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CHEST Physician

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COURTESY DR. GARY PARKES

Determining a patient's "lung age" can motivate smokers to make informed decisions about their health, said Dr. Gary Parkes.

Explaining 'Lung Age' Helped Smokers Quit

BY JOHN R. BELL
Elsevier Global Medical News

Smokers who were told their "lung age" after spirometry had more than double the rate of quitting 12 months later than did smokers who were given only a clinical measure of lung performance, according to findings of a randomized controlled trial.

Thus, telling smokers their lung age appeared to be as effective as nicotine replacement therapy, counseling, and bupropion—as well as potentially cheaper, the authors noted in their study.

Dr. Gary Parkes of the Limes Surgery, Hoddesdon, England, and colleagues enrolled 561 current smokers from five primary care practices in one English county. Patients were at least 35 years old (mean age, 53 years) and did not have a history of lung disease or use supplemental oxygen. All were given a series of spirometric tests, were advised during the visit to quit smoking, and were offered referral to a support service.

Each patient was then randomized to receive one of two types of information: Those patients in the intervention group received an individualized explanation of their level of forced expiratory volume in 1 second (FEV_1), along with a verbal explanation of their lung age and a graphic explaining the concept of lung age. Lung age was calculated using a previously established

See **Lung Age** • *page 2*

VITAL SIGNS

Current Smokers Account for Nearly Half of Emphysema Patients

Source: 2006 data, Centers for Disease Control and Prevention

ELSEVIER GLOBAL MEDICAL NEWS

Positive Outcomes Prompt ECMO Trial's Early End

One life saved for every six treated.

BY BETSY BATES
Elsevier Global Medical News

HONOLULU — One additional patient survived for every six patients treated with extracorporeal membrane oxygenation in a large randomized study comparing the modality to conventional ventilatory support in patients with severe but potentially reversible adult respiratory failure.

Among 90 patients assigned to receive extracorporeal membrane oxygenation (ECMO), 57 (63%) were alive without severe disability 6 months following treatment, compared with 41 (47%) who received conventional mechanical ventilation in specialized intensive care units in the United Kingdom.

The results of the CESAR trial (Conventional Ventilatory Support Versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure) were particularly striking because British researchers used an intent-to-treat analysis that included 22 patients who ultimately failed to receive ECMO, because they either began improving on their own or died before treatment could be initiated. That leaves the possibility that the magnitude of ECMO may be even greater among well-selected patients.

So profound was the impact of ECMO, in fact, that the data monitoring committee stopped the trial early, when 90 patients out of the planned enrollment of 120 had been randomized to each group.

The CESAR trial was conducted throughout the United Kingdom, and more than half of the intensive care units in the country participated by referring potential candidates for randomization. All ECMO was performed at Glenfield Hospital in Leicester, England, and the modality was available at no other center in the country during the study period.

Patients in the two groups

See **Early End** • *page 2*

INSIDE

Survival Up for Downstaged Lung Cancer

BY DAMIAN MCNAMARA
Elsevier Global Medical News

FORT LAUDERDALE, FLA. — Stage IIIa non–small cell lung cancer patients who achieve stage 0 or I disease following chemoradiotherapy induction have improved long-term surgery survival rates, but these are significantly lower than survival rates in stage I patients who have surgery only, according to a retrospective study.

Previous research demonstrated a survival benefit to downstaging stage IIIa non–small cell lung cancer (NSCLC). For example, of 53 patients treated with chemoradiotherapy induction, 22 achieved a major pathologic response and were reclassified as stage 0, I, or II in one report (J. Thorac. Cardiovasc. Surg. 2004; 127:108-13). Compared with a 24% survival rate among nonresponders, the downstaged group had a 48% survival rate. The 5-year actuarial survival was 31%. In another study, researchers found a 67% tumor downstaging and an "encouraging" 37% 5-year survival among 42 patients with advanced NSCLC who were also treated with chemoradiotherapy (J. Clin. Oncol. 1997;15:712-22). Again, a significantly better survival rate was observed among downstaged participants.

"Our study confirmed this," Dr. Stefano Margaritora said at the annual meeting of the Society of Thoracic Surgeons.

"But going further into this problem, do cases with stages 0-I after induction therapy have the same prognosis as surgery

See **Lung Cancer** • *page 10*

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ECMO Improved Survival in Adults

Early End • *from page 1*

were well balanced by age, hours of high pressure and/or high FiO_2 ventilation, underlying diagnosis (pneumonia, trauma, obstetric, or other acute respiratory distress syndrome), number of organs failed, and type of referral hospital.

Dr. Giles Peek, who presented preliminary study findings at the Society of Critical Care Medicine annual congress, said the "real-world" study design reflects current practice in the United Kingdom.

Currently, ECMO is widely used in neonatal intensive care units to temporarily provide gas exchange to provide rest for the lungs during respiratory failure. While ECMO is also in widespread use for children and newborns in the United States and Canada, only a handful of U.S. and Canadian hospitals practice adult ECMO, said Dr. Peek.

In both adults and infants, high airway pressures and oxygen concentrations associated with conventional mechanical ventilation are known to traumatize the lungs, yet previous studies of ECMO in adults have been inconsistent and inconclusive.

The CESAR trial was designed to determine on a large scale, in a randomized fashion, whether ECMO offers lung protective advantages to adults with a variety of conditions leading to respiratory distress.

Eligible patients included individuals aged 18-65 years with severe, potentially reversible adult respiratory failure, defined as having a Murray score of 3 or greater or hypercapnia with a pH of less than 7.2. If they met these criteria, they were randomized to be transferred to Glenfield Hospital, Leicester, where all ECMO was performed, or to receive continued conventional care at a tertiary center.

Patients were excluded if they had experienced prolonged (more than 7 days) of high peak pressure or high FiO_2 ventilation (more than 0.8), or if they had a contraindication to heparin.

Most enrolled patients suffered from pneumonia or nonobstetric acute respiratory distress syndrome (ARDS), followed by trauma. A significant number had failure of more than one organ system, demonstrating ECMO's usefulness in multiorgan failure, said Dr. Peek.

The median time on ventilation prior to randomization was about 35 hours in both treatment groups. Among patients randomized to receive venovenous ECMO, the mean time to beginning ECMO was 6.1 hours. The mean duration of ECMO was 9 days. The majority of patients had hypoxia, with a small number of patients experiencing uncompensated hypercapnia. The mean APACHE score assessing severity of illness was 20.

More patients died in the conventional treatment arm versus the ECMO group, 45 versus 33, but the difference was not statistically significant. Among patients who died, those receiving conventional care died more quickly.

Overall, ECMO reduced death or significant morbidity at 6 months regardless of patients' stratification criteria, including age, number of organs involved, or severity of illness.

"I expect conventional practice to slowly embrace the use of ECMO for adults with severe but potentially reversible respiratory failure," Dr. Peek predicted.

IN THIS ISSUE

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Approach Boosts Quit Rate

Lung Age • *from page 1*

formula. (See box.) Those patients in the control group received only a letter indicating their FEV_1 score, with no further explanation.

At 12 months, there were 249 control participants, 32 having been lost to follow-up. In the intervention group, there were also 249 patients remaining, with 31 lost to follow-up. However, those lost to follow-up were included as if they had continued to smoke. Among the controls, there were 18 patients (6%) who quit smoking, as verified by carbon-monoxide breath testing. In the intervention group, there were 38 patients who quit (14%).

The investigators analyzed the data among the intervention group to determine if those with a greater lung-age deficit were more likely to quit than those with a smaller deficit or none. Contrary to previously published findings, they found no significant difference in quit rates based on disclosed lung damage, although they cautioned that the study was not powered to detect such a difference. Anecdotally, they noted, some patients who were informed that their lung age was normal expressed relief that it was not too late for them to quit (BMJ 2008;336:598-600).

Dr. Parkes offered a note of caution, however. "I would emphasize that although comparisons have been made with treatments of those who have already decided to try to quit smoking, the aim of this study was not to compete with nicotine replacement therapy or bupropion therapy," he told CHEST PHYSICIAN.

In fact, more than 60% of smokers who came for a lung test in the study declared they had no intention of quitting in the next 1-6 months, he explained. In contrast, smokers who undergo nicotine replacement therapy have already decided to try to quit.

Instead, the study's aim was "to inform and motivate people about their health so that they could take informed decisions," Dr. Parkes said.

In an accompanying commentary, Dr. Raphaël Bize and Dr. Jacques Cornuz of the University of Lausanne (Switzerland) noted that a recent systematic review found no difference in quit rates between patients who were given spirometry testing results and counseling and those who were given counseling alone.

However, "providing feedback on lung age with graphic displays seems to be the best option so far for communicating the results of spirometry," Dr. Bize and Dr. Cornuz concluded (BMJ 2008;336:567-8).

The researchers disclosed no potential conflicts of interest.

Dr. Nicolas Hanania, FCCP, comments: *This study sheds light on a potential counseling tool that may help individuals quit smoking. Smokers who were informed about their "lung age" were more likely to quit smoking. This observation stresses the fact that providing smokers with details about their lung function test is an important adjunct to other behavioral counseling, in addition to pharmacological intervention.*

Lung-Age Calculations

- For men:
  Lung age = (2.87 × height [in inches]) – (31.25 × observed FEV_1 [in liters]) – 39.375
- For women:
  Lung age = (3.56 × height [in inches]) – (40 × observed FEV_1 [in liters]) – 77.28

CHEST PHYSICIAN

CHEST PHYSICIAN, the newspaper of the American College of Chest Physicians, provides cutting-edge reports from clinical meetings, FDA coverage, clinical trial results, expert commentary, and reporting on the business and politics of chest medicine. Each issue also provides material exclusive to the members of the American College of Chest Physicians. Content for **CHEST PHYSICIAN** is provided by International Medical News Group and Elsevier Global Medical News. Content for NEWS FROM THE COLLEGE is provided by the American College of Chest Physicians.

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Hot Tub Lung Eludes Diagnosis, Optimal Treatment

BY BRUCE JANCIN
Elsevier Global Medical News

KEYSTONE, COLO. — Hot tub lung is a common, frequently misdiagnosed, and particularly fascinating form of nontuberculous mycobacterial pulmonary disease, according to a researcher from the National Jewish Medical and Research Center, Denver.

Hot tub lung is believed to be a hypersensitivity pneumonitis caused by exposure to aerosolized *Mycobacterium avium* complex (MAC) and other nontuberculous mycobacteria (NTM) predisposed to grow in indoor hot tubs, enclosed swimming pools, spas, and therapy pools.

"The thought is the lung is overresponding to an antigen. What we don't know is whether it's simply an immune response to an antigen or a true infection with an NTM organism," Dr. Gwen A. Huitt said at a meeting on allergy and respiratory diseases sponsored by the National Jewish Medical and Research Center.

And that unresolved question bears on the issue of optimal treatment. "We still don't have a conclusion as to what the right treatment is: strict exposure avoidance and prednisone, or antibiotics as well. I think the jury is definitely still out," said Dr. Huitt, director of the adult infectious disease care unit and chairman of the infection control committee at the center.

Indeed, Dr. Huitt noted that in a recent series of 27 patients with hot tub lung reported by her colleagues in the occupational medicine group at National Jewish, the disease resolved or improved with treatment in all cases. However, one-third of patients were left with a mild fixed, permanent residual impairment in lung function as evidenced by a diffusing capacity of the lung for carbon monoxide less than 80% of normal. So hot tub lung is not necessarily a benign process.

All patients were treated with exposure avoidance, 13 got oral prednisone alone tapered over 4-8 weeks, and 12 got prednisone plus 3-6 months of triple-agent antimycobacterial therapy. There was no significant difference in the residual impairment rate between patients treated with or without the antimycobacterial medications (J. Occup. Environ. Hyg. 2007;4:831-40).

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A hot tub environment can expose people to aerosols of nontuberculous mycobacteria.

Her tentative conclusion? "Prednisone may be enough as long as you're avoiding the exposure."

Patients with hot tub lung typically are previously healthy and younger than those with other NTM-associated pulmonary disease.

Recreational tub and pool users aren't the only at-risk population. The disease also occurs in pool maintenance workers, lifeguards, and water therapists, raising occupational health issues.

The main presenting symptoms of hot tub lung are subacute-onset shortness of breath, cough, and fatigue.

"Many of these patients feel like they have a slow-onset flu. They're achy, tired, have a prominent cough or arthralgias," according to Dr. Huitt.

Chest x-rays will show diffuse infiltrates with prominent nodularity in all lung fields. CT scans often show intense inflammation with centrilobular nodules, ground glass opacities in a mosaic pattern, and air trapping.

The diagnosis of hot tub lung is based upon a history of exposure, compatible radiographic studies, and positive cultures for NTM obtained from the hot tub water as well as from sputum, bronchoalveolar lavage, or lung biopsy.

Pulmonologists at National Jewish have found that lidocaine is bacteriocidal to NTM; they've learned to rely instead on conscious sedation in order to avoid false-negative cultures when performing bronchoscopy in patients with suspected NTM.

Interestingly, the referral diagnosis was hypersensitivity pneumonitis in only 8 of the 27 patients in the recent National Jewish series. One-quarter of patients had a working diagnosis of sarcoidosis, probably because lung biopsies obtained at other centers showed granulomas. But the granulomas characteristic of hot tub lung are discrete, nonnecrotizing, and distributed in a bronchocentric and centrilobular fashion, in contrast to sarcoidosis.

The rest of the patients were misdiagnosed elsewhere as having asthma, pneumonia, emphysema, tuberculosis, bronchiolitis obliterans, or interstitial lung disease.

Dr. Huitt recalled a recent consult she received from public health workers regarding a family of five who had been diagnosed with TB and quarantined while undergoing anti-TB therapy.

It was a well-to-do white family living in an affluent community, and they had no history of travel to an endemic area. Dr. Huitt grew suspicious. Do they have an indoor hot tub? she asked. Sure enough, they did. And depressed by the quarantine and TB drug side effects, they were spending a lot more time in it than usual, and—strangely enough—feeling worse and worse. They hadn't changed the water in months and months—it's quite expensive—although they regularly dumped in disinfectant chemicals. A thorough workup revealed all five had hot tub lung rather than TB.

Dr. Huitt's preferred method of NTM exposure avoidance involves ripping out the hot tub. She stressed that while hot tub manufacturers tout their disinfectant systems, which often rely on UV light, bromine, chlorine, or ozone, none of them kills mycobacteria.

"The word needs to get out: The only thing that really works is changing the water," she said.

"After a nuclear bomb, there will still be cockroaches and mycobacteria."

Dr. Philip Marcus, FCCP, comments: *"Hot tub lung" has been recognized for several years. Clearly, this shows the importance of taking a complete history in terms of extraneous, environmental factors. As this article emphasizes, we need to focus on in-home factors as well. In addition, paying attention to the heating system, humidification, age of the home, and many other factors will help establish a diagnosis more quickly. Mycobacterial infection is something that can be treated when recognized. This study also points out the importance of common sense issues such as changing the water.*

FDA Issues Warning About Prescription Cough Product

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Deaths and life-threatening side effects associated with the misuse of a long-acting, prescription cough medicine that contains hydrocodone have prompted the Food and Drug Administration to issue a public health advisory about the dangers of the product when not used properly.

The product is marketed as Tussionex Pennkinetic Extended-Release Suspension, a combination of the narcotic hydrocodone and the antihistamine chlorpheniramine, which is approved for adults and for children over age 6.

It should not be given more frequently than every 12 hours and is contraindicated in children under age 6, according to the FDA advisory, which was issued on March 11.

The FDA has received "numerous" reports of deaths and other adverse events in adults and children "associated with the misuse and inappropriate use of this potent cough medicine," said the statement.

'NUMEROUS' REPORTS HAVE ASSOCIATED DEATHS AND OTHER ADVERSE EVENTS WITH IMPROPER USE OF TUSSIONEX.

The reports indicate that physicians and other health professionals have prescribed Tussionex for children who are under age 6, or more frequently than the labeled dosing interval of every 12 hours. In addition, the reports indicate that patients have taken the incorrect dose because they have misinterpreted the dosing directions or have utilized inappropriate devices to measure the suspension. (There are other hydrocodone-containing cough products that can be administered at an interval of every 4-6 hours.)

"There is a real and serious risk for overdosing if this medication is not used according to the labeling," said Dr. Curtis Rosebraugh, acting director of the FDA's Office of Drug Evaluation II, in the statement. Overdoses in children who are older than 6 years, adolescents, and adults have also resulted in life-threatening and fatal cases of respiratory depression.

Tussionex is manufactured by UCB Inc., which has agreed to update the labeling to include information that the product should not be used in children under age 6, and that it should be dosed accurately.

In addition to the warning not to use the product in children younger than age 6 years, the advisory recommends that health care professionals consult the prescribing information to determine the correct dose and dosing frequency of Tussionex. The FDA's other recommendations for using the product safely include the following:

- Health care professionals should not prescribe Tussionex to be taken more frequently than every 12 hours.
- Health care professionals and patients who use the product should be aware of the signs of hydrocodone overdose.
- Prescribers should clearly state the prescribed volume in milliliters. Pharmacists should clearly state directions in milliliters on the prescription container, and provide a measuring device that delivers the volume in milliliters. (The FDA has received some reports indicating that the volume prescribed by the physician was incorrectly converted to another volume on the prescription label, such as 2 mL to 2 teaspoons).
- Patients should be counseled about the amount of Tussionex that should be given and at what frequency.

More information is available at www.fda.gov/cder/drug/infopage/hydrocodone. Adverse reactions to this product should be reported to the FDA's MedWatch program at 800-332-1088 or www.fda.gov/medwatch.

Mepolizumab Helped Ease Hypereosinophilic Syndrome

Drug allowed patients to cut their daily prednisone dose to 10 mg or less for at least 8 weeks.

BY ROBERT FINN
Elsevier Global Medical News

Mepolizumab, a fully humanized monoclonal interleukin-5 antibody, significantly reduced the need for prednisone in patients with hypereosinophilic syndrome, according to an article published in the New England Journal of Medicine.

Hypereosinophilic syndrome (HES) is typically treated with prednisone or equivalent corticosteroids, and the 85 patients in the study were all stabilized on doses of 20-60 mg of prednisone daily before being randomized to mepolizumab or placebo.

By the end of the 36-week study, 84% of the patients taking mepolizumab were able to reduce their daily dose of prednisone to 10 mg or less for at least 8 weeks. In contrast, only 43% of the patients receiving placebo were able to decrease their daily dose of prednisone to 10 mg or less for 8 weeks (N. Engl. J. Med. 2008;358:1215-28).

On average, patients receiving mepolizumab were able to reduce their daily prednisone dose from 29.2 mg to 6.2 mg, while patients receiving placebo reduced their daily prednisone dose from 30.6 mg to 21.8 mg, a statistically significant difference.

The double-blind study, led by Dr. Marc E. Rothenberg of the University of Cincinnati and colleagues, involved 85 patients with HES who were seen at 1 of 26 sites in the United States, Canada, Belgium, France, Germany, Italy, Switzerland, and Australia. All patients had a blood eosinophil count greater than 1,500/mcL for at least 6 months, along with eosinophilia-related organ involvement and no identifiable secondary cause for eosinophilia. Patients who tested positive for the FIP1L1/PDGFRA fusion gene, which can cause HES, were excluded from the study.

Mepolizumab also proved superior to placebo on several secondary end points as well. About 95% of patients receiving mepolizumab had an eosinophil count of less than 600/mcL for 8 weeks or more, compared with 45% of the patients receiving placebo. Serum levels of the neurotoxins derived from eosinophils were significantly lower in the mepolizumab group than in the placebo group at all time points tested: 12, 24, and 36 weeks.

Seven patients receiving mepolizumab and five patients receiving placebo experienced serious adverse events, but none was judged to be related to the drug. Other adverse events occurred at similar rates in the two groups, with fatigue, pruritus, headache, and arthralgia the most common.

One patient in the mepolizumab group and four in the placebo group withdrew from the study because of adverse events.

Regulatory authorities in the United States and the European Union have granted mepolizumab orphan drug status.

According to some estimates, between 2,000 and 5,000 people in the United States suffer from HES.

Manufactured by GlaxoSmithKline, mepolizumab (trade name Bosatria) is still considered an investigational drug.

The study was supported in part by GlaxoSmithKline, several of the paper's coauthors are employees of GlaxoSmithKline, and Dr. Rothenberg and several other coauthors reported receiving consulting fees from that company.

Despite the encouraging results, several important questions remain unanswered, Dr. Michael E. Weschler of Harvard Medical School, Boston, wrote in an accompanying editorial. For example, it's unknown how long the effects of mepolizumab will last, whether rebound eosinophilia will occur when treatment is stopped, or what the ideal dose to achieve a sustained response will prove to be (N. Engl. J. Med. 2008;358:1293-4).

Mepolizumab is an anti-interleukin-5 antibody, and Dr. Weschler wondered whether this or other similar drugs would prove effective in other disorders such as eosinophilic esophagitis, eosinophilic pneumonia, asthma with eosinophil-predominant phenotypes, or Churg-Strauss syndrome.

"Anti-interleukin-5 treatment certainly brings new hope to many patients with the hypereosinophilic syndromes whose disease is currently refractory to conventional therapies or who have side effects from them," Dr. Weschler wrote.

"It is important to recognize that this therapy's greatest contribution may be to teach us about the biologic characteristics of the eosinophils," he added.

Dr. Weschler reported receiving research support, consulting fees, and lecture fees from GlaxoSmithKline and several other pharmaceutical companies.

FDA Investigating Reports of Suicidality in Singulair Users

BY ALICIA AULT
Elsevier Global Medical News

The Food and Drug Administration issued an "early communication" to health care professionals on March 27 that it is reviewing postmarketing reports it has received of behavior/mood changes, suicidality, and suicide in patients who have taken the asthma and allergy medication montelukast (Singulair), although the agency has declined to say how many reports it has received.

Dr. George Philip, senior director of clinical research at Merck & Co., which makes Singulair, also said the company would not reveal any more specific data at this time. "We think that sharing those numbers is ultimately not very useful," said Dr. Philip in an interview.

An FDA spokeswoman said the agency had received reports of three or four suicides in patients taking Singulair. But no causal relationship has been established, she noted.

Merck agreed that reports did not equal a relationship. "The fact that an adverse event has been reported to Merck and to regulatory agencies does not reflect a conclusion that the postmarketing event is caused by Singulair," said the company in a statement.

The company picked up a signal of potential psychiatric adverse events through anecdotal reports submitted to Merck over the last year or so as part of routine postmarketing surveillance, said Dr. Philip. Merck updated Singulair's label in October 2007 to reflect a potential association with suicidality.

In the past year, Merck has also added information that the leukotriene receptor antagonist has been associated with tremor, depression, and anxiousness. FDA and Merck officials met this past February to discuss how best to communicate the label changes to physicians, patients, and others, said Dr. Philip. Merck already had been—and will continue to—communicate directly with physicians through face-to-face meetings.

An initial review of clinical trial data found no evidence of an association with mood changes, according to Dr. Philip.

"In a cumulative analysis recently provided to the FDA of Merck's randomized, double blind, placebo-controlled clinical trials, which included over 11,000 adults and children in over 40 studies who were treated with Singulair, there were no reports of suicidal thoughts or actions and no completed suicides in the patients who received Singulair," the company's statement said.

The FDA has asked Merck to review all its clinical data for evidence of suicidality or suicide. And the agency said it will review the postmarketing reports it has received on behavior and mood changes, suicidality, and suicide. The FDA said its investigation will take 9 months to complete.

In the meantime, patients should not stop taking Singulair, said the FDA and Dr. Philip. The agency did urge physicians to monitor patients for signs of suicidality and other psychiatric events.

The FDA is also reviewing postmarketing reports it has received of behavior/mood changes, suicidality, and suicide in patients who took other leukotriene-modifying therapies, including zafirlukast (Accolate) and zileuton (Zyflo and Zyflo CR). The agency will then assess whether further investigation is warranted.

Oral Drug for CF Shows Promise in Early Trials

BY TERRY RUDD
Elsevier Global Medical News

A drug designed to fix a crucial defective protein in cystic fibrosis improved patients' lung function and sweat chloride levels, according to early results from a small randomized study.

The investigational oral drug, VX-770, is still in phase II trials. But the preliminary findings among 20 patients—particularly the impact on sweat chloride levels—are generating cautious optimism.

"These early results are an extraordinary endorsement of our hypothesis—that small molecules can correct the basic defect and affect the clinical indicators of cystic fibrosis," Robert J. Beall, Ph.D., president and CEO of the Cystic Fibrosis Foundation, said in a statement.

VX-770 targets defective Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) proteins in sweat duct epithelial cells. Dysfunctional CFTR proteins are believed to cause the fluid and salt imbalance that characterizes CF patients' airways.

The first part of the phase IIa trial included 20 patients who carry the G551D mutation in the CFTR gene. About 4% of CF patients in the United States carry the G551D mutation. Patients participated in two 14-day treatment periods. In addition to standard CF therapies, patients received either placebo or one of three VX-770 dosage levels during each 14-day period.

At the end of 14 days, patients who received the highest dose of VX-770 (150 mg twice daily) experienced an average 10.1% increase in forced expiratory volume in 1 second (FEV_1), compared with an average FEV_1 decrease of less than 1% in placebo patients.

For patients on high-dose VX-770, sweat chloride levels fell from an average 95.5 mmol/L at baseline to 53.2 mmol/L after 14 days of treatment. Patients on placebo had no significant change in sweat chloride levels. Sweat chloride levels for CF patients typically are greater than 60 mmol/L, compared with normal values of less than 40 mmol/L in people without CF.

The adverse events rate was similar between VX-770 and placebo. One patient experienced two serious adverse events, which researchers deemed were not related to VX-770.

The second stage of the drug's phase IIa trial is slated to begin later this year, and will enroll 16 patients for 28 days of randomized, placebo-controlled treatment. A phase IIb trial may begin in 2009, according to the Cystic Fibrosis Foundation.

Vertex Pharmaceutical Inc. is developing VX-770 and a second compound, VX-809, with funding support from the Cystic Fibrosis Foundation.

SAVE THE DATE

Inaugural Meeting of the
US Critical Illness and Injury Trials Group
held in conjunction with the
6th Symposium on the Functional Genomics of Critical Illness and Injury

November 17-19, 2008
National Institutes of Health
Bethesda, Maryland, USA

Scientific leaders within the United States critical illness and injury community met at the 5th NIH Functional Genomics of Critical Illness and Injury Symposium, November 14-15, 2007 to discuss a strategic plan for critical illness and injury clinical research in the United States. Representative views were gathered from a broad spectrum of stakeholders, including professional societies, academic centers, federal agencies, and industry. Group discussion affirmed that success could only come from cooperative and strategic actions that favor collaboration, standardization of protocols, and strong leadership.

The United States Critical Illness and Injury Trials Group (USCIITG) is funded by the National Institute of General Medical Sciences to create a clinical research framework that will reduce the barriers to investigation using the same investigator-initiated, evidence-driven, inclusive approach that has proven successful elsewhere. The USCIITG will not fund clinical trials, but rather will promote the development of evidence-based clinical protocols and the subsequent preparation of applications for funding to test specific hypotheses. Investigators that span the gamut of critical illness and injury specialties will be involved in this collaborative effort.

The specific aims of the USCIITG include the following:

- Establish an inclusive, nationwide network of experts to review published data, establish national priorities, vet hypotheses, write clinical protocols, and generate pilot data;
- Promote interactions and synergy across established programs — both academic and non-academic — to improve the robustness (power) of clinical trials and test hypotheses in U.S. populations across the patient age continuum;
- Provide a venue to discuss education and training in the science of clinical trial design including, conduct, analysis, and reporting for critically ill or injured patients; and
- Insure patient protection and privacy by addressing the ethical, legal, and social implications of research in the specialized circumstance of critical illness or injury.

It is expected that the USCIITG will not act in isolation, but will be part of a larger effort to bridge critical care trials groups worldwide. Its success will be based on collaborative leadership, non-hierarchical team culture, and open dialog among participants that will facilitate communication streams and help link new scientific knowledge with practice.

6th Functional Genomics of Critical Illness and Injury Symposium (November 17, 2008)

- Phenotyping for the future
- Update: Genetic predisposition in the ICU
- New technology for physiological genomics

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Budget Shortages Weaken Worldwide Fight Against TB

BY JONATHAN GARDNER
Elsevier Global Medical News

The pace of progress has slowed in the global battle against the tuberculosis epidemic, according to a World Health Organization report published March 17.

Between 2001 and 2005, the average rate at which new TB cases were detected was increasing by 6% per year; but between 2005 and 2006 that rate of increase was cut in half, to 3%, the WHO's 12th annual report on global tuberculosis control said.

The reason for the slowdown is that in some countries, programs that were having great success against TB have been unable to continue at the 2006 pace. Budget shortages are having a heavy impact on efforts: The 90 countries (with 91% of global cases) that provided data reported funding gaps totaling $385 million in 2008. Only 5 of the 22 high-burden countries reported no funding gap, the report said.

IN SOME COUNTRIES, PROGRAMS THAT WERE HAVING GREAT SUCCESS AGAINST TB HAVE BEEN UNABLE TO CONTINUE AT THE 2006 PACE.

The budget needed to meet the international goal set by the United Nations for 2008 is currently facing a shortfall of about $1 billion.

The WHO reported that in 2006 there were 9.2 million cases of tuberculosis (139 per 100,000 people), up from 9.1 million cases in 2005. In 1990 there was an incidence of 6.6 million cases (124 per 100,000).

The UN used 1990 as a baseline for measuring progress in TB control. The rate of decrease that occurred between 1990 and 2005, which was positively affected by population growth, appears to be encouraging. "If this trend is sustained, Millennium Development Goal 6, to have halted and begun to reverse the incidence of TB, will be achieved well before the target date of 2015," said the report.

WHO officials said the slowing in the growth of TB in 2006 ushers in a "new era" in global efforts to eradicate the disease, but added that public health programs still need support.

"To make progress, firstly public programmes must be further strengthened. Secondly, we need to fully tap the potential of other service providers," WHO Director-General Margaret Chan, M.D., said in a written statement.

The statement noted that other studies have documented "that many patients are treated by private care providers, and by non-governmental, faith-based and community organisations, thus escaping detection by the public programmes.

"Enlisting these other providers, working in partnership with national programs, will markedly increase diagnosis and treatment for people in need."

Coinfection with HIV also is a threat to progress, the WHO said, and despite a growth of HIV testing of TB patients from 22,000 in 2002 to 700,000 in 2006, testing fell well short of a goal of 1.6 million that was set in a global plan for TB control.

The organization's global strategy to treat TB has seen a major expansion since its first launch in 2006, according to the report. Directly-observed treatment, short-course, the recommended treatment protocol, has been implemented in 184 countries accounting for 99% of all estimated TB cases, the WHO said.

Other findings:

- There were 500,000 cases of multidrug resistant TB.
- The African region had the highest incidence rate at 363 per 100,000.
- 4.1 million of the new cases in 2006 were smear positive.
- 5.1 million of the 9.2 million new cases of TB were notified of their infections.
- India, China, Indonesia, South Africa, and Nigeria rank first to fifth in absolute numbers of cases.

FDA MedWatch Alert: Spiriva May Be Linked to Risk of Stroke

Use of Pfizer/Boehringer Ingelheim's chronic obstructive pulmonary medication Spiriva may be linked to stroke, the Food and Drug Administration said in a March 18 MedWatch alert.

According to the agency, manufacturer Boehringer Ingelheim conducted a pooled analysis of safety data from 29 studies of about 13,500 patients, and findings indicate that use of Spiriva (tiotropium bromide monohydrate) is linked to an excess risk of any type of stroke in 2 patients for every 1,000.

The company submitted the data from 25 studies of the Spiriva HandiHaler, and four trials of Spiriva Respimat, the formulation that is marketed in Europe.

The analyses showed an excess risk of stroke of 8 patients for every 1,000 taking Spiriva for 1 year, versus 6 patients for every 1,000 taking placebo.

"It is important to interpret these preliminary results with caution," the agency said in an accompanying "early communication about an ongoing safety review" as it noted that it "has not yet confirmed these analyses." In fact, the FDA has requested additional information and is currently reviewing post-marketing adverse events reports with Spiriva.

The agency points out it will have data from Boehringer Ingelheim's 4-year, long-term Spiriva trial, UPLIFT, in June, and that data likely will inform any ongoing review of potential safety issues.

The FDA approved Spiriva in 2004 for long-term treatment of bronchospasm associated with COPD.

—Brooke McManus, "The Pink Sheet"

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XDR-TB Coming to a Location Near You

U.S. cases in foreign-born patients on the rise.

BY BRUCE JANCIN
Elsevier Global Medical News

KEYSTONE, COLO. — Epidemiologic trends dictate American physicians will increasingly encounter extensively drug-resistant tuberculosis in coming years, Dr. Charles L. Daley predicted at a meeting on allergy and respiratory disease sponsored by the National Jewish Medical and Research Center, Denver.

In the mid-1990s, TB in the United States occurred chiefly in U.S.-born persons. Indeed, U.S.-born patients with TB outnumbered foreign-born patients with TB 2:1.

The No. 1 risk factor is foreign birth in areas where TB is endemic and TB control is poor.
DR. DALEY

Since then, however, the annual number of TB cases among U.S.-born individuals has declined sharply, while the number of cases arising in the foreign born has remained constant.

As a result of these crisscrossing trends, in each year since 2001 foreign-born persons have accounted for more than half of all TB cases in the United States.

"That's an important epidemiologic factor, because most of the XDR [extensively drug-resistant]-TB that's been reported has been outside the United States. With more cases here coming from those areas, no surprise, we're going to see more MDR [multidrug-resistant]- and XDR-TB," said Dr. Daley, head of the division of mycobacterial and respiratory infections at the center and professor of medicine at the University of Colorado, Denver.

The No.1 risk factor for MDR and XDR is foreign birth in areas where TB is endemic and TB control practices are poor.

Russia and many of its neighboring former Soviet republics constitute the biggest problem area worldwide. Astonishingly, more than 40% of people in that part of the world who've previously been treated for TB have MDR-TB.

"After the Berlin Wall came down, their health system was dismantled. There was no TB control," he explained.

Drug resistance in Russia was created mainly in the prisons—and mass pardons put many convicts with MDR-TB back into the community. A lot of transmission also took place in hospitals because of the lack of infection control protocols.

In the United States and Western Europe, roughly 6% of MDR-TB strains are XDR. In Russia, the rate is 14%.

South Africa is another hotbed of XDR. However, little TB drug resistance exists elsewhere on the continent. That's because MDR-TB and XDR-TB are caused by inadequate treatment—and for the most part Africans with TB outside of South Africa aren't receiving inadequate treatment, they're simply not being treated, period, Dr. Daley continued.

Suspect MDR-TB in a patient with TB symptoms who hails from or has traveled to an endemic area. "The highest risk is, 'I'm from Russia and I was in prison.' That's when you carefully back out the door of the examining room," Dr. Daley quipped.

Globally each year, there are more than 400,000 new cases of MDR-TB and 40,000 of XDR-TB. It's the XDR-TB that's captured the media's attention.

"The XDR strains aren't real virulent, so far as we know, but they're almost untreatable," according to Dr. Daley.

A handful of published reports show cure rates of about 30% in U.S. patients with XDR-TB, comparable to what's being reported elsewhere.

In contrast, treatment success rates of 60%-80% are reported with systematic treatment for MDR-TB.

A Centers for Disease Control and Prevention case series reported last year highlighted the changing epidemiology of XDR-TB in the United States during 1993-2006. In 1993-1999, 72% of cases in the series were men, 38% were foreign born, and 44% were HIV positive. In contrast, in 2000-2006, only 47% were men, 76% were foreign born, and just 12% were HIV infected.

"You might say, 'Well, this doesn't matter to my practice,' but it turns out the world has a way of reaching into the United States, including low-incidence areas," observed Dr. Daley.

He noted that in the past year and a half, there has been a handful of documented cases of MDR-TB diagnosed in Rocky Mountain states where TB hasn't historically been much of a problem. All involved foreign-born individuals.

Current treatment regimens for XDR-TB virtually always require utilization of third-line drugs that aren't very potent against *Mycobacterium tuberculosis*, such as amoxicillin/clavulanate, clofazimine, linezolid, and the macrolides. With cure rates for XDR-TB hovering around 30%, new drugs are clearly needed, Dr. Daley said.

ACIP Recommends Flu Shots for School-Age Children

BY MIRIAM E. TUCKER
Elsevier Global Medical News

ATLANTA — The unanimous vote by the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention at its winter meeting adds the 5- to 18-year age group to the previous recommendations for children aged 6 months through 5 years.

The new recommendation is "an important advance for children," Dr. Joseph A. Bocchini Jr. said in an interview.

The vote for the expanded recommendation was unanimous, but the decision about when it should go into effect was not. Some ACIP members said that it shouldn't become official until the 2009-2010 influenza season in order to allow time to prepare for implementation, while others felt that an immediate recommendation would get the ball rolling sooner. They ultimately voted for compromise language—the wording is subject to revision—that the recommendation should take effect "as soon as feasible, but no later than the 2009-2010 influenza season."

Although there are few deaths or hospitalizations for influenza among school-age children compared with younger children, the elderly, or those with chronic conditions, children aged 5-18 years make five to seven outpatient visits per 100 children annually for influenza, and they often receive antibiotics. About 10-30 influenza illnesses occur per 100 children, resulting in high rates of school absenteeism, Dr. Anthony Fiore of the Influenza Division of the CDC's National Center for Immunization and Respiratory Diseases, told the committee.

The recommendation also is expected to reduce transmission among adult contacts, and improve current low rates of immunization among the 50% of school-aged children who already have an indication for the vaccine because of a chronic condition or contact status. Data on cost-effectiveness of influenza vaccine in that age group suggest that it is more expensive than many currently recommended vaccines but that "models do not fully account for potential indirect effects," Dr. Fiore said.

The CDC is expected to follow the advice of the ACIP, which then must be "harmonized" with that of the American Academy of Pediatrics and other professional societies.

The AAP's Committee on Infectious Disease will discuss the recommendation at its April meeting, said Dr. Bocchini, one of two AAP liaisons to the ACIP.

He added that even with the language allowing a year's leeway, many pediatricians won't be able to start right away. "We recognize there will be significant potential impediments to getting this done, and most won't be able to consider this until the 2009-2010 season," said Dr. Bocchini, professor of pediatrics and chairman of the department of pediatrics at Louisiana State University Health Sciences Center in Shreveport, and chief of the section of pediatric infectious diseases and medical director of the Children's Hospital in Shreveport.

But pediatricians aren't expected to shoulder the entire burden. During the discussion, panel members agreed that broader approaches such as school- or community-based immunization programs will need to be developed in order to achieve the goal of immunizing all children every year during influenza season.

Dr. Kathleen Neuzil, who chaired the ACIP Influenza Vaccine Working Group, said that the decision to go forward at this time was based on the fact that there are no remaining critical data gaps, and no clear indication that more data will be available in the near-term on feasibility or indirect protection from influenza immunization to unimmunized contacts. Moreover, "There is no clear indication that steps will be taken to prepare in the absence of a recommendation."

The working group's document that was initially presented to the committee called for the recommendation to take effect beginning in the 2009-2010 season, primarily because many practitioners would have already ordered their vaccine supply for 2008-2009. Other reasons for waiting included the large number of new vaccine recommendations in the last 2-3 years, the need for education, and to allow time to harmonize with other professional organizations, said Dr. Neuzil of the University of Washington, Seattle.

Several panel members endorsed that cautious approach, but others urged the committee to move forward more quickly. Patricia Stinchfield, a nurse practitioner and director of pediatric infectious disease and immunology at the Children's Hospitals and Clinics of Minnesota, St. Paul, said that most of the clinicians she works with are already offering influenza vaccine to all children. "They don't feel fearful of a new implementation program. We have already ordered our vaccine, but we also know that at the end of every season we throw vaccine away."

States Rapidly Adopting Newborn Screening for CF

BY TIMOTHY F. KIRN
Elsevier Global Medical News

SALT LAKE CITY — Twenty-nine states required newborn cystic fibrosis screening as of this past summer, and more states are likely to do so soon, Dr. Michael Rock said at the annual meeting of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

"Cystic fibrosis newborn screening is really taking off across the country," said Dr. Rock, director of the cystic fibrosis center at the University of Wisconsin, Madison.

The Cystic Fibrosis Foundation has called for newborn testing in every state by 2010. "We're on track to meet that goal," he noted.

The number of states requiring newborn screening has been increasing rapidly since 2004 when the Centers for Disease Control and Prevention issued a statement that expert opinion considered the health benefits of screening to outweigh the costs.

Since then, an advisory committee to the secretary of the Department of Health and Human Services recommended that all states screen for 29 conditions in newborns. One of those tests was the immunoreactive trypsinogen test for cystic fibrosis.

A study conducted on all children diagnosed with cystic fibrosis in Wisconsin between 1984 and 1995 showed that earlier detection resulting from newborn screening resulted in better growth for those children (J. Pediatr. 2005;147:S30-6), and other evidence suggests that earlier detection can affect cognition, if efforts are made to improve vitamin E status in diagnosed children (Pediatrics 2004;113:1549-58), Dr. Rock said.

The states that did not mandate cystic fibrosis screening as of this summer were Alabama, Hawaii, Maine, Nevada, North Carolina, Utah, and Vermont. Connecticut and Pennsylvania have pilot programs in which testing is offered at some hospitals, but do not have universal screening. And Massachusetts has a pilot program whereby hospitals offer testing, but it is not required.

States that had decided to mandate universal testing but had not implemented the requirement as of this past summer are Arizona, Arkansas, Florida, Kansas, Illinois, Indiana, Michigan, Montana, Tennessee, Texas, and West Virginia, according to Dr. Rock.

Screening for cystic fibrosis is very cost effective, Dr. Rock said. According to data from two studies, the cost of offering newborn screening is $2.66 per infant, and the estimated yearly cost of treating that infant with earlier diagnosis is $7,228. In comparison, the cost of conventional diagnosis is $4.97 per patient and the yearly cost of treating that patient is $12,008.

Dr. Rock had no financial conflicts of interest to disclose.

According to a recent study—the Newborn Screening Report Card—conducted by the March of Dimes, as of June 2007, 88% of all newborns received 21 or more of the 29 newborn screening tests recommended by the American College of Medical Genetics, up from just 38% as recently as 2 years ago.

Less Delirium Seen With Precedex During Extended ICU Trial

BY BETSY BATES
Elsevier Global Medical News

HONOLULU — The sedative dexmedetomidine (Precedex) was significantly better than midazolam at controlling delirium in mechanically ventilated patients in a randomized, double-blind trial assessing its long-term use.

In the study of 366 intensive care patients sedated with one or the other drug for 1-8 days, the daily incidence of delirium was 55% in the dexmedetomidine patients and 76% in the midazolam patients, with most of the difference occurring early. The total time in delirium was 70 hours in the dexmedetomidine group, compared with almost 95 hours in the midazolam group, Dr. Richard Riker reported at the annual congress of the Society of Critical Care Medicine.

The Food and Drug Administration mandated the study in 1999, when dexmedetomidine was approved for sedating mechanically ventilated patients for a period not to exceed 24 hours at a maintenance dosage of 0.2-0.7 mcg/kg per hour.

Dr. Riker noted that practice registries suggest that "many of us are using the drug at higher doses and for longer durations than the current label [allows]. I think we'd all feel a bit better if we could bring the regulatory guidelines into [sync with] practice."

However, he added, "I won't even begin to try to second-guess the FDA."

The choice of medication to sedate mechanically ventilated patients is a conundrum in the ICU, because commonly used agents are associated with a variety of adverse effects, including oversedation, paradoxic agitation, myocardial depression, hypotension, tachyphylaxis, bradycardia, and delirium.

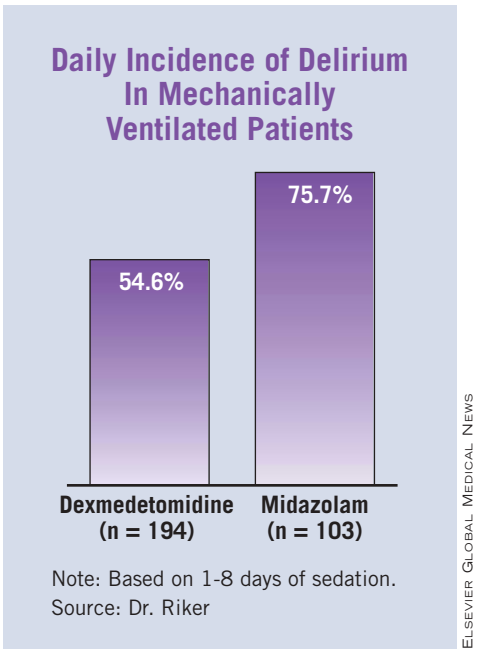
Daily awakening reduces oversedation, but predicting and minimizing the other potential side effects in critically ill patients can be challenging, said Dr. Riker, director of critical care research at Maine Medical Center Research Institute, Scarborough.

"There's no perfect sedation out there," he acknowledged, although he noted that any agent that can reduce delirium would be an important advance.

Delirium affects 60%-80% of mechanically ventilated patients and is associated with prolonged cognitive impairment and a threefold higher mortality over 6 months.

The researchers randomly assigned 366 adult ICU patients in a 2:1 ratio to dexmedetomidine, a relatively selective α_2-agonist, or midazolam, a benzodiazepine, at maintenance doses of 0.2-1.4 mcg/kg per hour and 0.02-0.1 mg/kg per hour, respectively. The average age of the patients was early 60s, and there were slightly more men than women. None of the women were pregnant. The subjects did not have unstable cardiac disease, burns, trauma, seizures or other central nervous system dysfunction, active hepatitis or advanced liver disease, or dialysis-dependent liver failure.

Randomization occurred within 96 hours of intubation. The Richmond Agitation-Sedation Scale (RASS)—which ranged from –5, unarousable, to +4, combative—was used to select eligible patients and to follow their progress. All randomized patients fell within a targeted sedation range of –2 to +1 prior to enrollment.



Daily awakening and arousal assessments were performed. Nurses assessed patients during each shift for communication, cooperation, and tolerance of mechanical ventilation.

Delirium was gauged using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).

Patients in both study arms could receive midazolam boluses of up to 4 mg every 8 hours if their RASS scale scores fell outside the targeted range of sedation. Fentanyl boluses were permitted for analgesia.

Of patients who received any dose of either sedative (244 received dexmedetomidine; 122, midazolam), 297 comprised the intent-to-treat population, having received either drug for more than 24 hours. In this group, 194 received dexmedetomidine and 103, midazolam. The groups were similar at baseline, with nearly identical initial CAM-ICU scores.

Time within the target range of sedation—the primary efficacy end point in the intent-to-treat population, was very similar between the two groups.

However, patients assigned to dexmedetomidine had significantly less delirium than did those receiving midazolam. The daily incidence of delirium, which started out fairly equally at about 55% of patients in each group, remained almost steady in patients on dexmedetomidine at 54.6% but increased to 75.7% of patients taking midazolam, with most of the difference occurring early in the study.

"If you look at days 1-8, you can see there is a dramatically higher incidence of delirium in the group receiving midazolam," Dr. Riker said.

Total time noted with delirium was 70 hours with dexmedetomidine and almost 95 hours with midazolam.

Time to extubation was abbreviated with dexmedetomidine: 94 hours vs. 138 hours, a 32% decrease in ventilator time.

Time to readiness for ICU discharge also was significantly shorter among patients assigned to dexmedetomidine: 6.2 days vs. 8 days for those receiving midazolam.

Nurses' assessments showed that the patients taking dexmedetomidine were more communicative and cooperative, although both groups were judged to tolerate mechanical ventilation equally.

Both drugs were safe, although there were more treatment-related adverse events in the dexmedetomidine arm. Moderate to severe adverse events were similar in both groups.

As expected from previous trials, dexmedetomidine was associated with more bradycardia and midazolam was associated with more tachycardia. More infections occurred in patients taking midazolam, "likely reflecting the longer duration of ventilation and time in the ICU," said Dr. Riker.

Dr. Riker disclosed that he has received grant support from a number of companies, including Hospira Inc., which manufactures dexmedetomidine and financed the FDA-mandated study.

ICU Bedside Exams Inconsistently Done

BY BETSY BATES
Elsevier Global Medical News

HONOLULU — Fewer than half of critically ill patients received a physical examination from their primary intensive care unit physicians each day, Canadian researchers have found.

Patients seen first during rounds, those with higher Sequential Organ Failure Assessment (SOFA) scores, and those not in isolation were more likely to be examined by their lead physicians during surreptitious line-of-sight observations of 195 patient/physician encounters, according to the findings of a study presented at the annual congress of the Society of Critical Care Medicine.

During multidisciplinary rounds, time spent at each ICU patient's bedside averaged 8 minutes, with progressively less time spent on each subsequent patient in the rounding order.

The amount of time spent at the patient's bedside increased with higher SOFA scores and with the number of health professionals attending medical rounds.

Dr. Adel Al-Sarraf led the study at Sunnybrook Health Sciences Centre in Toronto, Ont., in which an impartial observer with critical care experience timed patient encounters and noted whether each ICU patient received a physical examination each day.

The busy academic medical center intensive care unit had a mean 95.6% occupancy during the study, with a ratio of medical to surgical patients of 31:69. Nearly half of the patients were mechanically ventilated, and 9% were in isolation. The mean Acute Physiology and Chronic Health Evaluation (APACHE) score for the study population was 19.6.

Lead physicians physically examined their patients in 87 of 195 daily encounters, or 46.5%.

The duration of the primary ICU physician's time at the bedside averaged 11 minutes, with 69 seconds spent on physical examination.

The first patient seen by the lead physician was 2.5 times more likely than the last patient seen to receive a physical examination.

Patients who were in isolation were almost four times less likely to be examined, while higher SOFA scores were found to slightly but significantly increase the likelihood of an examination.

As clinical experience increased, the likelihood of a lead physician conducting a physical examination decreased, with fellows being most lax, said Dr. Al-Sarraf.

During briefer multidisciplinary rounds, just 8% of patients were physically examined.

Each patient seen during multidisciplinary rounds was seen for a shorter time than the previous patient was. When more health care professionals attended rounds, time spent at a patient's bedside increased, also true with a higher SOFA score.

THE FIRST PATIENT SEEN BY THE LEAD PHYSICIAN WAS 2.5 TIMES MORE LIKELY THAN WAS THE LAST PATIENT SEEN TO RECEIVE A PHYSICAL EXAM.

Dr. Al-Sarraf concluded that "patient, caregiver, and ICU organization factors significantly influence bedside clinical examination and assessment practices."

During the discussion following his talk, Dr. Al-Sarraf acknowledged that the study did not include any measures that would determine whether physical examinations correlated with improved outcome. He said that this might be a fruitful avenue for future research, particularly because technology has taken physicians increasingly away from patients' bedsides.

Dr. Philip Marcus, FCCP, comments: *Rounding in the ICU has changed over the last few decades. Our focus has moved from looking for subtle changes in the physical examination to using technology to evaluate our patients for us. Indeed, with the advent of ICU care from a distant location (telemedicine) in order to provide 24/7 coverage, we rely on numbers and their changes. Of course, we need to keep the focus on the patient and not just the numbers generated. Also, patients in isolation have always suffered from being the last seen and, now we see, perhaps not being "seen" at all.*

TBI Trials: Despite Setbacks, Promising Therapies Appear

BY BETSY BATES
Elsevier Global Medical News

HONOLULU — Disappointing clinical trial results should not suggest that outcomes cannot be improved in traumatic brain injury, only that study methodologies may need to be refined and study populations equalized as promising approaches come to the fore, Dr. D. James Cooper said during a plenary address at the annual congress of the Society of Critical Care Medicine.

To be sure, meaningful advances have been elusive, with various interventions producing hopeful improvements in animal models, then fizzling in human trials.

But the heterogeneity of the traumatic brain injury (TBI) population and "huge differences" in the specific trauma suffered may make study results look unfairly pessimistic, said Dr. Cooper, deputy director of the intensive care unit at Alfred Hospital, Melbourne.

Experimental treatments may be initiated too late, often because of logistical and informed-consent dilemmas, and older patients may be so unlikely to benefit that they negatively skew results.

Follow-up assessment periods may be too brief, since it increasingly appears that Glasgow Outcome Scale scores improve greatly over time, but very slowly, he said.

A number of lessons have indeed been learned, even from negative clinical trials, and a number of promising approaches are currently under review.

Serious doubt has been cast on the efficacy of early high-dose steroids, for example, following the curtailment of the 10,000-patient randomized controlled MRC-CRASH (Corticosteroid Randomisation After Significant Head Injury) trial in the United Kingdom after excess deaths were reported in the steroid arm. "It's abundantly clear . . . [that the] use of high-dose steroids should cease," said Dr. Cooper, who also serves as associate director of Australia's National Trauma Research Institute.

Because they lower vasopressor requirements in TBI patients, lower-dose steroids are used quite commonly in the intensive care environment, he noted. "There are no randomized controlled trials at all in this area, and it's clear to me, [based on the unequivocal MRC-CRASH results, that] there needs to be … a reevaluation" of this practice, said Dr. Cooper.

Another unexpected finding came from the Australian SAFE-TBI (Saline Versus Albumin Fluid Evaluation–Traumatic Brain Injury) study, in which Dr. Cooper participated. That study of nearly 500 patients confirmed that albumin is independently associated with mortality in TBI patients when it is used for intravascular fluid resuscitation in the first 28 days. In contrast, saline was associated with lower mortality and better neurologic outcomes in patients with moderate to severe TBI.

The reasons remain unclear, although Dr. Cooper hypothesized that albumin may increase brain edema, prompting the use of other agents that could contribute to mortality; that it may increase bleeding or cause more coagulopathy; or that it may be the result of hemodilution.

The possibility remains that albumin's negative effect on survival may be a class effect of colloids, he said.

A recent analysis of data from both the SAFE-TBI study and the earlier ATBIS (Australasian Traumatic Brain Injury Study) "[adds] to our strong feeling that saline alone might be worthwhile," he said.

As a final note, Dr. Cooper outlined two ongoing international clinical trials of early decompressive craniectomy to reduce intracranial pressure, an approach he said may offer "considerable promise."

The notion of temporarily removing the anterior portion of the skull is not a new idea, he stressed. But it has been controversial and not well studied, despite striking findings of benefit among young patients in small trials.

For example, the absolute risk of mortality was halved with early decompressive craniectomy versus medical therapy alone in a recent, 38-patient French study; but the trial was concluded early because of slow recruitment.

Dr. Cooper's government-sponsored DECRA (Early Decompression Craniectomy in Patients With Severe Traumatic Brain Injury) trial at 21 international sites (including 2 in the United States) is enrolling only patients younger than 60 years old with blunt diffuse brain injuries—strict criteria that may be more conducive to interpreting results, he said.

Thus far, 112 patients have been enrolled of 165 anticipated, which is "already many, many times higher than the largest study ever conducted of early decompressive craniectomy," Dr. Cooper noted.

In the first 42 patients randomized to surgery, the complication rate has been less than 10%, he said. While the trial is promising, Dr. Cooper urged colleagues to wait for study results in 2009 before implementing the procedure at their institutions.

Lung Transplants Less Likely in Black COPD Patients

BY BRUCE K. DIXON
Elsevier Global Medical News

Black Americans with chronic obstructive pulmonary disease were 17% less likely than were whites to undergo lung transplantation after being placed on a waiting list, according to the results of a large retrospective study.

A review of records from a 10-year period showed that 61% of blacks and 68% of whites on a waiting list received lung transplants. The study also detected a 19% greater risk of death or removal from the waiting list among blacks compared with whites, in spite of similar lung function at the time of listing.

"These disparities are consistent with those observed among patients awaiting kidney and liver transplantation, and among patients with other advanced lung diseases such as pulmonary arterial hypertension and pulmonary fibrosis," reported Dr. David J. Lederer and his colleagues at Columbia University, New York.

The investigators performed a retrospective cohort analysis of all non-Hispanic blacks and whites over age 39 with a diagnosis of chronic obstructive pulmonary disease (COPD) or emphysema who were placed on the United Network for Organ Sharing (UNOS) waiting list for lung transplantation in the United States between 1995 and 2004 (Am. J. Respir. Crit. Care Med. 2008;177:450-54).

The researchers obtained dates of transplantation and removal from the list from the UNOS file, and determined deaths using the Social Security Death Master File and the UNOS data set.

Analysis showed that after listing, 171 (61%) of 280 blacks and 3,580 (68%) of 5,272 whites received lung transplants. A total of 47 blacks (17%) and 804 whites (15%) died while waiting, and 39 blacks (14%) and 500 whites (9%) were removed from the waiting list.

"Of those removed from the list, 13 of 39 blacks and 229 of 500 whites subsequently died," they said, adding that at the conclusion of the study period, 23 blacks (8%) and 388 whites (7%) remained on the list.

The most common reasons for removal from the list were "too sick to transplant" (11 blacks and 145 whites) and "other" (12 blacks and 131 whites).

In both groups, the median time on the waiting list for those who either got a transplant, died, or were removed from the waiting list was about 400 days.

Blacks' reduced opportunity for a transplant was significant, even after adjustment for age, gender, disease severity, socioeconomic factors, transplant center volume, and access to health care, said Dr. Lederer.

"While we did not prove it in our study, one explanation for the lower transplant rate among blacks might be their higher rates of death and removal from the waiting list," Dr. Lederer said in an interview. "Differences in insurance, socioeconomic status, and cardiovascular risk factors explained some, but not all, of the higher risk of death or removal from the waiting list."

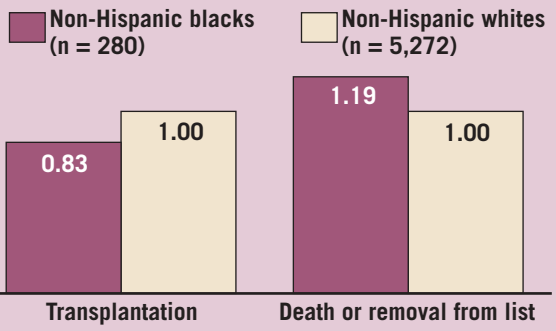
The investigators expressed concern about the finding that in this cohort of lung transplant candidates with COPD, the white-to-black ratio was 19:1, a considerably wider spread than the previously reported range of 9:1 to 11:1 for emphysema or chronic bronchitis.

Although confounding factors, reporting or misclassification bias, and random variation might explain this finding, one possible explanation is that blacks with COPD may not have accessed the lung transplantation waiting list as readily as whites during the study period, they said.

"It is apparent that over time, the mortality rate is increasing for blacks at a faster rate than it is for whites," said Dr. Lederer, adding that whether a transplant improves the long-term survival of those with COPD remains controversial.

"Still, patients with end-stage COPD should get on the list, because at that point, the assumption is that you've maxed everything else out," he said. "You've stopped smoking, you're using oxygen and bronchodilators, you're in a pulmonary exercise rehabilitation program, you've considered other experimental therapies, and you've considered or had lung reduction surgery."

Hazard Ratios Show Race Discrepancy In Chronic Obstructive Pulmonary Disease



Note: Data adjusted for age, sex, transplant center volume, forced vital capacity %, forced expiratory volume$_1$ %, pulmonary hypertension, 6-minute walk distance, diabetes, hypertension, body mass index, private insurance, and poverty level.
Source: American Journal of Respiratory and Critical Care Medicine

ELSEVIER GLOBAL MEDICAL NEWS

Study Examines Stage III Patients

Lung Cancer • *from page 1*

patients?" asked Dr. Margaritora, a thoracic surgeon at Catholic University, Rome.

To find out, Dr. Margaritora and his associates assessed 80 patients with stage IIIa or IIIb NSCLC downstaged to stage 0 or I by induction therapy. They compared the 3-year and 5-year survival rates in this group with 367 early-stage NSCLC patients scheduled for surgery only. Demographics were comparable between groups, he said.

Multimodal induction therapy included various chemotherapy protocols (for example, carboplatin, cisplatin/5-FU, or cisplatin and gemcitabine) and concurrent radiation. The 80 patients who responded were from a group of 226 patients treated with the induction protocol between 1992 and 2005.

Among the downstaged patients, 3-year survival was 48% and 5-year survival was 46%. Among the early-stage controls, 3-year survival was 82% and 5-year survival was 76%.

"This is an excellent study, elegantly presented," said study discussant Dr. Douglas E. Wood, chief of general thoracic surgery at the University of Washington Medical Center, Seattle. "It has the usual limitations that a retrospective study might have."

There may have been selection bias, for example, because the researchers included only patients who had surgery. On the other hand, its "enormous strengths include rigorous standardization of techniques, a great follow-up, and excellent clinical results."

There was no difference in 5-year survival between the 44 stage IIIa and 36 initial stage IIIb patients who responded to induction. Complication rates were similar between groups, Dr. Margaritora said. All the cancer in the first group was locally advanced; no patient in either group had a nodal metastasis, he added.

Dr. Wood asked why the researchers included stage IIIb NSCLC patients. "This was a selected group," Dr. Margaritora said. "The initial challenge from our oncologists was to include the IIIb group."

Despite the improved survival among the early-stage patients who had surgery without induction, Dr. Margaritora said, "downstaging to pathologic stage 0 or I after induction therapy for clinical stage III non–small cell lung cancer significantly improves long-term survival."

Dr. Michael Alberts, FCCP, comments: *The most appropriate treatment for patients with stage III lung cancer continues to be a subject of great debate. This article reports "encouraging results" among patients with stage III lung cancer who were "downstaged" with induction therapy prior to surgery. Questions remain, however, as to the best induction regimen, how to re-stage after induction, and how to treat those who were not "downstaged."*

Radiofrequency Ablation Shows Promise in Lung Cancer

The rates of tumor progression were 10.4% at 1 year and 17.5% at 2 years.

BY MIRIAM E. TUCKER
Elsevier Global Medical News

WASHINGTON — Radiofrequency ablation resulted in 70% survival at 2 years in a study of 244 lung cancer patients.

"Radiofrequency ablation is minimally invasive, with a high local success rate. It is a curative treatment in nonsurgical patients," Dr. Thierry de Baere said at the annual meeting of the Society of Interventional Radiology.

The patients, 60% of whom were men and were aged 27-85 years (mean, 62 years), had a total of 397 tumors. Of those, 19% were primary non–small cell lung cancer, and 81% were lung metastases (the majority from colon, rectum, or kidney).

Single tumors were present in about 57% of cases; the rest of the patients had two or more tumors. Bilateral tumors were present in 23% of the patients.

All were treated with CT-guided radiofrequency ablation (RFA) using expandable needles. Of a total 301 RFA sessions (1.23 sessions per patient), all but 5 were performed under general anesthesia. The technique was possible in all but two patients, said Dr. de Baere, an interventional radiologist at the Institut de Cancérologie Gustave Roussy, Villejuif, France.

Rates of local tumor progression were 6.1% per tumor at 1 year and 11.2% per tumor at 2 years. For tumors of 2 cm or smaller, progression rates were much lower: 3.7% at 1 year and 8.2% at 2 years.

In contrast, for tumors larger than 2 cm, progression occurred in 12.4% at 1 year and in 19.4% at 2 years. This 2-year survival difference between patients with tumors measuring 2 cm or smaller versus those with tumors greater than 2 cm was statistically significant.

Per patient, the rates of tumor progression were 10.4% at 1 year and 17.5% at 2 years. More than half of the patients (57.5%) had no viable lung tumors at 1 year, and 38.8% had no viable lung tumors at 2 years.

Median survival was 25 months, with 88.7% of patients surviving at 1 year and 70.3% at 2 years. The proportion of patients without pulmonary evolution was 57.5% at 1 year and 38.8% at 2 years.

Survival was 66% at 1 year and 52% at 2 years in patients with primary lung tumors, compared with 54% and 35% in those with pulmonary metastases.

These results are similar to those of RFA studies conducted in the United States, and the 2-year survival rate is similar to that reported in surgical series, Dr. de Baere noted.

Pneumothorax, an expected side effect, occurred in 60% of the patients. Of these, 28% were merely followed without treatment, 30% were treated with aspiration under CT guidance, 12% had drainage, and fewer than 1% each required thoracoscopy or thoracotomy/resection.

Early complications included death in 0.5% (one patient, from ventricular fibrillation), pleural effusion in 5% (all minimal/mild), alveolar hemorrhage in 14% (11% minimal, 3% mild), and cutaneous burn in 1%.

After discharge from the hospital, 66% had no symptoms, whereas about one-third had at least one symptom, including pain/pleural effusion (23%), hemoptysis (5%), pneumopathy (3%), and pneumothorax (2%).

Seven patients were readmitted to the hospital, none to the intensive care unit. Of those, two patients stayed just 1 day (both for pleurocentesis), one for 8 days (pneumopathy), and three for 10 days (two with pneumothorax, one with pleuroscopy). One patient who developed septicemia was hospitalized for 34 days, he reported.

Dr. de Baere has received grant support from Covidien AG and honoraria from Boston Scientific Corp. and Terumo Medical Corp.

Operating Room of the Future Already Here for Some Surgeons

BY JOHN R. BELL
Elsevier Global Medical News

A host of technological innovations in the operating theater will give surgeons faster access to more information, reduce the chance of errors, cut complication rates, and likely decrease malpractice insurance costs, according to one surgeon whose hospital has built two "futuristic" ORs and plans to build others.

Advances in imaging displays, communication, lighting, and even the shape of the operating room have already enhanced facilities at several U.S. hospitals, including New York–Presbyterian Hospital/Cornell University, New York, where Dr. Jeffrey Milsom is chief of colon and rectal surgery.

'Everything from the ceiling down to the floor is going to change dramatically.'
DR. MILSOM

"They're definitely going to improve efficiency, I think, as well as patient outcomes," Dr. Milsom said in an interview about two such ORs at his institution. More than 100 procedures have been performed thus far in these innovative units, and four additional futuristic ORs (sometimes called smart ORs) are planned.

Each unit includes six large high-definition monitors that display a patient's vital signs and allergies, all laparoscopic camera views, any external camera views, the electronic anesthetic record, and the names of all people in the operating theater. Such banks of monitors have long been a fixture of military, law enforcement, and intelligence operations centers, Dr. Milsom noted.

The monitors allow the surgeon to instantly view images sent from another OR, and even those sent by a pathologist or a referring physician, and to discuss them with the sender via a Bluetooth headset. Thus, for example, the surgeon can use a mouse and the high-definition monitor to pinpoint the precise area of a lesion to biopsy. Radiologic scans will also be available, via a picture archiving and communications system, he said. The accompanying software will allow video from the procedure to be streamed on the Internet or used in a live teleconference with other surgical staff.

The monitors also display checklists for each step in the procedure, with the option of an oral or written prompt for each. This system not only will help OR staff know instantly what comes next in an unfamiliar procedure but also will photographically document each step for future reference. "I'm planning photo documentation for standard operations as part of the operative record," Dr. Milsom said.

The system will also eliminate most paperwork for the surgeon. "I think this will become mandatory" in the future, he said, given the utility of such evidence in malpractice defense. In turn, he expects that eventually malpractice insurance costs will be reduced for institutions using such systems.

Dr. Milsom acknowledged that some surgeons have remained resistant to the new technology but added that most have not actually used the system. "There's a certain difficulty when you change culture in a working environment," he said. However, he added, "I'm pretty darn sure that if we design these things right … people are going to fight to work in these rooms."

The visual-imaging benefits of the futuristic ORs are most useful for laparoscopic or minimally invasive procedures, but the other elements can benefit open surgery as well.

Malfunctions—which have been rare thus far, he said—have occurred with the software. Hospital staff have been able to resolve the problems, although a 24-hour technical help line is available through LiveData Inc., maker of the visual display system. Dr. Milsom said he has no financial relationship with any of the equipment manufacturers.

CHARLES MANLEY/NEW YORK-PRESBYTERIAN HOSPITAL CORNELL MEDICAL CENTER

Dr. William Macaulay, Dr. Nitkin Kumar, and Dr. Charlie Jobin work in one of New York–Presbyterian's new operating rooms.

Training can be accomplished in a few weeks of daily sessions, although the actual time required will be affected by new features still in development. He estimated that a surgeon would need 5-10 hours of training time to become comfortable with the current systems.

The total cost to get a futuristic OR up and running is $200,000-$300,000 per room, Dr. Milsom estimated. His institution hopes to recoup part of this cost by licensing the design of some of the systems developed there.

New features on the horizon include:

- Additional light sources on ceilings to give the surgeon more options for directing light to a certain area—but without the ungainly support booms. The lights will have high-intensity LCD sources and allow fingertip adjustment.
- A 3-D x-ray machine with a C-arm for imaging a body part on the spot (pending Food and Drug Administration approval).
- The use of automated floor scrubbers and structural improvements to allow for faster sterilization and an environment less conducive to bacteria than what currently exists.

Dr. Milsom's department is also looking at ways to eliminate unneeded equipment and cumbersome electrical conduits from the OR.

"Everything from the ceiling down to the floor I think is going to change dramatically," he said. "The way a surgeon can and should operate has got to really undergo a lot of change for the betterment of the patient, the surgeon, and the whole working team."

Dr. Milsom said that eventually every operating room in his hospital will be a futuristic OR. "When something's really good, then people recognize it, and they don't want anything else."

Dr. Robert Cerfolio, FCCP, comments:
Dr. Milsom has presented a provocative and exciting concept of our future, and he probably is right. These ORs will eventually save money. However, the true cost savings of this incredibly expensive venture will be carefully weighed by hospital administrators before too many of these are built. And given the already skyrocketing cost of medical care in the United States, the expansion of these units will be slow at best.

OSAH May Increase Risk of Motor Vehicle Crashes

BY KERRI WACHTER
Elsevier Global Medical News

Patients with obstructive sleep apnea hypopnea had a greater rate of motor vehicle crashes than did matched controls, and they were three times more likely to be involved in crashes involving personal injury, according to researchers in British Columbia.

"Our data indicate that the increased risk of motor vehicle crash occurs at all levels of OSAH severity," Dr. Alan T. Mulgrew, of the University of British Columbia, Vancouver, and his colleagues wrote in an article in the journal Thorax published online.

The study involved 783 adult patients who were referred for overnight polysomnography for suspected sleep-disordered breathing.

Patients were excluded if they had symptoms of another sleep disorder known to cause daytime sleepiness (periodic limb movement disorder), or if they had another serious medical condition or overt psychiatric disease. They were also excluded if they were already being treated for OSAH.

Overnight polysomnography was performed using conventional instrumentation, and analysis was performed according to the American Academy of Sleep Medicine's recommendations on syndrome definition and measurement techniques.

Patients completed a number of surveys on the night of their polysomnography study. Daytime sleepiness was assessed using the Epworth Sleepiness Scale.

All motorists in British Columbia are insured by a single insurance corporation: the Insurance Corporation of British Columbia (ICBC). Objective crash data for patients—including crash severity type—was obtained for 3 years prior to the sleep study.

All patients were matched with an individual control from the ICBC database based on age, gender, type of license, driving experience, and postal region.

Patients were categorized by OSAH severity based on the apnea hypopnea index (AHI): normal polysomnography (AHI of 5 or fewer events per hour), mild OSAH (AHI greater than 5 and up to 15), moderate OSAH (AHI greater than 15 but less than 30), and severe OSAH (AHI of 30 or more per hour).

Most patients (71%) were men, and the average patient age was 50 years. The average AHI was 22.6 events per hour, and the average Epworth Sleepiness Scale score was 10. The mean body mass index (BMI) was 31.8 kg/m^2. The average distance driven each week was 236 km (145 miles).

In terms of OSAH severity, 18% of patients had normal polysomnography, 30% had mild OSAH, 26% had moderate OSAH, and 26% had severe OSAH.

In all, there were 374 crashes, of which 251 (67%) happened to patients. In the patient group, 94 of 251 crashes caused minor property damage, 83 crashes caused major property damage, and 74 crashes caused injuries. This compared with 48, 52, and 23 in the control group (Thorax 2008 Jan. 30 [Epub doi:10.1136/thx.2007.085464]).

When compared with controls, patients with OSAH had a significantly increased rate of motor vehicle crashes, with relative risks ranging from 1.9 to 2.6. (See table.)

In comparison, patients without OSAH (AHI 0-5 events per hour) were at lower risk of motor vehicle crashes than were patients with OSAH.

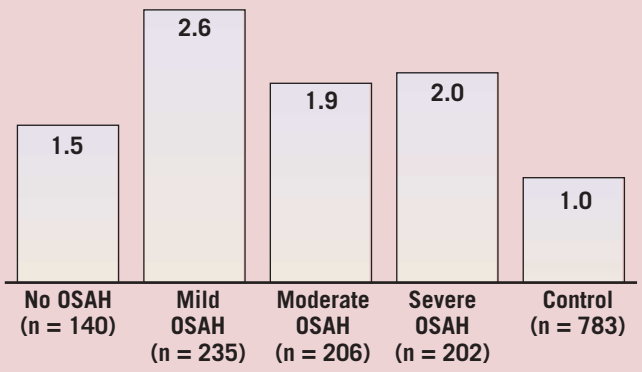
The presence of OSAH was linked with a 3.0- to 4.8-fold increase in the rate of more severe motor vehicle crashes. Within the patient group, there appeared to be a dose-response relationship between OSAH severity and the rate of motor vehicle crashes involving personal injury. In patients with an AHI of 0-5, motor vehicle crashes involving personal injury accounted for 9% of crashes, compared with 37% in those with an AHI greater than 30. Compared with patients with an AHI of 0-5, patients with severe OSAH were 6.1 times more likely to be in a crash involving personal injury.

In terms of subjective sleepiness, there was no significant difference in motor vehicle crash rates among the patient quartiles. Controlling for AHI group, Epworth Sleepiness Scale, BMI, gender, age, kilometers driven, and use of alcohol, sedatives, or caffeine, the presence of OSAH increased the rate ratio for any motor vehicle crash to 1.22, though this was not significant.

Notably, BMI and kilometers driven were both significant in the model. The presence of OSAH did increase the rate ratio for crashes causing personal injury to 3.67, which was also statistically significant.

"Caution should be exercised when assessing patient' driving risk, and all patients with OSAH should be advised of potential risk," the authors advised.

Relative Risk of Any Motor Vehicle Crash Is Highest With Mild Obstructive Sleep Apnea Hypopnea



Note: Based on a 3-year period.
Source: Thorax

ELSEVIER GLOBAL MEDICAL NEWS

Sleep Apnea May Be a Risk Factor for Diabetic Retinopathy

BY SARA FREEMAN
Elsevier Global Medical News

GLASGOW, SCOTLAND — Preliminary research presented at the annual professional conference of Diabetes U.K. suggests that sleep apnea could be a risk factor for diabetic retinopathy.

Dr. Simon Merritt of the Sleep Disorder Centre at St. Thomas' Hospital in London presented data showing that diabetes patients with severe retinopathy had significantly lower and more fluctuating levels of oxygen throughout the night than did those with normal or near-normal retinal scans.

"Sleep-disordered breathing occurs at the time when the rods are most metabolically active and is likely to add to retinal hypoxia and therefore increase angiogenesis and vascular permeability," said Dr. Merritt.

A total of 120 patients with type 2 diabetes who had undergone digital retinal photography within the past 6 months were included in the study. Data were presented on the first 21 patients with sight-threatening retinopathy and 23 with normal vision or minor background retinal changes.

The mean age of the patients was 60-61 years, and there was no significant difference among those with severe retinopathy and those with normal or near-normal sight in terms of hemoglobin A_{1c} level, body mass index, blood pressure, or duration of diabetes.

However, patients with severe eye disease were found to have significantly lower and more variable oxygen levels during the night than did the comparator group as measured by pulse oximeter.

The minimum and mean oxygen saturation was 72% and 93%, respectively, in patients with severe diabetic retinopathy, compared with 82% and 95% in those with normal or near-normal vision.

The mean number of times the oxygen saturation dipped by 4% or more per hour was 14 vs. 4 episodes, and 12.6% vs. 1.8% of the night was spent with an oxygen saturation of less than 90%.

Although not in the same league as more established risk factors for diabetic retinopathy, such as hyperglycemia and hypertension, Dr. Merritt suggested that sleep-disordered breathing should be added to the list.

"We're living longer and we're getting fatter, so the incidence of type 2 diabetes and indeed sleep apnea is increasing," Dr. Merritt said. Data have suggested that 22% of patients with type 2 diabetes also have obstructive sleep apnea.

Within the next few months, data should be available on all patients included in the study, and perhaps then it can be considered whether all patients with type 2 diabetes or just those with diabetic retinopathy should be screened or even treated for sleep apnea.

If sleep apnea continues to be a risk for retinopathy in this larger group of patients, then the question of which patients should be screened and/or treated will be raised.

Screening all patients with type 2 diabetes would not be a realistic target, Dr. Merritt said, since there would be far too many people for the available resources.

He proposed that if a patient with type 2 diabetes is obese, regularly snores, and appears sleepy in the daytime, then screen for sleep apnea.

At the very least, such a patient should be seen by a chest physician because they are at high risk of developing cardiovascular disease.

Whether limiting screening to only patients with diabetic retinopathy would be of value remains to be seen.

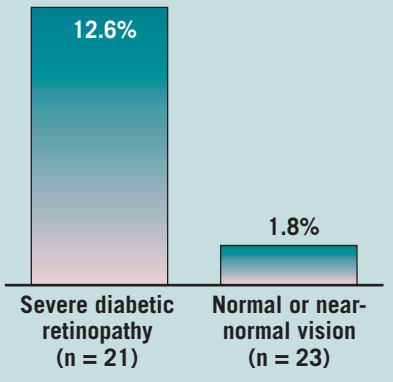
In response to a question from an audience member regarding whether giving oxygen to retinopathy patients would increase complications, Dr. Merritt noted that "by treating sleep apnea, you would only [be aiming to] normalize the oxygen levels; you wouldn't be providing supranormal partial pressures of oxygen."

Performing a treatment study may prove challenging, however, since this would involve treating a large number of asymptomatic patients with a continuous positive airway pressure device, Dr. Merritt explained.

"We have enough difficulty convincing patients who need it to use it, and it would be for a relatively long time," Dr. Merritt added.

The study was funded by ResMed (UK) Ltd., which makes devices to correct sleep-disordered breathing.

Percentage of Night With Oxygen Saturation <90%



Note: Based on a study of patients with sleep apnea.
Source: Dr. Merritt

ELSEVIER GLOBAL MEDICAL NEWS

Pulmonary Perspectives

Current NCI-Sponsored Screening Trials for Lung Cancer

Mass screening may reduce lung cancer mortality—or it might be an inappropriate allocation of resources.

Lung cancer is the deadliest malignancy, as it will cause approximately 162,000 deaths in the United States in 2008—more than the next four most commonly diagnosed deadly cancers (colon, breast, prostate, and pancreas) combined (Jemal et al. *CA Cancer J Clin* 2008; Feb 20, Epub ahead of print).

Overall, about 85% of patients with lung cancer die of this disease. Lung cancer usually remains clinically "silent" until it reaches an advanced stage, yet diagnosis at stage 1 is associated with survival rates that are reported to be as high as 60% to 90% with surgical resection. This has led to multiple efforts to screen patients for an early diagnosis.

There was no reduction in lung cancer mortality in the nonrandomized studies of chest radiograph screening prior to 1970.

Randomized, controlled trials in the 1970s (three in the United States, another in Czechoslovakia) used chest radiographs with or without sputum cytologic studies; all of them failed to demonstrate a mortality benefit from screening.

There were more early stage (stage 1 and 2) lung cancers in the screened populations; however, reanalysis of data at 20 years from the Mayo Lung Project again failed to reveal a mortality benefit, despite the excess of lung cancers found in the screened study arm.

This suggests an overdiagnosis bias, *ie*, the excess cancers were biologically less aggressive, and deaths occurred from other causes rather than from the lung cancer itself.

Moreover, a recent analysis by the Cochrane Library (Manser et al. *Cochrane Database Syst Rev* 2007; 4:[no page number]) led to the conclusion that there is an 11% relative increase in mortality from lung cancer associated with frequent chest radiograph screening (relative risk, 1.11; 95% CI, 1.00 to 1.23) and that frequent screening might be harmful.

There have been other criticisms of the earlier chest radiograph lung cancer screening studies, including small sample size; contamination of the control groups by the administered chest radiographs; and the possibility that there is a small, but clinically important, benefit from screening that was not detected.

TWO DIFFERENT, BUT COMPLEMENTARY, TRIALS SCREENING FOR LUNG CANCER ARE BEING CONDUCTED UNDER SPONSORSHIP FROM THE NATIONAL CANCER INSTITUTE.

Two different, but complementary, randomized, controlled trials screening for lung cancer are being conducted at the present time under sponsorship from the National Cancer Institute (NCI).

The first is a project designed to determine whether a screening program for prostate, lung, colon, and ovarian cancers (PLCO) will reduce mortality from each organ-specific cancer that is screened. A single posteroanterior (PA) chest radiograph is used as the screening tool for lung cancer in the PLCO study.

There are several important differences between the PLCO trial and earlier lung cancer screening trials. The PLCO trial includes women and people who have never smoked, and subjects in the control group are not screened with a scheduled chest radiograph.

Between 1993 and 2001, the PLCO trial recruited 154,934 individuals, aged 55 to 74, with 77,464 individuals in the intervention group. There was a near-equal number of men and women, and 51.6% of subjects were current or former smokers.

At our center, we enrolled 24,677 subjects, some who are now in their 15th year of follow-up. We are currently following 19,654 subjects after accounting for people who have dropped out or who have died.

This large population of subjects has required up to 27 full-time employees to perform the screening tests, as well as data entry, data analysis, and the other tasks involved with managing the information accumulated during the study. Even now, after screening has been completed, follow-up with the recovery of medical records, correctly abstracting the information, and ensuring error-free data entry requires a staff of 1 half-time and 10 full-time employees.

In the PLCO study, lung cancer screening initially included a baseline PA chest radiograph and three annual follow-up screening PA chest radiographs for all participants in the intervention group; the protocol was changed so that only smokers (current or former) were offered the third follow-up chest radiograph. Compliance with screening was high.

Ongoing analysis of the intervention group includes lung cancer detection rates, the patterns of care in the evaluation for lung cancer, the importance of abnormal results that are not suspicious for lung cancer, characteristics of the lung cancers in people who have never smoked, and differences between cancers that were detected by screening vs. cancers that were diagnosed in the intervals between screening.

UNTIL THEN, THE PULMONARY COMMUNITY MUST NOT BE MISLED BY THE MANY EFFORTS TO PROMOTE LDCT SCREENING FOR LUNG CANCER.

The Data and Safety Monitoring Board members are charged with the responsibility to look for the primary end result of mortality in the intervention (screened) arm and the control arm. At present, the investigators are blinded to these results, in order to avoid bias, while attempting to interpret the outcome of the study.

After the inception of the PLCO study, low-dose CT (LDCT) emerged as a more sensitive technique to screen for noncalcified lung nodules. Multiple observation studies generated enthusiasm that LDCT could detect smaller nodules than is possible with a chest radiograph, and that additional diagnostic-quality CTs and biopsies performed according to a strict protocol would lead to surgical resection with the intent to cure.

Indeed, survival from the time of diagnosis was excellent—projected to be up to 90% at 10 years from the initial diagnosis in one such study (Henschke et al. *N Engl J Med* 2006; 355:1763).

The problem with this study, and other observational studies, is that survival from the time of diagnosis does not account for the phenomenon of lead-time bias.

Diagnosis of the lung cancer will be made at an earlier date by any successful screening test; if the disease is going to lead to death because of its biological behavior at a given future date, there will be an increase in survival without any effect on mortality from the disease being screened. This is what is meant by lead-time bias.

Cognizant of this phenomenon, the NCI decided to sponsor a randomized, prospective, controlled trial that will compare LDCT with a PA chest radiograph to detect early-stage lung cancer.

The control group in the National Lung Screening Trial (NLST) received a PA chest radiograph instead of no screening, because the PLCO study was designed to answer the question of whether a chest radiograph provides a mortality benefit compared with no screening. In case there is an advantage demonstrated by screening by chest radiograph by the PLCO study, it was felt that denial of this potential advantage to the control group during their participation in the NLST could not be justified.

A total of 53,461 subjects were enrolled nationwide in the NLST.

As with the PLCO study, a prodigious staff of 14 employees was needed during the screening phase for the 3,395 subjects that we enrolled at our center. We still employ four people to manage and ensure the accuracy of all data that are accumulated during the follow-up phase after the screening is completed.

Note that the end point chosen for the PLCO study and the NLST is mortality, not survival. This distinguishes both studies from the observational studies that report survival from the time of diagnosis as their most important outcome variable.

The PLCO study and the NLST are statistically powered to detect significant differences in mortality, if there are such differences. Both studies also are designed to eliminate the potential for overdiagnosis and lead-time bias.

Welch et al (*Arch Intern Med* 2007; 167:2289) offer a more complete discussion of the problems associated with currently published observational studies that report survival as their end point.

The results of the PLCO study are expected to evolve; for the NLST, the results may be reported by 2010.

Until then, the pulmonary community and the public must not be misled by the many efforts to promote LDCT screening for lung cancer. Adoption of mass screening may prove beneficial and reduce lung cancer mortality, as well as increase survival, but it might be an inappropriate allocation of resources for a vexing disease with the highest death rate of any type of cancer.

There are risks that are associated with screening people who are asymptomatic; only well-conducted, randomized, controlled trials, such as the PLCO study and the NLST, will give us the information needed to determine whether lung cancer-specific mortality is reduced by screening with a chest radiograph and/or LDCT.

Dr. Kvale is Principal Investigator at Henry Ford Health System for the PLCO study and NLST.

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AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

PRESIDENT'S REPORT

Health Care Disparities: A Complex Issue

The presidential campaign, particularly the Democratic campaign, has been compelling. The issues of the economy and the Iraq war have been paramount, with a subtext of gender and racial issues, but the issue of health care reform remains quite large.

BY DR. ALVIN V. THOMAS, JR., FCCP

A discussion of the health status of the American populace cannot get very far without mention of the uninsured or underinsured, of which many are poor, underserved, and minority. The problem of health disparities of the poor, minorities, and underserved has been well documented, but solutions for the disparities in health care are much more difficult.

Disparities in health and health care are substantial for many of the patients we see in the ICU and many with pulmonary and sleep disorders. The reasons for such disparities are frequently complex and poorly understood but include poor access to quality health care; health care provider shortcomings; difficult and poorly responsive systems of care; patient-related issues, such as poor adherence to therapy; and social issues, such as poor socioeconomic status.

As most of us know, there are substantial health and health care disparities in asthma care. A recently published study (Erickson et al. *Arch Intern Med* 2007; 167:1846) evaluates the factors contributing to asthma health care disparities by studying them in a setting of uniform access to care (Kaiser Permanente of Northern California).

The effect of race on asthma management and outcomes in hospitalized patients in such a large, integrated managed care organization was prospectively studied over a 4-year period. Patients (678) were interviewed after hospital discharge, and information that included asthma history, health status, and socioeconomic status (SES) was obtained.

The authors found that black race was associated with a higher risk of ED visits (hazard ratio [HR] 1.93) and hospitalizations (HR 1.89). The findings persisted after adjusting for SES and differences in asthma therapy in blacks (*eg*, increased short-acting ß-agonist use and increased peak flow meter use).

The authors concluded that even in a setting of uniform access to care, black race was associated with worse asthma outcomes, including greater risk of ED visits and hospitalizations. They showed that the association was not explained by differences in SES, asthma severity (asthma severity score), or asthma therapy. They suggested that genetic differences might underlie the racial disparities, though they admitted that the reasons for the disparities in this study are not clear and are likely complex.

The authors acknowledged that unmeasured SES factors, comorbid diseases, specific health-related behaviors, health care provider decisions, and patient behavioral and cultural beliefs were unstudied and may individually or in aggregate confound study findings. The authors also did not evaluate the possible role that difficult patient navigation of a complex system of care might have played in the disparate asthma care.

Despite the cited concerns, the study has helped clarify the role of health care access in asthma care. It is one of a number of studies that suggests that the problem of health care disparities (in asthma and many other diseases) is far more complex than one of inadequate health care access. It suggests that a far more comprehensive approach is necessary to overcome disparities in health and health care.

A recent monograph published by the Center for Health Care Strategies (Angeles and Somers. Issue Brief: From policy to action: addressing racial and ethnic disparities at the ground-level: Center for Health Care Strategies, August 2007) states that a comprehensive, multistakeholder strategy is needed to reduce racial and ethnic disparities in health care delivery. They further state that progress in this area requires the engagement of the entire health care stake-holder community, including purchasers, managed care organizations, providers, consumers (patients), and, importantly, community-based organizations.

It is clear that if we are to overcome health and health care disparities in this country, a comprehensive approach to health reform is necessary. Helping to resolve the problem of access to care (health insurance), as is being debated in the presidential campaign, will only be part of a very complex approach to health reform.

ACCP WORLDWIDE

An Annual Education Medical Mission in the Philippines

Submitted by the ACCP Philippine Chapter

Concurrent with the ACCP Philippine Chapter Annual Scientific Meeting (ASM) for the past 5 years, the chapter has held an Education Medical Mission (EMM) that targets a needy community in the locale where the meeting is held.

These two back-to-back activities coincide with the mission of the ACCP: to promote the prevention and treatment of diseases of the chest through leadership, education, research, and communication. Through the EMM, members of the ACCP who come from different parts of the country for the ASM are engaged to provide service to indigents. Thus far, these lung specialists have been very willing to volunteer and lend a hand.

This undertaking is not the same as the common one-time treatment activity. Partnership with a local physician group ensures follow-up and continuing care. Free consultation and medications are provided, and these serve as incentives for patients with preexisting pulmonary complaints to attend. The real thrust is to empower patients to manage their disease through acquisition of basic and practical knowledge and development of skills needed for treatment. These patients can then prevent and control risk factors for exacerbations, recognize early symptoms of worsening disease, and implement appropriate primary interventions when needed. Long after the free medicine runs out, the knowledge learned and the skills acquired will continue to benefit these patients.

The mission specifically aims to:

1. Provide accurate diagnosis of the pulmonary condition.
2. Perform spirometry and other pulmonary function tests when indicated.
3. Give full courses of quality medicines and, if available, vaccines.
4. Give patients accurate and understandable information about their lung diseases through video presentations and interactive lectures.
5. Push advocacies on tobacco control, smoking cessation, TB PPM directly observed therapy, basic infection control, guided asthma self-management, and more.
6. Teach patient pursed-lip breathing and other basic pulmonary rehabilitation maneuvers.
7. Develop patients' skills in using inhalers, nebulizers, peak flow meters, and other devices whenever appropriate.
8. Identify patients with TB symptoms, and channel them to the local health center for microscopy and entry to the local TB program.

Indeed, by holding the ASM and the EMM outside metro Manila, the ACCP-Philippine Chapter continues its efforts to improve patients' lives and live up to its mission of being in the forefront of chest medicine.

This Month in *CHEST*: Editor's Picks

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

- **Portable Exhaled Nitric Oxide as a Screening Tool for Asthma in Young Adults During Pollen Season.** *By Dr. K. Kostikas, et al*
- **Ultrasound vs CT in Detecting Chest Wall Invasion by Tumor: A Prospective Study.** *By Dr. V. Bandi, et al*
- **Factors Associated With Failure to Complete Isoniazid Treatment for Latent Tuberculosis Infection in Rhode Island.** *By Dr. A. Kwara, et al*
- **Aerosolized Salbutamol Accelerates the Resolution of Pulmonary Edema After Lung Resection.** *By Dr. M. Licker, et al*
- **Definition of Cutoff Values for the Hypoxia Test Used for Preflight Testing in Young Children With Neonatal Chronic Lung Disease.** *By Dr. A. C. Martin, et al*
- **Air Travel Hypoxemia vs the Hypoxia Inhalation Test in Passengers With COPD.** *By Dr. P. T. Kelly, et al*
- **Hypoxia Altitude Simulation Test.** *By Dr. C. J. Dine, and Dr. M. E. Kreider*
- **The Hypoxia Altitude Simulation Test (Editorial).** *By Dr. L. C. Mohr, FCCP*
- **Affording EBUS (Editorial).** *By Dr. S. Manaker, FCCP, et al*

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NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

The CHEST Foundation 2008 Awards

The deadline of April 30, 2008, is drawing near. Whether you are involved in clinical research, humanitarian service, or you are a leader in end-of-life and/or palliative care, go to www.chestfoundation.org and apply for an award today!

Measuring the value of The CHEST Foundation's Awards Program in the words of previous award recipients …

Clinical Research Awards

Reena Mehra, MD, FCCP, Assistant Professor at the University Hospitals of Cleveland/Case Medical School in Cleveland, OH, was the 2005 recipient of the Association of Specialty Professors/CHEST Foundation Geriatric Development Research Award. The name of her research project was "Sleep-Disordered Breathing and Cardiac Arrhythmia Associations With Alcohol Use and Dependence in Elderly Men."

ACCP

Dr. Reena Mehra, FCCP, received a geriatric research award.

Dr. Mehra notes, *"The ASP/CHEST Foundation award has enhanced my career from many perspectives, as indicated by the following achievements occurring during the span of this award (2005 to 2007): promotion to Assistant Professor, attainment of funding and support from the K12 Multidisciplinary Clinical Research Training Program, and subsequent funding from the NIH/NHLBI K23 Mentored Patient-Oriented Research Career Development Award. In addition, I have had numerous manuscripts published, and I received an award from the Women Faculty School of Medicine to pursue professional development. My findings from the ASP/CHEST Foundation award have been presented as abstracts and oral presentations at national meetings and have resulted in a publication currently in press in the Journal of the American Geriatrics Society entitled, "Prevalence and Predictors of Sleep-Disordered Breathing in Older Men: The Outcomes of Sleep Disorders in Older Men."*

Dr. Mehra continues, *"Through the support of this award, I have had the opportunity to examine sleep-disordered breathing (SDB) prevalence and risk factor profile, investigate the important relationship between SDB and cardiac arrhythmias, and analyze the relationship between alcohol use and SDB in an older male cohort, while working with a mentorship team enriched with experts in the fields of pulmonary medicine, sleep medicine, geriatrics, epidemiology, and substance abuse."*

Humanitarian Project Development Grant

Debra J. Romberger, MD, FCCP, Nebraska Medical Center, Omaha, NE, was one of the recipients of the $25,000 Humanitarian Project Development Award in 2006. The name of her project was "One World Tuberculosis Control Program." Dr. Romberger has served as the co-director of the One World Tuberculosis Control Clinic since 1999. She and other dedicated volunteers and staff provide treatment for latent tuberculosis infection (LTBI), as well as active tuberculosis within the larger, first-generation immigrant population living in the Omaha area. About 350 patients have been treated at the clinic in the award year of 2006 to 2007.

ACCP

Dr. Debra J. Romberger, FCCP, received an award.

She writes, *"Funds from The CHEST Foundation Award were used to develop an "Express TB Visit" model to answer the need to improve the completion rates for medical therapy for patients with LTBI. Patients with LTBI must complete 9 months of medical therapy and, generally, were failing to follow-up for all of their scheduled visits to receive medication. This new model for care delivery provides lower cost service in a more convenient manner for patients with LTBI cared for at our clinic."*

Dr. Romberger continues, *"In addition, the award money supported the clinical pharmacist who developed the protocols and materials needed for the visit, as well as the training and coordination of the University of Nebraska Medical Center pharmacy students and faculty volunteers to manage the express visits. Grant dollars also helped support a volunteer coordinator from One World."*

THE CHEST FOUNDATION℠

Ambassadors Group News

▶ **Meet the 2007 Poster Contest Winner:** 11-year-old Natalie Gehred from Elm Grove, WI.

Natalie was in one of the classes in which Monir Almassi, an Ambassadors Group volunteer, taught the Lung Lessons℠ program last year. Natalie's art teacher, Julie Stockinger, followed up Mrs. Almassi's lesson with an assignment for her students to create a poster design that showed the Love Your Lungs® theme. The assignment was in response to the Ambassadors Group Poster Design Contest materials that Mrs. Almassi had distributed earlier at the school. Natalie's design was selected to be the winner of the CHEST 2007 Poster Contest from the 35 entries that were received at The CHEST Foundation.

Natalie said, *"I was extremely pleased and surprised to find out I had won the contest!"* Natalie is not only excellent in art, but also enjoys reading, playing the viola, playing volleyball, and hanging out with her friends in her free time.

ACCP

Natalie Gehred from Elm Grove, WI, submitted the winning entry in the CHEST 2007 Poster Contest.

ACCP members who have children, grandchildren, nieces, and nephews aged 8 to 14 years should encourage them to submit a colorful design that shows how to "Love Your Lungs®." Designs must be on 8-1/2 x 11-inch white paper and contain no more than 12 words for an effective message. Go to the Web site at www.chestfoundation.org/specialInitiatives/ambassadorsGroupProjects.php#poster to learn the rules and print out a submission form. Entries must be mailed to the attention of Sue Ciezadlo at The CHEST Foundation by June 1, 2008.

AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

NETWORKS

Growth in Practice Administration, Investigating Health Care–Associated Infections

Members In Industry

Perspectives on Clinical Research, Careers, and More

The relationship between the pharmaceutical industry and health-care providers has increasingly been the focus of discussion. The Members in Industry (MII) NetWork's mission is to promote cooperation between the ACCP and industry and foster advances in clinical research and medical education.

The important topic of the interface between the pharmaceutical industry and the rest of the health-care industry was discussed at CHEST 2007 in a session entitled, "Evolving Trends in the Relationship Between the Pharmaceutical Industry and the Health-Care Establishment." The discussion was led by a panel that included ACCP Past President Dr. W. Michael Alberts, FCCP, representing academia, as well as two industry representatives, Dr. James Roach, FCCP, who gave an industry perspective, and Mark Wanda, who offered a viewpoint from government.

A related topic, "Working With the Health-Care Community in a Complex Compliance Environment," was presented at the MII NetWork Open Meeting at CHEST 2007 by Dr. Mark Forshag, FCCP. This presentation is available for viewing on the MII Web site.

There was significant interest in the session, "Contemplating a Career Change: Alternative Careers in Industry," and in the Career Conversations table in ACCP Central, where MII steering committee members provided insight into pharmaceutical roles. A session exploring the impact of a product recall on physicians and patients was also successful. Many of these presentations will be available on the MII NetWork Web site.

The MII NetWork is excited about two sessions that have been accepted to the program for CHEST 2008, entitled, "Research Ethics and Oversight: Revolution, or Just Going Around in Circles?" and "The Drug Development Process: What Is New?" If these types of topics interest you and you would like to become involved in the MII NetWork, contact networks@chestnet.org or visit the NetWorks Web site at www.chestnet.org/networks/accp_industry/ for more information.

Dr. Dawn Carlson, FCCP
Members in Industry NetWork
Vice-Chair

Practice Administration

The Growth of Practice Administration: More Than a Decade of Success

Is your practice manager one of the many physicians or administrative practice professionals who belong to the Practice Administration NetWork (PAN)?

For more than a decade, PAN members have benefited from education, professional development, and networking within the ACCP. PAN members also have been integral to the expansion of several initiatives, such as the ACCP Practice Management Department. The PAN has provided postgraduate courses and educational sessions on practice management topics at CHEST since the mid-1990s.

Members of the NetWork have authored *CHEST* journal articles on important practice management topics, and many are contributing authors in the ACCP's *Coding for Chest Medicine 2008*.

Recently, the NetWork and the College have formed a strategic alliance with the Medical Group Management Association to provide quality, statistically relevant data about pulmonary, critical care, and sleep practices. The NetWork, along with key members of the College, has successfully assisted in the RUC and CPT® process, which aims to protect and improve physician reimbursement.

Building a national network of pulmonary practice administrators and managers provides a mechanism to compare and contrast performance criteria, such as physician compensation, clinical operations, practice financials, and administrative structure. The PAN is looking ahead to future challenges in practice management.

Attracting new members strengthens the NetWork's base of resources, benefits the College, and provides increased access to fellow practice managers with expertise in diverse disciplines. Members of the ACCP are encouraged to introduce their practice managers to the PAN.

For more information, contact Marla Brichta at mbrichta@chestnet.org, or visit www.chestnet.org/networks/practice_admin/index.php.

John Bauer, FACMPE, CPA, CFE
Ex Officio Steering Committee Member
Kim D. French, MHSA, CAPPM
Past Chair
Practice Administration NetWork

Respiratory Care

Payment System Brings Focus to Waterborne Health-Care-Associated Infection

Health-Care-associated infections (HAI) have a huge impact on morbid ity, mortality, and medical expenditures. The Centers for Medicare & Medicaid Services have zeroed in on this problem and will deny payment for certain infectious complications and other complications of hospitalization.

There is a renewed sense of urgency for health-care institutions to investigate the etiologies of HAI and implement effective measures to reduce the risk to patients.

Tap water is known to harbor potentially pathogenic microorganisms in health-care settings, where they may pose a substantial threat to patients.

Waterborne microbes enter the health-care environment in a number of ways, including direct contact with water streams, aerosols from showers and faucets, and ice from ice machines.

Many waterborne organisms thrive in the biofilms that inevitably inhabit hospital water systems. Bacteria in biofilm also may display a higher degree of resistance to antimicrobial agents than planktonic bacteria.

Microbes of clinical significance that may be isolated from water include *Pseudomonas aeruginosa*, *Legionella pneumophila*, *Stenotrophomonas maltophilia,* Acinetobacter spp, Klebsiella spp, atypical Mycobacteria, *Aspergillus fumigatus*, and *Fusarium solani*.

Highest-risk populations include recipients of bone marrow and solid organ transplants, burn victims, patients who are undergoing chemotherapy, and patients in ICUs.

In addition, individuals with less-recognized immunodeficiencies (*eg*, smokers with COPD) also may be at high risk of serious infections from waterborne pathogens.

Europe recognized the risk of waterborne HAI more than a decade ago and has widely adopted strategies, such as point-of-use (POU) water filtration, to reduce this risk.

Trautmann and colleagues (*Am J Infect Control* 2005; 33:S41) demonstrated that, in the midst of a serious outbreak of Pseudomonas infections in their ICU, POU filtration resulted in dramatic, statistically significant reductions in Pseudomonas infections and cost.

POU filtration, when strategically employed in areas where high-risk patients receive care, offers substantial cost advantages over the additional treatment costs for HAI.

Dr. James M. Maguire, FCCP
Respiratory Care NetWork
Steering Committee Member
Dr. Joseph S. Cervia

Thoracic Oncology

It has been a busy year for the Thoracic Oncology NetWork. Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition) was released in September 2007.

The membership of the Thoracic Oncology NetWork played a pivotal role in the development and publication of these guidelines, which provide an excellent framework for clinicians dealing with patients with known or suspected lung cancer.

The Thoracic Oncology NetWork recently took part in a project that explored the variation in experts' beliefs about lung cancer growth, progression, and prognosis. This brief report will appear in the *Journal of Thoracic Oncology* in the coming months.

The work being carried out by Dr. Michael Gould, FCCP, and colleagues at Stanford University will certainly help in developing decision-support tools for those faced with the dilemma of what to do with a solitary pulmonary nodule.

A second phase of this study will survey members of the Thoracic Oncology NetWork about their understanding and beliefs of the biology of lung cancer and how it may affect the way they manage patients.

The NetWork also has been busy assembling the content for the CHEST 2008 program. Some of the topics that will be covered are lung cancer in the older patient, lung cancer in nonsmokers, and the impact of gender on lung cancer.

There also will be an interactive tumor board and several sessions that will address the new clinical practice guidelines in lung cancer.

To find out more about how to become involved with the Thoracic Oncology NetWork, contact Jennifer Nemkovich at jnemkovich@chestnet.org.

Dr. Gerard A. Silvestri, FCCP
Thoracic Oncology NetWork
Chair

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

PRACTICE MANAGEMENT UPDATE

CMS Rules on CPAP Based on Home Sleep Testing

SUMMARIZED BY DIANE KRIER-MORROW, MBA, MPH, CCS-P

The 2005 National Coverage Determination (NCD) for Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea (OSA) was revised to allow coverage of CPAP based upon a diagnosis of OSA by home sleep testing (HST). The final NCD was published on March 13, 2008.

ACCP had participated in the September 17, 2007, MedCAC meeting and has commented on the proposed guidelines, and ACCP President, Dr. Alvin V. Thomas, Jr., FCCP, advised CMS that additional research is needed addressing clinical outcome in a variety of age and ethnic populations.

The decision summary and full memorandum can be viewed at www.cms.hhs.gov/mcd/viewdecisionmemo.asp?from2=viewdecisionmemo.asp&id=204&. CMS commissioned two technical assessments (Home Diagnosis of OSA-Hypopnea Syndrome and Modeling Different Diagnostic Strategies) from the National Committee on Quality Assurance that can be reviewed in their entirety at www.cms.hhs.gov/mcd/viewtechassess.asp?id=204. The 2005 coverage decision for CPAP for OSA in the Medicare manual can be read at www.cms.hhs.gov/manuals/downloads/ncd103c1_Part4.pdf.

Highlights of the final NCD are:

- Coverage of CPAP is initially limited to 12 weeks for Medicare and Medicaid beneficiaries diagnosed with obstructive sleep apnea (OSA). The CPT code for CPAP is 94660 and the ICD-9-CM diagnosis code for sleep apnea (OSA) is 327.23. CMS assumes that the treating physician will assess the beneficiary and if sleep apnea is indicated by the clinical findings, appropriate sleep testing will be ordered, and the results will assist in the management of the condition to make or exclude a diagnosis of OSA.
- Tests not ordered by the treating physician and not furnished with the required level of supervision are not considered reasonable and necessary, and payable under the physician fee schedule.
- CPAP for adults is covered when diagnosed using a clinical evaluation and a positive: (1) polysomnography (PSG) performed in a sleep laboratory; or (2) unattended home sleep monitoring device of Type II; or (3) unattended home sleep monitoring device of Type III; or (4) unattended home sleep monitoring device of Type IV, measuring at least 3 channels.
- A positive test for OSA is established if either of the following criterion using the apnea-hypopnea index (AHI) or respiratory distress index (RDI) is met. The AHI is equal to the average number of episodes of apnea and hypopnea per hour. The RDI is equal to the average number of respiratory disturbances per hour.

The criteria are:

1. AHI or RDI greater than or equal to 15 events per hour, or
2. AHI or RDI greater than or equal to 5 and less than or equal to 14 events per hour with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or history of stroke.

- If the AHI or RDI is calculated based on less than 2 hours of continuous recorded sleep, the total number of recorded events to calculate the AHI or RDI during sleep testing is at least the number of events that would have been required in a 2-hour period.
- CMS deleted the distinct requirements that an individual have "moderate to severe OSA" and that "surgery is a likely alternative" as a condition for CPAP coverage.
- Clinical study requirements are further delineated in the NCD.

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Providing Quality Critical Care: The Past, Present, and Future

An article published in the December 2007 issue of *CHEST PHYSICIAN* discussed patient safety in critical care, with all the inherent complexities of establishing and delivering the safest, most effective care possible. Going forward, as the need for critical care continues to increase, addressing the history, staffing (workforce numbers), and the organization of critical care services is paramount.

The Past

The history of critical care as a separate service demonstrates that it is still a fairly new concept in medicine and continues to evolve.

The modern construct of critical care started in Copenhagen during the polio epidemic in the 1950s. An anesthesiologist named Bjorn Ibsen realized that skillful airway management and the positive pressure ventilation required for treatment of patients with polio were similar to the requirements for an operating room. Working toward the goal of reducing mortality in these paralyzed patients with respiratory disease, anesthesiologists were the original leaders in critical care.

In the 1960s and 1970s, many technologic advances allowed for more intensive monitoring. It is these advances, especially in cardiopulmonary diseases, and a more thorough appreciation of the complex pathophysiology, that first attracted internists into critical care.

In the later 1970s, efforts to formalize critical care training and eventual certification were attempted. The American Board of Medical Specialties (ABMS), with the four primary boards—medicine, surgery, pediatrics, and anesthesiology—tried to resolve this issue. This group was unable to form a consensus and was disbanded a few years later. At this point, the ABMS allowed each individual board to develop its own criteria and qualifications. The American Board of Internal Medicine (ABIM) administered the first examination in 1987 for added qualification in critical care.

The Present

During the 1990s, and into the 2000s, great growth was experienced and continues in critical care and its training programs. Many pulmonary divisions added the term "and critical care" to their titles.

Although anesthesia programs dominated early critical care training, the predominant route now is through a combined 3-year pulmonary/critical care fellowship.

Testifying to the growing importance of critical care, The American College of Chest Physicians (ACCP)

Critical Care Institute
American College of Chest Physicians

Critical Care NetWork now has approximately 3,500 members registered and is the largest ACCP NetWork, just as the American Thoracic Society (ATS) Critical Care Assembly is its largest assembly. The ATS has changed its mission statement and journal name to include critical care.

CHEST PHYSICIAN, the ACCP news publication, includes a critical care commentary in six of its monthly issues each year.

The ACCP Critical Care Institute was formally created in 2004 to complement the Critical Care NetWork, with a focus on outreach and collaboration with other critical care professional societies. And, finally, the ABIM declared Critical Care a stand-alone specialty for recertification in the spring of 2006.

The increasing demand for critical care and its providers has a multifactorial basis. In part, the catalyst for this increase in demand is the fact that patient outcomes have been affected by practitioner training.

A major factor driving this increased need, however, is the aging of the American population (HRSA Report 2006. www.chestnet.org/practice/gr/hrsa.php). By the year 2020, the population older than 65 years will increase by 50%, and, by the year 2030, it is estimated to increase by 100%. In the United States, approximately 4 to 6 million people are admitted to an ICU each year, and there are about 6,000 ICUs across the country caring for approximately 55,000 people per day.

Critical care accounts for about 10% of all hospital beds, with an annual budget of about $180 billion, or 0.7% of the gross domestic product. About 18 million bed-days are used annually by critical care, and patients older than 65 years use more than 50%.

As a result of aging alone, the demand for intensivists would rise by 38% if all other factors remained the same. It is the changing paradigm in the delivery and organization of critical care that is also increasing the demand for trained staff.

Historically, there are three different delivery models in critical care: the open ICU; the mixed ICU; and the closed ICU. A recent review of services provided has designated them as low intensity vs. high intensity.

The open ICU, which is the traditional delivery system, has the primary attending with or without an intensivist deciding all aspects of the patient's care. This low intensity model exists in two-thirds of the hospitals around the United States. About 500,000 people in the United States die each year in the ICU, and intensivists do not manage 360,000 of these patients.

In the high intensity models (mixed and closed), an intensivist provides all (closed) or some (mixed) of the critical care portion, in collaboration with the primary attending. These models are only seen in one-third of US hospitals. It is estimated that 54,000 lives could be saved annually just by changing from a low intensity model to a high intensity model.

BY 2020, THERE WILL BE A NEED FOR ABOUT 4,300 CRITICAL CARE PROVIDERS. THIS SIGNIFICANT SHORTAGE WILL INCLUDE DOCTORS, NURSES, PHARMACISTS, AND RESPIRATORY TECHNICIANS.

Multiple research papers have demonstrated that critical care provided by trained intensivists leading multidisciplinary teams consistently yields the best results (Pronovost et al. *JAMA* 2002; 288:2151). These teams consist of doctors, nurses, dietitians, pharmacists, respiratory therapists, and unit managers.

The results of these studies were so stark that private industry, attempting to maximize the return on their insurance dollars, created "The LeapFrog" standards (www.leapfroggroup.org).

In addition to the lives saved, it was estimated that a savings of between $500,000 and $3,000,000 could be achieved annually in a 6- to 18-bed high intensity unit (Pronovost et al. *Crit Care Med* 2006; 34:S18).

At this time, about 20% of hospitals have been able to fully comply, despite recent easing of the standards.

If the proportion of care was increased as discussed above, the current demand for intensivists would rise by 63% above the current supply and to 129% by 2020.

There are over 2,000 critical care physicians in the United States now (self-reported). This number is expected to grow to about 3,000 by 2020. Even using two-thirds of critical patients as the target goal, by 2020, there will still be a need for about 4,300 providers. This significant shortage is not limited to doctors alone; critical care nurses, pharmacists, and respiratory technicians are in limited supply.

Leading critical care societies identified this problem in 2000 when the (COMPACCS) Committee on Manpower for Pulmonary and Critical Care Societies and the Framing Options for Critical Care in the United States (FOCCUS) (in 2004) outlined strategies to prevent a crisis in delivery of critical care. In May 2006, The HRSA Report to Congress highlighted the disparity in supply and demand of the critical care workforce.

Most recently, the PROMIS conference published possible solutions to the critical care workforce problem (Barnato et al. *Crit Care Med* 2007; 35:1003). In addition, in 2007, the Patient-Focused Critical Care Enhancement Act was introduced in the US Senate and the US House of Representatives.

The ACCP, as part of the Critical Care Workforce Partnership, had worked closely with Senators and Representatives to get this bill introduced. Other members of the Partnership include the American Thoracic Society, the American Association of Critical-Care Nurses, and the Society of Critical Care Medicine.

The proposed legislation specifically addresses the critical care workforce shortage by calling for appropriations for research and projects that will take the first steps toward optimizing the delivery of critical care medicine (www.chestnet.org/practice/gr/CCWorkforce.php).

The Future

In conclusion, presently recommended solutions fall into the following three categories: those that increase the efficiency of the critical care workforce, those that increase the critical care workforce itself, and those that address patient demand.

Methods suggested for increasing the efficiency of the critical care workforce

Continued on following page

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

ACCP President-Designate Honored by ACGME

Dr. Kalpalatha K. Guntupalli, FCCP, Chair of the ACCP Critical Care Institute and ACCP President-Designate, has recently been honored by the Accreditation Council for Graduate Medical Education (ACGME).

She was given the Parker J. Palmer "Courage to Teach" award "in recognition of extraordinary accomplishments in graduate medical education."

Dr. Guntupalli is the fellowship program director for the Pulmonary/Critical Care and Critical Care fellowships at Baylor College of Medicine in Houston, TX.

This award is given to 10 training program directors.

The winners are selected from nominations from training programs (residency and fellowships) in all specialties around the country.

There are about 8,500 training programs in United States.

ACCP

Dr. William H. Hartmann (left) stands with Palmer Award winner Dr. Kalpalatha K. Guntupalli, FCCP (center), and Dr. Thomas J. Nasca (right).

PRODUCT OF THE MONTH

Web Update on ICU Infections

View the newest ACCP product available online, which features audio tracks and faculty presentations from a CHEST 2007 satellite symposium.

This educational activity will update physicians on treatment protocols, therapeutic decision-making paradigms, and advances in the management of sepsis, pneumonia, and complex skin and soft tissue infections in the ICU.

To view this virtual satellite symposium, please visit the ACCP online education site at www.chestnet.org/education/online/index.php, and click on "Improving the Odds: Recognizing and Managing Complicated Infections in the ICU."

Continued from previous page

include conducting research on optimal critical care delivery models; developing incentives to better distribute critical care providers; supporting alternative delivery models, such as a tiered critical care delivery system; increasing the utilization of technology through telemedicine initiatives and electronic medical records; increasing the effective supply of critical care providers through cross-training; and simplifying the currently cumbersome reimbursement system.

Methods suggested for increasing the critical care workforce itself include increasing medical and nursing school capacity to train critical care providers; expanding federally funded GME slots for critical care providers; reducing the debt burden of critical care physicians graduating from medical school and nurses graduating from nursing school; and expanding the J-1 visa waiver program to allow more US-trained international medical graduates to practice in the United States in designated underserved areas.

Methods suggested that address patient demand include increasing support for critical care research in the elderly population; exploring alternative care pathways for elderly patients with high mortality conditions; and developing a patient-education campaign to teach Americans the benefits and limitations of critical care medicine.

None of these methods alone can avert this potential crisis. The only reasonable solutions will involve a collaboration among physicians, our patients, and the government.

Dr. Peter Spiro, FCCP
Assistant Professor of Clinical Medicine
Columbia University College of Physicians and Surgeons
Head, MICU
Harlem Hospital Center
New York, NY

Treat Request for Hastened Death as an Emergency

A patient who says, 'Doctor, will you help me die?' presents a remarkable therapeutic opportunity.

BY KERRI WACHTER
Elsevier Global Medical News

TAMPA — A patient's request for a hastened death—either an explicit request or a hint—should be considered a clinical emergency that offers an important therapeutic opportunity.

"When you're in the office and somebody asks, 'Doctor, will you help me die? I just want to end it all,' that is a true clinical emergency," Dr. Ira R. Byock said at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

"It's as if somebody develops crushing chest pain or fibrillates and codes in your office. Somebody's life is at risk here. That person may have a progressive illness, but that doesn't mean that [his or her] life is at any less risk or that it's any less of an emergency," said Dr. Byock, who is director of palliative medicine at Dartmouth-Hitchcock Medical Center in Lebanon, N.H.

Such a request is "a remarkable therapeutic opportunity," he said. "The very fact that the patient has shared this with you … opens up a therapeutic window."

Occasional thoughts of suicide or a desire for death are fairly common among people living with a serious illness.

In Oregon—where physician-assisted suicide is legal in certain circumstances—65 prescriptions for lethal medications were written in 2006, and 46 people died by lethal prescription that year (out of a total of roughly 31,000 deaths in the state). The 1997 Death with Dignity Act allows terminally ill Oregonians to end their lives through the voluntary self-administration of lethal medications, prescribed by a physician expressly for that purpose.

"Certain diagnoses are particularly associated with a request for assisted suicide and receipt of a lethal prescription," Dr. Byock said. Based on data through 2006 in Oregon, patients who have amyotrophic lateral sclerosis are about 35 times as likely to use physician-assisted suicide or to ask for a lethal prescription as do patients with chronic obstructive pulmonary disease, he said. HIV/AIDS and cancer also are particularly associated with a request for assisted suicide and receipt of a lethal prescription.

Research also has shown that many terminally ill patients meet the diagnostic criteria for major depression, which is an important risk factor for a request for suicide. "In treating depression, I think we often just reach for the SSRI [selective serotonin reuptake inhibitors] or the psychostimulant, all of which can be valuable," Dr. Byock said. But don't forget to look for other causes of the depression, such as hypothyroidism, adrenal dysfunction, or the side effects of other medications.

And because many of the somatic symptoms of depression—including fatigue, anorexia, loss of energy, sleep disturbance, and mild confusion—are common in terminal illness, the psychological symptoms are more useful in identifying depression in these patients. Look for hopelessness, helplessness, guilt, worthlessness, loss of meaning, and preoccupation with death and suicide.

Beyond that, the feeling of hopelessness has been shown to be more highly correlated with suicidal ideation in these patients than is depression. Think about recommending counseling to help patients address issues of hopelessness and helplessness.

MARK WASHBURN/DARTMOUTH-HITCHCOCK MEDICAL CENTER

What sounds like a request for death may simply be a desire "to be assured of a way of escaping suffering," said Dr. Ira R. Byock.

When a patient with advanced illness asks for help dying, it's important for physicians to recognize their own emotional responses to such requests. At the same time that a physician is moved by the patient's suffering, "at times, to a physician's ear, the expression of a wish to die can sound to us like a condemnation of our care," Dr. Byock observed. Acknowledging this is part of the therapeutic challenge.

The fact that the patient makes such a vulnerable statement is testament to the patient's trust in his or her physician. The most important thing a physician can do in these situations simply is to listen—an act that has therapeutic value in itself. The act of listening "helps people feel acknowledged and helps them feel like you're accompanying them on this difficult journey.

"Even if one is deeply, morally opposed to assisting a patient in suicide, it is possible and essential to be able to listen to the requests and accept the patient's feelings in a nonjudgmental manner," Dr. Byock said.

Expressing empathy—with comments such as "I can't imagine how hard this must be for you"—can also help to strengthen the therapeutic relationship, "which is itself a powerful tool for treatment," he said.

It's important to clarify a request for death, as many patients are confused about end-of-life care. Some assume that by not accepting every possible treatment—antibiotics and dialysis, for example—they are essentially committing suicide.

"We can often alleviate their anxiety and help them distinguish between actively shortening their lives and simply not using medical treatments that aren't consistent with their preferences and desires," said Dr. Byock.

Even simply informing patients that they can decline medically administered nutrition and hydration to allow a "natural" death can satisfy their concerns.

Sometimes patients won't directly express a desire for death but will hint at it or make deliberately provocative statements. One of Dr. Byock's patients told him that, "they should dig a hole and just shoot me." Statements like these are valuable openings because they express the patient's fears and feelings, he said. They are also a way for patients to test their physician. "If we respond 'oh, don't talk like that,' we've given a strong message," he said.

Patients also may use provocative statements like, "I hope you'll help me die when it's time" as a way of assessing their doctor's commitment to not letting them suffer. What may sound like a request for death could "simply [be a desire] to be assured of a way of escaping suffering if it becomes unbearable," he said. "It's important to understand whether they're referring to assisted suicide/euthanasia or just adequate analgesia," he said.

In treating pain in this patient group, Dr. Byock recommends making it explicit to the patient, in the chart, and to medical colleagues that there needs to be a detailed pain management plan in place, with lots of contingencies, in case pain gets out of control.

This means taking a multimodal, layered approach using patient-controlled analgesia and scheduled, as-necessary, and crisis medications. It's also important for patients to have specific telephone numbers to call after hours to get a prompt response.

"We pursue symptom-directed treatments even when patients are seriously ill," Dr. Byock said. These patients may benefit from regional blocks, axial analgesia, or neurolytic procedures.

In addition, it's a good idea to get a formal consultation with palliative care or pain services. Dr. Byock tells his patients that there always is the option of palliative sedation if no other options are working and pain is unbearable. "This is not only ethically acceptable, I would assert that it's ethically required, if nothing else is working," he said.

Another issue for many patients with advanced illness is the worry about being a burden on their families or caregivers. Dr. Byock tells his patients that although they can't take away the burden, their behavior and attitude can influence how their family responds to it. "The way people die stays in the minds and hearts of those they leave behind," he said.

There is some evidence that by committing suicide, a person is putting first-degree relatives at greater risk of suicide themselves. "I rarely say that, but there are some times when it's worth sharing," he said.

Patients who have children can provide a model for their children and grandchildren of living with dignity to the very end of life. A patient can be reassured that this, "has value in and of itself," said Dr. Byock.

A Hastened Death Request Addressed

One of Dr. Byock's patients, Mr. B, was a 68-year-old man with colon cancer that had metastasized to the liver, lungs, and bone. He presented with increasing, severe left hip pain after a minor injury. He was on hydrocodone/acetaminophen (Vicodin) every 4 hours for pain relief. He was very anxious, and at times seemed unable to understand the information given to him, Dr. Byock said.

Mr. B had retired after a career in industry. "He was a gentle, well-mannered man. His passions included walking in the wilderness and gardening, interests that he shared with his wife of 22 years," Dr. Byock recounted.

According to Dr. Byock, Mr. B volunteered that he had been thinking about "ending it all." He spoke of a neighbor who had committed suicide by gunshot to the head because of severe cancer pain. "I don't want to end up like that. I hope you will help me die before I get to that point," Mr. B told his physician.

While hospitalized for the hip pain resulting from the minor injury, he was treated with long-acting morphine, an NSAID, and lorazepam for his anxiety. A geriatric psychiatrist on the hospital staff was consulted about Mr. B's desire to die. Mr. B told the psychiatrist that he was feeling fine at the moment but he was in fear of being in constant, uncontrollable pain. He added that he knew his wife would be devastated if he committed suicide. When Dr. Byock learned that the real problem was fear of pain, he was able to reassure Mr. B that he could achieve sufficient pain control to live a high-quality life at home.

Mr. B was started on mirtazapine for depression, and his anxiety decreased during the course of his hospital stay. The medication also helped his sleep and appetite.

Before he went home, he was counseled about his pain management plan and assured that there was no circumstance in which he would suffer for more than a very short time.

Mr. B still talked about suicide when asked by a member of his palliative care team, but he no longer brought up the subject. He said that his feelings hadn't changed but that he felt more confident that he wouldn't have to turn to suicide, Dr. Byock said. He died at home in hospice care several months after he was discharged.

Pages 20a—20b

Tread Carefully With Palliative Sedation to Unconsciousness

BY KERRI WACHTER
Elsevier Global Medical News

TAMPA — Palliative sedation to unconsciousness can be an option for terminally ill patients, but its use should be rare, according to experts in palliative medicine.

"This is a big deal when you do this, in my opinion, and should be relatively rare," said Dr. Timothy E. Quill, director of the center for ethics, humanities, and palliative care at the University of Rochester (N.Y.) Medical Center.

Palliative sedation to unconsciousness is "for unusual circumstances when suffering is so hard to control and so great that you decide, as a team, to render somebody unconscious to relieve their suffering," Dr. Quill said at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

In 2006, the American Academy of Hospice and Palliative Medicine issued a revised position statement on palliative sedation (www.aahpm.org/positions/sedation.html). In the position statement, "we really tried to make a clear distinction between three types of sedation because in our review of the literature, these [types] are drastically confused," Dr. Quill said.

The position statement defined the three levels of sedation as follows:

- **Ordinary sedation.** This includes the use of sedative medications for the treatment of anxiety, agitated depression, insomnia, or related disorders. The goal is symptom relief without a reduction in the patient's level of consciousness.
- **Palliative sedation.** This is the use of sedative medication, at least in part, to reduce the patient's awareness of distressing symptoms that are not adequately controlled by symptom-specific therapies. The level of sedation should be proportional to the patient's level of distress. Alertness is preserved as much as possible.
- **Palliative sedation to unconsciousness.** This is the administration of sedatives to the point of unconsciousness, when less extreme sedation has not achieved sufficient relief of distressing symptoms. This practice should be reserved for the most severe and intractable suffering at the very end of life.

With all three levels of sedation, the intent is to relieve suffering in a way that is proportional to the severity of suffering. "This means that if you're going to sedate someone to unconsciousness, the level of suffering needs to be pretty profound and unrelievable," Dr. Quill said.

Palliative sedation to unconsciousness requires informed consent, which must come either from the patient or from the patient's surrogate, he added.

When treating severe and unremitting physical pain, "we do need to give some consideration to the doctrine of double effect," said Dr. Gregg K. VandeKieft, who is in private practice in Olympia, Wash.

MARIA MILELLA

Use palliative sedation to unconsciousness "for unusual circumstances," said Dr. Timothy E. Quill.

Medical ethicists describe the following four components of the double-effect doctrine:

- The act itself must be good or at least morally neutral.
- The bad effect may be foreseen but is not intended.
- The bad effect must not be a means to the good effect.
- The need for the good effect outweighs the risk of the bad effect.

In the case of a patient with severe, unremitting pain, the good effect is pain control. The bad effect of shortening the patient's life is a foreseen but acceptable consequence. The intent is to relieve suffering, not to shorten life, and the relief of suffering is not achieved by death but by sedation. Lastly, this action is considered only after all other options have been explored.

"You can fall into the trap of prolonging a patient's suffering to exhaust every option, because of our moral discomfort, as opposed to what the patient truly needs," Dr. VandeKieft said.

One audience member asked about ending pain versus ending suffering.

"I would argue that it's not a semantic distinction, [but rather] that pain versus suffering are two very different [phenomena]," Dr. VandeKieft said. Pain is a biomedical phenomenon, whereas suffering has biological, psychological, social, and possibly even spiritual components. Pain is not the sum total of suffering.

In discussing a clinical case, Dr. Mark V. Blum, a geriatrician who specializes in palliative care for Kaiser Permanente Medical Group Inc. in Sacramento, asked whether it's acceptable for the medical team to bring up the issue of palliative sedation to unconsciousness if the patient or the patient's surrogate has not already done so.

The audience generally found that scenario acceptable, with one audience member stating, "informed consent for whichever course of action would imply that you've got to give them all of the different options. So you have to bring it up; you're obligated to bring it up."

Dr. Blum agreed, likening the situation to dealing with coronary artery disease detected by angiography. All treatment options are offered: angioplasty, bypass, medical management.

Dr. Blum also asked the audience if surrogate decision makers can choose palliative sedation even if the patient had not considered this option. In general, the audience found this acceptable. One audience member suggested that the palliative care team really has not done its job properly if a surrogate must consider palliative sedation in the absence of a previous discussion of the subject with the patient.

Dr. Blum noted that he doesn't bring the subject of palliative sedation up with every patient. But he tells patients who have a significant symptom burden that palliative sedation is an option to ensure that they don't suffer too much.

Dr. Gary A. Johanson, of Memorial Hospice and Palliative Care Center in Santa Rosa, Calif., described a case involving the question of using palliative sedation to unconsciousness to control physical symptoms other than pain (for example, nausea, retching, and weakness) and to ease existential suffering (such as distress about the thought of death itself, or worry about being a burden to family and caregivers).

In such cases, the amount of time that the patient is likely to live can be an important consideration. If a patient who just had lumbar surgery is suffering a lot from back pain and has 40 years left, the situation is different than it would be for a patient who has only 3-4 days left and is classified as NPO (nothing by mouth), Dr. Johanson said.

One audience member asked what to do about a patient who is experiencing only existential suffering. "If you are contemplating sedating such a person to unconsciousness, for sure that is a case where you get a second palliative care consult, and an ethics consult, and a psychiatric consult, because you are way out on the edge," Dr. Quill said.

Expect Conflicts To Occur During End-of-Life Care

BY KERRI WACHTER
Elsevier Global Medical News

TAMPA — When conflicts over end-of-life care arise, try to understand the conflict and keep the lines of communication open, said three experts in palliative medicine at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

"There's no question that conflicts will occur. The question is how to approach them," said Dr. Kimberly S. Johnson, an attending physician at the Duke University Center for Palliative Care in Durham, N.C.

"The challenge for us is to be able to recognize the conflict and the nature of the conflict," said Jennifer Gentry, an adult and geriatric nurse practitioner at the center.

Conflicts can arise when there are different views of the expected roles of family members and of the medical team, noted Dr. Toni Cutson, an attending physician at the center.

For example, the husband of a dying woman might not act supportive of her, or a husband might wish to discontinue lifesaving treatments but parents and siblings disagree. Family members might challenge physician authority regarding treatment, even threatening to take legal action or call the local media.

Physicians should remember that the family could have a history of problems before the medical team enters the picture. "We're not marriage or family counselors," Dr. Cutson said. "We're certainly not asked to fix these relationships."

In addition, the team doesn't always know all of the facts. Even the "villain" has his own side to the story. In the case of an unsupportive husband, he might be trying to protect his children from their mother's illness and decline.

"When you see conflict, you're going to see emotion," Ms. Gentry said. In handling emotions that arise in situations of conflict, she recommends remembering the mnemonic acronym NURSE: name the emotion; understand and relate to that emotion; respect everyone's feelings; support the patient; and explore the emotion by asking the patient and family to tell you more.

"Clear communication and transparency are important tools to resolve conflict," Dr. Johnson said. Take the time to find out what the patient's and family's goals are, and avoid making assumptions, particularly about a patient/family's culture and relationships, Ms. Gentry advised.

When faced with a patient and family members experiencing conflict, Ms. Gentry recommended that physicians do the following:

- Try to understand that each family member might be at a different stage in terms of acceptance of a terminal illness.
- Realize that prior family conflict could be contributing to the current conflict over care.
- Try to define areas of agreement and disagreement to clarify the problem.
- Try time-limited trials of therapies to allow the family more time to make decisions.
- Schedule follow-up meetings to discuss concerns about care.
- When appropriate, suggest the family consult a psychiatric professional, ethics consultant, or spiritual adviser.

"Finally, and I think most importantly, the fact is that we take patients and family with all of their baggage and we simply do the best that we can," Dr. Johnson noted.

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Employer-Based Health Insurance Has Wide Support

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

Most Americans favor a continuation of the employer-based health insurance system and say that they believe health insurance costs should be shared among individuals, employers, and the government, according to the results of a survey conducted by the Commonwealth Fund.

More than two-thirds of Americans who took part would favor a mandate for individuals to obtain health insurance in an effort to provide universal health coverage.

These findings indicate that on certain health reform issues Americans' views may be more closely aligned with the proposals put forth by Democratic candidates for president than those outlined by Republicans.

For example, the leading Democratic candidates for president would require employers to offer health coverage to employees or pay for part of their coverage, while most of the Republican candidates proposed changes to the tax code that could potentially reduce the role of employers in the health insurance market, according to a Commonwealth Fund analysis.

Sen. Hillary Clinton (D-N.Y.) would support an individual health insurance mandate, while Sen. Barack Obama (D-Ill.) would mandate coverage for all children. Of all the Republican candidates, no one proposed an individual insurance mandate, according to the Commonwealth Fund.

In the period from June to October 2007, the Commonwealth Fund conducted a telephone survey of 3,501 adults aged 19 years and older as part of its biennial health insurance survey. The group released the results from four health reform queries before it announced the other findings, which are scheduled to be released in March.

The survey respondents expressed broad support for an employer-based system of health insurance coverage. About 81% of respondents said that employers should either provide health insurance or contribute to a fund in order to cover all Americans.

Support for an employer-based health insurance system was high among respondents regardless of political affiliation, race, gender, age, and income.

The support for an individual insurance mandate to ensure coverage for all was lower; 68% of the respondents said that they strongly or somewhat favor a requirement that all individuals obtain health insurance. About 25% of the respondents said they strongly or somewhat opposed the idea. About 7% said they did not know, or refused to answer.

When respondents were asked who should pay for health insurance for all Americans, 66% favored a system in which costs would be shared by individuals, employers, and the government. About 15% of respondents said it should be mostly government financed, 8% said it should be paid for mostly by employers, and 6% favored a system in which individuals pick up the tab. Another 5% of the respondents said they didn't know, or refused to answer.

The survey also indicated that the candidates' views on health care reform will be important in determining votes. About 86% of the respondents said that health care reform is very or somewhat important in determining their vote during the presidential election.

Dr. Philip Marcus, FCCP, comments: *Health insurance continues to be a major discussion point, and the interest increases during a national election. We continue to debate whether health care is a privilege or a right. Should we just expand the Medicare program to all Americans, including children, so that no one lacks insurance? Should this be financed by an addition to the already existing Medicare tax deduction, with a portion paid by the employer and another by the employee? We are faced with major decisions concerning how we fund our health care. Each candidate has views to solve the problem, but may or may not be able to "fix" the problem at this time.*

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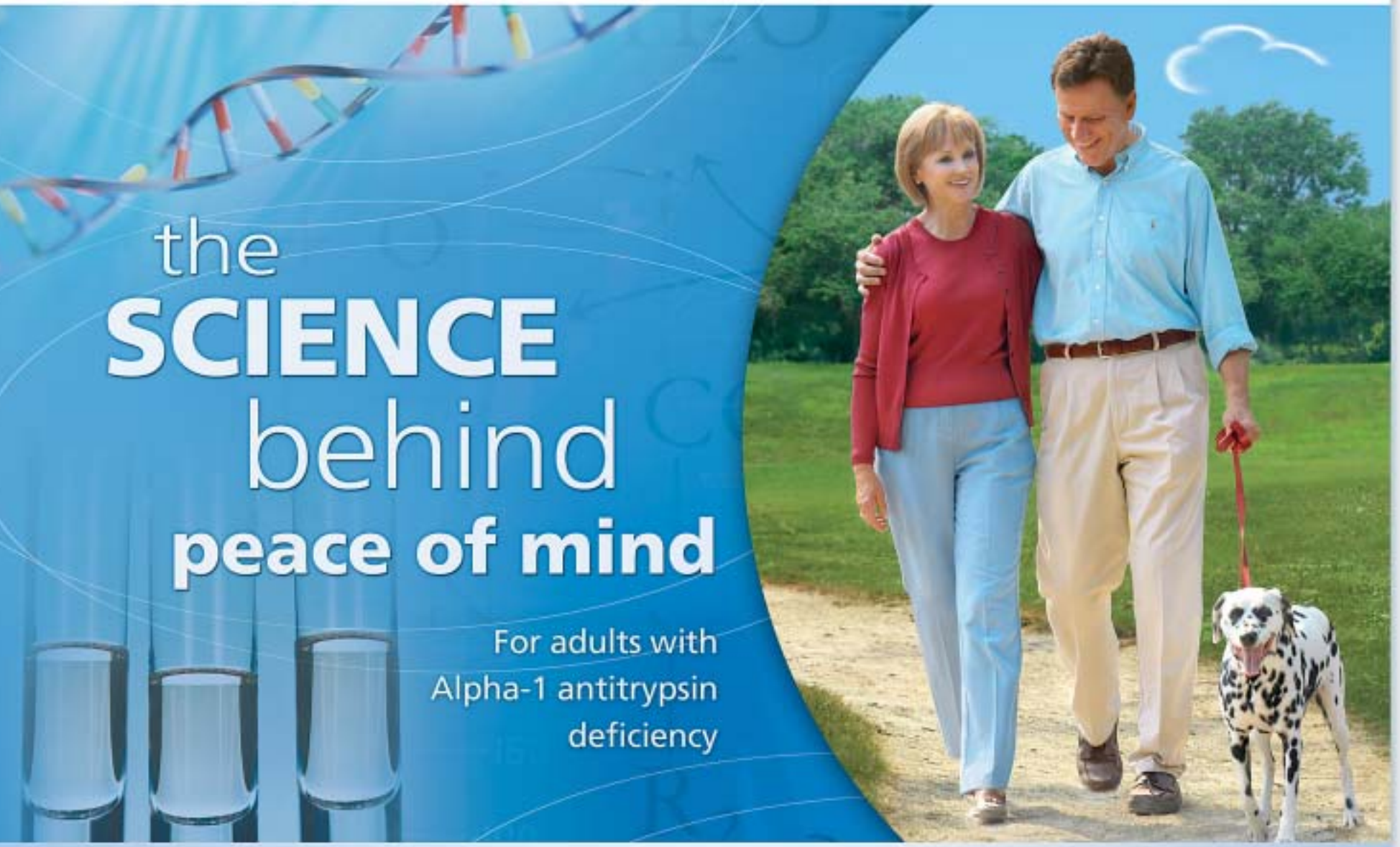

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