VOL. 2 • NO. 2 • FEBRUARY 2007

CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

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Initiatives will counteract the reality that "most people don't even know what COPD is," said ACCP President Dr. Mark J. Rosen, FCCP.

Campaign, Research to Shine Spotlight on COPD

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

The National Heart, Lung, and Blood Institute is set to spend millions of dollars to raise patients' and physicians' awareness about chronic obstructive pulmonary disease and to accelerate research to improve treatment of the disease.

The 3-year, $2.4 million awareness campaign, "Learn More Breathe Better," kicked off last month. It is aimed at emphasizing the warning signs of COPD and ensuring that more people are diagnosed and treated early. The campaign will include print and radio public service announcements, fact sheets for patients, fact cards for physicians and other practitioners, and a Web site.

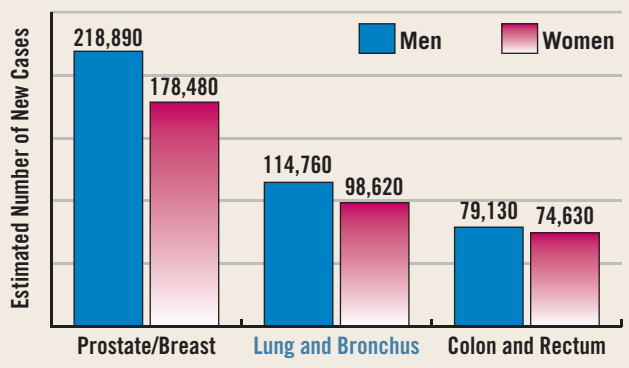
COPD affects a quarter of Americans older than 45 years, according to the National Heart, Lung, and Blood Institute (NHLBI). Yet "most people don't even know what COPD is," said Dr. Mark J. Rosen, FCCP, president of the American College of Chest Physicians, which is a campaign partner with NHLBI, the American Academy of Family Physicians, the American Thoracic Society, and other organizations.

NHLBI has also joined forces with the COPD Foundation and will offer information and spirometry screening to at-risk patients around the country this year.

See **Spotlight** • *page 2*

VITAL SIGNS

Estimates for 2007 Rank Lung Cancer Second Among Men and Women



Note: Data estimates from American Cancer Society.
Source: CA Cancer J. Clin. 2007;57:43-66

ELSEVIER GLOBAL MEDICAL NEWS

Genetic Signature Predicted Clinical Outcome in NSCLC

A step toward personalized therapy.

BY ROBERT FINN
Elsevier Global Medical News

A risk score based on the activity of just five genes accurately predicted which patients with non–small cell lung cancer are likely to die in the years after surgical resection, according to a new study.

The advance may lead to a better staging system, may help select patients for aggressive adjuvant therapy, and may provide specific targets for lung-cancer therapy, wrote Hsuan-Yu Chen and colleagues of the National Taiwan University College of Public Health, Taipei.

Patients who have a high risk genetic signature on the basis of those five genes are three to four times more likely to die of any cause within 5 years after surgery than are those with a low risk signature. The median survival for patients with a high risk signature was 20 months, compared with 40 months for patients with a low risk signature (N. Engl. J. Med. 007;356:11-20).

This work "reflects the maturation of the first phase of lung-cancer genomics," wrote Dr. Roy S. Herbst and Dr. Scott M. Lippman in an accompanying editorial. "The field is now poised to begin its next phase—conducting prospective trials of adjuvant chemotherapy in patients with early lung cancer who are selected because they have a high risk of relapse or metastasis according to the molecular signature identified by Chen et al. or others" (N. Engl. J. Med. 2007;356:76-8).

Previously, the investigators had identified 672 genes associated with invasive cancer. They placed these genes on microarrays and looked at their resulting activity when challenged with specimens of lung-cancer tissue. The investigators identified 16 genes whose activity was associated significantly with the patients' survival. For some genes, high activity increased the risk of death from

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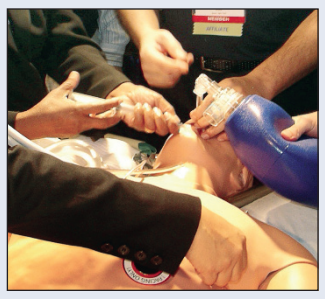
INSIDE



Steroid Insensitivity Thwarts Asthma Tx

BY TIMOTHY F. KIRN
Elsevier Global Medical News

VAIL, COLO. — The new concept in asthma management is that one size does not fit all.

Asthma is a heterogeneous entity, and it is increasingly recognized that most, but not all, asthma patients respond adequately to corticosteroid treatment, Dr. Carolyn M. Kercsmar said at a meeting sponsored by the American Academy of Pediatrics.

In fact, there have even been recent, serious calls for abolishing the term "asthma" in favor of "complex wheezing disorders," to reflect this new understanding that asthma can be very different in different individuals, said Dr. Kercsmar, director of the children's asthma center at Rainbow Babies and Children's Hospital, Cleveland.

Because many patients are not sensitive to corticosteroids, physicians need to be careful about raising the dose excessively when a patient fails to achieve control, she said. Rather, the prudent approach should be to add another type of drug.

Dr. Kercsmar used to attribute much treatment failure to nonadherence to the drug regimen, because it is so common. But the current estimates are that around 30% of patients do not respond to corticosteroid treatment, by any measure.

"If you see someone who says they are not doing well, you've got to believe them," she said.

She noted four studies in particular that have documented inhaled-corticosteroid insensitivity.

One clinical study in a pediatric

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Risk Profile Uses Five Genes

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any cause, and for other genes, high activity decreased the risk of death.

The investigators conducted reverse transcriptase–polymerase chain reaction (RT-PCR) analysis of the 16 genes and determined that just 5 genes showed good correlations between activity as assessed by microarray and by RT-PCR.

The five genes were for dual-specificity phosphatase 6 (DUSP6), monocyte-to-macrophage differentiation-associated protein (MMD), signal transducer and activator of transcription 1 (STAT1), v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3 (ERBB3), and lymphocyte-specific protein tyrosine kinase (LCK).

Investigators used the level of expression of these five genes to construct risk scores. Patients below the 50th percentile of risk score were classified as low risk, and those above the 50th percentile were classified as high risk.

To validate these risk scores, the investigators studied two independent cohorts of 60 and 86 patients with non–small cell lung cancer, conducting RT-PCR analysis and examining patient survival. Those with high risk scores experienced significantly shorter survival times than those with low risk scores.

This study constitutes an important step toward personalized cancer therapy, wrote Dr. Herbst and Dr. Lippman. When genomic profiles are combined with proteomic, clinical, and imaging factors, patients with early-stage cancers will receive particular drugs on the basis of the molecular characteristics of individual tumors. ■

NHLBI Awards $41M for Research

Spotlight • *from page 1*

The message to patients is even if your physician doesn't bring up COPD, ask about it, said Dr. Rosen, who also is chief of the divisions of pulmonary, critical care, and sleep medicine at North Shore University Hospital in Manhasset, N.Y., and Long Island Jewish Medical Center in New Hyde Park, N.Y.

The campaign also will target primary care physicians, who are usually in the best position to diagnose COPD early, said Dr. Robert M. Pallay, a family physician in Hillsborough, N.J.

Along with the awareness campaign, NHLBI officials are investing in COPD research. NHLBI recently awarded $41 million in grants to three Specialized Centers for Clinically Oriented Research in COPD. The centers—Weill Cornell Medical College in New York City, the University of Pittsburgh, and Washington University in St. Louis—will conduct both basic and clinical research over the next 5 years.

Officials at the American College of Chest Physicians also are working with Congress to obtain better funding for pulmonary rehabilitation. "Currently, Medicare payments are variable, based on the policy of the local carrier," Dr. Rosen said. However, legislation introduced in January would require Medicare to cover both physician-supervised pulmonary and cardiac rehabilitation programs. This legislation, the "Pulmonary and Cardiac Rehabilitation Act of 2007" (H.R. 552, S. 329), was introduced in the House by Rep. John Lewis (D-Ga.) and in the Senate by Sen. Mike Crapo (R-Idaho). ■

More information about the campaign is available online at www.learnaboutcopd.org.

Guidelines Focus on Control

Insensitivity • *from page 1*

population of 126 asthma patients with relatively high pulmonary function and allergy found that more than half failed to respond to 8 weeks of fluticasone or montelukast treatment, where response was defined as a 7.5% improvement in forced expiratory volume in 1 second (FEV_1) (J. Allergy Clin. Immunol. 2005;115:233-42).

A study of 30 adults with moderate asthma treated with one of two corticosteroids found that around 30% had no improvement in FEV_1 when treated with one of the steroids, and it was clear that this lack of effect was not caused by poor drug adherence because cortisol levels were measured as well, Dr. Kercsmar noted (J. Allergy Clin. Immunol. 2002;109:410-8).

In a study of 87 adolescents with difficult to control asthma, 24% had no improvement in FEV_1 after 7 days of oral prednisone treatment (J. Allergy Clin. Immunol. 1998;101:594-601).

There also is evidence that when patients are corticosteroid unresponsive, they have no decrease in T cells expressing inflammatory cytokines in their bronchial passages when given a steroid (J. Exp. Med. 1995;181:33-40).

Inhaled steroid therapy for asthma control will continue to be the backbone of asthma management, but this new concept of steroid unresponsiveness probably means that when a patient is not responding to an adequate, low-dose corticosteroid treatment, increasing the dose to the highest levels is unlikely to result in a complete response in all patients, Dr. Kercsmar said.

She recommended staying with as low a dose as possible for children and adolescents, and noted that if a patient is responding, symptoms improve in a few days, pulmonary function increases in a few weeks, and airway hyperreactivity decreases over a few months.

There is little dose-response with inhaled steroids beyond a certain low to moderate dose, depending on the drug, and so generally, there is very little additional asthma improvement for most patients when a steroid dose is increased, she explained.

On the other hand, adverse effects can increase much more significantly and rapidly with dose escalations.

The new understanding of asthma management is reflected in the most recent guidelines, Dr. Kercsmar said. She noted that the just-released guidelines from the Global Initiative for Asthma focus on asthma control rather than asthma severity.

The guidelines do not require a physician to identify the patient's asthma severity and apply a specific treatment for that severity; instead, they place a greater onus on a physician to assess the patient's asthma control and adjust treatment to maintain it.

Asthma control means that children should be able to participate in daily activities, be relatively asymptomatic, not have severe exacerbations, and have minimal use of β-agonists, Dr. Kercsmar said. ■

Dr. LeRoy M. Graham, FCCP, comments: *GINA guidelines clearly recognize that control is the key in asthma. Logically, effective disease classification should fit this recognition.*

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Address Changes: Send editorial correspondence and address changes to Circulation, CHEST PHYSICIAN, 5635 Fishers Lane, Suite 6000, Rockville, MD 20852.

POSTMASTER: Send change of address (with old mailing label) to CHEST PHYSICIAN, 5635 Fishers Lane, Suite 6000, Rockville, MD 20852.

CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Elsevier Inc., 60 Columbia Rd., Building B, Morristown, NJ 07960, 973-290-8200, fax 973-290-8250.

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Rapid Antigen Test Impacts Care of Adult Flu Patients

BY DIANA MAHONEY
Elsevier Global Medical News

The use of rapid antigen testing modestly reduced antibiotic use in adults hospitalized with influenza, a new study has shown.

Yet physician concerns about secondary bacterial infections kept antibiotic use in this population high, despite the diagnosis of influenza, Dr. Ann R. Falsey and colleagues at the University of Rochester (N.Y.) reported.

While rapid influenza testing has been shown to decrease the use of antibiotics and ancillary tests in febrile infants (see story, p. 9), its impact on the care of hospitalized adults has not previously been measured, according to the authors. The researchers undertook a review to compare the clinical management of hospitalized adults with positive rapid antigen tests on admission to that of patients who were diagnosed by either means (Arch. Intern. Med. 2007 Jan. 22 [Epub doi:10/1001/archinternmed.167.4.ioi.60207]).

The study population included 166 patients older than 18 years who were hospitalized for documented influenza A or B at Rochester General Hospital during four winters (1999-2003). As per hospital protocol, patients presenting between Nov. 15 and April 15 with acute cardiopulmonary symptoms underwent rapid antigen testing, excluding those patients with acute coronary syndrome, pulmonary embolism, or witnessed aspiration.

Viral nasal and pharyngeal swabs were obtained from all patients on admission, and viral culture was performed on all samples. Upon documentation of influenza activity, all samples underwent rapid testing, followed by viral culture for negative antigen test results.

Of the 166 patients, 86 were influenza antigen positive, and 80 were considered antigen-0—meaning that either they were antigen negative on rapid testing and were subsequently diagnosed by another means, or they did not have the test performed and were diagnosed primarily by another means.

A 105-patient subset of the study population participated in an epidemiologic study of respiratory illnesses and had reverse transcriptase polymerase chain reaction (RT-PCR) and serologic tests performed in addition to antigen testing and viral culture.

Of the 80 antigen-0 patients, 30 were viral culture positive, 30 were culture negative and RT-PCR-positive, and 20 were seropositive only, the authors noted.

Influenza testing was ordered by the emergency department or admitting health care provider for fewer than half (78) of the study group. "Of the 88 patients who would have been missed if the influenza screening program were not in place, 37 were potentially infectious at admission," the authors wrote.

While antibiotic use was reported in 153 (92%) of the patients, testing for bacterial infection was not universal. Of the 166 patients, only 115 had blood cultures, and only 66 had sputum cultures.

In all, 93 of the patients who received antibiotics were placed on combination therapy—usually ceftriaxone and a macrolide— and 60 received monotherapy, most commonly with quinolone or a macrolide.

The antigen-positive and antigen-0 groups had similar age, race, and sex distributions, but different frequencies of underlying conditions. The antigen-0 patients had higher rates of chronic obstructive pulmonary disease, inhaled steroid use, and home oxygen use, but less cardiac disease.

The antigen- positive patients had a shorter duration of illness before presentation to the hospital, were more often febrile, and were less likely to experience wheezing on examination. However, there were no differences in peripheral white blood cell count, infiltrates noted on [chest radiographs], or bacterial culture results.

As expected, the use of antiviral medications was greater in the antigen-positive group, the authors said. In 83 of the 86 antigen-positive patients and in 8 of the 80 patients in the antigen-0 group, the health care provider was aware of the influenza test result. This awareness led to a management change in response to the result in 27 of the antigen-positive patients, including a discontinuation of all antibiotics in 12 patients, a discontinuation of one of two antibiotics in 4 patients, and a change from intravenous to oral antibiotics in 11 patients.

To control for differences in clinical presentation, the investigators performed an analysis that showed that a positive rapid test result was significantly associated with a decision to withhold or discontinue antibiotic therapy (odds ratio of 6.9). ■

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Lavage Falls Short for Scleroderma Lung Disease

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — An underappreciated, practice-changing finding in the landmark Scleroderma Lung Study is that baseline bronchoalveolar lavage results had no value in predicting which patients would respond to cyclophosphamide, Dr. Charlie Strange, FCCP, said at the annual meeting of the American College of Chest Physicians.

"I think this is kind of the final nail in the coffin for BAL [bronchoalveolar lavage] in scleroderma," said Dr. Strange, a study coinvestigator and professor of pulmonary and critical care medicine at the Medical University of South Carolina, Charleston.

"Our rheumatology colleagues often are still knocking on our doors asking us to do lavage to help them figure out this treatment decision about cyclophosphamide. I personally think those days are over," the physician added.

The Scleroderma Lung Study, sponsored by the National Institutes of Health, was a multicenter, double-blind, placebo-controlled year-long trial of oral cyclophosphamide in 158 randomized patients with symptomatic scleroderma-related interstitial lung disease and active alveolitis.

The modest but statistically significant gains in forced vital capacity and total lung capacity along with the clinically meaningful improvement in symptoms seen in the cyclophosphamide arm of the trial constitute the first positive results of a placebo-controlled treatment study in scleroderma lung disease, according to Dr. Strange.

BAL in scleroderma has been a controversial issue. Many European studies have concluded that the procedure has no role in identifying those patients whose scleroderma lung disease is likely to benefit from cyclophosphamide.

In contrast, several American studies have concluded that the presence of extensive eosinophilia and/or neutrophilia in BAL fluid marks the patient at greatest risk of pulmonary disease progression and hence likely to respond to cyclophosphamide. But these earlier U.S. studies were retrospective in nature or methodologically flawed, according to Dr. Strange.

The sole significant predictor of response to cyclophosphamide in the Scleroderma Lung Study was the degree of pulmonary fibrosis on a 1-4 scale on baseline high-resolution CT scan. Patients with more severe baseline fibrosis tended to show the greatest improvement with cyclophosphamide in terms of the primary end point of the study—change in forced vital capacity (FVC) at 12 months—and the greatest deterioration on placebo.

'I think this is kind of the final nail in the coffin for BAL [bronchoalveolar lavage] in scleroderma.'
DR. STRANGE

No other findings on baseline high-resolution CT, including pure ground-glass opacity or the degree of honeycombing, proved predictive of response to cyclophosphamide. Neither did patient demographic variables.

The main results of the Scleroderma Lung Study have been published (N. Engl. J. Med. 2006;3564:2707-9). The mean absolute difference in FVC at 12 months between the cyclophosphamide and placebo groups was 2.5%, favoring cyclophosphamide.

Forty-nine percent of patients in the cyclophosphamide arm had an improvement in FVC, compared with 26% on placebo. At 2 years of follow-up, after 12 months of observation off treatment, the mean 1.95% absolute difference in FVC between the two groups remained significant.

Based on this study, it is appropriate for any scleroderma patient with severe fibrosis on high-resolution CT to undergo treatment with cyclophosphamide, Dr. Strange said.

Some physicians now order the CT scan at the time of diagnosis. Dr. Strange's own practice is to screen patients every 6 months with a chest radiograph, spirometry, a 6-minute walk test, and a lung diffusion capacity measurement. If he finds evidence of progressing lung disease, he moves on to CT.

Just how severe the fibrosis needs to be in order to trigger treatment with cyclophosphamide, a highly toxic drug, is an issue being addressed in an ongoing follow-up study, as is how best to maintain the therapeutic benefits over time. ■

Antibiotic Guidelines May Hamper Pneumonia Care

BY DIANA MAHONEY
Elsevier Global Medical News

TORONTO — Adherence to guidelines that recommend early use of antibiotics may lead to inaccurate diagnosis of community-acquired pneumonia and inappropriate use of antibiotics, according to a study presented at the annual meeting of the Infectious Diseases Society of America.

The IDSA guidelines for community-acquired pneumonia (CAP), published in November 2003, recommend the initiation of antibiotics within 4 hours of hospitalization—an indicator that has been linked to incentive compensation of third-party payers to hospitals, said Dr. Manreet K. Kanwar of St. John Hospital and Medical Center in Detroit.

Given the potential for providing less than optimal care by promoting compliance with the current CAP quality indicator, a more feasible target should be established, Dr. Kanwar suggested. "It's possible that prolonging the antibiotic window to 6 hours may be enough time to better evaluate a patient," he said.

To determine the effect of this recommendation on the diagnosis of CAP and the use of antibiotics, Dr. Kanwar and colleagues reviewed the charts of 518 patients older than 21 years who were admitted to their institution through the emergency department both before (January through June 2003) and after (January through June 2005) the publication of the guidelines. They collected data on clinical signs and symptoms at presentation, chest x-ray findings, preantibiotic blood cultures, time to antibiotic administration, Pneumonia Severity Index (PSI) scores, intensive care unit transfer rates, and mortality.

There were no significant differences between the 199 patients in the preguideline group and the 319 in the postguideline group in age, gender, PSI score, ICU transfer rates, or mortality. In the postguideline group, 66% of patients received antibiotics within 4 hours of triage, compared with 54% of the preguideline patients. The percentage of blood cultures prior to antibiotic administration was higher in the 2005 group (70%) than in the 2003 group (47%). But the final diagnosis of CAP dropped significantly, from about 76% in 2003 to 59% in 2005, and the mean antibiotic utilization per patient increased significantly, Dr. Kanwar reported in a poster presentation.

The increases in both the misdiagnosis in CAP and inappropriate antibiotic use as a result of compliance with the 4-hour antibiotic rule suggest that many patients received antibiotics for noninfectious processes. The increase in blood cultures obtained without indication suggests potential antibiotic use for contaminant-related positive cultures, Dr. Kanwar said. He reported having no financial disclosures related to this presentation. ■

Study: Travel Restrictions Can Halve Infection Rates in Epidemic

BY JONATHAN GARDNER
Elsevier Global Medical News

Banning all trips of greater than 50 km in an epidemic similar to severe acute respiratory syndrome would reduce the number of cases by more than half, even with compliance as low as 70%, Swedish epidemiologists reported.

Prohibiting trips longer than 20 km would reduce the spread of the infection even more, they found.

The researchers, led by Martin Camitz, of the Swedish Institute for Infectious Disease Control, modeled the spread of a SARS-like illness starting with a single infection in Stockholm and testing its spread without travel restrictions, and with limiting of all travel of more than 50 km and 20 km (BMC Med. 2006 Dec. 14 [Epub doi:10.1186/1741-7015-4-32]). The scenario assumed the country would be free from any outside influx of disease.

The model was based on the data contained in a survey of 17,000 Swedes who traveled between municipalities. All single, intercity trips were included, regardless of the destination, aim of the trip, and mode of transport.

If usual travel patterns are followed, 320,555 people, or 3.6% of the population, would be infected. If public health authorities limited travel to 50 km, the number drops to 154,517, or 1.7%, and if limited to 20 km, 64,307, or 0.7% of the population, would be infected. Control of the infection persists even if 30% of the population does not comply, researchers reported.

"The model and results are robust and there is no reason to believe that the results are not generally applicable to any country or region," the researchers wrote.

If all trips of more than 50 km were limited, the mean distance of the disease's spread would be 276 km. The farthest the disease would travel is 1,471 km, protecting the major population center of Malmo, a metropolitan area of 605,000 on the southern tip of Sweden, researchers said.

Under the 20-km restriction, the mean distance of the disease's spread would be 34 km. The farthest it would spread is 441 km. The 50-km restriction also would eliminate infection in 9 of 20 cities listed, and the 20-km restriction would eliminate infection in 3 more.

The researchers reported no conflicts of interest. ■

Dr. Aymarah Robles, FCCP, comments: *Limiting spread of respiratory infectious diseases is a huge challenge. Novel ways to achieve this are laudable. Quarantine in the "warp speed" modern world seems a difficult enterprise. Two potential drawbacks to the success of this proposed model are varying resistance to travel restrictions (quarantine) based on economic, sociopolitical, and cultural issues within countries; and the lack of accounting for influx of new disease after the outbreak, an unlikely scenario in today's world.*

Scintigraphy Aids Diagnosis of Thromboembolic Hypertension

BY KERRI WACHTER
Elsevier Global Medical News

BETHESDA, MD. — Patients with unexplained pulmonary hypertension or with pulmonary hypertension and a history of pulmonary embolism should undergo ventilation-perfusion scintigraphy to look for signs of chronic thromboembolic pulmonary hypertension, said one expert speaking at a meeting on pulmonary hypertension sponsored by the National Institutes of Health.

Patients with chronic thromboembolic pulmonary hypertension (CTEPH) may or may not have symptoms. "Many of these patients have no history at all of acute pulmonary embolism … so the overall prevalence of this disease is virtually unknown," said Dr. Marius M. Hoeper, clinical director of the pulmonary intensive care unit at the University of Hanover (Germany).

Most experts put the true incidence of CTEPH at 0.5%-1% of patients who survive an episode of acute pulmonary embolism, said Dr. Hoeper.

Dr. Hoeper and his colleagues have proposed a diagnostic algorithm for CTEPH (Circulation 2006;113:2011-20). Ventilation-perfusion scintigraphy is recommended in cases of unexplained pulmonary hypertension, or in patients who have pulmonary hypertension combined with a history of pulmonary embolism. A normal perfusion scan rules out CTEPH.

For those with multiple perfusion defects or indeterminate scans, further imaging should be pursued, including CT angiography, MR angiography, and pulmonary angiography. In those patients showing evidence of CTEPH on further imaging, a multidisciplinary approach—involving chest physicians, radiologists, and surgeons—should be adopted to tailor therapy.

CT angiography can distinguish between the typical findings of acute and chronic pulmonary embolism. CTA can also show the presence of bronchial arterial collaterals, which are typical of CTEPH and almost never seen in idiopathic pulmonary arterial hypertension. CTA can also reveal mosaic attenuation of the pulmonary parenchyma, which is virtually pathognomic for chronic thromboembolic disease. While MR angiography provides detailed images of the pulmonary vascular tree, it is time consuming. Surgeons tend to rely on pulmonary angiography.

"CTEPH carries a poor prognosis if left untreated, and most of these patients are going to die within a couple of years, especially if mean pulmonary artery pressures are higher than 30 mm Hg," said Dr. Hoeper.

In patients who are surgical candidates, pulmonary endarterectomy is the treatment of choice, he said. Long-term survival after this procedure is fairly good, ranging from 50% to 75% at 5 years. The main cause of death related to surgery is persistent pulmonary hypertension.

Some patient populations have been proposed for medical therapy, including those who are hemodynamically unstable, those with comorbidities that preclude surgery, and those with predominant peripheral involvement or persistent pulmonary hypertension after endarterectomy.

In uncontrolled studies, epoprostenol (a prostaglandin), sildenafil (a phosphodiesterase-5 inhibitor), and bosentan (endothelin receptor antagonist) show some promise for the treatment of CTEPH.

The etiology of CTEPH is not fully understood. Up to half of patients with this disorder have no history of clinically overt acute pulmonary embolism. Deep vein thrombosis is detected in only 30%-60% of patients. "The classic thrombophilic conditions are quite rare [in these patients], except for antiphospholipid syndrome," Dr. Hoeper said. In addition, it does not appear that fibrinolysis is impaired in these patients.

"On the other hand, they have quite typical and distinct risk factors," he said, including splenectomy, the presence of atrial ventricular shunt, myeloproliferative disorders, and chronic inflammation. However, the vast majority of patients diagnosed with CTEPH may not have any of these underlying conditions.

The classical hypothesis for pathogenesis is that patients have a deep vein thrombosis—either acute or more commonly recurrent pulmonary embolism—and for unknown reasons there is incomplete resolution. This leads to vascular obstruction, which sets up a cascade of events resulting in pulmonary vascular remodeling and prothrombotic disease.

However, this view has been challenged by some who suggest that at least some of these patients suffer from pulmonary arteriopathy resulting in respiratory obstruction and possibly caused by *in situ* thrombosis of large pulmonary vessels.

The concept of the two-compartment pulmonary vascular bed has been used to describe the disorder. In this model, part of the pulmonary vasculature has centrally obstructed vessels, while peripheral vessels are protected from pulmonary hypertensive changes (i.e., are normal).

However, vessels in areas that are not protected by central obstructions are exposed to high flow, high pressure, and high shear stress, which lead to progressive peripheral pulmonary vascular remodeling. "So in the peripheral vessels of these patients, what is going on is obviously quite similar to what we see in other forms of pulmonary artery hypertension," said Dr. Hoeper.

Dr. Hoeper disclosed that he has financial ties to several pharmaceutical companies. ■

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Low-Dose Aspirin May Head Off Adult-Onset Asthma

BY ROBERT FINN
Elsevier Global Medical News

Men who take low-dose aspirin are 22% less likely to develop asthma as adults, according to a secondary analysis of the large Physicians' Health Study.

Among 11,023 physicians taking 325 mg of aspirin every other day for an average of 4.5 years, 113 developed asthma. In contrast, among the 11,017 physicians randomized to the placebo group, 145 developed asthma during that period, a significant difference, reported Dr. R. Graham Barr of Columbia University Medical Center, New York, and colleagues (Am. J. Respir. Crit. Care Med. 2007;175:120-5).

The finding supports an earlier observational cohort study of analgesic use and adult-onset asthma among women.

The authors cautioned that the Physicians' Health Study was not designed to examine the relationship between aspirin and asthma. Instead, it was designed to see if aspirin would protect against the development of cardiovascular disease. That relationship was so strong that the study was stopped prematurely. A trial designed a priori to examine the relationship between aspirin and asthma would be needed to confirm this new finding.

The relationship between low-dose aspirin and asthma was especially strong among men who had never smoked and among men younger than 46 years.

The investigators proposed several mechanisms by which aspirin may prevent new-onset asthma, including some mechanisms that rely on COX-1 inhibition.

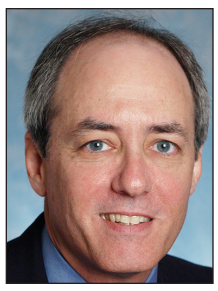
Dr. Barr disclosed that he has no financial relationships with a commercial entity that has interest in the subject of the study. Several of his coauthors, however, disclosed relationships with various pharmaceutical companies, including Bayer AG, the company that introduced aspirin in 1899. The study was supported by grants from the Robert Wood Johnson Foundation, the National Cancer Institute, and the National Heart, Lung, and Blood Institute. ■

Use IgE Testing To Identify Asthma Triggers

WASHINGTON — Allergen-specific immunoglobulin E testing is an effective tool for accurately diagnosing atopic triggers in patients with asthma, but it is underused in the United States, Dr. Leonard Fromer said at the annual meeting of the American Academy of Family Physicians.

Only 1 in 20 asthmatics in the U.S. is tested for triggers, he added.

Primary care physicians manage most patients with mild to moderate asthma. In about 70%-90% of children and 60% of adults with asthma, the disease is atopic. Often, the emphasis is on what drugs to prescribe and not on identifying allergen exposures, said Dr. Fromer, who is a professor of family medicine at the University of California, Los Angeles.



Too often, the emphasis is on what medications to prescribe and not on identifying allergen exposures.
DR. FROMER

Skin-prick testing for allergy remains the cornerstone for many physicians, but it cannot be performed on patients with uncontrolled asthma, and it requires the cessation of medication prior to testing, he said. These shortcomings of the skin-prick test do not apply to blood-based IgE testing. Newer-generation IgE tests allow for accurate testing in children as young as 6 months old, he said.

Some studies have shown IgE testing to have sensitivity and specificity similar to that of skin-prick testing (J. Allergy Clin. Immunol. 1999;103:773-9). Moreover, there is significant variability in the way skin tests are performed, interpreted, and documented (Ann. Allergy Asthma Immunol. 2006;96:19-23), Dr. Fromer said.

There are more than 300 available reagents when ordering an IgE test. The respiratory panel is most important in young children and adults because by 3 years of age, respiratory allergens start to dominate, Dr. Fromer said. Testing requires 2 mL of blood for children and 4 mL for adults, with results typically available in 48 hours.

—Patrice Wendling

Obesity Improved Survival in Bloodstream Infections

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Critically ill obese and morbidly obese ICU patients with bloodstream infections have a higher survival rate than nonobese ones, Dr. Luis Carlos Murillo reported at the annual meeting of the American College of Chest Physicians.

This finding from a retrospective observational study is counterintuitive. After all, obesity is associated with increased levels of inflammatory markers linked to poor cardiovascular and other outcomes. The observed survival advantage suggests obesity might be associated with as-yet unidentified beneficial alterations in immune function or metabolism in response to serious infection, according to Dr. Murillo of Geisinger Medical Center, Danville, Pa.

Efforts to characterize these hypothesized distinctive immunologic and metabolic responses of obese patients to bloodstream infections could eventually lead to novel treatments for septic patients of all weight categories, added Dr. Murillo.

He reported on 185 patients with bloodstream infections in the Geisinger ICU. Of the 98 patients with a body mass index of 30 kg/m^2 or more, 69% survived their hospitalization, compared with only 52% of those with a BMI of 17.5-29.9. That difference was statistically significant.

In contrast, there were no significant differences between the combined obese/morbidly obese groups and nonobese patients in terms of age, sex, APACHE critical illness severity scores, comorbid conditions, number of days on mechanical ventilation, or length of stay in the ICU or hospital.

There was, however, a trend for longer hospital stays in morbidly obese patients who survived. Mean length of stay for patients with a BMI of 17.5-29.9 was 24.6 days, compared with 31.5 days for those with a BMI of 30 or more. Stays among the 32 patients whose BMI was at least 40 were even longer. ■

In HIV Cases, Antiretrovirals Cut ICU Pneumonia Deaths

BY TIMOTHY F. KIRN
Elsevier Global Medical News

SAN FRANCISCO — Patients found to have HIV infection when they are admitted to the intensive care unit with pneumocystis pneumonia should have antiretroviral therapy started, even though there are no trial data to support the practice, Dr. Lawrence Huang said at a meeting on HIV management sponsored by the University of California, San Francisco.

Pneumocystis jiroveci (formerly known as *Pneumocystis carinii*) pneumonia is still a commonly presenting condition in patients who are infected with HIV, said Dr. Huang of the division of pulmonary and critical care medicine at San Francisco General Hospital.

It is estimated that one-fourth of those infected with HIV in the United States are unaware of their infection. They are the patients at risk of pneumocystis pneumonia. And 40% of HIV-infected patients who are admitted to the intensive care unit are unaware of their HIV status as well.

Although limited, the data to support the practice of initiating antiretroviral therapy in HIV-infected patients admitted with pneumonia and respiratory failure come from a cohort at San Francisco General reviewed by Dr. Huang and his colleagues, he said.

The investigators looked at 58 HIV-infected patients with pneumocystis pneumonia admitted to the ICU. In the cohort, 21% were on antiretroviral therapy or started antiretrovirals. The mortality rate was 25% in the patients whose HIV was treated. The rate was 63% in those whose disease was not treated.

The investigators were unable to identify any risk factor other than antiretroviral therapy that might have produced the difference (AIDS 2003;17:73-80).

Of course, the physicians choosing to treat or not treat may have seen something in the patients not reflected by the numbers in the chart, Dr. Huang said.

"The bottom line is that I don't know the answer," he said.

"My argument—that I make with no data—is, 'Oh, what the heck, try it,' " he added. "I don't mean there are no data. There are no randomized, controlled trial data."

Pneumocystis pneumonia is highly fatal in HIV-infected ICU patients, he noted. "PCP is the only HIV diagnosis for which mortality is greater than 50%." ■

Dr. Aymarah Robles, FCCP, comments: *This 4-year-old and still provocative article demonstrated a marked survival benefit in the cohort of patients with respiratory failure from PCP as the sentinel diagnosis of AIDS. Dr. Huang's approach, initiating ART with the first diagnosis of PCP, is a good one, even in the absence of randomized controlled trials, given the high mortality with PCP-related respiratory failure. Initiating ART without a patient willingness contract in new-onset AIDS with respiratory failure from PCP allows for a survival advantage, so that the patient can subsequently make an informed consent and perhaps have a personal incentive to adhere to therapy. What would be welcome now are data about the incidence of the PCP immune reconstitution syndrome, the length of steroid therapy to modify the inflammatory/immune reconstitution response, and the long-term survival benefit.*

Combo Tx No Better In *P. aeruginosa* Pneumonia Cases

BARCELONA — Combination antibiotic therapy confers no additional benefit over monotherapy in treating ventilator-associated *Pseudomonas aeruginosa* pneumonia, Dr. A.M. Escoresca reported at the annual congress of the European Society of Intensive Care Medicine.

Dr. Escoresca, of the Hospital Virgen del Rocío, Seville, Spain, presented a retrospective study of 183 patients who developed nosocomial *P. aeruginosa* pneumonia while mechanically ventilated in the intensive care unit. Monotherapy, defined as one antibiotic agent active against *P. aeruginosa*, was used in 69 patients. Combination therapy patients received β-lactam plus aminoglycosides; β-lactam plus fluoroquinolones; or fluoroquinolones plus aminoglycosides.

There were no statistically significant differences in mortality among the groups. There was a trend toward higher mortality in patients who received β-lactam plus fluoroquinolones, but multivariate analysis revealed that those patients were older and more likely to have chronic cardiac disease.

—Michele G. Sullivan

Excess Body Weight Lowers Quality of Life for Asthmatics

BY LESLIE B. SABBAGH
Elsevier Global Medical News

Children with excessive body weight who also have asthma have significantly poorer quality-of-life scores than do children who have only excessive body weight or are only asthmatic, according to study findings published in the Journal of Allergy and Clinical Immunology.

Dr. Rene van Gent and colleagues from Maxima Medical Center, Veldhoven, the Netherlands, conducted a cross-sectional design study of four groups (asthmatic children with and without excessive body weight, and healthy controls with and without excessive body weight) to determine whether asthma and excessive body weight have more impact on quality of life in children than asthma alone or excessive body weight alone. Excessive body weight was defined using international cutoff points for children with overweight and obesity stratified by sex. Healthy normal weight children served as controls (J. Allergy Clin. Immunol. 2006 [Epub doi:10.1016/j.jaci.2006.11.007]).

IT IS IMPORTANT FOR CLINICIANS TO REALIZE THAT CHILDREN WITH ASTHMA NEED EXTRA ATTENTION IF THEY ALSO HAVE EXCESSIVE BODY WEIGHT.

Of 1,614 participants aged 7-10 years in the researchers' preliminary lung-function study, 204 (13%) were diagnosed with asthma. Of those, 171 (84%) were normal weight and 33 (16%) had excessive body weight. Of the 200 healthy controls, each selected randomly from the same classroom as an asthma patient, 174 (87%) were normal weight, and 26 (13%) had excessive body weight. There were 24 (73% of the excessive-weight children) overweight children in the asthma group and 23 (89%) among the healthy controls. There were nine (27%) obese children in the asthma group and three (11%) among the healthy controls.

Quality of life in children with asthma and excessive body weight was "lower than expected on the basis of the sum of the separate effects of asthma alone or excessive body weight alone."

Quality-of-life scores were 25% lower in asthmatic children with excessive body weight, 14% lower in normal weight asthmatic children, and 1% lower in healthy controls with excessive body weight, compared with healthy normal weight controls. The first two differences were statistically significant, whereas the third difference was not.

"Excessive body weight is associated with an additional decrease in quality of life in children with asthma," the researchers concluded. They suggest clinicians "realize that children with asthma need extra attention if they also have excessive body weight. … Treatment by specialized multidisciplinary teams will have the largest beneficial effect in these children." ■

Dr. LeRoy M. Graham, FCCP, comments: *Obesity is an important comorbidity when noted in children with asthma. Effective management must address both conditions, which may be interdependent.*

Bacterial Tracheitis Gains Prominence In Dangerous Airway Infections

BY HEIDI SPLETE
Elsevier Global Medical News

Bacterial tracheitis, a relatively uncommon infection, may have outpaced viral croup and epiglottitis as the most common potentially life-threatening upper airway infection in children, based on data from patients treated in a single hospital between 1997 and 2006.

The widespread immunization of children against *Haemophilus influenza* type b and the use of corticosteroids to treat viral croup have likely contributed to the decline in viral croup and epiglottitis, and the resulting prevalence of cases of bacterial tracheitis, reported Dr. Amelia Hopkins of the University of Colorado School of Medicine, Denver, and her colleagues (Pediatrics 2006;118:1418-21).

Respiratory failures were three times more likely to be caused by bacterial tracheitis than by viral croup and epiglottitis combined, they said.

The researchers reviewed a series of 127 patients admitted to Vermont Children's Hospital with viral croup, epiglottitis, or bacterial tracheitis. Overall, 35 children were sent to the pediatric intensive care unit: 17 (48%) were diagnosed with bacterial tracheitis, 16 (46%) were diagnosed with viral croup, and 2 (6%) were diagnosed with epiglottitis. Of the 20 children in the PICU who developed respiratory failure, 15 (75%) had bacterial tracheitis, compared with only 3 (15%) who had viral croup and 2 (10%) who had nonclassic epiglottitis.

Of the 18 cases of bacterial tracheitis that were reviewed, 17 (94%) children were sent to the PICU and 15 (83%) of these children needed to be intubated.

In addition, five of the patients with bacterial tracheitis developed serious complications—four experienced acute respiratory distress syndrome accompanied by multiple organ dysfunction syndrome, and a fifth patient developed subglottic stenosis and underwent a tracheostomy.

By contrast, only 16 (15%) of the 107 cases of viral croup that were reviewed were sent to the PICU, and 3 of these children needed to be intubated, but none experienced serious complications.

Clinical characteristics of bacterial tracheitis included cough and retractions in 17 (94%) patients, stridor in 16 (89%) patients, and hoarseness in 12 (67%) patients. ■

Dr. LeRoy Graham, FCCP, comments: *Bacterial tracheitis appears to be rising in prevalence as compared to decreasing trends in viral croup and epiglottitis as a cause of potentially life-threatening airway infection in children.*

Neonatal Lung Function Linked to Later Asthma

Two measures have predictive value.

BY MARY ANN MOON
Elsevier Global Medical News

Infants who have reduced lung function a few days after birth are at elevated risk of developing asthma by 10 years of age, reported Dr. Geir Håland of Ulleval University Hospital, Oslo, and associates.

The study findings suggest that airway dysfunction associated with later asthma may be present and detectable in the newborn population a few days following birth.

"To our knowledge, no study to date has shown an association between lung function in early infancy and asthma after 3 years of age," the researchers said in the New England Journal of Medicine.

Dr. Håland and colleagues assessed the predictive value of lung function using data from the Environment and Childhood Asthma study, a prospective study of 3,754 healthy full-term infants born in Oslo over a 15-month period beginning in 1992. Tidal breathing flow-volume loops and passive respiratory mechanics were evaluated using a face mask while the newborns were calm and awake.

At 10-years' follow-up, 614 of these subjects were found to have a history of asthma or current asthma.

Infants whose tidal breathing values were at or below the median were significantly more likely to develop asthma over the intervening years than were those whose values were above the median. They also were more likely to develop severe bronchial hyperresponsiveness and to use inhaled corticosteroids.

Similarly, those newborn children whose values for respiratory system compliance were at or below the median level were significantly more likely to develop asthma by the age of 10 than newborn children whose values were higher than the median.

In the subset of 33 children whose values for both measures of lung function were less than the median at birth, the prevalence of a history of asthma was 46% and of current asthma was 28%; both of these values were significantly higher than the rates of 19% and 10%, respectively, that were observed in the other subjects tested.

The strengths of the associations between lung function measures and past or current asthma were equivalent to those of a family history of asthma, Dr. Håland and associates noted (N. Engl. J. Med. 2006;355:1682-9).

These associations remained strong after the data were adjusted to allow for a number of variables, such as gender, parental asthma, parental rhinoconjunctivitis, and prenatal exposure to tobacco smoke. ■

Rapid Flu Test Cuts Further Testing

Rapid viral testing for influenza as part of the routine care plan for febrile infants reduced antibiotic use, emergency department visits, and the use of additional tests, based on data from a prospective study of 206 infants during the course of two flu seasons.

Nonspecific fevers without obvious signs of infection send many infants to the pediatric emergency department, and rapid flu testing in these settings can help triage patients more effectively and reduce unnecessary tests and treatment, wrote Dr. Javier Benito-Fernandez of the pediatric emergency department in Hospital de Cruces, Barakaldo, Spain, and his colleagues.

Overall, 84 of 206 (41%) infants aged 0-36 months tested positive based on commercially available rapid flu tests. The influenza-positive infants were significantly less likely than influenza-negative infants to undergo blood tests (33% vs. 100%), urinalysis (81% vs. 100%), chest radiographs (14% vs. 32%), and lumbar punctures for cerebrospinal fluid analysis (2% vs. 21%).

In addition, none of the influenza-positive infants received antibiotics at the time of diagnosis, compared with a 39% of the influenza-negative infants (Pediatr. Infect. Dis. J. 2006;25:1153-7).

Only two influenza-positive infants (2%) required hospital stays for observation, compared with 20 influenza-negative infants (16%) admitted for diagnoses including pneumonia, meningitis, urinary tract infection, and bacteremia. Approximately 12% of both influenza-positive and influenza-negative patients returned to the emergency department for consultation within a few days, and four patients in each group were diagnosed with either otitis media or pneumonia.

All influenza-positive patients had a favorable clinical course, the investigators said.

—Heidi Splete

Pneumonectomy Mortality Tripled in Elderly Patients

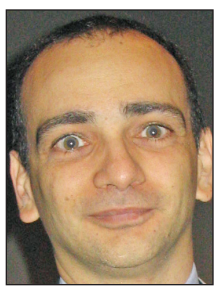
BY JANE SALODOF MACNEIL
Elsevier Global Medical News

STOCKHOLM — Lung cancer patients over 70 years of age face about three times the risk of death after pneumonectomy, compared with younger patients with comparable disease and comorbidities, according to the outcomes of a case-control study presented at a meeting of the European Association for Cardio-Thoracic Surgery.

Dr. Francesco Leo, FCCP, reported that respiratory complications occurred significantly more often in the elderly patients and were a primary reason for the disparity in mortality.

"Respiratory function has been confirmed as the most accurate predictor of mortality," said Dr. Leo of the department of thoracic surgery at the European Institute of Oncology in Milan.

The study identified 35 patients who were aged 70 and older and underwent pneumonectomy for lung cancer between 1998 and 2005 at the institute. This group of patients was predominantly male, had a median age of 73.8 years, and underwent 15 right-handed procedures.



'Respiratory function has been confirmed as the most accurate predictor of mortality.'
DR. LEO

Dr. Leo and his colleagues matched the elderly patients to a control group of 70 younger patients with a median age of 59.3 years. There were no other significant differences between the two groups with respect to sex, cardiovascular comorbidity, respiratory function, tumor side or stage, and preoperative chemotherapy.

Postoperative mortality was more than twice as high, 11.4% vs. 4.3%, in the older patients. The difference reached statistical significance at 90 days when mortality was reported as 14.2% of the elderly vs. 5.7% of the control group.

Overall morbidity was slightly higher in the elderly (54.2% vs. 41.6%). Respiratory complications occurred significantly more often in the elderly (25.7% vs. 8.3%), as did cardiac complications (28.5% vs. 11.4%). Surgical complications were comparable, however (8.5% vs. 7.1%).

Dr. Leo reported that preoperative chemotherapy did not affect postoperative mortality, but that respiratory function and complications did have an effect.

Among patients whose forced expiratory volume in 1 second (FEV_1) was less than 70%, the respiratory complication rate was 43.7% in the elderly but only 11.5% in younger patients. Mortality in patients with poor respiratory function likewise was much higher with advanced age: 12.5% vs. 3.8%.

Elderly patients with FEV_1 above 70% also had higher morbidity and mortality, but neither occurred as often. Their rate of respiratory complications was 11.1% vs. 6.8% in younger patients with FEV_1 above 70%. The mortality rate in older patients with better respiratory function was 5.2% vs. 4.5% in the control group.

In an interview at the meeting, which was held with the European Society of Thoracic Surgeons, Dr. Leo said the elderly should not be precluded from pneumonectomy, but that surgeons need to become more selective in identifying which older patients would benefit from the operation.

"The problem is the alternative. The alternative is chemoradiotherapy," Dr. Leo said.

Only about half of elderly patients are able to complete chemoradiation, according to Dr. Leo. Their 5-year survival rate is only about 3%-5%, he said, compared with 17% for elderly patients who have all or part of a lung removed.

"We should define specific criteria of eligibility for [pneumonectomy in] elderly patients," he said, predicting that improved criteria would lead to lower mortality and maximum survival.

"Respiratory function is the predictor of life expectancy. We have to be more selective on the respiratory function," said Dr. Leo.

Dr. Robert Cerfolio, FCCP, comments: *Dr. Leo and colleagues have presented further evidence for the growing body of data that suggested an increased risk of pneumonectomy, especially right pneumonectomy. In this manuscript, the target patient population is elderly patients. However, many studies have shown that properly selected elderly patients can safely undergo all types of pulmonary resection.*

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Sleep Disorders Can Affect Pregnancy Outcomes

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SCOTTSDALE, ARIZ. — Even mild sleep disorders have the potential to affect fetal outcomes during pregnancy, Dr. Susan M. Harding, FCCP, said at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

Recent research suggests that obstructive sleep apnea might impact hypertension in pregnant women with preeclampsia, said Dr. Harding, professor of medicine at the University of Alabama at Birmingham, and medical director of the Sleep/Wake Disorders Center there.

Other studies cited by Dr. Harding reported a higher risk of lower-birth-weight babies in women who work night shifts, and increases in labor duration and in cesarean section rates when women sleep poorly.

Dr. Harding cited a Swedish study of 502 singleton pregnancies that diagnosed hypertension in 14% of 113 snorers but in only 6% of 389 nonsnorers (Chest 2000; 117:137-41). Preeclampsia also was more prevalent in the snorers.

The investigators concluded that habitual snoring is an independent predictor of hypertension (odds ratio 2.03) and growth retardation (OR 3.45). Dr. Harding noted that snorers' babies were significantly more likely to have Apgar scores of 7 or lower at 1 minute after birth (12.4% vs. 3.6%) and to be small for gestational age (7.1% vs. 2.6%). Only 4% of women snored before becoming pregnant, whereas 23% snored during their final week of pregnancy.

Another study cited by Dr. Harding delivered continuous positive airway pressure (CPAP) to 11 pregnant women with severe preeclampsia and findings of upper airway resistance syndrome (Am. J. Respir. Crit. Care Med. 2000;162:252-7). CPAP reduced blood pressure in these women.

The shift-work study reviewed 41,150 pregnancies in a Danish database (Am. J. Obstet. Gynecol. 2004;191:285-91). Women on permanent night shifts had a higher risk of post-term birth (OR 1.35) and delivering a low-birth-weight baby at term (OR 1.80).

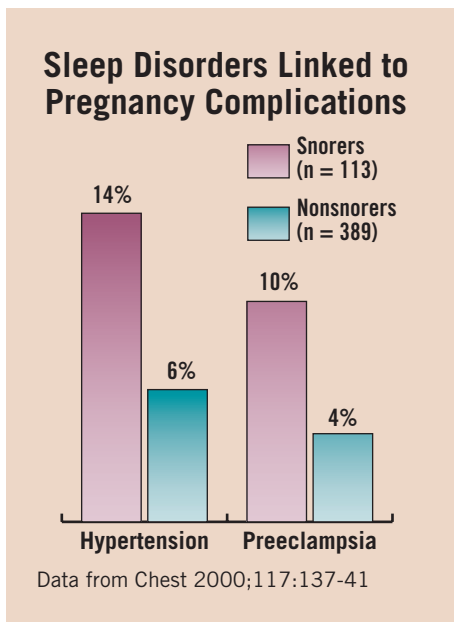
Dr. Harding also cited an American study of 131 women in their ninth month of pregnancy (Am. J. Obstet. Gynecol. 2004; 191:2041-6). Women who slept fewer than 6 hours each night had a longer labor (29 hours vs. 18 hours) and a higher cesarean rate (37% vs. 11%), compared with women who slept more hours. Longer labors and higher cesarean rates also were linked with disrupted sleep.

Consider screening pregnant women for sleep apnea, especially when hypertension is an issue.
DR. HARDING

Although these studies are not conclusive, the evidence so far is strong enough that physicians should consider screening pregnant women for obstructive sleep apnea, especially when hypertension is an issue.

Treating two other sleep disorders—restless legs syndrome (RLS) and narcolepsy—is problematic because the medications used in treating them are contraindicated during pregnancy, Dr. Harding said. Pregnancy is a risk factor for development of RLS. Up to a third of pregnant women have RLS symptoms, she said

Dr. Harding recommended educating women under treatment for RLS or other sleep disorders about the need to discontinue modafinil, stimulants, and other medications prior to becoming pregnant. She called on physicians to assess risks, such as patients' driving when drowsy, if drug therapies are stopped. "Off medication, they may have significant problems with sleepiness," she said. ■



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NEWS FROM THE COLLEGE

March Is DVT Awareness Month

ACCP

(L-R) Dr. Sam Goldhaber, FCCP; Dr. Victor Tapson, FCCP; Melanie Bloom; Sydney Parker, PhD; and Dr. Henry Bussey, FCCP.

DVT Awareness by Design

The Coalition to Prevent Deep-Vein Thrombosis, of which the ACCP is a member, invites you and your health-care community to participate in *DVT Awareness by Design*. By actively empowering health-care communities and individuals, *DVT Awareness by Design* goes beyond building awareness of signs and symptoms of deep-vein thrombosis, by asking individuals and health-care communities to design and personalize their own socks to illustrate how they have personally been affected by DVT.

In preparation for DVT Awareness Month 2007 in March, the Coalition has developed a *DVT Awareness by Design Kit*. The design kit is a tool to encourage individuals to get engaged in DVT Awareness and to submit photo entries of their DVT designed socks on preventdvt.org. The design kit will include socks, markers, DVT pins, ribbon stencils, instructions on "How to Design Your Own DVT Sock," DVT backgrounder, a disposable camera, the 2007 Turnkey Kit, and a list of DVT activities nationwide.

We need your help in alerting the health-care community to show its support and get actively involved in the *DVT Awareness by Design* program. During February, the Coalition will be mailing design kits to hospitals and Coalition member organizations for participation in designing your own DVT socks (see photo at upper right).

To learn more about requesting your own design kit and how to share your DVT personalized socks, visit www.preventdvt.org. The design kits will be available for distribution throughout February and March 2007. If you have questions, contact Hampton Shaddock at (202) 530-4677. Visit www.preventdvt.org.

Online Services From ClotCare

Up-to-date information and expert insight on issues relating to anticoagulation and antithrombotic therapy are available at no cost on ClotCare Online Resource, www.clotcare.com. This interactive Web site for patients, their caregivers, and clinicians has a searchable database, will respond to questions, and provides information alerts to its listserv members.

► **For clinicians:** ClotCare provides online summaries with commentary and links to new anticoagulation publications. These summaries are written by members of ClotCare's world-class, interdisciplinary editorial board, which consists of 19 experts from across the US and Canada. These same carefully selected experts also provide their specialized expertise in addressing submitted questions. Additionally, the site provides information on relevant continuing education opportunities and various anticoagulation training programs, some of which may be completed online. Clinicians also have access to all patient education materials available on the site.

► **For patients:** ClotCare has a wealth of education materials. A dedicated lay editor ensures that patient postings are presented in terms a layperson will understand. These materials provide information on specific conditions, such as deep vein thrombosis and postthrombotic syndrome, and on

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treatment issues, such as an explanation of key issues relating to warfarin therapy, an explanation of the PT-INR test, and information on the use of graduated compression stockings. ClotCare also has teamed up with the National Alliance for Thrombosis and Thrombophilia to make presentations from a recent patient education seminar available online.

▶ **Services in development:** ClotCare is currently developing an anticoagulation patient education video that can be downloaded and viewed on a computer or saved to a disk. Another feature in development is an online conference for patients on anticoagulation issues that will be moderated by ClotCare editorial board members. ClotCare also is developing an international registry to track observed interactions between vitamin K antagonists and dietary or herbal supplements. This registry will be available early in 2007, and any clinician may contribute.

▶ **Finding information on ClotCare:** When using ClotCare.com, site visitors can review a list of new postings or browse for information on a specific medicine, class of medications, specific condition, lab procedure, or management issue. The site can also be searched based on any keyword(s). ClotCare sends e-mail alerts summarizing new information to individuals on ClotCare's free listserv.

ClotCare has developed an online anticoagulation management system, the Clot*Free* System. ClotCare has made it available at no cost for research purposes, and options are being developed to provide it at no cost for routine patient management.

ClotCare is a member of the Coalition to Prevent Deep-Vein Thrombosis and has received the HONcode endorsement for quality health information on the Web. ClotCare is funded by unrestricted educational grants and sponsorships from Astra-Zeneca, sanofi-aventis U.S. L.L.C, Upsher-Smith, Pharmion, and Boehringer Ingelheim. ■

Henry I. Bussey, PharmD, FCCP; and Marie B. Walker, BBA

AMA, ACCP to Conduct Physician Practice Survey

The American Medical Association (AMA), with the support of the American College of Chest Physicians (ACCP) and more than 60 other medical specialty societies, will begin conducting a multispecialty survey of America's physician practices beginning in 2007. The survey will collect up-to-date information on physician practice characteristics to develop and redefine AMA and ACCP policy. Data related to professional practice expenses will also be collected. The AMA and the ACCP will survey thousands of physicians from virtually all physician specialties. You may be contacted by the Gallup Organization to participate. We encourage your participation, which ensures that the information collected will represent you and your patients' concerns to national policy makers. ■

ACCP Participates in 11th APSR Congress

ACCP leadership attended the 11th APSR Congress held November 19-22, 2006, in Kyoto, Japan. The ACCP delegation gave lectures and planned the 12th APSR and 2nd joint APSR/ACCP Congress to be held November 30 - December 4, 2007 on the Gold Coast of Queensland, Australia. ACCP attendees included President, Mark J. Rosen, MD, FCCP; Immediate Past President, W. Michael Alberts, MD, FCCP; Past President and *CHEST* Editor in Chief, Richard S. Irwin, MD, FCCP; Executive Vice President and CEO, Alvin Lever, MA, FCCP(Hon); and VP of Publications and *CHEST* Executive Editor, Stephen Welch. ■

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AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

BY DR. MARK J. ROSEN, FCCP

PRESIDENT'S REPORT

Simulation Technology's Time Has Come

"See one, do one, teach one" is a cornerstone of medical education, probably for millennia. But would you happily sign the consent form for insertion of your subclavian line by an intern who cheerfully informs you, "This will be my first line, but I've seen a few, and I will be supervised by an excellent resident"? Not likely.

Simulations are used widely to educate and evaluate professionals, with technologies ranging from low-end (boxers punching a sandbag) to super-high-end (fighter pilots playing out tricky scenarios in multimillion-dollar virtual cockpit flight simulators). In medicine, computer-controlled patient simulators offer mannequins that look, act, sound, feel, and get sick almost like the real thing. The pulses pulse, the chest moves, and you hear realistic sounds through your stethoscope, and the heartbeat is palpable and audible, with any murmurs and gallops you program in.

Put one of these in a simulated ICU, and things get even more interesting. The mannequin blinks, looks you in the eye, and moans, "I can't breathe!" as the pulse quickens and the chest moves faster. As your "patient" is crashing, the monitor shows the oxygen saturation dropping and blood pressure rising, and you decide to intubate. Then, under the watchful eyes of a video camera and an expert instructor who will review the event and the tape with you and point out ways you could improve, you assemble your equipment, call over your team to help, and start bagging.

If all goes well, you visualize real-looking vocal cords with a real laryngoscope, intubate with a real tube, ventilate the patient with a real bag, watch the vital signs stabilize and improve, and get high fives all around.

WITH A SIMULATOR, WE CAN LEARN AND PRACTICE NEW SKILLS WITHOUT RISK OF HARM, OTHER THAN TO OUR OWN BRUISED EGOS.

On the other hand, if you make a serious mistake, the simulator knows it, and the mannequin dies a simulated death. Then, you curse yourself, discuss what happened while reviewing the tape with your instructor, learn what went wrong, and try again. Unlike a real ICU, you also go back and repeat this process until you do everything right.

Medical simulation technology has been adopted mainly in anesthesiology, surgery, and nursing, but, surprisingly, not in critical care training, where it would seem to be particularly useful. With experience on a simulator, we can learn and practice new skills without risk of harm, other than to our own bruised egos when we learn that we aren't as proficient as we thought. With a simulator, we can objectively assess our skills and our progress and keep running the simulation until we do it perfectly. Unusual events like a "difficult airway" can be programmed with remarkable realism, so the learner can practice dealing with one when it happens in real life. Better still, the patient care team can train like a flight crew, practicing together to function cohesively and effectively in a variety of scenarios.

The obstacles to starting a simulation program are formidable: the equipment is expensive, the facilities to set up a realistic environment are lacking, and the expertise to use simulators in an organized and effective fashion is rare. Many schools and hospitals invest in the equipment, only to have it sit in boxes for lack of space and people to make it work.

The ACCP is moving ahead to incorporate simulation as an central component of its education programs. After seeing its potential in our first simulation lab at CHEST 2005, the College recruited Viva Siddall, MS, as Assistant Vice President, Educational Resources. Ms. Siddall, a former respiratory therapist with Masters degrees in both Education and in Outcomes Research, had been Director of Education of the Patient Safety Simulator Center at Northwestern University, where she wrote the curricula and coordinated the Center's activities, while pursuing an active line of research linking simulation training with improved clinical outcomes.

At the College, she will play a leading role (along with Ed Dellert, Vice President of Educational Resources, and our Fellows with expertise and interest) in developing our programs in patient simulation. The outstanding and capacity-crowd CHEST 2006 simulation lab will be replicated and expanded at CHEST 2007 and at future meetings (see article on page 16). We are developing new simulation-based programs to teach new skills and evaluate proficiency, to train hospital-based teams, and to train new educators.

The ACCP will be a leader in education using simulation, because we believe that properly used, this technology will vastly improve our effectiveness and, more important, help to make the world a safer and better place for our patients. ■

Creating Healthy Work Environments: Skilled Communication

BY DAVID MAXFIELD

"Nurses must be as proficient in communication skills as they are in clinical skills." This is the conclusion of a blue-ribbon set of scholars convened by the American Association of Critical-Care Nurses (AACN).

The full report, titled AACN Standards for Establishing and Sustaining Healthy Work Environments, prescribes six essential standards:

- Skilled communication
- True collaboration
- Effective decision making
- Appropriate staffing
- Meaningful recognition
- Authentic leadership

JCAHO studies cite communication breakdowns as a major cause in more than two thirds of sentinel events. Why has communication become so critical to the health of health care?

Hospitals are "knowledge organizations." In fact, they are the cutting, bleeding edge of what scholars mean when they describe knowledge organizations. The key to success in knowledge organizations is to get the right information from the right person to the right person at the right time. When communication fails, the team fails. Communication is the lifeblood of a knowledge organization.

In hospitals, you expect the unexpected. Jet fighters landing on carriers at sea and squads of firefighters parachuting into forest fires provide the best models for the communication skills required in hospitals. What they share are frequent unexpected emergencies. In predictable environments, success depends on planning and controlling the future. But on aircraft carriers, in firefighting teams, and in many parts of a hospital, the best don't look at the future beyond about 4 hours. Instead, they focus on managing the complexity of the present—the three planes landing, the explosion of flame, or the multiple complexities of an operating room. Juggling these multiple inputs and outputs in realtime requires a much higher and better level of communication.

How can you improve communication on your team? When communication breaks down, it breaks down in two very different ways. These different kinds of failures require different kinds of solutions.

The first failure mode is unintentional slips and errors. Health care is rife with thousands of examples of these breakdowns: poor handwriting, medications with similar sounding names, and batons dropped between shifts, between units, between professions, or between employees and patients. Computerized physician order entry systems, automated drug dispensing systems, and a variety of hand-off protocols are all examples of actions hospitals are taking to prevent these unintentional slips and errors.

The second failure mode is high-stakes, emotional, differences of opinion. The second failure mode occurs when a person knows something is wrong but fails to speak up. Or, maybe the person speaks up, but it's like touching a land mine. Soon, everyone learns to leave the problem alone. It becomes an unspeakable, an elephant in the room that stomps on patient safety, quality of care, employee engagement, and everything else in its path. The good news about these crucial conversations is that most organizations and most teams suffer from only two or three elephants. If they can address and resolve these two or three issues, then many of their problems will improve.

Find out more about the AACN Standards for Establishing and Sustaining Healthy Work Environments at www.aacn.org/hwe. ■

DAVID MAXFIELD is the director of research for the VitalSmarts consulting firm, which conducted the Silence Kills: The Seven Crucial Conversations for Healthcare study, showing that poor communication and collaboration among health professionals relates significantly to continued medical errors and staff turnover. He is currently leading a series of studies on the role that crucial conversations play in organizations, teams, and relationships. Over the last 25 years, he has taught at Stanford and at Brigham Young University, and he has consulted with more than 200 organizations.

Pulmonary Perspectives

The CFC to HFA Transition for Albuterol

Part 1.
CFCs: The Problem

Albuterol administered by metered-dose inhaler (MDI) is the seventh most commonly used drug in the United States. About 52 million albuterol MDIs are sold in the United States annually for the acute management of asthma and COPD symptoms.

Although albuterol MDIs have many desirable attributes, they do have one serious drawback. They were all originally formulated with chlorofluorocarbons (CFCs) as the propellant. CFC release into the atmosphere results in depletion of stratospheric ozone, which is a serious public health concern.

Over the past 30 years, there has been a highly successful global effort coordinated through the Montreal Protocol to eliminate CFC production and use. The next phase of this campaign is to eliminate MDIs using CFC propellants.

This step is now beginning in the United States with the mandated removal of albuterol MDIs using CFCs from the market by December 2008.

This brief, two-part review will explain why CFCs are a public health problem (Part 1. CFCs: The Problem) and how hydrofluoroalkanes (HFAs) have been developed as a safe, alternative propellant for MDIs (Part 2. HFAs: The Solution, scheduled for March 2007 *CHEST PHYSICIAN*).

ALTHOUGH ALBUTEROL MDIs HAVE MANY DESIRABLE ATTRIBUTES, THEY DO HAVE ONE SERIOUS DRAWBACK. THEY WERE ALL ORIGINALLY FORMULATED WITH CFCs AS THE PROPELLANT.

Evolution of MDIs

Inhalation devices have been used for at least 4,000 years to deliver medications but only became efficient and reliable with the development of the MDI, by Riker Laboratories (now 3M), in 1956.

The MDI concept originated with the daughter of Riker Laboratories' president. She asked if her asthma medication could be put in a spray can, like her hair spray.

The first design used Coca Cola bottles and CFC-12 and CFC-114. Subsequently, a 50-microliter metering valve and a 10-mL vinyl plastic enclosed glass vial, both originally developed for perfume aerosols, were adapted as a prototypical MDI. A plastic mouthpiece, about 3 inches long, with a separately molded nozzle, was used as an adaptor.

The first MDI products were Medihaler-Iso and Medihaler-Epi (both created by Riker Laboratories).

Initial MDIs were plagued by technical problems. The drug formulation for aerosolization was difficult. Drugs were initially dissolved in water and then emulsified with propellant with the aid of surfactants.

Later, work with hydrocortisone acetate led to a suspension of micronized drug made directly in the propellant, with surfactants used as dispersing agents.

Drug formulations tended to be unstable over time. Active drug would cream to the surface and stick to the walls of the vial. Moisture contamination was the cause, which, fortunately, could be controlled by adding desiccants. Products stored upright for any length of time did not function properly, because propellant drained out of the metering valve. Addition of a retaining cup minimized this "loss of prime." Unacceptable leakage rates from MDIs could be corrected by placing an O-ring around the neck of the vial. The O-ring seal tightens as pressure in the vial increases.

By the 1970s, MDI technology had improved sufficiently to support the development of a variety of highly effective bronchodilators (among them albuterol) and corticosteroids, and MDIs became the foundation of inhalation therapy in the United States.

CFCs and the Environment

CFCs are not naturally occurring chemicals. Frederic Swarts pioneered fluorocarbon chemistry in the late 1890s. In 1928, two scientists in the Frigidaire Division of General Motors selected CFC-12 as an ideal refrigerant for home refrigerators.

The use of CFCs for industrial purposes rapidly diversified to foam-blowing agents for polystyrene and polyurethane, industrial solvents and cleaning agents, and multiple other industrial applications.

However, in 1971, James Lovelock found CFC-11 in the atmosphere (Lovelock. *Nature* 1971; 230:379). Although the significance of this finding was not initially understood, as a prescient step, DuPont, a world leader in the manufacture of CFCs, convened an industry seminar in 1972 on the ecology of CFCs. This seminar prompted further research into the fate of CFCs in the atmosphere.

In 1974, Molina and Rowland (*Nature* 1974; 249:810) noted that the worldwide production of various CFCs was probably about 1 million tons per year, with production increasing about 8% each year.

CFC inertness made them appealing for industrial use but also meant that their biologic interaction with the environment was minimal.

CFCs released into the atmosphere had a life cycle of possibly 40 to 150 years. They are not removed by rainfall from the lower atmosphere, because they are relatively insoluble in water. They are also not subject to photolysis at those altitudes, because they are transparent to light wavelengths longer than 2,500 Å.

However, CFCs are metabolized by photolysis in the stratosphere. Light of wavelength 1,750 to 2,200 Å will lead to the photolytic dissociation of CFCs with the release of chlorine. Chlorine, in turn, acts to metabolize ozone.

Molina and Rowland speculated that stratospheric chlorine accumulation derived from CFCs might be an important cause of stratospheric ozone depletion.

The FDA was sufficiently concerned about these findings to specify in 1978 that "any food, drug, device, or cosmetic in a self-pressurized container that contains a CFC propellant is adulterated and/or misbranded in violation of the (Food, Drug, and Cosmetic) act …" This statement was later modified to not apply to essential uses of CFC propellants in MDIs.

Furthermore, new products could be approved with CFCs as propellants, if there were no technically feasible alternatives to the use of CFC propellants and the product provided a substantial health benefit.

Although this step led to a decline in the use of CFCs for aerosols, other industrial applications increased substantially. By 1987, the world production of CFCs peaked at about 1 million metric tons. About 8,000 metric tons (0.8%) of the total were devoted to production of MDIs (D'Sousa. *J Aerosol Med* 1995; 8:S13).

In 1984, scientific concern about the extent of stratospheric ozone depletion increased when British scientists detected a stratospheric ozone hole (*ie*, a complete absence) above Antarctica. In the late 1980s, the Ozone Trends Panel found thinning of the stratospheric ozone layer in the mid-latitudes using NASA satellite technology.

Loss of stratospheric ozone has serious public health consequences. The stratospheric ozone layer, which is found 15 to 25 km above the earth's surface, is transparent to ultraviolet A wavelengths of 320 to 400 nm, completely absorbs ultraviolet C wavelengths of <280 nm, and partially absorbs ultraviolet B wavelengths of 280 to 320 nm.

Ultraviolet B radiation is principally responsible for causing epithelial DNA lesions. Epidemiologic data indicate increasing risk of both melanoma and nonmelanoma skin cancers with cumulative lifetime ultraviolet B exposure. A 10% decrease in stratospheric ozone levels was estimated to cause a yearly increase of 300,000 nonmelanomas and 4,500 melanomas (World Health Organization Fact Sheet 1996; 33).

Both the cornea and the lens absorb ultraviolet B radiation. Photokeratitis has been associated with exposure to ultraviolet B radiation. High cumulative exposures to ultraviolet B radiation significantly increase the risk of all types of cataracts.

Animal and human studies suggest that ultraviolet B exposure suppresses cell-mediated immune responses. The implications of these experimental findings for human disease are not understood.

In 1985, the United States and 26 other nations signed the Vienna Convention, which recognized the potential harmful effects of stratospheric ozone depletion. The parties met again in 1987 and signed the Montreal Protocol, which called for a 50% reduction in the use of ozone-depleting substances, including CFCs, by developed countries, by 1998.

However, concerns about increasing evidence of ozone depletion led the parties at subsequent meetings to amend the Protocol and require developed nations to cease ozone-depleting substances use altogether by 1996. US participation in this Protocol was formalized when the US Congress amended the Clean Air Act in 1990.

At present, 188 countries have signed this Protocol, and international action has been highly successful in reducing use of ozone-depleting substances worldwide.

Conclusion

Recognizing that stratospheric ozone depletion represented a serious public health concern related to CFC release was a critical first step. Gaining international agreement to reduce CFC production was a second step. CFCs were relatively quickly replaced in various industrial processes.

However, development of alternative propellants for use in MDIs was a more complicated process that required cooperative efforts by the pharmaceutical industry and worldwide regulatory agencies. ■

Dr. Gene L. Colice, FCCP
Editor, Pulmonary Perspectives
Professor of Medicine
The George Washington University
School of Medicine
Director, Pulmonary, Critical Care, and
Respiratory Services
Washington Hospital Center
Washington, DC

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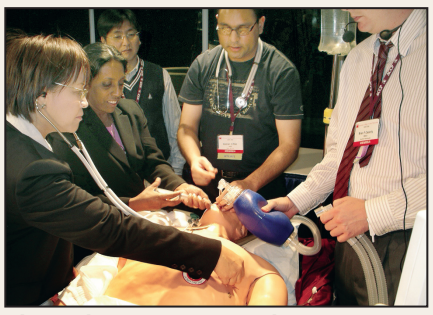
CHEST 2006 WRAP-UP

Simulation Offers Hands-On Learning

BY VIVA JO SIDDALL, MS, MS, RRT
Assistant VP, ACCP Educational Resources

As a part of the ongoing effort to provide innovative education to the ACCP membership, a simulation center was offered during CHEST 2006. Various stations covering acute airway, ultrasonography, bronchoscopy, polysomnography, and critical care offered hands-on educational experiences.

The educational format consisted of written pretests, an educational intervention, a simulation exercise, followed by a peer debrief and, lastly, a written posttest. Simulation-based education can serve as an enhancement to traditional lecture-based offerings that the ACCP has offered. Simulation provides a nonthreatening forum to practice, explore, and fine tune skills and behaviors, which occur in everyday practice or to gain exposure to more complex or less common procedures.



ACCP

Simulation-based education enhanced lecture-based learning at CHEST 2006.

The acute airway station incorporated crew resource management, as well as establishment of a difficult airway. The critical care station focused on the simultaneous care of two patients with various forms of shock; one required intubation and ventilation. Participants were encouraged to employ the current shock guidelines in the care of these simulated patients. The polysomnography station offered instruction on sleep staging, as well as identifying the polysomnographic findings of obstructive sleep apnea and other sleep disorders.

Ultrasonography was proctored by international clinical experts who facilitated image acquisition techniques on standardized patients. Bronchoscopy allowed learners to fine tune skills guided by a pre- and postsimulation checklist.

Upcoming ACCP educational offerings will include simulation: Pediatric Pulmonology course (March 2007), Fellows courses (April 2007), Ultrasonography course (April 2007), and an expanded Simulation Center at CHEST 2007 (October 20-25). ■

The CHEST Foundation Names Lilly Distinguished Scholar in Critical Care Medicine

The Second Eli Lilly and Company Distinguished Scholar in Critical Care Medicine is Dr. Kalpalatha K. Guntupalli, FCCP. Her project will be "Development and Validation of the Educational Materials for Use by the Critical Care Health-care Team (Physician Trainees, Nurses, Respiratory Therapists, Physician Assistants) and Patient/Family for Use in Critical Care Units." During her 3-year tenure as the Distinguished Scholar, she plans to develop and produce the following: (1) an interactive multimedia CD and booklet on "Critical Care Procedures"; (2) an interactive multimedia CD and booklet on teaching patient communication to the house staff; (3) an educational CD and booklet on "Ventilator Waveforms"; and (4) an interactive multimedia CD and booklet on "Patient Education—FAQs in the ICU." ■

ACCP

Dr. Kalpalatha K. Guntupalli, FCCP, receives the award from Dr. W. Michael Alberts, FCCP (left) and Dr. Nicholas Hill, FCCP.

CHEST 2006 WRAP-UP

AMERICAN COLLEGE OF CHEST PHYSICIANS®

'Love, Love, Love Your Lungs'

BY SUE CIEZADLO
Community Outreach Coordinator, The CHEST Foundation

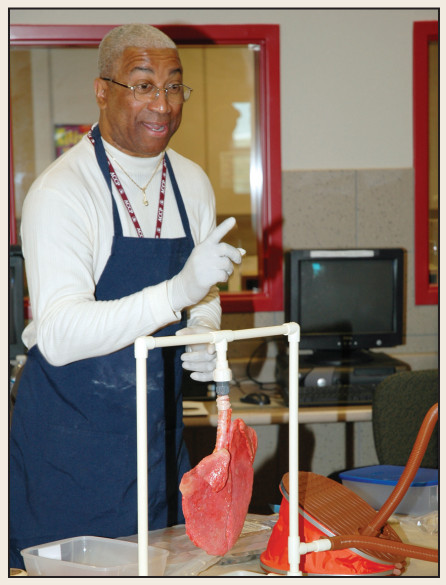
More than 30 enthusiastic ACCP volunteers visited the North Star Elementary School in Salt Lake City, Utah, during CHEST 2006, for the annual CHEST Foundation and ACCP Industry Advisory Council's Community Outreach Event.

The assistant principal, Mrs. Pam Pederson, greeted the volunteers, and the 117 fourth, fifth, and sixth graders, and Ambassadors Group member, Mrs. Susan Kvale, started the program rolling by teaching the children two verses of "Love, Love, Love Your Lungs" to the tune of "Row, Row, Row Your Boat."

Next, the children were divided into groups and proceeded to five different areas for the lesson that is based on the Lung Lessons™ curriculum, which was developed by The CHEST Foundation. Using a laminated diagram of human lungs, a Pig Lungs Education kit (composed of a healthy lung and a diseased lung), and a "Jar of Tar," the children learned about the parts and function of their lungs, the facts about asthma, and the impact that smoking has on their lungs and overall general health. The students received a Love Your Lungs™ wristband and a "Puffree" dog keychain from The CHEST Foundation and a certificate of participation and a pen and pencil from the American Lung Association of Utah. At the end of the lesson, the children enthusiastically signed a large poster entitled, "I Pledge To Never Smoke."

The CHEST Foundation extends its gratitude to the staff and children at the North Star Elementary School, and to the American Lung Association of Utah, the ACCP Industry Advisory Council, and the volunteers from the ACCP and The CHEST Foundation's Ambassadors Group.

Additionally, the ACCP Industry Advisory Council should be recognized for its support and presentation of a $10,000 check to the American Lung Association of Utah at the Making a Difference Awards Dinner. ■

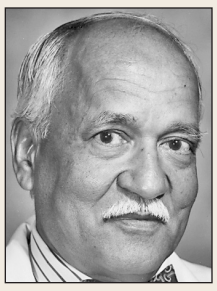


ACCP

Alfred Keith, RRT, teaches students about good lung health.

Newest Master Fellow Honored at CHEST 2006

Dr. Om P. Sharma, Master FCCP, is Professor of Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA. He is world-recognized for his expertise in sarcoidosis and has made significant contributions in the field of interstitial lung diseases.



DR. OM P. SHARMA, MASTER FCCP

A lifelong teacher and mentor and a prolific author, Dr. Sharma has lectured around the world and has an extensive bibliography of journal articles, abstracts, book chapters, and books.

He was a member of the *CHEST* Editorial Board from 1984 to 1990 and has served as an editor to several medical journals, including *Current Opinion in Pulmonary Medicine*. Dr. Sharma has been President of the World Association of Sarcoidosis and Other Granulomatous Disorders since 1999 and enjoys professional affiliations with numerous other organizations.

The Master Fellow title was established in 1980 to honor Fellows of the ACCP who have achieved national or international professional prominence due to their personal character, leadership, eminence in clinical practice, contributions to medical research, or years of outstanding service to the College.

The position of Master is conferred by a majority vote of the ACCP Board of Regents. ■

ACCP Master Fellows

2006: Dr. Om P. Sharma, Master FCCP
2004: Dr. Allen I. Goldberg, Master FCCP
2004: Dr. Paul D. Stein, Master FCCP
2003: Dr. D. Robert McCaffree, Master FCCP
2002: Dr. John G. Weg, Master FCCP
2001: Dr. Dick D. Briggs, Jr., Master FCCP
2001: Dr. Ronald B. George, Master FCCP
2000: Dr. A. Jay Block, Master FCCP
2000: Dr. James E. Dalen, Master FCCP
2000: Dr. Deborah Shure, Master FCCP
1999: Dr. Bart Chernow, Master FCCP
1997: Dr. Farokh E. Udwadia, Master FCCP
1997: Dr. Max Harry Weil, Master FCCP
1996: Dr. Marvin I. Dunn, Master FCCP
1996: *Dr. Shigeto Ikeda, Master FCCP
1996: Dr. Edward C. Rosenow III, Master FCCP
1995: *Dr. Roger C. Bone, Master FCCP
1995: Dr. Thomas L. Petty, Master FCCP
1995: *Dr. Aquiles J. Roncoroni, Master FCCP
1993: *Dr. Antonio Blasi, Master FCCP
1992: Dr. Alfred Soffer, Master FCCP
1980: *Dr. Arthur M. Olsen, Master FCCP
* Deceased

AMERICAN COLLEGE OF CHEST PHYSICIANS®

CHEST 2006 WRAP-UP

International Pulmonary Fellows Mentoring Program 2006

BY DR. LOREN GREENWAY, FCCP

The International Pulmonary Fellows Mentoring Program took place in Salt Lake City during the week prior to the opening of CHEST 2006.

The mentoring program was organized under the direction of the ACCP and was sponsored by Altana Pharmaceuticals. Fifteen international pulmonary fellows from England, Germany, Australia, Belgium, Brazil, Canada, Italy, France, Spain, Netherlands, and Portugal participated.

The experiences that these pulmonary fellows received from their interaction here at Intermountain Healthcare (LDS Hospital) included the following (space constraints do not allow a more exhaustive detailed description):

- Dialogue concerning sleep and hyperbaric medicine (both critical care monoplace and multiplace hyperbaric medicine).
- A tour of our new facility, a 550-bed acute care center being completed at this time.

THE PROGRAM INCLUDED INTERACTIVE DISCUSSIONS WITH INTERNATIONALLY RENOWNED PULMONARY PHYSIOLOGISTS.

- Having time in the new multiplace hyperbaric chamber and interacting with hyperbaricists of international renown.
- Touring two long-term acute care (LTAC) hospitals to discuss ventilator management, specifically that of weaning patients in the long-term care arena.
- Detailed discussions on medical decision support and data-driven protocols.
- Meeting with the leadership of the American College of Chest Physicians.
- Interactive discussion about pulmonary function and physiology and interacting with internationally renowned pulmonary physiologists.
- Lectures on wilderness medicine and practical demonstrations during a hike in one of our beautiful canyons here in Salt Lake City.

This was an exciting process for me, spearheading this mentoring program.

It was a privilege for me to be asked and to be able to participate with these young bright pulmonary fellows.

Their evaluations were exemplary in their nature and flattering in their comments.

I have reflected upon many of the experiences with fondness, and a few individuals have contacted me to develop further fellowship opportunities here in our Pulmonary/Critical Care Division.

It has always been an honor for me to be associated with the ACCP, and I am especially honored to have had the opportunity to organize this mentoring program for the international fellows.

This has been a rewarding professional experience and an excellent educational experience for the fellows. ■

Participating Fellows

Australia: Dr. Andrew Kyoong
Brazil: Dr. Ricardo Teixeira
Belgium: Dr. Laurent Godinas
Canada: Dr. Nicole Drost
France: Dr. Cecile Durand
Germany: Dr. Florian Bornitz, Dr. Timm Greulich
Italy: Dr. Angelo Petroianni, Dr. Giovanna E. Carpagnano
Netherlands: Dr. Bernt van der Blink, Dr. Upama Rai
Portugal: Dr. Maria Teresa Padrao de Brito Camara
Spain: Dr. Isabel Blanco
UK: Dr. Philip Raines, Dr. Danie Watson

Congratulations to These 2006 Winners

CHEST Challenge

Nine teams won spots for the play-offs that took place at CHEST 2006:

- University Hospitals of Cleveland Case Western Reserve University
- Coney Island Hospital
- University of Oklahoma Health Sciences Center
- Hospital of University of Pennsylvania
- Brown University
- University of South Florida
- University of Toronto
- Maimonides Medical Center
- Ohio State University Medical Center

And the winning teams were:

- **1st Place**
  Hospital of University of Pennsylvania, Philadelphia, PA
  Dr. Giora Netzer
  Dr. Nirav P. Patel
  Dr. Chirag V. Shah
- **2nd Place**
  University of Toronto, Toronto, ON, Canada
  Dr. Stephen C. Juvet
  Dr. H.S. Jeffrey Man
  Dr. Mony Punam Singh
- **3rd Place**
  Coney Island Hospital, Brooklyn, NY
  Dr. George N. Gandev
  Dr. Muhammad U. Rehman
  Dr. Julian L. Williams

Supported by grants from AstraZeneca LP (Play-offs) and ALTANA Pharma (Championship).

CHEST Bingo

Attendees visited specified exhibit booths to obtain the letter of a disease state for their bingo cards. Each day, a different disease was sponsored, a drawing was held, and a new prize was awarded. The winners were:

- **Asthma Bingo**
  Dr. Melvin T. Saludes, FCCP
  Wheeling, IL
  Desktop computer
- **COPD Bingo**
  Alfred J. Keith, RRT
  Chicago, IL
  27" TV/DVD combination
- **Sleep Bingo**
  CAPT Joshua M. Sill, MC, USAF
  San Antonio, TX
  Palm® handheld

Supported by ALTANA Pharma US; AstraZeneca LP; Genentech and Novartis; Kos Pharmaceuticals, Inc.; Merck & Co., Inc.; and Schering-Plough.

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

EDUCATION INSIGHTS

Consensus Statement Development: The ACCP Process

BY CARLA HERRERIAS, MPH
Clinical Research Analyst, Health and Science Policy

The ACCP develops two types of policy: evidence-based clinical practice guidelines and consensus statements.

There are fundamental differences between these two types of policies. Evidence-based clinical practice guidelines are developed through a rigorous, systematic review of clinical literature and analysis of the data from these published studies. Recommendations are based solely on the quality of the evidence and follow the ACCP Board of Regents-approved system for grading evidence and recommendations.

Consensus statements, usually developed by ACCP NetWorks, are written documents that represent the collective opinions of a convened panel of clinical experts. The opinions expressed in consensus statements may be derived from a review of the literature. Suggestions incorporated into consensus statements must be differentiated from formal recommendations in clinical practice guidelines.

The following principles apply when developing consensus statements:

1. Consensus statements can issue opinions or suggestion but cannot make recommendations, as these are reserved for clinical practice guidelines.
2. A methods section should be included in the consensus statement document to detail how the literature was reviewed and if any formal or informal method was used to achieve consensus.
3. If questionnaires were used to achieve consensus, these must be validated using appropriate statistical methods.
4. NetWorks or Institutes developing consensus statements should have their topics reviewed and accepted by the ACCP Board of Regents prior to undertaking development.
5. The Editor in Chief of *CHEST* should be notified of the topic and an anticipated completion date. Periodic updates should be provided to the Editor in Chief of *CHEST*. (This applies only if the consensus statement will be submitted to *CHEST*.)
6. The consensus panel chair will be chosen by the NetWork or Institute based upon expertise in the topic area; the chair must be an FCCP.
7. Panel members should be chosen based on clinical and scientific expertise in the topic area, diversity in geographic location, writing skills, and the ability to work appropriately in a group atmosphere.

Consensus can be achieved by a formal process, such as the Delphi Method, or another informal process, whereby the majority of panel members reach agreement. The formal method is preferred. The Delphi Method was developed by RAND Corp (Santa Monica, CA, 1962) and is considered to be the standard for formal consensus achievement.

Consensus statements should be written in a standard format that includes an executive summary; abstract; methods section; text, including opinions and suggestions; and areas for future research. The format should follow that of the *CHEST* Instructions to Authors document found at www.chestjournal.org.

In summary, consensus statements represent a very important part of ACCP policy and may address new and emerging issues for which substantial evidence may not yet be available.

For more information on developing clinical practice guidelines and consensus statements, please go to the ACCP education page at www.chestnet.org/education/index.php. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Mass Casualty Critical Care Allocation of Scarce Ventilator Resources and Ethical Triage of Patients

The severe acute respiratory syndrome (SARS) epidemic of 2002-2003, recent natural disasters, burgeoning concerns regarding intentional catastrophes, and the looming threat of an influenza pandemic have stimulated much recent debate about how to plan for and implement large-scale critical care disaster response.

Daily critical care workforce shortages, tight hospital operating margins, just-in-time purchasing, and expensive critical care medical equipment are some of the major challenges to preparing for mass casualty critical care responses (Daugherty et al. *Curr Opin Crit Care* 2007; 13:51). Even with emergency augmentation of critical care capability, crucial critical care resources may remain overwhelmed by patient need. The ACCP Critical Care Institute (CCI) has convened a task force consisting of key individuals from various public health and private organizations to make recommendations on some of the difficult ethical and management issues involved in the delivery of mass critical care.

In the United States, there are approximately 87,400 ICU beds distributed among 3,581 nonfederal acute care hospitals. These ICUs are usually functioning at near capacity, with small surges requiring temporary shifts of patients to postanesthesia care units, EDs, or other facilities. Such strategies can usually handle a handful of additional critically ill and injured patients. For larger surge needs, the Working Group on Emergency Mass Critical Care provided recommendations that may increase local critical care capability by 100 to 500% (Rubinson et al. *Crit Care Med* 2005; 33:2393). The current ACCP/CCI task force will further define critical care surge strategies for mass casualty events. However, there are plausible situations, such as a severe influenza pandemic, where the number of critically ill patients may far outweigh the additional critical care capability.

Based on the Flu Surge template from the Centers for Disease Control and Prevention (CDC), it is estimated that approximately 15 to 35% of the US population may be affected by pandemic influenza, of which 15% may require ICU level care, and half will require mechanical ventilation.

Average length of stay is estimated to be 10 days in the ICU, which is similar to the average ICU length of stay for a patient with SARS (10.5 days) (www.cdc.gov/flu/pdf/FluSurge2.0_Manual_060705.pdf, accessed December 31, 2006). Hick and O'Lauglin recently published data from a drill using a 10% affected rate and found that there were only 16 additional ventilators available for an anticipated surge of 3,000 patients, of which 210 would need mechanical ventilation in the Minneapolis metropolitan area (Hick et al. *Acad Emerg Med* 2006; 13:223). Exercises such as these have brought disaster preparedness into the critical care arena and highlighted some vital shortfalls in supplies and ICU staffing.

The CDC, Agency for Healthcare Research and Quality (AHRQ), American Association for Respiratory Care (AARC), New York City, Minnesota Department of Public Health, and Canadian Public Health have all published guidelines and recommendations regarding the allocation of scarce resources. The list above offers Web sites for some of the relevant material.

Web Resources

- www.cdc.gov
- www.ahrq.gov
- www.health.gov.on.ca/english/providers/program/emu/pan_flu/pan_flu_plan.html
- www.pandemicflu.gov/plan/states/newyork.html
- www.aarc.org/resources/mass_casualty/index.asp

These recommendations are based on sound ethical principles as follows:
1. Transparency
2. Involvement and accountability for political leadership
3. Fairness—all patients will receive care
4. Autonomy—where individual rights may need to be altered for the greater good

For the equitable delivery of health care during scarce resource allocation, transparency in policy and decision-making needs to occur. Patients need to understand that limitations will occur, and health-care workers will need to mentally prepare themselves for situations in which they may not be able to provide everything possible for their patient. The ethical triage of patients who may not benefit from medical care needs to be discussed and accepted within society and the health-care industry. These ethical discussions regularly occur in the ICU with family and health-care providers regarding

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The Task Force Steering Committee

Lewis Rubinson, MD, PhD
Disaster Medicine Director
Public Health Seattle King County
Seattle, WA
Asha Devereaux, MD, FCCP
Chair, Disaster Response
NetWork-ACCP
Lead Physician-Medical Reserve Corps, SD
Pulmonary and Critical Care Medicine
Sharp Coronado Hospital, CA
Jeff Dichter, MD
Presbyterian Hospital
Director of the Critical Care Service
Albuquerque, NM
James Geiling, MD, FCCP
Chief, Medical Service
Veterans Affairs Medical Center
White River Junction, VT
Associate Professor of Medicine
Dartmouth Medical School
Hanover, NH
Michael M. Bourisaw
Director, ACCP Critical Care Institute
Northbrook, IL

CHEST Physician—Coming in March

- New *CHEST* journal benefits
- Pulmonary Perspectives "The CFC to HFA Transition for Albuterol—Part 2. HFAs: The Solution"
- Ambassadors Group antitobacco efforts
- Important deadlines approaching for CHEST Foundation awards

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the delivery of futile treatments to patients who would not benefit or who are terminally ill. It is intuitive to foresee that this is the environment in which this situation will occur during a pandemic or mass casualty event. These recommendations are anticipated to generate debate, deliberation, discussion, and further research within the pulmonary/critical care community.

Since 9/11, the CDC has invested a great deal of time and energy in maintaining a warehouse of medical supplies, pharmaceuticals, and ventilators (approximately 4,100). States and many hospitals are beginning to mobilize and maintain their own pool of resources to better manage disasters locally. It is hoped that resource allocation and triage decisions will not be necessary if a community is adequately staffed and prepared to face a large number of stricken people. ■

Asha Devereaux, MD, FCCP
Chair, ACCP Disaster Response NetWork
and James Geiling, MD, FCCP
Vice-Chair, ACCP Disaster Response NetWork

Product of the Month

Study or review obstructive sleep apnea through the convenience of this on-demand Webcast. Sleep apnea sessions from the ACCP Sleep Medicine 2006 course are featured to offer the latest clinical information for effective evaluation, diagnosis, and treatment. Up to 1 hour of CME is available for each presentation.

To learn more about obstructive sleep apnea, epidemiology, and pathophysiology and positive airway pressure from the Sleep Medicine 2006 course, visit www.chestnet.org/education/online/webinar/sleep/index.php.

NetWorks: Providing Helpful Information to Chest Physicians

Cultural Diversity

As we approach the end of life, we seek comfort in the traditions and language of our heritage. In palliative care, this presents unique challenges to its principle goal: determining the individual patient's goals of care.

First, remember that our complex preferences incorporate our cultural differences. Individual cultures reflect national origin, religion, country of birth, education, economics, and gender issues.

► **Who Should Make Decisions?** In 2007, "autonomy" is a sacrosanct principle of medical ethics. Patients or other surrogates have the right to determine their treatment. Determine up front who should make decisions when the patient can no longer make them. Although HIPAA has undoubtedly complicated our communication, and privacy is a core value, an inability to communicate is an inability to provide care.

► **How Much Should Be Told and to Whom?** In some cultures, speak the word "cancer" or "death," and you are thought to have caused it. Determine how, how much, and from whom the patient wants to hear.

► **Ask About Customs.** Whatever the tradition, notify the family when death is imminent, to allow them to be present and to guide you in the dying process. We know the medical facts; the family (and sometimes the patient) can guide us in the cultural aspects. Many cultures provide specific traditions to follow. Most patients and families value the opportunity to say "goodbye" and to resolve any unfinished business. In many traditions, patients cannot die until they are at peace. Often this means waiting for someone to arrive or for some event to occur, even if the patient is not conscious.

Death itself, like birth, is the ultimate "life" experience: it is always steeped in tradition and ritual. When we open our minds and freely ask about traditions, we enhance our ability to eliminate the cultural divide that otherwise precludes what we each want for our patients, our families, and, ultimately, for ourselves: excellent end-of-life care.

Dr. Alice Beal, FCCP
Cultural Diversity in Medicine
Steering Committee Member

Clinical Pulmonary Medicine

Does Your Patient Have Osteoporosis?

Even in the absence of other well-known risk factors (thin, female, family history, tobacco abuse, ethanol abuse, Caucasian or Asian ethnicity), pulmonary patients have an increased risk for osteoporosis. Contributors to this are the frequent need for corticosteroid therapy and likelihood of being sedentary. Although somewhat controversial, COPD alone seems to be an important independent risk factor. Prevention of osteoporosis helps avoid other complications in this often chronically ill population.

The Clinical Pulmonary Medicine (CPM) NetWork has a goal for all physicians who treat patients with lung disease to be aware of the potential for osteoporosis. NetWork efforts in this area span several years, and further efforts have continued under the direction of Dr. Nicola Hanania, FCCP. With the assistance of the NetWork Steering Committee and the fellows in his division, Dr. Hanania has developed a survey, which has been sent out to assess awareness of this problem in the pulmonary community. Watch for results of this survey in a future issue of *CHEST Physician*. On the heels of the survey, a Web guide outlining the diagnostic approach and treatment for

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osteoporosis is in the last phases of development and production.

The CPM NetWork plans continued efforts to increase awareness and offer guidance to colleagues in this endeavor.

Suggested Reading

1. American College of Rheumatology. Guidelines for management of glucocorticoid-induced-osteoporosis. Arthritis Rheum 2001; 44:1496-1503
2. Gluck O, Colice G. Recognizing and treating glucocorticoid-induced osteoporosis in patients with pulmonary diseases. Chest 2004; 125:1859-1876
3. LaRosa DF, Apter AJ. Assessing the risk of osteoporosis in patients with asthma and COPD. J Respir Dis 2004; 25:377-384
4. LaRosa DF, Apter AJ. Preventing and managing osteoporosis in patients with asthma and COPD. J Respir Dis 2004; 25:426-430

Home Care

The Home Care NetWork welcomes participation from ACCP members who are academic medical experts, durable medical suppliers, members of patient societies and advocacy groups, as well as those professionals who are also ventilator users. The NetWork is involved in teaching the knowledge, skills, and attitudes required to collaboratively manage patients requiring respiratory assistance (oxygen, mechanical ventilation, and others) beginning in the ICU and continuing through to home.

A project of the NetWork, the Home Ventilation Resource Center, will provide a Web-based resource to assist health-care providers in the provision of home mechanical ventilation. It will include a product matrix in graph-type format, which will reference the type of ventilator, define features, characteristics, and indications for use. Another section, Home Ventilator Management 101, will be a guide to aid in decision-making for patient discharge and treatment plan considerations. A ventilator acquisition checklist will include items needed to utilize ventilators listed in the product matrix. In addition to providing this Web-based resource, the NetWork is redesigning its Web page, www.chestnet.org/networks/home_care, to better illustrate the work that is being done.

The Steering Committee is moving forward to suggest a new name for the NetWork, which would more accurately describe the nature of the patient population and the clinical and academic focus.

Interstitial and Diffuse Lung Disease

NIH-Sponsored Consortium Seeks To Improve Outcomes in IPF

Idiopathic pulmonary fibrosis (IPF) continues to be a burden to patients and their families.

This devastating illness, characterized by progressive lung fibrosis, affects over 100,000 Americans and is usually fatal.

The IPF Network, an 11-center consortium sponsored by the National Institutes of Health, has the objective of designing and conducting well-controlled randomized clinical trials in the treatment of IPF.

Patients are often treated with immunosuppressants, even though the effectiveness of this strategy has not been tested in randomized prospective trials.

The IPF Network aims to evaluate this strategy while also spearheading trials with new agents.

The studies will be placebo-controlled randomized trials targeting patients with early and advanced disease. "Because of the large number of patients required to test the effectiveness of single and combination agents in IPF, the early referral of patients to the Network is essential" explained Network member Dr. Fernando Martinez, FCCP.

For this reason, the IPF Network will emphasize early patient recruitment and easy access to clinical trials.

The IPF Network also intends to generate written guidelines about the diagnosis, treatment, and long-term management of IPF and generate consensus statements that address poorly understood areas related to IPF exacerbations, the usefulness of new imaging techniques, and research needs, among others.

This is important because IPF continues to be an elusive and difficult-to-treat condition.

Patients and referring physicians can gain access to information about the IPF Network and clinical trials in IPF through its Web site at www.ipfnet.org. ■

CHEST Physician Welcomes New Editorial Advisory Board Member

DR. KEITH M. WILLE, FCCP

CHEST PHYSICIAN *is pleased to introduce our readers to the newest member of our Editorial Advisory Board:*

Dr. Keith M. Wille, FCCP, is Assistant Professor of Medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine at the University of Alabama at Birmingham, where he serves as Medical Director of the Lung Transplantation Program. He is boarded in Pulmonary, Critical Care, and Sleep Medicine. Dr. Wille is a past attendee of the ACCP Leadership Development Program and is the ACCP Governor for Alabama. ■

This Month in *CHEST*: Editor's Picks

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

▶ **The Association Between Body Mass Index and Clinical Outcomes in Acute Lung Injury.** *Dr. Amy E. Morris, et al*

▶ **Spirometric Criteria for Airway Obstruction.** *Dr. James E. Hansen, FCCP, et al*

▶ **Age and Sex Differences in Malignant Mesothelioma After Residential Exposure to Blue Asbestos (Crocidolite).** *Dr. Alison Reid, et al*

▶ **Airway Stenting.** *Dr. Mark E. Lund, FCCP, et al*

▶ **Clinical Application of Tissue Doppler Imaging in Patients With Idiopathic Pulmonary Hypertension.** *Dr. Qinyun Ruan; and Dr. Sherif F. Nagueh*

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Gainsharing Slowed by Hospitals' Legal Fears

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

Hospitals are reluctant to offer physicians a portion of the savings generated by reducing clinical costs—a concept known as gainsharing—because of legal fears, D. McCarty Thornton said during an audioconference on gainsharing sponsored by the Integrated Healthcare Association.

"It's clear, I think, that gainsharing is not on the fast track," said Mr. Thornton, a partner with the law firm of Sonnenschein, Nath, and Rosenthal LLP, based in Washington.

In the long run, gainsharing approaches that can save money without impacting patient care are likely to take hold, he said, but first hospitals need clarification from Congress, the Health and Human Services secretary, and the Office of Inspector General about what arrangements are allowed.

In 1999, the HHS Office of Inspector General issued a special advisory bulletin saying that the civil monetary penalty provision of the Social Security Act prohibits most gainsharing arrangements. Under that provision, hospitals are prohibited from making payments to physicians to reduce or limit services to Medicare and Medicaid beneficiaries. The bulletin said that these types of arrangements could also trigger the antikickback provisions of the Social Security Act, which prohibits arrangements used to influence the referral of patients in federal health care programs.

"Historically, the office has been somewhat leery of gainsharing arrangements," said Catherine A. Martin, OIG senior counsel.

Since the 1999 bulletin, the OIG has issued a number of advisory opinions which outline gainsharing arrangements that would be allowable. In general, in order to give the green light to a gainsharing arrangement, the OIG looks for transparency and accountability, quality of care controls, and safeguards against kickbacks, Ms. Martin said.

In order to be transparent, any actions taken to save costs need to be clearly and separately identified and fully disclosed to patients. Hospitals must also put in place controls to ensure that cost savings do not result in the inappropriate reduction of services. OIG officials also want to see ongoing monitoring of quality by the hospital and an independent outside reviewer, Ms. Martin said.

But OIG is not the only regulator that hospitals and physicians need to consider when embarking on gainsharing arrangements, Ms. Martin said. Hospitals and physicians must also keep from running afoul of the Stark self-referral prohibitions, which fall under the purview of the Centers for Medicare and Medicaid Services. Gainsharing arrangements must also meet Internal Revenue Service rules, and hospitals are at risk for private lawsuits, she said.

But the industry is keeping an eye on two demonstration projects that test the gainsharing concept in the Medicare fee-for-service program. Both projects are set to begin this year.

The first project, which is required under the Deficit Reduction Act of 2005, will involve six hospitals and will focus on quality and efficiency in inpatient episodes and during the 30-day postdischarge period. The DRA provision waives civil monetary penalty restrictions that would otherwise prohibit gainsharing.

The second project will focus on physician groups and integrated delivery systems and their affiliated hospitals. The demonstration will include inpatient episodes, as well as the pre- and posthospital care over the duration of the project. This demonstration was mandated the Medicare Modernization Act of 2003.

Participants in both demonstrations will be required to standardize quality and efficiency improvement initiatives, internal cost savings measurement, and physician payment methodology, said Lisa R. Waters, a project officer with the division of payment policy demonstrations at CMS. ■

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