"Everyone in the room can go get it [a flu shot] at the supermarket, but the people who are actually really sick are not getting it anywhere because they either think they don't need it or they think they are too sick or their doctor didn't bring it up," she said with the admonition: "Somebody has to bring it up." ■

FDA Panel Ponders Efficacy of Phenylephrine Doses

Review prompted by allegations that 10-mg dose in OTC decongestant medications is not effective.

BY ALICIA AULT
Elsevier Global Medical News

SILVER SPRING, MD. — Phenylephrine, a primary ingredient in hundreds of over-the-counter nasal decongestants, appears to be effective at the current dose, but further research is needed to determine whether higher doses might be more effective, according to a Food and Drug Administration advisory panel.

The ingredient's safety was not a particular concern to the Nonprescription Drugs Advisory Committee. Although it is an α-adrenergic receptor antagonist, phenylephrine (PE) appears to be poorly absorbed systemically, at least when taken orally in doses used for decongestion.

The panel convened Dec. 14 to weigh a February 2007 citizen's petition submitted to the FDA that alleged that OTC medications containing 10 mg of PE are not effective. The dose should be increased to 25 mg, said the petitioners, a group of pharmacologists from the University of Florida. They also urged the FDA to prohibit use of PE-containing medicines by children under the age of 12, but the panel did not discuss that issue. The FDA is addressing OTC cough and cold medicines for children separately, according to the agency.

The committee voted 11-1 that PE was effective at 10 mg, but members were not confident about the efficacy data, which were largely from trials conducted decades ago with small numbers of patients and end points that the FDA no longer deems acceptable. When asked if the 10-mg dose worked, Dean Follman, Ph.D., a temporary voting member who is chief of the biostatistics research branch at the National Institute of Allergy and Infectious Diseases, said, "it probably does, but I don't really know based on the studies I've seen here today."

The evidence on the 10-mg dose "would not meet today's standards of evidence," Dr. Mary E. Tinetti, committee chair, said after the meeting. The data suggest that the 10-mg dose may be effective "but we need to understand a lot more in terms of who benefits," said Dr. Tinetti, professor of medicine at Yale University, New Haven, Conn.

Modern trials of the 10-mg and the 25-mg doses are needed, committee members said. Ralph B. D'Agostino, Ph.D., recommended randomized, controlled, double-blind studies that measure symptom relief in common colds and rhinitis. And, the studies should attempt to determine whether PE has any effect on blood pressure, which could be expected, despite the lack of adverse event reports, said Dr. D'Agostino, professor of mathematics and statistics at Boston University.

"What we really need are studies that relate dose to plasma concentration to effect," said Dr. Garret A. FitzGerald, chairman of the pharmacology department at the University of Pennsylvania, Philadelphia.

The FDA usually follows the advice of its panels. To affect how PE is studied now or in the future, the FDA would have to change the "monograph" for cold, cough, allergy, bronchodilator and antiasthmatic drug products. Monographs dictate how OTC products are regulated. Changing the documents can be cumbersome, but Dr. Charles Ganley, director of the FDA's OTC drug products division, said that the agency would do so, if necessary.

However, he said he believes PE drugmakers will be cooperative. "I'm confident we can get the support of the industry to do new studies," Dr. Ganley told reporters after the meeting.

The agency has no timeline for any action, said Susan Johnson, associate director of the FDA's office of nonprescription products.

PE, which is in products such as Sudafed PE, was determined to be generally safe and effective in 1994. A 10-mg dose also has been approved in Canada, Australia, and several European Union countries, according to the Consumer Healthcare Products Association (CHPA). More than 5 billion doses of PE have been distributed in the United States, Linda Suydam, CHPA president, said at the meeting.

SHERI MATTES/ELSEVIER GLOBAL MEDICAL NEWS

The evidence on the 10-mg dose "would not meet today's standards of evidence," Dr. Mary E. Tinetti said at a Food and Drug Administration advisory panel meeting.

CHPA presented analyses of 14 studies that evaluated the 10-mg dose in patients with upper respiratory infections or allergic rhinitis. In seven of the studies, PE had an effect on nasal airway resistance; in five of those seven, PE also improved nasal symptom scores, considered to be more indicative of a clinical effect. There was no significant effect in the remaining seven studies. A meta-analysis was supportive of the efficacy of 10 mg, said Ms. Suydam.

Two newer studies, however, failed to show any effect over placebo. Those trials, conducted in Canada and Austria in sophisticated enclosed chambers, did not demonstrate a significant effect for PE at 10 mg or 12 mg, said Melvyn Danzig, project director in allergy and respiratory clinical research for Schering-Plough/Merck Pharmaceuticals.

Lead petitioner Leslie Hendeles, Pharm.D., a professor of pharmacy and pediatrics at the University of Florida, told the panel that his review of the literature found that of 12 studies of the 10-mg dose, only 5 had a statistically significant difference from placebo. Eight of 10 studies of a 25-mg dose showed a difference, according to the petition.

Dr. Hendeles and his colleagues recommended dose-response studies and a moratorium on broadcast advertising of PE-containing products, calling them "grossly misleading."

The FDA reviewers said the agency prefers to see clinical symptom scores instead of mechanical outcomes such as nasal airway resistance. Only 7 of the 14 studies showed some positive effect, and there was symptom relief in only 5 of 12 studies with that end point, said Michael Koenig, a reviewer in the FDA's Office of Nonprescription Products.

There has been no signal that safety is an issue. From 1969 to 2007, there were 26 reports of an event associated with single-ingredient PE, said Mr. Koenig. Thirteen cases involved overdoses, five of which were medication errors, and only three were known to be intentional, he said. ■

Readmission of Trauma Patients Tied to Pulmonary Disease

BY KATE JOHNSON
Elsevier Global Medical News

MONTREAL — Pulmonary pathology is the most frequent reason for hospital readmission of multisystem trauma patients and should be ruled out before they are discharged, Dr. Jaime Bohl said at a meeting sponsored by the International Society of Surgery.

"In our experience, readmitted patients have a large burden of pulmonary disease and will require invasive treatment for pulmonary rehabilitation," said Dr. Bohl of Vanderbilt University, Nashville, Tenn.

In a retrospective review of 3,998 surviving multisystem trauma patients admitted to Dr. Bohl's level I trauma center between January 2002 and June 2004, she identified 156 patients (3.9%) who were readmitted within 30 days of discharge. The patients, whose average age was 40 years, were predominantly male (73%), and 81% were blunt trauma victims.

"We hypothesized that a subgroup of trauma patients could be identified who are at increased risk for readmission and that strategies could be developed to attenuate that risk," she explained.

Readmitted patients did not differ from nonreadmitted patients in terms of gender, mechanism of injury, ventilator days, location of discharge, or insurance group. "Patient risk factors for admission included age greater than 80 years, prolonged intensive care unit stay [more than 17 days], tube thoracostomy, and severe head and neck injury," said Dr. Bohl.

"Patients with any one of these characteristics had twice the risk of readmission."

Pulmonary diagnoses were the most frequent causes for readmission, occurring in 30% of patients. They included pneumonia (30%), pleural effusion (21%), retained hemothorax (13%), and empyema and pneumothorax (13%), she said.

In the case of one patient, a 32-year-old male admitted with a pneumohemothorax in the right chest, a chest tube was placed and then discontinued on post-injury day 3 as he appeared to have no significant fluid collection or retained hemothorax. Two days later, however, he was readmitted with fever, hypoxia, and leukocytosis. After undergoing video-assisted thoracopic surgery for retained hemothorax, he was given antibiotics and discharged 3 days later.

Chest x-ray in patients at risk of readmission is inadequate, according to Dr. Bohl. For this patient, she said, chest CT prior to discharge may have prevented his readmission.

"Despite the large burden of pulmonary pathology in our readmitted patients, thoracic injury was not associated with an increased risk of readmission. However, tube thoracostomy at initial hospitalization was associated with risk of readmission," she noted.

In addition to aggressive screening for pulmonary pathology, Dr. Bohl recommended drainage of fluid from the pleural cavity before discharge to avoid the risk of retained hemothorax and empyema.

Patients at risk of readmission should also have a short-interval follow-up; anyone hospitalized for more than 7 days should be seen within 7 days of discharge, she advised. ■

Lung Function Mildly Impaired After Roadside Walks

BY MARY ANN MOON
Elsevier Global Medical News

Asthmatic adults who took a leisurely 2-hour walk in London's shopping district showed significant but largely asymptomatic declines in lung function from exposure to diesel exhaust, study results suggest.

Study participants also showed inflammatory changes in sputum samples and exhaled breath condensate after their walks. These effects occurred even though particulate-matter concentrations were below those considered harmful under current World Health Organization guidelines and U.S. Environmental Protection Agency standards, investigators reported in the New England Journal of Medicine.

Dr. James McCreanor of the National Heart and Lung Institute of Imperial College, London, and his associates assessed lung function in real-world settings among 31 adults with mild asthma and 29 with moderate asthma. The subjects took 2-hour walks at their own pace, with several stops to rest, first along busy Oxford Street where traffic is restricted to diesel-powered taxis and buses, and some weeks later in Hyde Park, which is off-limits to vehicles. Exposure to particulate matter, ultrafine particles, elemental carbon, and nitrogen dioxide was markedly higher along the roadside than in the park.

The subjects walked about 6 km along predefined paths at midday in both settings. They were studied on weekdays between November and March to avoid confounding exposure to pollens.

The subjects showed significant declines in FEV_1 and forced vital capacity during their roadside walks, which persisted for a full day afterward. These decrements were larger in the subjects with moderate asthma than in those with mild asthma.

Sputum neutrophil counts and interleukin-8 concentrations increased only after exposure to diesel fumes. "We did not detect, even in participants with more severe asthma, an eosinophilic response characteristic of asthmatic inflammation," the investigators said (N. Engl. J. Med. 2007;357:2348-58).

Despite the declines in lung function, concomitant changes in respiratory symptoms were insignificant, and the use of treatments for asthma relief did not change significantly over the following week.

"The most consistent relationships between changes in respiratory variables and specific pollutant concentrations were for ultrafine particles and elemental carbon, a finding consistent with growing evidence that the adverse respiratory effects of diesel-generated particles are attributable to those in the very small size range," Dr. McCreanor and his associates noted.

"With their higher ratio of surface area to mass, ultrafine particles can adsorb greater fractions of potentially toxic substances onto their surface, and they are deposited more deeply and in greater numbers within the lung than are larger particles," they added.

The researchers cautioned that their findings shouldn't be taken as proving that ultrafine particles and elemental carbon caused the lung impairment, "since these may simply be a sensitive proxy for the entirety of a roadside diesel-traffic exposure, which is composed not only of the complex diesel exhaust mixture but also of resuspended coarse … particles from road dust and engine or tire debris, which we did not measure."

In an editorial comment accompanying this report, Dr. Morton Lippmann of New York University, New York, said the study was "highly structured and well executed, with realistic street-level exposures."

The findings clearly show that diesel exhaust at levels typical of a modern city "does produce acute small-airway effects in people with mild or moderate asthma and that greater, clinically significant effects are likely in people with more severe asthma," he said (N. Engl. J. Med. 2007; 357:2395-7).

Combo Asthma Therapies May Deliver Equivalent Control

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — Equivalent or perhaps better asthma control using combination therapy may be achieved with less budesonide/formoterol than fluticasone/salmeterol in the first year of use, Samy Suissa, Ph.D., said at the annual meeting of the American College of Chest Physicians.

Dr. Suissa and Dr. Pierre Ernst of McGill University Health Center, Montreal, reported the results of an observational study in 23,075 patients, aged 4-95 years, with long-standing asthma, who were first-time users of either budesonide/formoterol (6,918 patients) or fluticasone/salmeterol (16,157 patients). The two therapies are the only combination treatments currently available in a single inhaler.

The investigators used the United Kingdom's General Research Database, which includes 6 million patients from about 450 practices, to identify patients who received their first budesonide/formoterol or fluticasone/salmeterol prescription from May 2001 (when both therapies became available in the United Kingdom) to December 2005.

In an effort to emulate a prospective randomized trial, both intent-to-treat and persistent-treatment analyses were conducted on the frequency of prescriptions and health care events in the year after the first prescription; investigators adjusted for covariates measured during the year before this prescription.

A wide range of dosages and inhalers was used in each group. Patients with chronic obstructive pulmonary disease were excluded, said Dr. Suissa, who disclosed that both he and Dr. Ernst have received research grants and speaker fees from, and have served on advisory boards for, AstraZeneca Pharmaceuticals LP which manufactures budesonide/formoterol as Symbicort, and GlaxoSmithKline Inc., which manufactures fluticasone/salmeterol as Advair.

At baseline, budesonide/formoterol patients had a generally less severe asthma profile, compared with fluticasone/salmeterol patients, said Dr. Suissa, director of McGill's pharmacoepidemiology research unit, and professor of epidemiology, biostatistics, and medicine.

Budesonide/formoterol patients used fewer short-acting (83% vs. 85%) and long-acting (23% vs. 36%) β-agonists, and fewer oral (28% vs. 32%) and inhaled (47% vs. 57%) corticosteroids, and were less likely to have an asthma-related hospital visit (1% vs. 1.7%). Both groups saw their general practitioner an average of 10 times during the year prior to their combination therapy prescription. The groups' mean ages were 44 years (budesonide/formoterol) and 43 years (fluticasone/salmeterol).

In the intent-to-treat analysis, budesonide/formoterol patients received 14% fewer prescriptions for their study drug than did fluticasone/salmeterol patients, 8% fewer prescriptions for other asthma medications, and 9% fewer antibiotic prescriptions.

Persistent treatment, defined as two prescriptions with a gap of less than 7 days between them, averaged 3.1 months in the budesonide/formoterol group and 2.8 months in the fluticasone/salmeterol group. After adjustment for all baseline determinants, the duration of persistent use was 15% longer for budesonide/formoterol patients, Dr. Suissa said.

In the persistent-treatment analysis, which covered only the 3 months on average of continuous use, budesonide/formoterol patients received 11% fewer prescriptions for their therapy than did fluticasone/salmeterol patients, 8% fewer prescriptions for other asthma medications, and 11% fewer antibiotic prescriptions.

The rate of asthma hospitalization was also 16% lower in budesonide/formoterol patients, Dr. Suissa said.

Although the findings are promising, the study is limited by its observational design, he cautioned, and the findings need to be confirmed using a randomized trial approach.

Smoking Linked to Greater Risk of Type 2 Diabetes

BY MARY ANN MOON
Elsevier Global Medical News

Cigarette smoking is associated with an increased risk of developing type 2 diabetes, results of a meta-analysis suggest.

"Active smokers had an increased risk of developing type 2 diabetes, compared with nonsmokers, with a pooled relative risk of 1.44," study investigators reported in the Dec. 12 issue of JAMA.

The researchers conducted a meta-analysis of all 25 prospective cohort studies on this issue in the United States, Europe, Japan, and Israel that were published between 1992 and 2006. All of the studies examined a possible link between smoking and irregularities of glucose metabolism, and all but one found a positive association, Dr. Carole Willi of the University of Lausanne (Switzerland) and her associates wrote.

The number of study subjects ranged from 630 people to more than 700,000 people, for a total of 1.2 million subjects and 45,844 cases of incident diabetes in the meta-analysis.

Overall, 35% of the people were current smokers. Follow-up ranged from 5 to 30 years.

The association between smoking and diabetes remained robust through numerous statistical analyses that explored study factors as well as clinical variables. The findings also suggested a dose-response relationship, because the association with diabetes was stronger among heavy smokers than among light smokers, and was stronger in active smokers than in former smokers.

"Given this consistency, we conclude that the relevant question should no longer be whether this association exists, but rather whether this established association is causal," Dr. Willi and her associates said (JAMA 2007;298:2654-64).

The adverse effect of smoking on diabetes risk "has been generally underrecognized," Dr. Eric L. Ding and Dr. Frank B. Hu of the Harvard School of Public Health, Boston, said in an editorial accompanying the report.

Dr. Ding and Dr. Hu estimated that 12% of all type 2 diabetes in the United States may be attributable to smoking, based on this study's estimates, statistics on smoking prevalence, and an accepted population-attributable risk formula (JAMA 2007;298:2675-6).

In addition, "an estimated 2.3 million cases of diabetes in the United States and a corresponding $14.9 billion of the annual U.S. $132 billion diabetes cost burden may be attributable to smoking," they said.

Although the exact mechanism by which smoking may contribute to the development of diabetes hasn't been identified, smoking is known to be related to central adiposity. It is also known to increase inflammation and oxidative stress, to directly damage beta-cell function, to impair endothelial function, and to impair insulin sensitivity and glucose tolerance, said Dr. Ding and Dr. Hu.

PHOTODISC

Active smokers had a pooled relative risk of 1.44 for developing type 2 diabetes.

Given the findings of Dr. Willi and her associates, it is "important and prudent for clinicians to screen for and carefully monitor glucose levels among current and former smokers," they added. ■

Adults With Type 1 Diabetes Are More Likely to Smoke

BY MIRIAM E. TUCKER
Elsevier Global Medical News

CHICAGO — Adults with type 1 diabetes appear to be more likely than nondiabetics to smoke cigarettes but less likely to drink alcohol, researchers reported at the annual scientific sessions of the American Diabetes Association.

In addition, women with type 1 diabetes report that they engage in less physical activity and have higher body mass indexes than do nondiabetic women, whereas the reverse is true for men.

"Adults with type 1 diabetes could benefit from more intensive interventions targeting smoking cessation and increased physical activity in women," Franziska K. Bishop and her associates of the University of Colorado, Denver, wrote in a poster presentation at the meeting.

The researchers analyzed data from validated questionnaires distributed to 582 patients with type 1 diabetes and 724 nondiabetic controls who participated in the Coronary Artery Calcification in Type 1 Diabetes (CACTI) study. The patients with type 1 disease had a mean age of 37 years, and 46% were men. The nondiabetics had a mean age of 39 years, and 51% were men.

Overall, a total of 12.3% of the diabetic group reported being current smokers, compared with 8.6% of the nondiabetics.

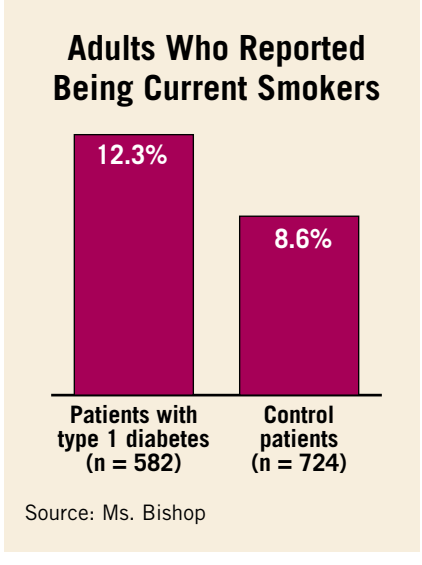
The type 1 diabetic group was more likely to report no lifetime history of alcohol use (10% vs. 4%), and those who did drink alcohol reported consuming fewer alcoholic drinks per month than did the subjects in the nondiabetic group (19 vs. 24 for the men, 9 vs. 13 for the women).

Men with type 1 diabetes reported more physical activity than did the nondiabetic men (34 vs. 31 kcal/kg per week), but the reverse was true for women: Those with diabetes averaged 28 kcal/kg per week, compared with 32 kcal/kg per week for the nondiabetic women.

Among men, the mean BMI value (kg/m^2) was higher for the nondiabetics (27.2 vs. 26.5), but again, the reverse was true for the women, with BMIs of 26 for the diabetics and 25 for the nondiabetics, Ms. Bishop and her associates reported.

The findings are of concern because cardiovascular disease is widely known to be a leading cause of death in people with type 1 diabetes.

Adults who have type 1 diabetes smoke more than do nondiabetic controls, which could increase their already elevated risk of diabetic nephropathy and cardiovascular disease, the investigators noted in their poster. ■



ELSEVIER GLOBAL MEDICAL NEWS

Reasons for Quitting Smoking Found to Vary With Smoker's Age

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — Older smokers are motivated to quit smoking by very different factors than are younger smokers, and tailoring cessation services to recognize these unique differences can improve quit rates, Virginia Reichert, N.P., said at the annual meeting of the American College of Chest Physicians.

Ms. Reichert and colleagues at the Center for Tobacco Control, North Shore–Long Island Jewish Health System, Great Neck, N.Y., reported the findings of a comparison study of 2,052 smokers; 143 were aged older than 65 years and 1,909 were aged 65 years or younger.

Older smokers were significantly more likely to report quitting smoking because of physician pressure (32% vs. 19%) and a recent change in health status (27% vs. 19%). Younger smokers attributed their reasons for quitting to general health concerns (81% vs. 68%), the cost of cigarettes (37% vs. 22%), and cigarette odor (33% vs. 18%).

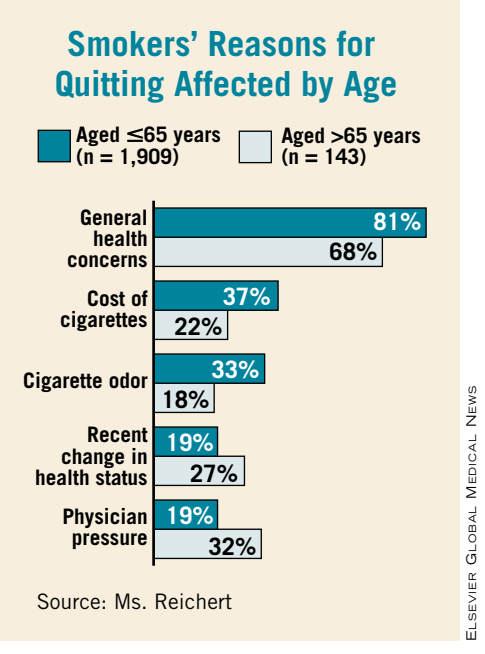
Older smokers were significantly more likely to report a recent hospitalization (23% vs. 13%), a diagnosis of cardiac disease (78% vs. 38%), cancer (20% vs. 6%), and chronic obstructive pulmonary disease and/or asthma (37% vs. 23%). Significantly more older smokers also reported smoking more than two packs per day (15% vs. 11%).

Older smokers were significantly more likely to report not wanting to give up their first cigarette in the morning as an obstacle to quitting (69% vs. 54%). In contrast, younger smokers were significantly more likely to cite weight gain (29% vs. 15%), handling social situations (24% vs. 7%), and stress relief without cigarettes (59% vs. 45%) as obstacles to quitting.

"If you're talking to an older person, you're not going to talk about weight gain and going out drinking in the clubs, you're going to go right into how this is impacting that person's health in particular," Ms. Reichert said in an interview. "With the younger smokers . . . you can develop strategies to manage stress and weight before they quit, so it's not an issue that will keep them from doing it."

Most of both the younger and older smokers erroneously believe that nicotine causes cancer. "They're not going to use the patches if they believe nicotine causes cancer," she said.

Roughly three-fourths of patients in both groups reported feeling guilty about smoking; while 72% of younger and 60% of older smokers worried that smoking would give them cancer. Nearly one-third of patients reported being depressed for much of the previous year, and a similar percentage reported receiving help or medication for their depression. At 30 days, 57% of younger and 58% of older smokers were smoke free. Of those who quit, 34% of younger smokers and 52% of older smokers remained smoke free at 1 year, Ms. Reichert said. ■



ELSEVIER GLOBAL MEDICAL NEWS

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Follow-Up X-Rays Not Needed in Some Severe CAP

Resolution of radiograph abnormalities may lag behind clinical improvement.

BY BRUCE K. DIXON
Elsevier Global Medical News

CHICAGO — Routine, short-term follow-up chest radiography may not be appropriate for patients with severe community-acquired pneumonia who clinically respond to initial antibiotic therapy, according to a multicenter study presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy.

"In addition, chest radiographs obtained prior to hospital discharge … seem to be unnecessary," according to the authors, whose study was published shortly after the conference (Clin. Infect. Dis. 2007; 45:983-91).

The use of follow-up chest x-rays of patients hospitalized for severe community-acquired pneumonia (CAP) has become common, and the absence of guidelines for this disease leaves physicians reliant on recommendations derived from grade D evidence, said lead author and presenter Dr. Anke H.W. Bruns, a research fellow in the Department of Internal Medicine and Infectious Diseases at the University Medical Center Utrecht in the Netherlands.

"Furthermore, the timing of those follow-up chest x-rays is difficult, in part because we know little about the time-to-resolution of findings related to infection on a film," Dr. Bruns said.

"So, follow-up radiographs probably are ordered unnecessarily."

To address the question of whether chest radiography is an appropriate follow-up measure, the researchers studied 288 patients enrolled between July 2000 and June 2003 from a prospective randomized trial on the cost-effectiveness of an early switch from parenteral to oral therapy for severe CAP.

The mean age of the patients in the study was 70 years, and two-thirds were men. The mean pneumonia severity index at hospital admission was 113, half the patients had comorbidities, and virtually all patients had been placed on a β-lactam (82%) or β-lactam–macrolide combination (14%).

'CHEST RADIOGRAPH DETERIORATION DURING FOLLOW-UP WAS NOT ASSOCIATED WITH POOR OUTCOME.'

Of the 140 cases with proven microbiological etiology, 44% had *Streptococcus pneumoniae*. Another 20% had atypical pathogens, including *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Legionella pneumophila*.

Patients were observed for a maximum period of 28 days, and those who were still hospitalized on day 7 underwent follow-up chest radiography. After hospital discharge, all patients were asked to return to the outpatient clinic for clinical evaluation, blood chemistry analysis, and a chest radiograph at day 28. The investigators calculated scores for clinical improvement on day 7 and for clinical cure on day 28 for each patient.

The cumulative dropout rate for radiographs was 21% at day 7 and 32% at day 28.

Radiologists reviewed the radiographs for the presence of pulmonary infiltrates, pleural fluid, atelectasis, pulmonary edema, and other findings. During follow-up, clearance of pulmonary infiltrates and resolution of chest radiograph abnormalities were established.

At 1 week, 33% of patients exhibited clearance of pulmonary infiltrates, and only 25% demonstrated resolution of chest radiograph abnormalities. At 1 month, 62% of patients showed clearance of infiltrates, and 53% had resolution of radiograph abnormalities. Resolution of abnormalities occurred more slowly in patients with proven *S. pneumoniae* pneumonia, the investigators reported.

Resolution of radiograph abnormalities lagged behind clinical improvement: At 1 week, clinical improvement was observed in more than half of patients, while resolution of chest radiograph abnormalities was seen in only one-quarter of patients. At 1 month, 78% of patients had clinical cures, and 53% showed resolution on radiograph.

The cohort was then split into two groups of equal size: one with radiographic deterioration, and one without radiographic deterioration. The researchers compared the groups for outcomes that included clinical cure at 1 month, mortality, and intervention during follow-up.

"We saw no difference in any of those three parameters; so, we can state that chest radiograph deterioration during follow-up was not associated with poor outcome," Dr. Bruns said at the conference sponsored by the American Society for Microbiology.

Clinical parameters that independently predicted delayed resolution of chest radiograph findings at 1 week included dullness to percussion, multilobar disease, high respiratory rate, and high C-reactive protein (CRP) level.

CRP level greater than 200 mg/L at admission also predicted delayed resolution of chest radiograph abnormalities at day 28.

The investigators noted that the number of interventions in patients with deterioration of chest radiograph findings was comparable to the number of interventions in other patients, suggesting that physicians' decisions were not made solely on the basis of chest radiograph findings.

"Performing a chest x-ray to exclude a noninfectious cause of pneumonia within 4 weeks of initial diagnosis is not indicated, because at this point half of patients have radiographic findings that are a result of normal clinical course and do not necessarily indicate pathology," Dr. Bruns said.

"Chest radiograph deterioration during follow-up was not associated with poor outcome, so in our opinion, routine in-hospital follow-up radiographs in severe CAP have no additional value," Dr. Bruns concluded. ■

First Rapid MRSA Blood Test Gets The Green Light From the FDA

BY ROBERT FINN
Elsevier Global Medical News

The Food and Drug Administration has recently approved the first rapid blood test for methicillin-resistant *Staphylococcus aureus*.

The test, called the BD GeneOhm Staph SR, can detect both methicillin-resistant *S. aureus* (MRSA) and more common and less dangerous strains of the staph bacterium in just 2 hours. Manufactured by BD Diagnostics, a subsidiary of BD of Franklin Lakes, N.J., the rapid blood test uses polymerase chain reaction techniques to detect a gene sequence unique to the drug-resistant strain of *S. aureus*. Traditional microbiology-based cultures require 24-72 hours to return results.

In 2005, BD received approval for a similar rapid test, the BD GeneOhm MRSA Assay, which detects MRSA in nasal specimens that are taken from patients.

That test is used primarily to screen patients who are about to enter the hospital for the presence of asymptomatic MRSA so that preventive measures can be taken.

The new rapid blood test will be used primarily to help health care practitioners choose among treatment options for patients already suspected of having an invasive staph infection.

According to BD spokesperson Barbara Kalavik, the company plans to begin marketing the BD GeneOhm Staph SR as soon as February in the United States. The company began marketing the test in Europe at the end of December.

Both versions of the test require the use of a specialized piece of equipment, called a PCR-thermocycler, which costs about $35,000.

Not counting the capital cost of this equipment, the new BD GeneOhm Staph SR blood test is expected to cost about $35 per patient, compared with about $25 for the older BD GeneOhm MRSA Assay.

The approval of the rapid blood test was based on the results of a multicenter clinical trial that demonstrated that the BD GeneOhm Staph SR correctly identified 100% of the MRSA-positive specimens and more than 98% of other staph infections.

According to the FDA, "In order to preserve the integrity of positive test results, this test should be used only in patients suspected of a staph infection. The test should not be used to monitor treatment for staph infections because it cannot quantify a patient's response to treatment."

In addition, the FDA warned that results from the test should not be used as the sole basis for diagnosis, since positive results may reflect the bacteria's presence in patients who have already been successfully treated for staph infections.

Furthermore, the agency cautioned, the test will not rule out other complicating conditions or infections. ■

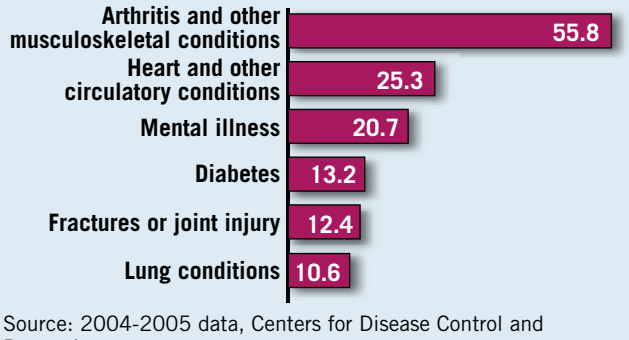
National Asthma Screening Drive Set to Begin in May

The American College of Allergy, Asthma, and Immunization is planning its 12th Annual Nationwide Asthma Screening Program. The screening campaign, in response to government guidelines on asthma control, will target those who are at risk for the disease and those already diagnosed but who may be missing school or work because of their condition.

To register as a participant in the program, go to www.acaai.org, where there are also online self-tests and information on managing asthma. Screening sites will be posted on the site in mid-March; screenings will be held in mid-May. ■

DATA WATCH

Activity Limitations Caused by Chronic Health Conditions in Adults Aged 45-54 Years
(per 1,000 population)



Source: 2004-2005 data, Centers for Disease Control and Prevention

ELSEVIER GLOBAL MEDICAL NEWS

Early Cytokine Changes Predicted Multiple Organ Failure

BY BRUCE JANCIN
Elsevier Global Medical News

COLORADO SPRINGS — A pattern of dramatically elevated serum cytokine levels within the first 6 hours following major torso trauma appears to identify patients at increased risk for subsequent multiple organ failure more effectively than do the Injury Severity Score and other traditional predictors, Dr. David W. Mercer said at the annual meeting of the Western Surgical Association.

These early changes in cytokine production not only mark a high-risk patient subset, but may also point the way to novel therapies aimed at preventing multiple organ failure (MOF), the leading cause of death among acutely injured patients in the ICU, added Dr. Mercer, professor and vice chairman of the department of surgery and chief of general surgery, trauma, and critical care at the University of Texas, Houston.

He presented a prospective, observational study of 48 patients with major torso trauma who underwent a standardized shock resuscitation protocol with measurement of numerous serum cytokines via multiplex suspension immunoassay every 4 hours for the first 24 hours after beginning resuscitation.

In all, 11 patients developed MOF, of whom 7 died. In contrast, mortality occurred in only 1 of 37 patients without MOF. That's an in-hospital mortality of 64% in the MOF group and less than 3% in the non-MOF group.

In addition, the MOF group had an average of 3.5 ICU-free days, compared with 17.8 days for non-MOF patients.

None of the traditional predictors of MOF—Injury Severity Score, age, admission hemoglobin, base deficit, and international normalized ratio—differed significantly between patients who subsequently developed MOF and those who didn't.

Serum cytokines were markedly elevated in the MOF group within 6 hours after trauma.
DR. MERCER

However, levels of both inflammatory and anti-inflammatory cytokines were markedly elevated in the MOF group within 6 hours after trauma.

Among them were the inflammatory cytokines interleukins-6 and -8, tumor necrosis factor–α, and interferon-γ, as well as the anti-inflammatory cytokines IL-10 and IL-1-receptor antagonist. Also elevated in the MOF group were several nontraditional cytokines: eotaxin, a chemotactic agent for eosinophils; granulocyte colony-stimulating factor; and granulocyte-macrophage colony-stimulating factor.

For years, Dr. Mercer has studied the hypothesis that shock-induced gut inflammation and the resultant derangement of the gut's normal barrier and immune defense mechanisms play a major role in the pathogenesis of MOF.

Recently, he has shown that ketamine, an anesthetic with anti-inflammatory actions, inhibits lipopolysaccharide-induced gastric dysfunction and prevents endotoxic shock from progressing to MOF (Eur. Surg. Res. 2007; 40:184-9).

Discussant Dr. James G. Tyburski of Detroit Receiving Hospital observed that in this 48-patient study, many of the traditional MOF predictors tended to differ between the MOF and non-MOF groups. He speculated that with higher patient numbers, the trend would have firmed up, and the traditional predictors would have achieved statistical significance. Dr. Mercer agreed that this was quite likely, but he noted that even in this relatively small study the cytokine differences did reach significance.

Pressed by Dr. Tyburski to name the single cytokine most worth measuring to predict MOF risk, Dr. Mercer said most researchers in the field would argue that it's IL-6. If two cytokines are to be measured, he'd recommend IL-6 and IL-10.

But Dr. Mercer added that the case for routinely measuring early cytokine levels in the ICU would become much stronger should future work show that therapies aimed at reversing the cytokine elevations actually prevent MOF. ■

FDA Eyes Risks Linked to Erythropoiesis Agents

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

More evidence associating erythropoiesis-stimulating agents with increased tumor growth and mortality in patients with cancer is being reviewed at the Food and Drug Administration and could result in additional action by the agency.

The new data are from two studies, according to an FDA statement issued on Jan. 3. In one study of 733 women who received chemotherapy before breast cancer surgery, 14% of those who received Aranesp, one of the ESAs marketed in the United States, had died 3 years later, compared with 9.8% of those who did not receive the drug; tumor growth also was faster among the former. In another study of patients receiving chemotherapy and radiation for cervical cancer, 59% of those who received Procrit were alive and free of cancer growth 3 years later, compared with 66% of those who did not receive Procrit. (In that study, patients received Procrit to maintain a hemoglobin level above 12 g/dL, or blood transfusions as needed.)

These two studies, along with six other studies that were summarized in recent revisions to ESA labels, "show more rapid tumor growth or shortened survival when patients with breast, non–small cell lung, head and neck, lymphoid or cervical cancers received ESAs compared to patients who did not receive this treatment," according to the FDA statement.

The agency might take additional action regarding the ESAs, and plans to hold a public advisory panel meeting in early 2008 to discuss the new data. Until then, the agency "recommends that health care providers review the risks and benefits of ESAs outlined in the product label and discuss this information with their patients," Dr. Janet Woodcock, the FDA's chief medical officer and acting director of the FDA's Center for Drug Evaluation and Research, said in the statement.

Previous FDA advisory panel meetings on the risks of ESAs resulted in revisions to their labels. In November, the FDA approved major revisions to the boxed warnings and other safety-related changes in ESA labels, reflecting evidence associating ESAs with an increased risk of tumor progression and lower survival rates when used to treat patients with certain cancers.

IN 733 WOMEN TREATED WITH CHEMOTHERAPY BEFORE BREAST CANCER SURGERY, TUMORS GREW FASTER IN THOSE WHO RECEIVED ARANESP.

In the United States, two epoetin alfa products (Epogen and Procrit) and darbepoetin alfa (Aranesp) are approved for treating anemia in patients with chronic kidney failure and for treating anemia caused by chemotherapy in certain patients with cancer. Epogen and Procrit also are approved for use during or shortly after surgery to reduce the need for blood transfusions in patients undergoing major surgery and for treating anemia caused by zidovudine treatment in patients with HIV. ■

VAP Prevention Impact Varies

Bundles • *from page 1*

then those bundles need to be revised and made more relevant to trauma/surgical patients so hospitals and surgeons aren't unfairly penalized, Dr. Offner said.

Ventilator-associated pneumonia (VAP) is the most common ICU-acquired infection and accounts for substantial morbidity, mortality, and health care cost. Numerous medical centers have reported success in sustaining extremely low VAP rates since introducing ventilator bundles. But these reports emanate from medical ICUs, not trauma/surgical ICUs, according to Dr. Offner.

St. Anthony is a busy urban tertiary referral center with just under 3,000 trauma admissions per year. The hospital has trauma surgeons and critical care medicine physicians on-site 24/7, and they do rounds together.

The hospital introduced the four-pronged ventilator bundle—the same as that advocated in the 5 Million Lives Campaign of the Institute for Healthcare Improvement—as a quality improvement initiative in August 2005.

Prior to implementation, ICU nurses and respiratory therapists received several months of intensive education. Compliance with the ventilator bundle was tracked daily, and VAP diagnosis was based upon the Centers for Disease Control and Prevention definition.

The VAP rate in the medical ICU fell from 7.8 cases/1,000 ventilator days at baseline to 2.0/1,000 ventilator days in the seventh quarter following introduction of the ventilator bundle.

In contrast, the rate increased slightly in the trauma/surgical ICU from 10 to 11.9 cases.

When the study period was divided into halves, the VAP rate dropped from 9.2 cases/1,000 ventilator days in the first half to 1.4 in the latter months. In the trauma/surgical ICU, the VAP rate was 13.7 cases/1,000 ventilator days in the first half and 11.6 in the second half, a nonsignificant difference.

The VAP rate in the cardiac and pulmonary ICU went from 6.2 to 3.0 cases/1,000 ventilator days.

Discussant Dr. Gregory J. Jurkovich said these results support the notion that the pneumonia commonly seen in trauma patients differs from that encountered in medical or coronary ICUs.

"Rather than calling it ventilator-associated pneumonia in these trauma patients, perhaps we should call it CTAP—chest trauma–associated pneumonia; or IAP—injury-associated pneumonia; or RAP—resuscitation-associated pneumonia," added Dr. Jurkovich, professor of surgery at the University of Washington and chief of the trauma service at Harborview Medical Center, Seattle.

"The four strategies in the ventilator bundle are advocated by the medicine-dominated critical care societies," he continued.

"This type of work [by Dr. Offner] is important as we become more beholden to national norms and practice guidelines," he added.

Asked which of the four bundle elements had the poorest compliance, Dr. Offner said it was, to his considerable surprise, elevating the head of the bed.

"I thought that would be the one that would be easiest to implement. But the nurses are concerned about elevating the head of the bed. They worry about pressure ulcers, the patient sliding out of the bed, things like that," Dr. Offner explained. ■

DVT Prophylaxis Underused in Hospitalized Patients

BY JEFF EVANS
Elsevier Global Medical News

BALTIMORE — Methods for determining how and when to use pharmacologic and mechanical interventions to prevent venous thromboembolism in surgical patients may remain open to debate, but the need for prophylaxis should not, Dr. Morey A. Blinder said at the annual meeting of the American Society of Plastic Surgeons.

Prophylaxis is underused because many clinicians believe that the incidence of deep venous thrombosis (DVT) in hospitalized patients is "too low" to warrant its consideration, said Dr. Blinder of the division of hematology and the department of pathology and immunology at Washington University, St. Louis.

Other physicians voice concerns about bleeding complications—particularly in surgical patients—and about heparin-induced thrombocytopenia, which occurs in 1%-2% of patients on heparin. Some doctors also seem unaware that broad applications of prophylaxis against DVTs can be cost-effective, he noted.

WITHOUT PROPHYLAXIS, STUDIES HAVE FOUND A DVT PREVALENCE OF 10%-20% IN MEDICAL PATIENTS AND 15%-40% IN GENERAL SURGERY PATIENTS.

"Many clinicians have the sense that venous thrombosis is not a particular problem in their practice," because they have not seen a DVT in one of their patients for several years or may have not known that a patient had a DVT diagnosed a week after surgery by an internist or at the emergency department, Dr. Blinder said.

In the absence of prophylaxis, studies have found a DVT prevalence of 10%-20% in medical patients, 15%-40% in general surgery patients, and about 20%-50% in stroke and orthopedic surgery patients. Even though most patients did not have symptomatic thrombosis in those studies, each patient underwent venography or a fibrinogen uptake procedure. Most series of major procedures in plastic surgery have found a risk of 1%-2% for DVT and/or pulmonary embolism, generally without prophylaxis, he said.

Risk factors that are temporary, like surgical procedures, immobilization, medical illness, in-dwelling venous catheters, prolonged travel, and pregnancy or estrogen-related therapies, appear to convey a lower recurrence rate to patients than those that are persistent, such as an underlying cancer, antiphospholipid antibody syndrome, or a previous venous thromboembolism.

In a study of patients who received warfarin for 3 months for an underlying thrombosis, those with persistent risk factors had about a 10% risk of recurrence in the following year, compared with a rate close to zero for patients with just a temporary risk factor, Dr. Blinder said.

Deficiencies in the body's natural anticoagulants, such as antithrombin, protein C, or protein S, lead to a substantial risk of thrombosis. An antithrombin deficiency may occur in only 1 of 5,000 blood donors, but it could occur in several percent of patients with a blood clot. About 5% of people with European heritage carry a mutation in the blood-clotting factor V Leiden, which increases the risk of thrombosis. In fact, 20%-30% of people who have venous thrombosis without an identified cause later turn out to be positive for the factor V Leiden mutation, he said.

"We've seen many, many patients who have [a factor V Leiden mutation] as an inherited risk factor, and then you add on a second risk factor like surgery or like an estrogen-containing hormone, and that is enough to trigger a blood clot," said Dr. Blinder.

The American College of Chest Physicians' evidence-based guidelines for preventing venous thromboembolism stratify patients undergoing general surgery as low, moderate, high, or highest risk, according to their age, the type of operation, and underlying risk factors (Chest 2004;126:338S-400S).

The guidelines advise early and frequent mobilization for low-risk patients and low-dose unfractionated heparin (LDUH) or low-molecular-weight heparin (LMWH) for moderate-risk patients. High-risk patients generally should receive LDUH every 8 hours, or an LMWH such as enoxaparin (Lovenox). Patients at highest risk for DVT need a full dose of an LMWH such as enoxaparin or the factor Xa inhibitor fondaparinux (Arixtra) in combination with intermittent pneumatic compression or graduated compression stockings.

Continued on following page

Continued from previous page

Surgeons in some specialties, such as orthopedics, recommend vitamin K antagonists or warfarin for very high-risk patients, but others do not do this because of difficulties, according to Dr. Blinder, who is on the speakers bureau for GlaxoSmithKline Inc., which manufactures fondaparinux.

Other guidelines issued by the American Society of Plastic Surgeons largely follow these recommendations but instead divide surgical patients into low-, moderate-, and high-risk groups (Plast. Reconstr. Surg. 2002;110:1337-42).

Dr. Blinder suggested that intermittent pneumatic compression (IPC) devices may see rising use because newer, fanny pack–size devices are much smaller than previous ones. Graduated compression stockings are thought to increase blood circulation by restricting the venous diameter. IPC devices also restrict venous diameter and are known to more than double the velocity of blood and increase fibrinolytic activity.

A meta-analysis of 15 randomized, controlled trials using IPC to prevent DVT in surgical patients found that the devices could drop the risk of DVT by 60%, vs. no prophylaxis (Thromb. Haemost. 2005; 94:1181-5). IPC might be useful in trauma and orthopedic surgery patients who should not receive enoxaparin or fondaparinux, Dr. Blinder said. However, IPC suffers from poor compliance and patient intolerance because the machines become warmer over the course of hours of operation. Some patients also find the IPC devices difficult to use properly.

Investigators have not resolved which type of mechanical device is best to use or the appropriate time to start or stop prophylaxis, but some type of pharmacologic prophylaxis should be included along with mechanical methods, he advised. ■

Endovascular Aortic Repair Deemed Best

BY MITCHEL L. ZOLER
Elsevier Global Medical News

BALTIMORE — Endovascular repair was safer than open surgical repair of traumatic, thoracic aortic transections in a meta-analysis that included almost 700 patients.

A large, prospective, randomized comparison of endovascular and open repairs for thoracic aortic transections has never been done, and may never be done, Dr. Gale L. Tang said at the Vascular Annual Meeting. Without direct comparison data, a meta-analysis of small studies may be the best alternative available for comparing the two treatment options.

A systematic review of retrospective, nonrandomized studies that assessed the repair of traumatic thoracic aortic transections and were published during 2001-2006 identified 33 reports involving a total of 370 patients who underwent endovascular repairs and 329 who had open repairs. The average age of the patients, their injury severity scores, and the technical success of repairs were similar in the two treatment arms.

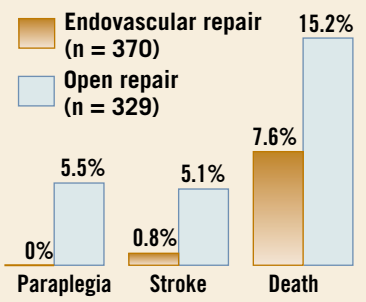
The study focused on three indicators of safety during follow-up: death, paraplegia, and stroke. The incidence of all three was significantly lower in the endovascular group, compared with the open-repair group, said Dr. Tang, a vascular surgeon at Northwestern University, Chicago (see graphic).

The incidence of postrepair complications also favored endovascular repair. The most common complications were iliac-artery injury in the endovascular-repair group, and recurrent laryngeal nerve injury in the open-repair group.

The only question that remains is whether the long-term durability of endovascular repairs will rival the durability of open repairs, Dr. Tang said.

"It seems clear that endovascular repair is the way to go for traumatic tears," commented Dr. Richard P. Cambria, chief of vascular surgery at the Massachusetts General Hospital in Boston. "There has not been an open repair of [a traumatic thoracic aortic transection] at our hospital for 3 years." ■

Outcomes From Endovascular and Open Thoracic Repairs



Note: All differences were statistically significant.
Source: Dr. Tang

ELSEVIER GLOBAL MEDICAL NEWS

Consider Deactivating ICD Near End of Life

BY SHERRY BOSCHERT
Elsevier Global Medical News

SAN FRANCISCO — One reason that few implantable cardioverter defibrillators get shut off to prevent a painful, unnecessary shock near the end of a patient's life is that physicians disagree about who should begin the deactivation discussion, Dr. Amy S. Kelley said.

In addition, some physicians prefer further aggressive medical treatments and they postpone discussing deactivation of implantable cardioverter defibrillators (ICDs), according to a survey that was mailed to 4,876 physicians and completed by 558. Inadequate knowledge about or awareness of ICDs also contributed to physicians' lack of attention to the issue, Dr. Kelley reported in a poster presentation at the annual meeting of the Gerontological Society of America.

"People at the bedside caring for a dying patient . . . may not be familiar with how the ICD works, and the fact that they are very easy to deactivate," said Dr. Kelley of the University of California, Los Angeles. "Even if it's functioning as a pacemaker, the shut-off function is entirely separate and could be deactivated in a moment's time at the bedside with a magnet and an electrophysiologist or even a nurse."

The 96 general internists, 106 cardiologists, 163 geriatricians, and 193 electrophysiologists surveyed were asked if they would discuss ICD deactivation, advance directives, and "do not resuscitate" orders with terminally ill patients described in five vignettes. (See box.) The survey also solicited comments.

Of the 177 physicians who provided comments, 6% said they had never thought about deactivating an ICD, 2% were unaware of the separate pacer and defibrillator functions, and 1% declared a lack of knowledge about defibrillators. Overall, 21% of the commenters expressed a preference for further medical treatments over deactivation of the ICD.

Of the 177, 13% accepted primary responsibility for initiating discussions about deactivating pacemakers, 10% said another specialist should start the discussion, and 7% said the patient or family should bring it up first.

Data from a previous retrospective study that surveyed next of kin after a patient's death suggest that fewer than a fourth of ICDs get deactivated near the end of life, and then only after the patient suffered a painful shock from the device, she said.

Informed consent for ICD implantation should include information about deactivation options, 77% of physicians in the current survey agreed. A majority (58%) said guidance from experts on management of patients with ICDs would be helpful in their practices. There are no guidelines for managing the deactivation of ICDs.

The study has been accepted for publication in the American Journal of Geriatric Cardiology, Dr. Kelley said. ■

Dr. Thomas Behrenbeck, FCCP, comments: *Dr. Kelley addresses an important ethical and psychological issue. ICD devices are an important armamentarium in the treatment of patients with severe congestive heart failure. They have been proven to prevent sudden cardiac death and prolong life at a high quality of life, both by using their ability to deliver effective shocks to terminate ventricular fibrillation and by pacing in the presence of symptomatic bradycardia.*

Interestingly, because of the way they are applied (implanted subcutaneously), they have not become part of the algorithm when patients or their power of attorney decide to discontinue life-prolonging measures, i.e., medication, dialysis, etc. This can pose a potential dilemma, since indeed an ICD may, unwantedly, continue to perform its task regulating cardiac rhythm.

This article is important in the discussion to switch off the ICD, when the overall decision has been made to let nature take its course. This article is just the beginning, albeit an important one, to address the multiple layers that are associated with the issues to discontinue life supporting therapy.

End-of-Life Scenarios Surveyed

In the following scenarios, the percentages indicate how many of the 558 surveyed physicians would discuss ICD deactivation, advance directives, or do not resuscitate (DNR) orders with patients.

- A man with severe chronic obstructive pulmonary disease who reports a poor quality of life:
  ICD deactivation: 56%
  Advance directives: 88%
  DNR: 82%
- A man with advanced dementia who is agitated by medical appointments and tests:
  ICD deactivation: 71%
  Advance directives: 84%
  DNR: 84%
- A woman with stage IV ovarian cancer who requests palliative care:
  ICD deactivation: 79%
  Advance directives: 94%
  DNR: 93%
- A man with end-stage renal failure who declines dialysis:
  ICD deactivation: 76%
  Advance directives: 90%
  DNR: 90%
- A woman with a massive stroke whose family has requested ventilator withdrawal:
  ICD deactivation: 83%
  Advance directives: 80%
  DNR: 83%

Death Rattle Can Be Limited By a Few Simple Measures

DALLAS — The key point in preventing the death rattle that's so distressing to the family of a dying patient is to avoid the natural inclination to perform suctioning, Dr. Steven Pantilat said at the annual meeting of the Society of Hospital Medicine.

Put one or two drops of atropine 1% ophthalmic solution under the tongue every 1-2 hours.
DR. PANTILAT

"It's tempting when you hear it to want to suction," noted Dr. Pantilat, director of the palliative care program at the University of California, San Francisco.

But he explained that suctioning will simply make the patient gag and feel more uncomfortable.

The death rattle is caused by pooling of secretions in the upper airway. Several measures are effective in preventing or alleviating this unnerving sound. One is simply to turn the patient onto his or her other side, since it takes time for fluids to pool in the new position. Minimizing intravenous fluids also is helpful.

Placing one or two drops of atropine 1% ophthalmic solution under the tongue every 1-2 hours can be effective at decreasing secretions. "What's nice about this is you can send the patient home with it, or it gives the family something to do in the hospital," Dr. Pantilat said.

For a patient who is conscious, a better alternative anticholinergic agent is intravenous glycopyrrolate. Unlike atropine, this drug doesn't readily cross the blood-brain barrier, so it decreases secretions without causing sedation. The dose is 0.2-0.4 mg every 4 hours.

A scopolamine patch also is highly effective for preventing the death rattle. It's a lot more convenient than administering sublingual atropine drops every 1-2 hours. However, it's much more expensive, and many patients who develop the death rattle are so close to the end of life that they're unlikely to obtain the full 3 days' worth of benefit from the patch.

(Medical editor's note: These medications are not FDA-approved for this indication.)

—Bruce Jancin

Pulmonary Perspectives

Endobronchial Valves in COPD

COPD is a highly prevalent condition with frequent morbidity and mortality. Emphysema alone afflicts approximately 3 million people in the United States, with associated costs of US $ 2.5 billion annually and nearly 14,000 deaths each year. In the most advanced stages, it causes debilitating breathlessness that is not improved despite maximal medical therapy, including smoking cessation, bronchodilators, corticosteroids, and supplemental oxygen. The limitations of medical therapy led to the development of several surgical techniques to improve quality of life.

The National Emphysema Treatment Trial (NETT) compared the efficacy of lung volume reduction surgery (LVRS) with standard medical therapy and reported improvements in survival and functional benefits in a subgroup of patients with upper-lobe-predominant, heterogeneous emphysema and limited exercise capacity (Fishman et al. *N Engl J Med* 2003; 348:2059). However, it still carries a substantial morbidity, even if the mortality is low at centers with a larger realm of experience. Hence, investigators are vigorously pursuing research into innovative, alternative methods for achieving LVR.

Endobronchial devices, working as one-way valves, allow air to exit the lung parenchyma but not to re-enter, potentially leading to atelectasis of the desired area of the lung. By obstructing air supply to the most hyperinflated, emphysematous areas of the lung, endobronchial valves could promote collapse of these areas through absorption atelectasis. These valves might also have benefits, even in the absence of atelectasis, by reducing physiologic dead space and improving efficiency of ventilation. They could also reduce dynamic hyperinflation by diverting air flow to less obstructed areas of the lung. Two devices are currently under clinical evaluation: Spiration IBV Valve System and the Emphasys one-way valve.

The Spiration® IBV® Valve System (Spiration Inc; Redmond, WA) has a nitinol (nickel-titanium) framework with five anchors that engage the airway and provide stability. The proximal support struts are covered by a synthetic polymer that allows the valve to conform to the airway wall. This device looks like a semi-opened umbrella, which opens further during inspiration to prevent air entry and closes during expiration to allow air and secretions to escape. It is designed to be delivered through the working channel of a flexible bronchoscope. The valve design also includes a proximal central rod that allows repositioning or removal.

The results of the first human pilot study with IBV were recently reported (Wood et al. *J Thorac Cardiovasc Surg* 2007; 133:65). In a prospective, open-enrollment, multicenter trial, 30 patients with heterogenous upper-lobe-predominant emphysema underwent flexible bronchoscopic placement of valves into segmental or subsegmental airways. A mean of 6.1 valves were placed per patient, and patients were followed for 1 to 12 months. Patients underwent general anesthesia with endotracheal intubation, and airways were then sequentially sized with a calibrated balloon to determine valve size. Six-month follow-up data were available for 28 patients. There were no reported episodes of valve migration, erosion, or significant bleeding. Valves were removed in seven patients (LVRS, two patients; pneumonia, two patients; and nonresponse, three patients). There were no unanticipated serious adverse events, and the clinical events committee judged that no adverse events were definitively attributable to the valves. Anticipated adverse events, including COPD exacerbation and pneumonia, occurred in two patients. Although the clinical trial was not designed to establish efficacy of the valves, data were collected to provide guidance for future studies. No significant improvement was shown in FEV_1, lung volumes, or exercise capacity following valve placement in this study. In contrast, significant improvements were found in disease-specific quality of life, as measured by the St. George's Respiratory Questionnaire. The mean improvement at 1 month in this series was eight points, which was both clinically meaningful and sustained at 6 months. These results demonstrate the ease of use and low complication rates for the IBV. Further studies are needed to determine effects on lung function, exercise capacity, and quality of life, and to establish possible mechanisms of action.

The Emphasys endobronchial valve (EBV) (Emphasys; Redwood City, CA) is a one-way silicone, duck-bill valve mounted inside a nitinol frame with a proximal silicone seal. This particular device has undergone several design modifications. The latest version (Zephyr®) can be easily placed using a flexible bronchoscope and can also be removed easily. Snell and colleagues (*Chest* 2003; 124:1073) performed the initial human pilot study and showed that these bronchoscopic prostheses can be safely and reliably placed into the human lung, but absence of segmental or lobar collapse was the most surprising finding.

The first multicenter experience on treatment of end-stage emphysema using the EBV was recently reported (Wan et al. *Chest* 2006;129:518). Ninety-eight patients were treated in nine centers in several countries over a period of 20 months. A mean of 4.0± 1.6 valves were placed per patient, predominantly in the right upper lobe. Significant improvements were seen in FEV_1 (10.7 ±26.2% p=0.007), FVC (9.0 ±23.9% p=0.024), residual volume (-4.9 ±17.4%, p=0.025), and exercise capacity (23 ±55.3%, p=0.063). Eight serious complications (8.2%) and one death were reported. Patients treated unilaterally showed greater improvements than those treated bilaterally, and patients who had the whole lobe treated improved more so than patients who had only one to two bronchopulmonary segments treated. Follow-up information was recently reported for 19 patients who were followed with serial bronchoscopies at 1, 3, 6, 12, and 24 months (de Oliveira et al. *Chest* 2006; 130:190). The authors noted granulomas, not requiring treatment, as the main complication. Improvements in FEV_1 and FVC of >12% or >150 mL were observed, respectively, in 4 of 18 and 8 of 18 patients at 1 month. However, these results were attenuated at 24 months. Significant and clinically meaningful (greater than 4 unit change) improvements in the St. George's Respiratory Questionnaire persisted at 6 months in three of four domains, raising the question of long-term efficacy of these EBVs.

Hopkinson and coworkers investigated the effects of endobronchial valve placement on exercise capacity in patients with emphysema and related this change to dynamic hyperinflation (*Am J Respir Crit Care Med* 2005; 171:453). They reported an increase in cycle endurance time at 80% of peak workload (p=0.03) and a reduction in end-expiratory lung volume at peak exercise (p=0.03). The authors concluded that EBV placement in patients with emphysema improves lung volume and gas transfer and prolongs exercise time by improving dynamic hyperinflation.

The results of the recently completed Emphasys bronchial **V**alve for **E**mphysema palliatio**N** **T**rial (VENT study) were presented at the 17th annual congress of the European Respiratory Society in September 2007. This multicenter study, conducted in 31 centers in the United States and Europe, enrolled 321 patients with severe heterogeneous emphysema and randomly assigned them to either treatment with EBV therapy with the Zephyr® endobronchial valve or to a control group in a ratio of 2:1. Both groups received optimal medical management, including pulmonary rehabilitation. In the treated group, the FEV_1 improved by 5.8% at 6 months, whereas it declined by 0.6% in the control group (p=0.0047). Significant improvement was also noted in the 6-min walk distance (p=0.0073). Protocol-defined major complications occurred in 5.9% of the treated patients as compared with 1.0% of the control subjects (p > 0.05). Emphasys Medical, Inc, has used the results of the VENT study to support a premarket approval application to the US Food and Drug Administration.

Other techniques of bronchoscopic LVR involve using biological reagents to remodel and shrink emphysematous regions. Results from an open label phase 1 trial, which enrolled six patients, have recently been reported (Reilly et al. *Chest* 2007; 131:1108). The procedure involves instillation of a primer solution followed by a fibrinogen solution and a thrombin solution, delivered separately but simultaneously to promote formation of a fibrin hydrogel. This hydrogel promotes atelectasis and inflammation, facilitating remodeling of the hyperinflated segment through scar tissue formation. Investigators noted that the procedure was well-tolerated, and no serious complications were encountered. Improvements in vital capacity, residual volume, 6-min walk distance, and dyspnea scores were also noted. These preliminary results indicate that there may be benefits with this procedure in appropriately selected patients with advanced heterogenous emphysema.

In summary, EBV placement appears to be a relatively safe procedure with minimal morbidity. The ability of EBVs to allow mucus to escape, and their ease of deployment and removal, are advantages of this technique. However, questions remain regarding efficacy, patient selection criteria, optimal number of valves, and their area of deployment. Some of these questions will be answered by the VENT study. Others will have to await further investigation in this developing field. ■

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Editor's Comments

We are undergoing a quiet but remarkable evolution in our thinking about heterogeneous emphysema. The NETT trial confirmed the possible benefits of surgical resection of these areas in selected patients.

Endobronchial valve placement may be an easier and safer step forward in providing options for managing these difficult patients. These procedures are intended, though, for patients with stable disease. The most recent lung cancer guidelines (Colice et al. *Chest* 2007; 132[suppl]:161S) suggest an intriguing approach to the surgical treatment of patients with a localized lung cancer in an upper lobe affected by heterogeneous emphysema and very poor lung function.

Combining lung volume reduction surgery with resection of the cancer might simultaneously provide curative treatment and improve lung function.

These are encouraging steps, although I agree with the authors that additional data are clearly needed to support the efficacy and safety of these approaches.

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

EDUCATION INSIGHTS

Health and Science Policy—How Current Are the Guidelines?

BY DR. SANDRA ZELMAN LEWIS
Assistant Vice President, Health and Science Policy/Quality Improvement

The Health and Science Policy (HSP) Committee has labored to develop rigorous methodologies and carefully crafted policies and procedures (Baumann et al. *Chest* 2007; 132:1015) that will lead to well-crafted, scientifically accurate, and clinically feasible recommendations. The HSP Guidelines Subcommittee is responsible, in part, for the maintenance of ACCP guidelines over time. Just how can a reader tell whether the evidence and recommendations are current in an ACCP guideline?

Each summer, ACCP staff send inquiries to the panel chairs of the guidelines that are more than 1 year past publication. These panel chairs know that their responsibilities include keeping current on the literature relevant to the recommendations and informing HSP staff if the guidelines become out-of-date or need updating. Some guidelines cover so many topic areas that chairs may appoint a small subcommittee of chapter editors to respond to the HSP Committee. For the first time, in 2007, a standardized form was prepared for the panelists to facilitate their review and response.

Starting in 2008, the HSP Web site now includes a posting of the guidelines classified according to the ranking system below, based on their level of currency relevant to the existing literature:

▶ **Rank: 1.** This guideline is new and represents the best available evidence at this time. It will be reviewed on an annual basis to determine if it remains current.

▶ **Rank: 2.** This guideline is reviewed on an annual basis, and there have been new studies published since the guideline was developed. However, the HSP Committee determined that these studies are not sufficient to warrant changing the guideline at this time. The information contained in this guideline provides the user with the best evidence available at the time the guideline was published. Readers are encouraged to search the current literature as a supplement to using this guideline.

▶ **Rank: 3.** This guideline is reviewed on an annual basis. The HSP Committee determined that new studies have been published that warrant an update of the chapter/section of this practice guideline. The HSP Committee also determined that the remainder of the chapters/sections does not require updating, and these recommendations remain current.

▶ **Rank: 4.** This guideline is reviewed on an annual basis. The HSP Committee determined that new data are available that are sufficient to potentially change guideline recommendations, and a full revision is warranted.

▶ **Rank: 5.** This guideline has been reviewed on an annual basis. The HSP Committee has decided it is outdated; however, it has been retained for historical and/or educational purposes. These guidelines should be used with caution for clinical decision-making purposes.

On the newly revised HSP Web site, users can access the guidelines directly from a grid that lists all HSP guidelines and any associated products (*eg,* clinical resources) based on those guidelines. In addition, the publication dates and complete references are provided, as well as the currency rankings and the date of the last currency assessment.

It is the aim of the HSP Committee members and staff to make access to our guidelines and information about our guidelines as simple as possible. Watch for future articles in CHEST PHYSICIAN about how HSP will make guidelines more easily implemented.

For responses to this article or other HSP matters, please contact Dr. Sandra Zelman Lewis at slewis@chestnet.org. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CHEST 2007 Practice Management Consultations

Some members took advantage of a service provided for the second year by the Practice Management Department during CHEST 2007 as part of the new pulmonary office exhibit.

Diane Krier-Morrow, MBA, MPH, CCS-P, coding and reimbursement consultant to the College, provided one-on-one consultations on any practice management issue of interest to ACCP members and their practice.

Thirty-three College members participated in these consultations and were pleased to speak with someone on issues of interest to their particular practice situation.

The discussions were as varied as the types of practice situations that exist. A sampling of the discussions follow:

- An Illinois second-year fellow planning to open a solo practice in Florida wanted to talk about where to begin in that he has not learned anything about practice management in his fellowship.
- A Pennsylvania interventional pulmonologist wanted to talk about developing a bronchoscopy suite in the office.
- A Florida member is developing an ambulatory surgical center for bronchoscopy and wanted advice.
- A pulmonary, critical care physician from Jordan wanted to talk about patient retention.
- A Texas physician wanted to talk about development of an electronic medical record in a pulmonary practice.
- A Pennsylvania practice wanted to talk about Medicare payment denials for vascular access codes with critical care code reporting. We talked with his billing staff to review the exact codes denied.

We provided him with his pulmonary Medicare Contractor Advisory Committee (CAC) members who attend quarterly meetings on behalf of all pulmonologists in most states.

- A Texas pediatric pulmonologist wanted to talk about billing sleep medicine codes and difference in payment in negotiated third-party payor contracts.
- A Minnesota practice wanted advice about patients receiving home oxygen and issues with DME providers.

Check the 2008 edition of the renamed ACCP coding book, *Coding for Chest Medicine 2008: A Practice Management Tool*, for details on the new procedure and service codes.

Most importantly, there are new smoking cessation counseling codes, **99406**, **99407** and subcutaneous infusion codes for immune globulin, **90769-90771** in CPT®.

All the new codes were discussed at the individual meetings and the roundtables.

In the Surgery Section, the Lungs and Pleural subsection codes were renumbered. ■

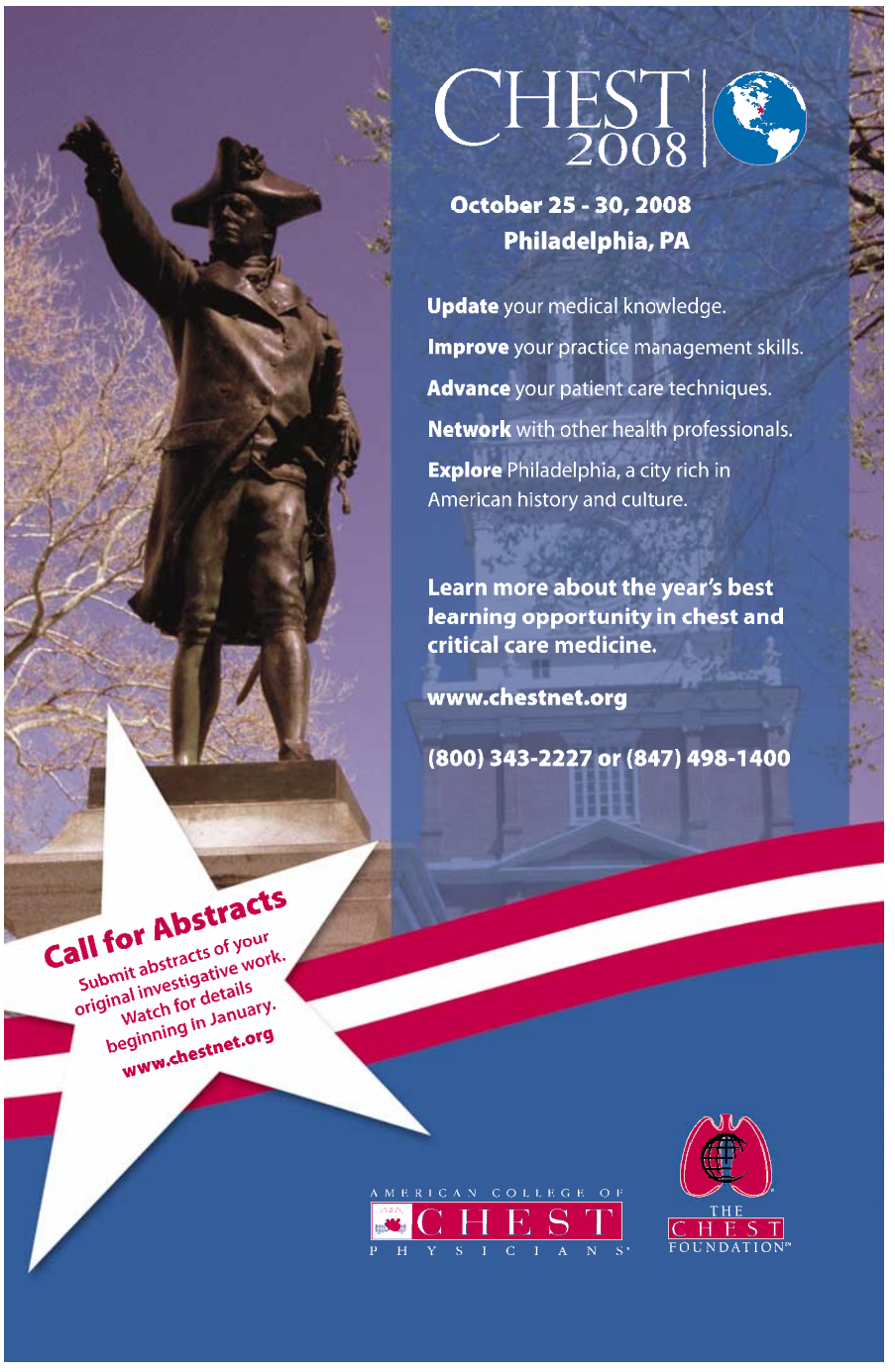
ACCP WORLDWIDE

Leadership Attends APSR/ACCP Congress

The ACCP and the Asia Pacific Society of Respirology (APSR) held their second joint congress November 30 to December 4, 2007, on the Gold Coast of Australia.

ACCP organized a postgraduate course on "ACCP Lung Cancer Guidelines: What's New in the Second Edition," as well as sessions in critical care and other topics. ACCP faculty and representatives included Dr. James A. L. Mathers, Jr., FCCP; Dr. W. Michael Alberts, FCCP; Dr. Richard S. Irwin, FCCP; Dr. Mark Rosen, FCCP; Dr. Gene Colice, FCCP; Dr. Curtis Sessler, FCCP; Dr. Gerard Silvestri, FCCP; Dr. Jeffery Vender, FCCP; and Alvin Lever, MA, FCCP(Hon).

Thank you to all of our Australia, New Zealand, and Asia Pacific region members who stopped by the ACCP booth to say hello and get information on upcoming ACCP programs. ■



NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

PATIENT INFORMATION ORGANIZATIONS

Ten Reasons Breathing Matters to All of Us

Allergy & Asthma Network Mothers of Asthmatics (AANMA) is dedicated to helping patients and families overcome asthma and allergies. We offer patient education resources and advocacy tools for patients and medical professionals, including our Breathing Matters™ 2008 conference held May 5-7, 2008, in Washington, DC. The conference brings together patients, medical-care providers, nonprofit organizations, and legislators.

1. Prepare for disasters: Dangerous air quality and lack of medication are a few of the problems people with asthma and allergies may face after a disaster. Learn what you can do to prepare your practice and your patients.

2. Make the move: *Smart Moves to an HFA Inhaler*™: AANMA offers practical resources to help health-care providers and patients make a safe, efficient transition from chlorofluorocarbon (CFC)-propelled bronchodilators to other devices, such as hydrofluoroalkane (HFA) inhalers.

3. Improve patient/provider communication: New asthma treatment guidelines stress the importance of patient/provider communication, yet often patients, families, and medical-care teams speak different languages. Learn what each side understands and expects from common asthma terms, and access resources for working with Hispanic patients and families.

4. Avoid risk from illegal nebulizer medications: The US Food and Drug Administration (FDA) is pursuing companies that mass manufacture nebulizer medications under the guise of patient-specific compounding. Until these companies are out of the manufacturing business, patient health is at risk, and medical care providers face liability risks. Learn how to identify FDA-approved medications and avoid imposters. (See related article in the November 2007 issue of CHEST PHYSICIAN at www.chestnet.org/about/publications/chestPhysicianArchives.php.)

5. Connect asthma with allergies and indoor air quality: Many asthma patients do not know the basic steps to minimize allergic reactions at home, school, work, and outdoors. Learn about available patient education resources.

6. Prepare students to self-carry medications: Whether students have immediate access to prescribed asthma and anaphylaxis medications can be a life-or-death situation. Find out how new state laws affect your patients and how you can keep students safe at school.

7. Meet with your elected officials: The key to effective advocacy is how you present your message and to whom it is presented. Learn practical communication and outreach skills that you can use locally and on Capitol Hill.

8. Work with the media: The media can be a powerful ally in your advocacy efforts. Learn the secrets of effective messaging.

9. Earn medical education credits: Medical professionals can receive continuing education credits for attending the conference and Capitol Hill events.

10. Inspire the patient advocates of tomorrow: From a hands-on overview of medications and devices to interactive sessions about meeting with members of Congress, youth attendees (10 to 16 years old) will learn how to make a difference for themselves and other children living with asthma, allergies, and food allergies.

For more information on AANMA's Breathing Matters™: Advocacy Conference and Asthma Awareness Day Capitol Hill 2008, visit www.breatherville.org/cityhall or call (800) 878-4403. ■

Media Highlights From CHEST 2007

CHEST 2007 in Chicago offered an exciting array of new scientific research, and the media took notice. To date, CHEST 2007 has yielded nearly 450 press mentions across print, broadcast, and Internet media outlets, and they're still coming!

In total, the ACCP actively promoted 56 abstracts for this year's meeting, 9 through press releases and 47 through categorized news briefs. Some of the most well received by the press included inhaler misuse, infrared imaging for sleep disorders, new uses for pulse CO-oximeters, 9/11 firefighters and corticosteroid treatment, and the association of chronic cough and iron deficiency in women.

The ACCP pressroom was active throughout the week, as researchers and medical experts made their way in and out to provide interviews. Two press conferences were held for reporters—Monday's focused on new developments in tobacco cessation and Wednesday's concentrated on new developments in the prevention and management of airways disorders. By the end of the week, 29 members of the press had attended at least 1 day of the meeting, with the majority spending 3 days or more covering the events.

Articles mentioning CHEST 2007 appeared around the country in the *Chicago Tribune*, *The New York Times*, *The Washington Post*, *The Wall Street Journal*, and *The Atlanta Journal-Constitution*, as well as in many trade publications. CHEST 2007 even appeared on newsstands abroad, in an article in *The Times of India*, the world's largest selling English broadsheet newspaper.

CHEST 2007 research also fared well in the broadcast medium, with multiple mentions on ABC, NBC, CBS, and FOX affiliates. Two separate live, on-air interviews were also provided to ABC's 24-hour news feed by Dr. Alvin Thomas, FCCP, President of the ACCP, and Dr. David Prezant, FCCP, Chief Medical Officer and Co-Director of the WTC Medical Monitoring and Treatment Programs for the NYC Fire Department.

Thanks to everyone who helped with the successful CHEST 2007 media campaign. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

NETWORKS

Disaster Simulation, Familial Pulmonary Fibrosis, and More

Cultural Diversity in Medicine

The Cultural Diversity in Medicine (CDM) NetWork was originally focused on making a difference in the lung health of minorities and children. Over the last few years, the NetWork has expanded its scope into two major areas: (1) cultural diversity education, and (2) health and health-care disparities topic discussions and involvement.

At CHEST 2006 in Salt Lake City, the NetWork provided a postgraduate course entitled: "Culturally Competent Health Care: An Education Program for Chest Physicians," and plans to use it as a resource for pulmonary fellows-in-training curricula. A presentation at CHEST 2008 is planned to begin addressing some solutions to this extensive problem in US medicine. The NetWork and The CHEST Foundation are involved with the Commission to End Health Care Disparities, co-chaired by the American Medical Association and the National Medical Association, to promote their four areas of interest: increasing awareness of disparities, promoting better data gathering, promoting workforce diversity, and increasing education and training. Please check www.ama-assn.org/ama/pub/category/12809.html for more information about this commission.

The NetWork is available to collaborate with all other ACCP NetWorks on educational activities. Utilize the resources that are posted on the Cultural Diversity in Medicine NetWork Web pages at www.chestnet.org/networks/cultural_diversity/index.php. Educational slide presentations for both health-care providers and the community are featured. Included are two PowerPoint presentations designed for community presentations to minority groups on lung health—"Healthy Lungs for African Americans" and "La Salud del Pulmon." To contact this NetWork, e-mail Lee Ann Fulton at lfulton@chestnet.org.

Disaster Response

Disaster simulation offers a learning experience that allows practitioners to perform skills that are part of the everyday clinical experience, such as intubation, airway care, auscultation, and drug administration, while wearing a level B biohazard suit and breathing apparatus. This learning event is invaluable for those practitioners who are part of a mass casualty (hospital disaster) planning scenario or have the potential of being called to the ED as part of an ongoing disaster event.

As part of CHEST 2007, the disaster simulation team used didactic lecture and slides, along with hands-on training on wearing the biohazard suit while functioning in various hazardous scenarios, such as exposure to chemical and/or biological agents. Training also included the use of real antidote kits. The simulation mannequin used was an advanced model that allowed for changing scenarios and clinical responses based on clinical interventions by the learner.

The learner was taught how to use a hazard suit correctly, along with the breathing apparatus, boots, and gloves, and to correctly remove the suit without self-contamination upon leaving the scenario. Following an all-hazards approach, the learner was taught how to function in an alternate way without the use of a stethoscope or the usual tactile use of the hands, or to be able to hear over the sound of the air blower. The learner was given an overview of the characteristics of particular chemical and biological agents (event recognition) that represented the potential for respiratory involvement of the patient. At the end of the scenario, the learner was also given an overview of the particular decision-making logic to cover the main points, such as control of contamination, personal protective equipment, and personal and physical adjustments to wearing a biohazard suit.

This real-time training will help participants understand the issues of safety for both the patient and practitioner. The overwhelming feedback was that this learning experience was extremely helpful and provided critical information for institutions' planning purposes and stockpiling equipment requirements.

Alan Roth, RRT
Disaster Response NetWork
Steering Committee Member

Home Care

The Home Care NetWork continues to encourage the active participation of health-care professionals in the fields of critical care, pulmonary, and sleep medicine, as well as inviting essential contributions from ventilator users, patient advocacy groups, and home care vendors. It is an exciting time for home care, as the rapid introduction of new technologies allows for the increasing application of life-sustaining treatments outside of the ICU. This includes the use of mechanical ventilators, oxygen therapy, and devices for sleep-related breathing disorders and involves physicians and health-care professionals throughout the continuum from home to ICU and back again.

The Home Care NetWork is involved in patient advocacy, expressing collective views through the Government Relations Committee to legislators on a number of issues, including capped rentals for bilevel devices with a back-up rate, the tendering of home care services, changes in oxygen reimbursement, and competitive bidding. Decisions on these issues could have significant effects on the availability of home care services and supplies.

The Home Care NetWork plans to utilize its NetWork Web pages to provide important resources, *ie*, a Web-based home ventilation resource center that will include the following:

- Information sections on specific ventilator products, both current and out of production.
- A primer on home ventilator management.
- A ventilator acquisition checklist.

This resource will assist health-care providers, particularly those in developing countries, by providing the education necessary to match clinical needs to specific technology and manage available ventilators outside the ICU setting.

New projects under consideration include one on assessment of noninvasive ventilation (NIV) clinical practices with a focus on the needs of patients supported by NIV and what would happen in the event of a disaster and one on using downloaded information from bilevel equipment for patient management.

Members of the NetWork continue to participate in national and international meetings in order to provide continuous improvements in the care of technology-dependent home care patients. More information about the Home Care NetWork is available at www.chestnet.org/networks/home_care/index.php.

Interstitial and Diffuse Lung Disease

Familial Pulmonary Fibrosis: New Insights

For the vast majority of patients with progressive pulmonary fibrosis, the underlying etiology is unclear. New genetic findings suggest that for at least a small subset of these patients, we may be one step closer to an answer. There are families in which multiple first-degree blood relatives develop interstitial lung disease (ILD). The family members with ILD are classified as having familial interstitial pneumonia (FIP). Approximately 80% of these patients with FIP have the familial form of idiopathic pulmonary fibrosis (IPF). Two recent genetic studies focused on FIP families with familial IPF have shed new light on the pathogenesis of pulmonary fibrosis.

Two groups (Armanios et al. *N Engl J Med* 2007; 356:1317; Tsakiri et al. *Proc Natl Acad Sci USA* 2007; 104:7552) independently identified important abnormalities in the same gene, *TERT*. This gene encodes the protein component of an enzyme complex called telomerase. Telomerase activity maintains telomeres, structures at the ends of human chromosomes that allow chromosomes to be copied during cell division. Interfering with telomerase function ultimately leads to cell death.

Both groups showed that within a few of these FIP families, inactivating mutations in one copy of *TERT* were present, consistent with the dominant inheritance pattern seen.

As with nearly every genetic "breakthrough," the ability to test individuals for gene mutations progresses faster than our understanding of the results. The identification of telomerase abnormalities in these patients has rapidly led to the development of commercially available genetic testing. The utility of this testing for most patients with pulmonary fibrosis is, at best, unclear.

Similar to previously identified genetic abnormalities in patients with pulmonary fibrosis (*eg*, surfactant protein C), these mutations are not common. Even among FIP families with well-defined familial IPF cases, the majority of family members will test negative for *TERT* mutations. In the studied FIP families, 90% did not carry the mutation. Remaining unanswered is whether telomerase dysfunction plays any role in the overwhelmingly more common sporadic IPF.

A positive mutation test also has limitations. For asymptomatic individuals testing positive, nothing is known regarding the lifetime risk of pulmonary fibrosis related to these mutations. Given these and the other inherent limitations and risks of genetic testing, it appears too early to embrace or recommend this testing for patients or families with pulmonary fibrosis. ■

Dr. Sonye K. Danoff, FCCP
Interstitial and Diffuse Lung Disease NetWork
Steering Committee Member

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

The CHEST Foundation Announces Awards for 2008

▶ AST/CHEST Foundation Clinical Research Award in Lung Transplantation

New amount and extended length of time for research

For 2008, the American Society of Transplantation (AST) and The CHEST Foundation have renewed their partnership and are offering a 2-year, $80,000 clinical research award in lung transplantation. Payments of $40,000 each year will be granted to the successful candidate who submits an outstanding research project in the field of lung transplantation. Second-year payment of $40,000 will be granted upon a written progress report showing substantial progress, subject to the approval of AST and The CHEST Foundation. This award opportunity is extended to current ACCP and AST members who work in Canada, Mexico, or the United States who meet the qualifications described in the application.

▶ The CHEST Foundation/LUNGevity Foundation Clinical Research Award in Lung Cancer

Based on the exceptional quality of the applications received in previous years for The CHEST Foundation/LUNGevity Foundation Clinical Research Award in Lung Cancer, this successful partnership continues in 2008. A 2-year, $75,000 award in the area of lung cancer research will be granted to the successful candidate who submits an outstanding research project. NEW for 2008: This award opportunity is open to all Canadian, US, and international ACCP members who meet the requirements described in the application.

▶ New Focus for The CHEST Foundation Humanitarian Awards

Based on recommendations from The CHEST Foundation's Pro Bono Committee, the 2008 Humanitarian Recognition Awards, in the amount of $5,000 each, will be granted to ACCP volunteer projects/programs at international locations only. The Project Development Grants, in the amount of $25,000 each, will be granted to US or international pro bono projects/programs.

ACCP members who have been granted funds to support their volunteer projects/programs in the past may apply in 2008, but members who have been humanitarian award recipients (or Governors Community Service Award recipients) two times may not apply for additional funding in 2008. Award checks are issued to projects or programs that are affiliated with a nonprofit or nongovernmental organization, of which documentation, via official letter or certificate, must be provided with the completed application.

Go to www.chestfoundation.org for details on the above awards, as well as others: the Second GlaxoSmithKline Distinguished Scholar in Thrombosis, the Association of Specialty Professors/CHEST Foundation Geriatric Development Research Award, The CHEST Foundation Clinical Research Award in Women's Health, and the Roger C. Bone Advances in End-of-Life Care Award.

The deadline for ALL applications is **April 30, 2008**.

This Month in *CHEST*: Editor's Picks

BY DR. RICHARD S. IRWIN, FCCP

Editor in Chief, CHEST

▶ Prevalence of COPD in Five Colombian Cities Situated at Low, Medium, and High Altitude (PREPOCOL Study). *By Dr. A. Caballero, et al*

▶ Prognostic Value of the Echocardiographic Right/Left Ventricular End-Diastolic Diameter Ratio in Patients With Acute Pulmonary Embolism: Results From a Monocenter Registry of 1,416 Patients. *By Dr. B. Frémont, et al*

▶ The Modified Apache II Score Outperforms CURB65 Pneumonia Severity Score as a Predictor of 30-Day Mortality in Patients With Methicillin-Resistant *Staphylococcus aureus* Pneumonia. *By Dr. K. E. Kollef, et al*

▶ Effects of One-Legged Exercise Training of Patients With COPD. *By Dr. T. E. Dolmage; and Dr. Roger S. Goldstein, FCCP*

▶ The Impact of Critical Illness on Perceived Health-Related Quality of Life During ICU Treatment, Hospital Stay, and After Hospital Discharge: A Long-term Follow-up Study. *By Dr. J.G.M. Hofhuis, et al*

▶ COPD in Asia: Where East Meets West. *By Dr. W. C. Tan, FCCP; and Dr. T. P. Ng*

www.chestjournal.org

The GlaxoSmithKline Distinguished Scholar in Respiratory Health

In 2000, The CHEST Foundation embarked on an endowment campaign designed to provide a significant base of funding in support of CHEST Foundation education and awards programming. The Distinguished Scholar Program was developed to incorporate a specific area of cardiopulmonary and critical care medicine in order for ACCP members to extend their impact in clinical practice. The projects and programs undertaken by The CHEST Foundation Distinguished Scholars address public health issues or clinical practice issues that link to improvements in patients' lives.

The ACCP, The CHEST Foundation, and GlaxoSmithKline created the GlaxoSmithKline Distinguished Scholar in Respiratory Health Award in 2003. By endowing the Distinguished Scholar, GlaxoSmithKline (GSK) reflects the importance of developing new scientific innovations, educating physicians and their patients, and heightening public awareness regarding airways disorders.

At CHEST 2007, The CHEST Foundation announced that **Dr. Sidney S. Braman, FCCP**, had been selected as the Second GlaxoSmithKline Distinguished Scholar in Respiratory Health. Dr. Braman is the Division Director of Pulmonary and Critical Care Medicine at the Warren Albert Medical School of Brown University in Providence, Rhode Island. His project is "The ACCP Chronic Care Model for COPD and Its Comorbidities: An Initiative for Primary Care Physicians and Other Health-care Providers To Improve the Quality of Life and Health Outcomes for Patients With COPD." The focus of his project is: (1) to develop an evidence-based, guideline-driven COPD chronic care model for primary care physicians and other health-care providers that encourages high-quality chronic disease management; and (2) to study whether this model is effective in improving disease recognition and disease outcomes in COPD.

ACCP

Dr. Braman (left) receives distinguished scholar award during Convocation 2007 from Dr. Mark Rosen, FCCP.

Donate Your Honoraria To Make a Difference

The ACCP spring board meetings have provided ACCP membership with another option with which to give to The CHEST Foundation. In recent years, a philanthropic theme has emerged, largely due to the commitment of ACCP members attending focus groups or teaching fellows' courses. The CHEST Foundation invites ACCP members who are going to participate in a focus group sponsored by a pharmaceutical company to donate all or a portion of their honorarium to The Foundation. ACCP members have been very generous and have increasingly taken advantage of donating in this way.

Members who donate at the spring meeting can be first-time donors who become familiar with The Foundation's mission during a personalized appeal from a Foundation Trustee at the beginning of a focus group or they are long-time, committed donors. Last year, The Foundation introduced charitable giving to participants in the fellows' courses by distributing a brochure about the *Making a Difference Society for New ACCP Members*. This opportunity is available throughout the year. ACCP members serving as faculty for courses held throughout the year have the opportunity to donate their honorarium to The CHEST Foundation.

Honoraria, whether from focus groups or educational courses, provide much needed funding for The CHEST Foundation. These donations are directed to the general fund that supports The Foundation's four core program areas: clinical research, critical and end-of-life care, humanitarian programs, and tobacco prevention. To learn how to donate an honorarium, contact Teri Ruiz at truiz@chestnet.org.

FDA Advises Against Cold Remedies for Very Young

Agency cites risk of 'serious and potentially life-threatening side effects' in children under age 2.

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

The Food and Drug Administration has released a public health advisory strongly recommending against the use of over-the-counter cough and cold products in children and infants aged under 2 years, but will not issue recommendations until the spring about the use of these products in children aged 2-11 years.

During a telebriefing, Dr. Charles Ganley, director of the FDA's Office of Nonprescription Products, said that the agency had completed its safety review of these products in children aged under 2 years and concluded that the products should not be used in this age group because of the risk of "serious and potentially life-threatening side effects."

The advisory is based on a review of information the agency received about serious side effects—including deaths and seizures—associated with the use of these products in children this young. Also contributing to the decision were discussions and recommendations made at the FDA's Nonprescription Drugs Advisory Committee and Pediatric Advisory Committee joint meeting in October 2007. At that meeting, the advisory panel members agreed that there was no available scientific evidence that these products were safe and effective in children aged under 12 years, and they voted 21-1 that these products should not be used in children younger than 2 years.

Still pending, however, is the final decision about the use of over-the-counter (OTC) cough and cold products in children aged 2-11 years. An internal working group is continuing to deliberate over what to recommend for this age group.

At the October meeting, the panels voted 13-9 that these products should not be used in children aged 2-5 years, but they voted 15-7 in favor of keeping them available for children aged 6-11 years. Dr. Ganley said that there was debate over differences of opinion among the working group, which has been reviewing this issue since the panel meeting in October. The agency plans to make final recommendations in the spring, he said.

But the group unanimously agreed that the data in children under 2 years raised significant concerns and that OTC cough and cold products should not be used in this age group. Part of the reason the FDA decided to release the advisory now is that it is the middle of cough and cold season, and there is evidence that parents and caregivers of children may be continuing to administer these products to children younger than 2 years without consulting their health care providers, according to Dr. Ganley.

He referred to a survey of parents of children younger than 2 years of age—conducted by National Public Radio, the Kaiser Family Foundation, and Harvard School of Public Health, in November 2007. When asked what best described their reaction to the recent news about the safety and effectiveness of the OTC cough and cold products for children, 20% said they planned to continue using these products, 26% were undecided, and 15% had not heard about the discussions. (Sixteen percent said they planned to stop using these products, 22% said they had never used or planned to use them, and 1% were in the "other" category.)

And at a workshop on OTC product use among adolescents, held by the FDA and Consumer Healthcare Products Association (CHPA) last fall, the results of a survey of parents aged 16-25 years with infants younger than 12 months of age found that 86% considered the use of OTC cough and cold medications appropriate for children under age 2 years, without consulting a physician.

The agency has never endorsed the use of these products in children this young, and in the past has left it up to the discretion of the health care provider to decide whether their use was appropriate. Shortly before the panel meeting in October, manufacturers of products with wording and images of infants on the packaging of these products voluntarily pulled them off the market, and the CHPA and its member companies recommended to the FDA that the "ask a doctor" statement on the labels of these products be changed to "do not use" in children younger than 2 years—a suggestion which is supported by the agency, Dr. Ganley said.

Until the FDA makes recommendations about older children, the advisory includes recommendations for consumers. These recommendations include using only measuring spoons, droppers, or cups that come with the product itself; not using these products to sedate the child or make a child sleepy; and calling a physician, pharmacist, or other health care professional for any questions about the use of these medicines in children aged 2 years and older. ■

The public health advisory is available at: www.fda.gov/cder/drug/advisory/cough_cold_2008.htm. A consumer information sheet is available at www.fda.gov/consumer/updates/coughcold011708.html.

Pediatric *S. aureus* Resistance to Clindamycin Is Stable

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — The overall rates of resistance of pediatric *Staphylococcus aureus* isolates to clindamycin remained stable at around 11% in Southern California between 2004 and the first half of 2007, results from a large study of patients from that area have demonstrated.

At the same time, overall resistance to both a β-lactam and clindamycin remained stable at 2.8%, Dr. Mark B. Salzman reported at the annual meeting of the Infectious Diseases Society of America.

"We need to continue to monitor resistance rates of clindamycin and other antimicrobials," said Dr. Salzman, who is a pediatrician at Kaiser Permanente West Los Angeles Medical Center.

'Clindamycin can still be used as empiric therapy for most nonserious *S. aureus* infections.'
DR. SALZMAN

He and his associate, Susan M. Novak-Weekley, Ph.D., identified all *S. aureus* isolates from Kaiser Permanente Southern California patients under the age of 18 years between January 2004 and June of 2007. Kaiser Permanente Southern California is a large HMO system with 11 hospitals, 110 medical offices, and 839,000 patients younger than 18 years.

The researchers categorized the *S. aureus* isolates by year and by methicillin-resistant *S. aureus* (MRSA) status, methicillin-susceptible *S. aureus* (MSSA) status, and clindamycin susceptibility.

"Only one isolate per patient per year was counted unless it was different in susceptibility to either clindamycin or oxacillin or if it was from a different source cultured more than 6 months later," Dr. Salzman said.

In 2004, there were 2,095 *S. aureus* isolates in patients younger than 18 years, compared with 3,406 in 2005, 4,801 in 2006, and 2,329 in the first 6 months of 2007.

MRSA accounted for 33% of isolates in 2004, 43% of isolates in 2005, 45% of isolates in 2006, and 46% of isolates in the first 6 months of 2007. "Since 2005 the pediatric MRSA rates seemed to have reached a plateau," he said.

The number of clindamycin suspension prescriptions nearly tripled over the time period, from 1,276 in 2004 to a projected 3,300 in 2007 based on data extrapolated from the first 6 months of 2007. The number of prescriptions for clindamycin capsules also rose significantly over the time period, from 41,427 to 70,000 in 2007 based on data extrapolated from the first 6 months of 2007.

Clindamycin resistance rates to MRSA isolates were 8% in 2004, 7% in 2005, 6% in 2006, and 7% in the first 6 months of 2007, while the rates of resistance to MSSA isolates were 13%, 17%, 15%, and 15%, respectively.

The overall rates of clindamycin resistance to *S. aureus*, including both MRSA and MSSA, were 11.2% in 2004, 12.3% in 2005, 10.9% in 2006, and 11.2% in 2007. The rates "do not seem to be increasing," he said. "They're around 11.4% overall."

The percentages of isolates resistant to both β-lactams and clindamycin were 7% in 2004, 2.9% in 2005, 2.7% in 2006, and 3.1% in the first 6 months of 2007, for an overall rate of 2.8%. The researchers also found that overall resistance to trimethoprim sulfamethoxazole is low, about 0.5%, and is lower for MRSA isolates (0.4%).

Dr. Salzman offered several recommendations based on the study's findings. "All presumed *S. aureus* infections should be cultured if possible," he said. "Clindamycin can still be used as empiric therapy for most nonserious *S. aureus* infections, but I think that combining a β-lactam with clindamycin should be considered for empiric therapy of more serious *S. aureus* infections."

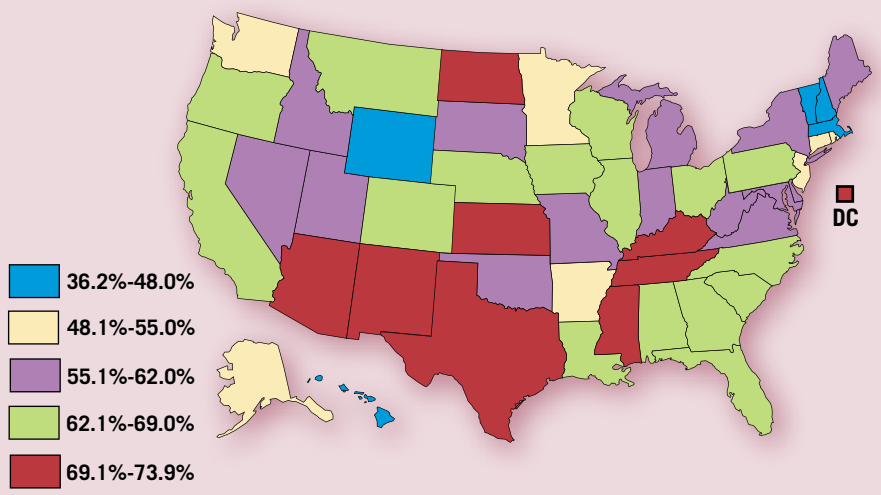
He advised that vancomycin be reserved "for life-threatening infections or very serious infections or empiric therapy when other therapies fail in the absence of culture and susceptibility confirmation."

Trimethoprim sulfamethoxazole provides "excellent coverage for empiric therapy, but if infection due to a β-hemolytic streptococcus is being considered, then a β-lactam should be added."

Dr. Salzman disclosed that he is on the speakers bureau for Sanofi Pasteur. ■

DATA WATCH

Percentage of Uninsured Children Living in Poor Families



Note: Based on children aged 0-18 years who are living in families below 200% of the federal poverty level.
Source: 2003-2005 data, Robert Wood Johnson Foundation

ELSEVIER GLOBAL MEDICAL NEWS

Diet During Pregnancy May Affect Child's Asthma Risk

BY JONATHAN GARDNER
Elsevier Global Medical News

Women who follow a Mediterranean diet during pregnancy may avert asthma-like symptoms and atopy in their children, suggest results of a population study published in the journal Thorax.

Researchers studying a birth cohort of 412 children in Menorca, Spain, found that offspring of mothers who closely followed a Mediterranean diet in pregnancy were less likely to experience persistent wheeze (adjusted odds ratio 0.22), atopic wheeze (OR 0.30), or atopy (OR 0.55) at a 6.5-year follow-up, compared with children of mothers who were less adherent to the diet.

Micronutrients such as antioxidants or polyphenols contained in the fruits, vegetables, legumes, and oils that are key ingredients of the Mediterranean diet may have protective effects against asthma, may protect the airways against oxidative damage, or may have anti-inflammatory effects, wrote Dr. Leda Chatzi of the University of Crete, Heraklion, Greece, and associates (Thorax 2008 Jan. 15 [doi:10.1136/thx.2007.081745]).

Over a 12-month period beginning in mid-1997, the researchers enrolled 507 women seeking antenatal care at general practices in Menorca. A total of 412 children of these women underwent skin-prick tests for allergies at a 6.5 year follow-up.

In addition, 468 parents completed questionnaires on children's respiratory and allergic symptoms, and supplied information on the mother's diet during pregnancy and the children's diet at 6.5 years using a food frequency questionnaire. The questionnaires were then scored according to how much of the food intake matched a traditional Mediterranean diet. A total of 36% of mothers had a low-quality Mediterranean diet in pregnancy; the remainder had a high-quality diet.

Approximately 13% of the children at follow-up had persistent wheeze, 6% had atopic wheeze, and 17% had atopy.

Maternal intake of vegetables more than eight times a week in pregnancy was significantly associated with a reduced risk of persistent wheeze (odds ratio 0.36) and atopy (OR 0.4) in their children, compared with children of mothers who ate fewer servings.

Eating fish two to three times a week and legumes at least once a week during pregnancy each was also significantly linked to a lower risk of persistent wheeze (OR 0.34 and OR 0.36, respectively).

Although there was a trend toward a high-quality Mediterranean diet in pregnancy having a protective effect against atopic wheeze, the association was not significant, possibly because of the small number of children affected (n = 20), the investigators wrote.

At 6.5 years, 9% of the children had a diet that scored low, 54% scored intermediate, and 37% scored high on the Mediterranean diet measures. Although a high score was found to be protective against persistent wheeze, the effect was only marginally significant, the researchers said. ■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Pregnant women in the study followed a traditional Mediterranean diet.

Dr. Nicola Hanania, FCCP, comments: *This study sheds more light on factors that determine the development of allergies and asthma in early childhood. Previous studies supporting the "hygiene hypothesis" suggest that exposures during early childhood to certain environmental hazards and infections (such as rhinovirus) may indeed be protective from developing a Th2-type immunologic response that favors allergies and asthma. The current study now suggests that there may be other exposures in utero that can indeed affect such a response.*

In this single-center cohort study, Mediterranean diet, which contains a significant amount of fruits, vegetables, legumes, and oils, in pregnant women was shown to be protective from developing asthma and allergies. Although the exact mechanism for such a protective effect is not known, it is speculated that many of the Mediterranean diet ingredients contain antioxidants that may play a major role.

While these findings are very interesting, future studies are needed to confirm the results in larger populations, especially given that many confounding variables that may have affected the results of the study were not accounted for.

Assess Asthma More Frequently

Unstable • *from page 1*

At 3 months, asthma control had deteriorated in 46% of the children who had mild intermittent asthma at baseline and in 33% of those with mild persistent asthma at baseline. Changes in control also were seen at 3 months in more than half of the children with moderate persistent asthma at baseline and in about half of those with severe persistent asthma at baseline.

Among children with persistent symptoms at baseline, "even greater shifts were observed between baseline and 6 months," at which time a change in the degree of asthma control was seen in more than two-thirds of the children with persistent symptoms at baseline in this study that appeared in the journal Pediatrics (2007;120:e1174-81).

These results "underscore the labile nature of asthma," and suggest that assessments of asthma control in young, inner-city children "should be repeated at least every 3 months to take advantage of opportunities to prevent future morbidity," Dr. Sharma and his associates said.

Poor control of asthma was an independent predictor of the children's use of asthma-related health care (unscheduled doctor visits, emergency department visits, and hospitalizations) during the preceding 3 months, with a significant association between poor asthma control and recent use of asthma-related health care, "suggesting that asthma control is related to overall recent disease activity," they said.

For example, 5% of those with mild intermittent asthma had an unscheduled doctor visit related to asthma within the previous 3 months, compared with 23% of those with moderate persistent asthma, and 42% of those with severe persistent asthma.

Their reported use of long-term controller medications, however, was not an independent predictor of their use of asthma-related health care.

The ability to accurately identify children who are at the greatest risk of morbidity in the future is a "key component" of successfully preventing asthma-related health care use and targeting high-risk children, but information about which clinical factors predict the risk of future asthma-related health care use among children is lacking, the authors wrote.

The investigators added that while these findings may not be applicable to other populations, they have "direct implications to inner-city black children, who bear much of the asthma burden in the United States."

Dr. Sharma and his associates added that this was the first study they knew of that found baseline control was predictive of future use of asthma-related health care in this population, noting other studies that found current asthma control was predictive of future use of health care resources in adults.

The authors indicated they have no financial relationships to disclose. ■

Dr. LeRoy Graham, FCCP, comments: *Frequent clinical monitoring of asthma control in young African American children in the inner city appears to be a logical strategy to reduce the disparate disease burden experienced in this population.*

Benign Parasomnias Call for Thorough Evaluation

Consider a comprehensive evaluation with EEG and brain MRI in REM sleep behavior disorder cases.

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SCOTTSDALE, ARIZ. — Even though sleepwalking, night terrors, and other parasomnias are usually benign and do not call for specific interventions, Dr. Teofilo L. Lee-Chiong Jr., FCCP, urged that they be thoroughly evaluated in children and adults.

Violent and potentially injurious behavior can endanger the person and/or the person's bed partner, according to Dr. Lee-Chiong, head of the sleep medicine section at National Jewish Medical and Research Center in Denver. A recent patient, for example, walked for 4 hours along a busy interstate highway while fast asleep, Dr. Lee-Chiong said at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

Another concern, he added, is that a patient with REM sleep behavior disorder could have undiagnosed Parkinson's disease or another neurological disorder. Characteristics of this condition include abnormal behavior during REM sleep, REM sleep without muscle atonia, and the enactment of altered, unpleasant, or violent dreams.

"I believe assessment should be extensive," Dr. Lee-Chiong said, recommending a comprehensive neurological evaluation with EEG and brain MRI in REM sleep behavior disorder cases. Even if these tests prove negative, he urged that the patient be closely monitored for years afterward in case a neurological disorder is late in emerging.

Another concern is that a patient could have undiagnosed Parkinson's disease.
DR. LEE-CHIONG, FCCP

Dr. Lee-Chiong defined parasomnias as undesirable physical phenomena or behaviors that appear "alongside sleep," but are not associated with more common complaints such as excess sleepiness or insomnia. "We all seem to know what it is, but deep down we know very little," he said, adding afterward in an interview, "If you take [posttraumatic stress disorder] away, there really is no psychopathology that predicts the development of parasomnias."

A variety of factors make evaluation difficult, according to Dr. Lee-Chiong. Patients are unaware of some parasomnias. Descriptions are often inaccurate or misleading. The clinician rarely sees the parasomnia. If it is not related to sleep architecture, then polysomnography may not be useful. Moreover, a single negative test does not rule out infrequent events.

Polysomnography is indicated when an underlying seizure disorder is suspected, someone has been injured, the case has medical-legal implications, or the person presents with REM sleep behavior disorder, according to Dr. Lee-Chiong. A seizure montage using many EEG electrodes should be used if seizures are a possibility during polysomnography. In REM sleep behavior disorder cases, he also recommends EMG monitoring of the upper extremities. Often four to six studies are required before a diagnosis can be made, he advised, and technicians need to be trained to recognize subtle features.

Dr. Lee-Chiong characterized sleepwalking, sleep terrors, and confusional

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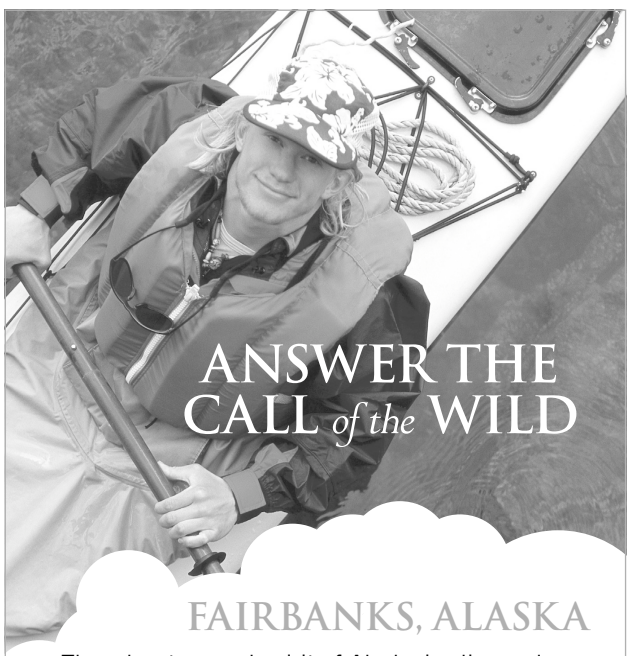

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arousals as disorders of arousal that usually occur in non-REM sleep during the first third of the night. These are four times as common in childhood, he said, with a prevalence of 16% vs. 4% in adults. Febrile illness in children and medications in the elderly are among the predisposing factors, though sleep terrors are uncommon in older people.

Genetics appears to play a role in sleepwalking, according to Dr. Lee-Chiong. Prevalence is 45% if one parent engaged in sleepwalking, and 60% if both parents had the condition. In addition, the DQB1*0501 allele is more common among sleepwalkers.

Treatments can range from proper sleep hygiene and relaxation techniques to pharmacologic agents, including low-dose benzodiazepines, SSRIs, tricyclic antidepressants, and trazodone. In cases of confusional arousals (waking with disorientation, inappropriate behavior, or inability to be consoled), Dr. Lee-Chiong suggested attempting to break the cycle by waking a child about 15 minutes before the time these usually occur.

REM sleep parasomnias typically occur during early morning hours, he said. Unlike sleepwalkers, people with REM sleep behavior disorder usually keep their eyes closed and can recall their dreams afterward. The condition is more common in older men and can include screaming, punching, kicking, jumping, and running. "True intent to harm" should be considered in the differential diagnosis.

A host of medications—for example, alcohol, amphetamines, anticholinergics, antidepressants other than bupropion, biperiden, cocaine, sedative-hypnotics, and selegiline—might precipitate REM sleep behavior disorder, as can withdrawal from alcohol, hypnotic agents, and REM suppressants.

Deciding whether and how to treat can be problematic, according to Dr. Lee-Chiong. Daily medication might be riskier than infrequent parasomnias. Clonazepam has been successful in 87% of REM sleep behavior disorder cases, he said.

Other REM sleep parasomnias include recurrent sleep paralysis and recurrent nightmares. Although brief and benign, the former is often mistaken for stroke. Dr. Lee-Chiong estimated 10%-50% of children and 1%-5% of adults, most of them women, suffer from recurrent nightmares. He recommended imagery training for people who repeat the same frightening scenario. A person attacked by a bear, for example, writes out a plausible alternative ending in which he or she finds a car and escapes.

Yet other parasomnias include sleep-related groaning in the absence of a physical complaint and exploding head syndrome, in which the person hears a loud imagined noise, which can be accompanied by a flash of light or myoclonic jerk. In all parasomnias, even if no cause is found or treatment given, Dr. Lee-Chiong emphasized that making the bedroom safe is a priority. "Environmental precautions are essential," he said. ■

Steps to Make Bedrooms Safe

Removing weapons such as guns and knives from the bedroom is a given when people present with parasomnias that put them and their bed partners in harm's way. Other, less obvious changes are at least as important, Dr. Teofilo L. Lee-Chiong Jr. said, offering the following recommendations for a safe bedroom:

- Keep the floor very clean. There should be no object on the floor that could cause a person to slide or trip.
- Make sure nothing breakable is within reach of the person. Glasses and mirrors might have to be removed from the bedroom.
- Exclude sharp objects, including pens.
- Pad sharp edges of bedroom furniture.
- Close the bathroom door—add a barrier, if necessary—to keep out a person having a parasomnia. The floor is harder, and fixtures can create a dangerous obstacle course for a person who is not fully awake.
- Sleep on the first floor if possible. Stairs and upper story windows are hazards.
- Use heavy curtains to prevent cuts to the hand and forearm, if a person strikes out and breaks the glass.

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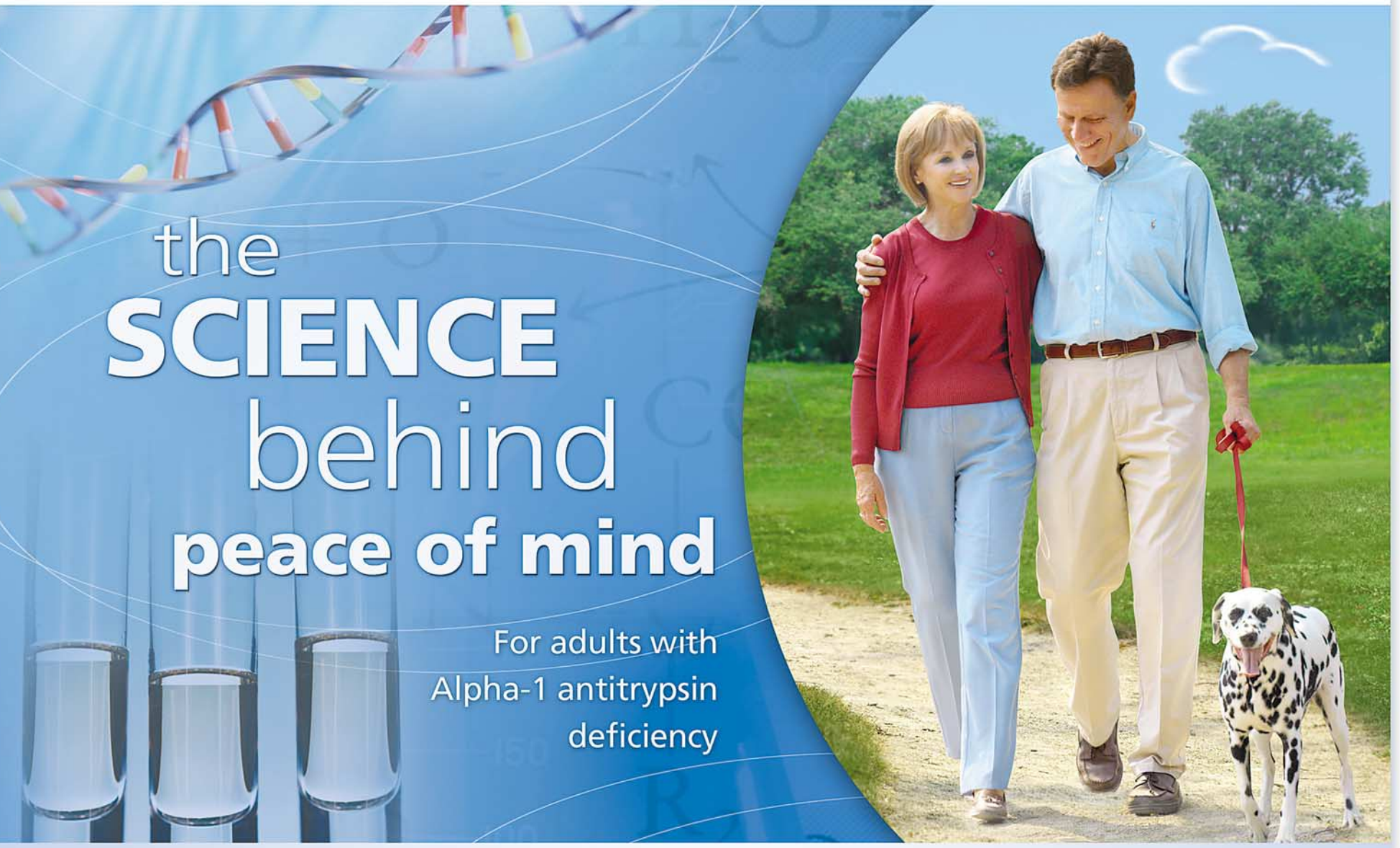

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