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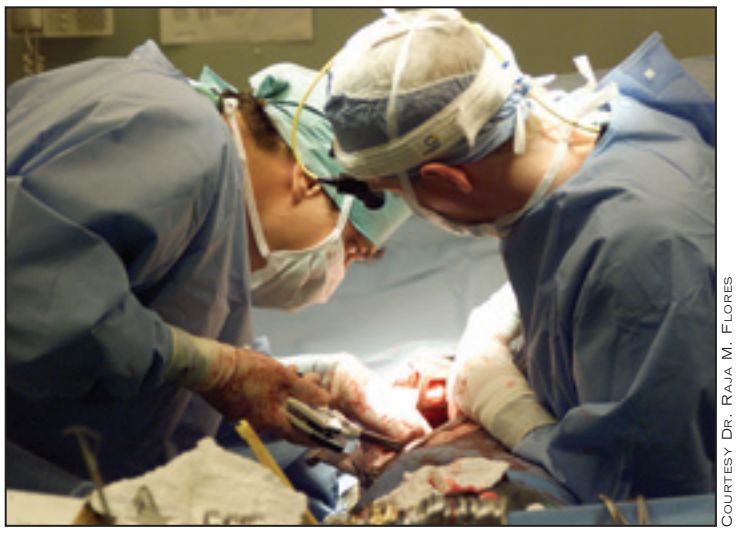

Courtesy Dr. Raja M. Flores

Dr. Raja M. Flores (left) transects the main pulmonary artery of a mesothelioma patient with the assistance of a thoracic fellow.

Mesothelioma Surgery Choice Is Complex

BY MARK S. LESNEY
Elsevier Global Medical News

Surgery for malignant pleural mesothelioma remains a complicated and controversial issue. Thus far, the benefits of surgery vs. nonsurgical treatment have yet to be demonstrated.

Complete resection with surgery alone (R0) appears theoretically unattainable since it is impossible to eradicate residual microscopic disease, regardless of the surgical method used. Hence, most surgical treatment today is coupled with various adjuvant treatments, primarily a trimodality mode with radiotherapy and chemotherapy, according to Dr. Raja M. Flores, FCCP, professor and chief of thoracic surgery, Mount Sinai School of Medicine, New York.

A "curative" surgical procedure remains an elusive goal, and thus the focus of lung surgery for malignant pleural mesothelioma (MPM) has shifted to R1 surgical resection for cytoreduction in the hope of prolonging life, relieving symptoms, and enhancing the effectiveness of adjuvant therapies. This approach has often meant a shift from the more radical extrapleural pneumonectomy (EPP), when possible, to the more lung-sparing pleurectomy/decortication (PD) procedure, according to Dr. Flores (Sem. Thorac. Cardiovasc. Surg. 2009;21:149-53).

EPP involves a radical en bloc resection of the lung, pleura, diaphragm, and pericardium. PD involves resection of the parietal and visceral pleurae, pericardium, and – when necessary – the diaphragm, but it spares the entire lung. Both operations are technically complex and require extensive surgical expertise.

The operative mortality rate of EPP in the literature ranges from 4% to 15%, compared with 1%-5% for PD. In addition, PD has lower morbidity than does EPP. But the two techniques are not interchangeable, according to Dr. Flores. The choice of surgical technique depends on multiple

See **Mesothelioma** • *page 6*

AHA: 'Smokeless' Tobacco Not a Safe Alternative

Products linked to higher disease risk.

BY LORINDA BULLOCK
Elsevier Global Medical News

Smokeless tobacco products are not safer alternatives to cigarette smoking and do not help smokers quit; in addition, their long-term use can increase the risk of fatal heart attack, fatal stroke, and cancer, the American Heart Association warned in a scientific statement.

The researchers, led by Mariann R. Piano, Ph.D., examined several international studies to compare smokeless tobacco use and its health risks. Meta-analysis data involving male Swedish smokers in 1976-2002 showed a significant decrease in cigarette smoking that corresponded with an increase in use of smokeless tobacco products, the investigators wrote (Circulation 2010 Sept. 13 [doi:10.1161/CIR.0b013e3181f432c3).

Despite the decline in cigarette use, concern is warranted. "Smokeless tobacco products are harmful and addictive – that does not translate to a better alternative," Dr. Piano, professor of biobehavioral science at the University of Illinois at Chicago, said in a written statement released by the American Heart Association (AHA).

"Scientists and policy makers need to assess the effect of 'reduced risk' messages related to smokeless tobacco use on public perception, especially among smokers who might be trying to quit," Dr. Piano and her colleagues wrote.

Citing "inadequate evidence of smoking cessation efficacy and safety," the researchers deemed as inappropriate the promotion of smokeless tobacco as a way of reducing smoking-related diseases.

See **AHA** • *page 3*

INSIDE

Rivaroxaban Scores High Marks for DVT

BY BRUCE JANCIN
Elsevier Global Medical News

STOCKHOLM – Fixed-dose rivaroxaban is at least as effective as current standard treatment for acute deep vein thrombosis – and far simpler to use, according to the large phase III EINSTEIN-DVT trial presented in a hotline session at the annual congress of the European Society of Cardiology.

"Results from EINSTEIN-DVT could transform the way physicians treat deep vein thrombosis," Dr. Harry R. Büller predicted in presenting the data.

Congress program chair Dr. Fausto J. Pinto of Lisbon University agreed. Indeed, in a wrap-up session at the close of the conference, he singled out EINSTEIN-DVT as one of the meeting's highlights, citing the trial's likely practice-changing impact on the treatment of a problem that affects 2-3/1,000 adults every year in the Western world.

EINSTEIN-DVT was an open-label study involving 3,449 patients at 253 centers in

See **Rivaroxaban** • *page 7*

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Decline in Smoking Stalled; Secondhand Smoke Down

Virtually all children who live with a smoker have detectable serum cotinine levels.

BY ROBERT FINN
Elsevier Global Medical News

Smoking rates, which declined precipitously in the United States from 1964 to 2004, have remained virtually unchanged since then, according to data from the 2009 National Health Interview Survey. In 2009, 20.6% of adult Americans smoked cigarettes, compared with 20.9% of Americans in 2005, a difference that was not statistically significant.

On the other hand, data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) demonstrated a significant drop in the proportion of nonsmoking Americans aged 3 years and above with detectable levels of serum cotinine, an indication of exposure to secondhand smoke. That rate fell from 52.5% in the 1999-2000 survey to 40.1% in the 2007-2008 survey.

Both studies appeared in the Sept. 7, 2010, issue of the Morbidity and Mortality Weekly Report, published by the Centers for Disease Control and Prevention (MMWR 2010;59:1-6 and 7-12).

In announcing the results at a press briefing, Dr. Thomas R. Frieden, director of the CDC, said that both the tobacco industry and federal, state, and local governments bear the blame for the failure of smoking rates to decline. "The industry has gotten even better at sidestepping laws designed to get people to stop smoking," he said. "They ensure that every cigarette they sell delivers nicotine quickly and efficiently to keep people addicted."

THE INDUSTRY ENSURES THAT 'EVERY CIGARETTE THEY SELL DELIVERS NICOTINE QUICKLY AND EFFICIENTLY TO KEEP PEOPLE ADDICTED.'

In addition, the industry has found ways to sidestep regulations banning the sale of flavored cigarettes, which can encourage children to start smoking, Dr. Frieden said. And while tobacco companies are not permitted to market their products as having lower levels of tar and nicotine, "they continue to deceive smokers with color coding and other subtle and not-so-subtle ways of sending the message that some cigarettes are less deadly than others, when in fact all cigarettes kill equally," he said.

Furthermore, "government is also not doing what it needs to reduce smoking," he charged. "Comprehensive, evidence-based programs are not being widely implemented. Last year, states took in about $25 billion from tobacco taxes and the [Tobacco] Master Settlement Agreement but spent only about $700 million – about 3 cents on every dollar [on tobacco control]. By 2015, if all states funded tobacco control at the CDC recommended level – 15 cents on the dollar of tobacco revenue – there would be an estimated 5 million fewer smokers in this country and that would prevent at least 1 million deaths in the future."


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In 2009, 20.6% of adult Americans smoked cigarettes vs. 20.9% in 2005, a decline that is not statistically significant.

While the NHANES study did find significant overall declines in the proportion of nonsmokers with detectable levels of serum cotinine, that decline did not extend to children who live with a smoker. Virtually all such children – 98.3% – had detectable cotinine levels, compared with 39.9% of children not living with someone who smoked inside the home. For nonsmoking adults, the corresponding figures were 93.4% and 33.4%.

The first study used data collected in 2009 by the National Health Interview Survey, which involved telephone interviews with 27,603 Americans aged 18 years and older. The second study used NHANES data collected from a nationally representative sample of 30,451 nonsmoking Americans aged 3 years and older.

In answer to a reporter's question, Dr. Frieden said, "There's a lot that doctors can do. Doctors can ask every patient if they smoke, and they can advise every patient who does to quit and quit today, and, if not today, then to set a date when they can quit. [Physicians] should also know what services are available in their community to help smokers quit and refer people to quit [telephone] lines. With the Affordable Care Act, tobacco cessation medication will be free of charge, so it should be easier for people to quit smoking in the future."

No disclosures were reported. ■

COMMENTARY

Dr. Philip Marcus, FCCP, comments: Whereas smoking rates have stalled as a percentage of the population smoking, the actual number of people who smoke in the United States has not appreciably declined over time. The dangers of secondhand smoke exposure are well known and can only decline if the number of people who smoke declines.

Why people continue to take up the smoking habit is still hard to comprehend, but increasing the cost of cigarettes may be one way to reduce smoking rates.

IN THIS ISSUE

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CHEST PHYSICIAN

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Smokeless Tobacco Assessed

AHA • *from page 1*

The AHA does recommend nicotine-replacement therapy (nicotine gum or a nicotine-releasing patch placed on the skin) as a safer option for cigarette smokers who want to quit. "Clinical studies have found no increased risk of heart attack or stroke with either type of nicotine replacement therapy," the AHA said in the written statement.

Meta-analysis data in the AHA scientific statement indicated that smokeless tobacco use was associated with an increased risk of heart disease (relative risk 1.12) (Int. J. Epidemiol. 2007;36:789-804). In addition, a subanalysis of INTERHEART (a study of 15,152 cases of first myocardial infarction in 52 countries) showed that tobacco chewers had a significantly increased risk of first myocardial infarction (odds ratio 2.23), compared with those who never used tobacco. Two other meta-analyses indicated that smokeless tobacco use was also associated with an increased risk of fatal stroke (RR 1.42 and 1.40).

The researchers explained that, like cigarettes, smokeless tobacco (ST) products still contain nicotine of varying concentrations, as well as a number of carcinogens that are just as harmful. Cigarettes and oral snuff have similar amounts of nicotine, while chewing tobacco appears to have "somewhat lower" amounts compared with cigarettes, Dr. Piano and her colleagues wrote.

"Even though certain manufacturing techniques are used to reduce the level of these compounds in some products, they remain present in substantial concentrations in ST products, including Swedish snus," they said.

In a comparison of nicotine concentration between three types of smokeless tobacco products (chewing tobacco, dry snuff, and moist snuff) and cigarettes sold in the United States, all of the smokeless tobacco products had nicotine concentrations that were similar to cigarettes with the highest concentrations. (See box.)

Dr. Piano and her colleagues found that unlike the aforementioned Swedish cohorts, there was no reduction in smoking rates among people in the United States using smokeless tobacco. (The sale of smokeless tobacco products such as moist snuff or snus is banned in most of the European Union, with the exception of Sweden and Norway.)

In the United States about 8.1 million people are users of smokeless tobacco. Its use is more prevalent in men than women, and people aged 18-25 years are the most likely to use smokeless tobacco, the researchers wrote. According to the study, educational background and socioeconomic status coincided with smokeless tobacco use. High prevalence was reported among people with a high-school diploma as their highest level of education, and among people who live in southern states and rural areas. Blue-collar workers and service or labor workers, as well as the unemployed, were among the most regular users of smokeless tobacco products. Native Americans have the highest prevalence of use (9%), followed by whites (5.8%), African Americans (1.9%), Hispanics (0.8%), and Asian Americans (0.6%).

It also appears that while U.S. chewing tobacco use has been on the decline since the 1980s, snuff consumption and production are increasing, the researchers said.

Dr. Piano reported that she received a grant from the National Institutes of Health. The researchers reported no relvant conflicts of interest. ■

COMMENTARY

Dr. Philip Marcus, FCCP, comments: Tobacco is tobacco. For smokers trying to quit, effective smoking cessation products exist and include nicotine-replacement therapy, bupropion, and varenicline. The use of smokeless tobacco has not been found to be effective nor protective against the other known adverse effects of tobacco. In addition, the use of electronic cigarettes has not been shown to be effective as a smoking cessation aid for smokers trying to quit.

Nicotine Concentrations in Smokeless Tobacco Products and Cigarettes Sold in the United States

	Chewing tobacco* (mean range)	Dry snuff* (mean range)	Moist snuff* (mean range)	Cigarettes High	Cigarettes Moderate	Cigarettes Low
Nicotine (mg/g)	9.9 (3.41-39.7)	16.8 (10.5-24.8)	12.6 (4.7-24.3)	9.5-13.4	8.9-11.4	7.2-11.5

*Smokeless products sold in Massachusetts in 2003.
Source: Circulation

Elsevier Global Medical News

COPD With Frequent Exacerbations a Distinct Phenotype

BY MARY ANN MOON
Elsevier Global Medical News

It appears that chronic obstructive pulmonary disease with frequent exacerbations constitutes a distinct phenotype of the disease that can occur at mild, moderate, or severe levels of illness, according to results from a dta analysis.

The frequency of COPD exacerbations appears to be relatively stable over time, and a distinct subgroup of patients

THE BEST WAY TO PREDICT EXACERBATIONS WAS TO ASK HOW MANY THE PATIENT HAD IN THE PRECEDING YEAR.

appears to be prone to frequent (two or more times per year) exacerbations year after year, said Dr. John R. Hurst of University College London Medical School and his associates.

"Despite the importance of exacerbations, we know relatively little about their incidence, their determinants, and their effects in patients with COPD at various levels of severity," the investigators noted. They used data from a large observational study – the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) – to examine exacerbation frequency.

The international ECLIPSE study included 2,138 patients aged 40-75 years with a history of 10 or more pack-years of smoking, a forced expiratory volume in 1 second (FEV_1) of less than 80% of predicted value, and an FEV_1-to-forced vital capacity ratio of 0.7 or less after use of a bronchodilator.

The participants had a wide range of COPD severity, and were evaluated at baseline, 3 months, and 6 months, and at 6-month intervals thereafter for 3 years.

Although exacerbations tended to increase with increasing disease severity, patients also tended to fall into and remain in one of two groups: those with infrequent exacerbations (0 or 1 per year) or those with more frequent exacerbations.

For example, 1,187 patients had infrequent exacerbations in the first year of the study, and 987 (83%) of them also had infrequent exacerbations in the second year. Another 492 patients had frequent exacerbations in year 1, and 296 of them (60%) had frequent exacerbations in year 2 as well.

"Thus, exacerbation frequency in the first year had a sensitivity of 60% and a specificity of 83%" for predicting the frequency in the second year, Dr. Hurst and his colleagues said (N. Engl. J. Med. 2010;363:1128-38).

Similarly, 994 (84%) of the 1,187 patients with infrequent exacerbations also had infrequent exacerbations during the third study year, while 276 (56%) of the 496 with frequent exacerbations also had frequent exacerbations during the third study year.

And 210 (71%) of those with frequent exacerbations during years 1 and 2 went on to have frequent exacerbations in year 3, while 388 (74%) of those who had no exacerbations during years 1 and 2 also had no exacerbations in year 3.

The easiest and most accurate way of predicting a patient's susceptibility to exacerbations was simply to ask that patient how many exacerbations they had had the preceding year, the researchers said.

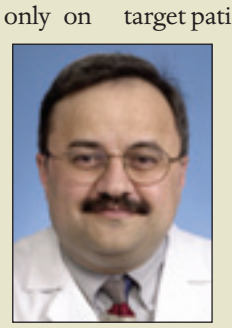
A full 22% of the patients with moderate COPD were found to have frequent exacerbations, which is an important observation, considering that such patients had relatively mild disease according to FEV_1 criteria, they noted.

Conversely, 29% of the subjects who had very severe COPD appeared to have some resistance to exacerbations, since they experienced none or very few exacerbations during the study.

The ECLIPSE study was funded by GlaxoSmithKline. Dr. Hurst and his associates reported ties to numerous pharmaceutical companies. ■

COMMENTARY

Dr. Nicola Hanania, FCCP, comments: This study sheds light on yet another important phenotype of COPD. For many years we focused only on the "pink puffers" and the "blue bloaters" of this disease. We now realize that these two "classic" phenotypes are not the only ones that exist, and we need to become aware of other clinically important faces of COPD. The current study results reveal that an "exacerbator" phenotype can indeed be identified that is independent of disease severity. The observation that one or more exacerbations in the preceding year increases the risk of subsequent exacerbations has significant therapeutic implication, as it leads us to target patients belonging to this phenoearly with pharmacologic and nonpharmacologic interventions. However, many patients fail to recognize exacerbations when they occur and therefore underreport them. It is thus imperative that clinicians educate patients with COPD about the signs and symptoms of such episodes so that they recognize them and report them if they occur.



Quick Test Identified Rifampin-Resistant TB

BY MARY ANN MOON
Elsevier Global Medical News

An automated assay designed for use in Third World regions rapidly and accurately detected *Mycobacterium tuberculosis* infection and resistance to rifampin, according to a report published online.

In a multicenter, prospective trial in South Africa, Peru, India, and Azerbaijan involving 1,730 patients suspected of having TB, the Xpert MTB/RIF correctly identified 72% of patients whose sputum smears were negative, as well as 98% of those with positive smears. It also correctly identified 98% of rifampin-resistant bacteria and 98% of rifampin-sensitive bacteria, said Dr. Catharina C. Boehme of the Foundation for Innovative New Diagnostics (FIND), Geneva, and her associates.

"Only a small fraction" of patients worldwide with drug-resistant TB currently has access to sufficiently sensitive diagnostic testing and drug-susceptibility testing, Dr. Boehme noted, because of the complex technologies required for mycobacterial culture and nucleic-acid amplification (N. Engl. J. Med. 2010 Sept. 1 [doi:10.1056/NEJMoa0907847]).

"Globally, ineffective tuberculosis detection and the rise of multidrug resistance and extensively drug-resistant TB have led to calls for dramatic expansion of culture capability and drug-susceptibility testing in countries in which the disease is endemic," Dr. Boehme and her colleagues noted. "Unfortunately, the infrastructure and trained personnel required for such testing are not available except in a limited number of reference centers, and results of testing are often not available for at least 4 months, which dramatically reduces its clinical utility."

FIND developed the new assay to address those needs. FIND also designed, supervised, and sponsored the study evaluating the assay's performance.

The Xpert MTB/RIF kit includes a disposable plastic cartridge that contains all the reagents needed for bacterial analysis, nucleic acid extraction, PCR amplification, and amplicon detection. The only manual step is the "nonprecise" addition of a bactericidal buffer to sputum before transferring the sample to the cartridge. Because the cartridge is never reopened, there is little chance of amplicon contamination, the investigators noted. In addition, the sputum is inactivated at the same time it is liquified, thus making a biosafety cabinet unnecessary.

The cartridge is then inserted into the GeneXpert device, which delivers test results within 2 hours. Relatively unskilled health care workers at all the study locations became proficient in the assay's use after brief training. Data from a separate study confirm that the assay generates no infectious aerosols, which obviates the need for laboratories equipped for advanced biosafety.

Of the 1,462 patients (4,386 sputum samples) assessed, 567 patients had smear-positive and culture-positive TB; 174 had smear-negative but culture-positive TB; 105 had clinically defined but smear-negative, culture-negative TB; and 616 had no clinical, smear, or culture evidence of TB. The remaining 268 patients were excluded from the study for a variety of reasons, including 103 who had an inadequate number of sputum samples and 10 who had an inadequate volume of sputum samples.

Overall sensitivity of the device in patients with culture-positive TB was 97.6%, with no significant variation in performance across study sites.

Sensitivity was 99.8% for smear-positive and culture-positive cases, and 90.2% for smear-negative but culture-positive cases. The assay was specific in 604 of the 609 patients who proved not to have TB (99.2%).

In addition, "the MTB/RIF test correctly detected rifampin resistance in 209 of 211 patients (99.1% sensitivity)" and correctly identified rifampin susceptibility in all 506 patients who had it (100% specificity).

It is not yet known whether the results can be replicated in settings where temperature and electricity supply will be more variable. "Large-scale projects to show the feasibility and effect of MTB/RIF testing at such sites are under way," they added.

The study was designed and supervised by the sponsor (and maker) of the Xpert MTB/RIF, FIND, with additional development support provided by the National Institutes of Health, Cepheid, and the Bill and Melinda Gates Foundation. The investigators reported no additional disclosures. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments:

This report on the development of the Xpert MTB/RIF provides encouraging information regarding enhanced ability to rapidly confirm suspected tuberculosis in Third World regions where traditional methods are limited. This technology also allows rapid detection of rifampin resistance. Although the results need confirmation in other clinical settings, this diagnostic assay appears to have promise in an area of significant need.

Influenza Mortality Varies Widely Across Seasons

Range of 1.4-16.7 deaths per 100,000 persons seen.

BY DIANA MAHONEY
Elsevier Global Medical News

Annual estimates of influenza-associated deaths from 1976 to 2007 varied substantially by season, influenza virus type, underlying cause of death, and age group, according to revised statistical models, the Centers for Disease Control and Prevention reported in its Morbidity and Mortality Weekly Report.

The "incredible variation" indicates that using a single, average estimate insufficiently communicates the mortality burden of influenza, Dr. David Shay, medical officer with the CDC's National Center for Immunization and Respiratory Diseases, said in a media briefing.

With a low of 3,349 estimated deaths in 1986-1987 and a high of 48,614 deaths in 2003-2004, the estimated annual rate of influenza-associated deaths in the United States from 1976 to 2007 ranged from 1.4 to 16.7 deaths per 100,000 persons, according to the new models, which update the CDC's previously published estimates for 1976-2003 and include new data from 2006-2007.

Because of the wide variability across influenza seasons, "it is relatively meaningless to try to summarize [influenza burden] with one number," Dr. Shay stressed.

For this reason, the CDC advises quantifying influenza-associated deaths in the context of circulating virus strains and underlying causes of death among age groups. Toward this end, the influenza-associated mortality estimates in the CDC's revised models are provided for three age groups (younger than 19 years, 19-64 years, and 65 years or older) and for two categories of underlying cause of death codes: pneumonia and influenza causes and respiratory and circulatory causes.

For pneumonia and influenza causes, the respective estimated annual average of influenza-associated deaths and the rate of influenza-associated deaths per 100,000 people were 6,309 and 2.4 for the U.S. population overall; 97 and 0.1 for persons younger than 19 years; 666 and 0.4 for adults age 19-64 years; and 5,546 and 17.0 for adults 65 years and older, the report states.

For deaths with underlying respiratory and circulatory causes, the respective estimated number and rate of influenza-associated deaths per 100,000 were 23,607 and 9.0 for the United States overall; 124 and 0.2 for people younger than age 19 years; 2,385 and 1.5 among adults age 19-64 years; and 21,098 and 66.1 among adults age 65 years and older (MMWR 2010;33:1057-62).

For both causes, "the average mortality rates for the 22 seasons during which influenza A(H3N2) was a prominent strain were 2.7 times higher than for the nine seasons that it was not," the authors reported. "The average annual number of influenza-associated deaths during influenza A(H3N2) prominent seasons was 7,722 for pneumonia and influenza causes and 28,909 for respiratory and circulatory causes, compared with 2,856 deaths for pneumonia and influenza causes and 10,648 deaths for respiratory and circulatory causes in seasons in which it was not."

The findings represented in the revised model are limited by several factors, including the failure to account for co-circulating pathogens such as respiratory syncytial virus; the possibility that changing virus surveillance data may reduce the relevance of comparing estimates over time; and the possibility that the increase in the number of adults older than age 65 years during the study period could have contributed to an increase in influenza-associated mortality, according to the authors. Also, because the models rely on national death certificate data through 2007, preliminary estimates of 2009 influenza A(H1N1)–associated deaths are not comparable, they wrote. ■

FDA: Tigecycline Not Advised For Serious Infections

Alternatives to tigecycline "should be considered" when treating patients with serious infections because the intravenous antibiotic has been associated with increased mortality in this population, according to a safety alert issued last month by the Food and Drug Administration.

In a pooled analysis of 13 clinical trials, treatment with tigecycline (Tygacil) was associated with increased mortality when compared with other antibiotics, according to the FDA.

The higher risk was seen "most clearly" in patients with ventilator-associated pneumonia (VAP): 19.1% of those treated with tigecycline died, vs. 12.3% of those treated with other antibiotics. Tigecycline is not approved for this condition.

Mortality was also increased in patients treated with tigecycline for complicated skin and skin structure infections (cSSSI) and complicated intra-abdominal infections (cIAI) – both approved indications – and diabetic foot infections – an unapproved indication – compared with other antibiotics.

In patients with cSSSI, 1.4% of those treated with tigecycline died, vs. 0.7% of those who received other antibiotics. For cIAI, the mortality rates were 3.0% and 2.2%, respectively; and for diabetic foot infections, the mortality rates were 1.3% and 0.6%, respectively.

The notice is available at www.fda.gov/Drugs/DrugSafety/ucm224370.htm.

—Elizabeth Mechatie

This Month in *CHEST*: Editor's Picks

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

▶ **Combined Endoscopic-Endobronchial Ultrasound-Guided Fine-Needle Aspiration of Mediastinal Lymph Nodes Through a Single Bronchoscope in 150 Patients With Suspected Lung Cancer.** *By Dr F. J. F. Herth, et al.*

▶ **Transbronchial and Transesophageal Fine-Needle Aspiration Using an Ultrasound Bronchoscope in Mediastinal Staging of Potentially Operable Lung Cancer.** *By Dr B. Hwangbo, et al.*

▶ **Respiratory Viruses in Adults With Community-Acquired Pneumonia.** *By Dr D. Lieberman, et al.*

▶ **Real Prevalence of Pulmonary Right-to-Left Shunt According to Genotype in Patients With Hereditary Hemorrhagic Telangiectasia: A Transthoracic Contrast Echocardiography Study.** *By Dr M.W. F. van Gent, et al.*

▶ **Safety of Uninterrupted Anticoagulation in Patients Requiring Elective Coronary Angiography With or Without Percutaneous Coronary Intervention.** *By Dr E. Jamula, et al.*

▶ **The New Local Coverage Determination Criteria for Adherence to Positive Airway Pressure Treatment: Testing the Limits?** *By Dr M. S. Aloia, et al.*

POINT/COUNTERPOINT

▶ **Efficacy of Extracorporeal Membrane Oxygenation in 2009 Influenza A(H1N1): Sufficient Evidence?**
Point: By Dr P. Park, et al. Counterpoint: By Dr A. H. Morris, et al.

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October Lessons

▶ **Pain Management in the ICU: Essentials for the Intensivist.** *By Dr C. Spencer Yost; and Dr Michael A. Gropper, FCCP*

▶ **Approaching Glucose Management in the ICU.** *By Dr Shyoko Honiden, MSc*

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PCCSU
PULMONARY, CRITICAL CARE, SLEEP UPDATE

NETWORKS
Transplant, Script Theory, Bronchoscopy

Transplant

The Transplant NetWork has been involved in many projects over the last few years that are currently in different stages. The survey on Barriers to Palliative Care has been sent to the membership of the Transplant NetWork and the Pulmonary Council of the International Society for Heart and Lung Transplantation. The chair of this project, Dr Lianne Singer, is in the process of analyzing the data and compiling the results. The second project is the "Consensus Statement on the Management of the Organ Donor." This effort has been done in collaboration with many other societies, and it is in the final stages of preparation for publication in *Critical Care Medicine*. Many members of the NetWork have participated in the project. The third project deals with medical complications (noninfectious and nonrejection) after lung transplantation. It has been approved and is being circulated to the steering committee (and then to the NetWork membership) for further ideas in order to reach its final form. A consensus statement is being considered. Another project being considered is the creation of a working group to study variations on the diagnosis of bronchiolitis obliterans syndrome (BOS). There are definitions for its diagnosis (Estenne et al. *J Heart Lung Transplant*. 2002;21[3]:297); however, different experts can sometimes have differing opinions for individual patients. In addition, BOS needs to be diagnosed prospectively for clinical trials and management but can only be diagnosed retrospectively with great confidence. We will keep our NetWork and the ACCP membership updated on these projects.

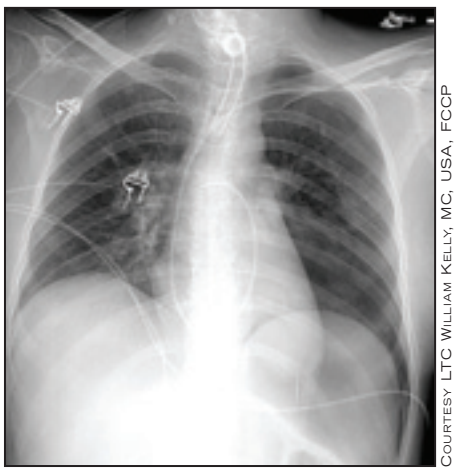
Dr Denis Hadjiliadis, MHS, FCCP
Vice-Chair

Affiliate

CHEST 2010: The Right PreSCRIPTion for Learning

Script theory postulates that physicians in clinical practice apply prestored knowledge sets (or "scripts") to understand a situation and then either accept or reject their hypothesis when presented with additional information (Charlin et al. *Teach Learn Med*. 2000;12[4]:189). The scripts of experienced clinicians vary to a degree, but essential elements are similar, and students (including residents, fellows) can be measured against this standard (Fournier et al. *BMC Med Inform Decis Mak*. 2008;8[May 6]:18). A script concordance test measures how well your answer agrees, or is in concordance with, a group of experts.

Vignette: You are called to see a 57-year-old critically ill patient with sudden-onset respiratory distress and hypoxia. You suspect pulmonary embolism [=hypothesis], and then the pictured radiograph becomes available [=new information]. Is your diagnosis more likely, less likely, or unchanged? (See answer at end.)



Courtesy LTC William Kelly, MC, USA, FCCP

This patient had an initial diagnosis of PE. After viewing this radiograph, would you change your diagnosis?

The CHEST 2010 meeting's core learning program, essential updates, and other resources will help you build and refine your personal bank of scripts. Some proudly sponsored by the Affiliate NetWork include:

Monday–Wednesday, 8:00 AM: CHEST Challenge Play-offs. Test yourself as you cheer for fellows from around the country as they compete in this "Jeopardy" game-show-style competition of pulmonary/critical care/sleep knowledge.

Monday: "Chest CT for the Pulmonologist – Anatomic Correlation, Interpretation, and Case Review"

Tuesday: "Lung Histopathology Review: Preparation for Boards, Preparation for Practice"

Wednesday: "Critical Care Radiology: Indications, Interpretation, and Case Review for the Intensivist" and "Academic vs Private Practice: Which To Choose and What To Look for in the Contract"

With all of this script enhancement going on, don't forget your lunch. Affiliate members (fellows-in-training programs) have a free lunch Monday during which they will hear about "Leadership Styles." And last but not least, mingle and relax in the Lung Health Lounge. There will be special group discussions for fellows on contract negotiations and pursuing careers in private practice or academic medicine, but the Lung Health Lounge will be open to all members to facilitate your networking.

Answer: LESS LIKELY. A left pneumothorax is shown. In addition to the lateral white pleural line, there is a "deep sulcus" sign due to air overlying the anterior pleural reflection as can be seen in supine patients. The radiograph in pulmonary embolism may be normal or show nonspecific findings, including atelectasis, pleural effusion, elevated hemidiaphragm, or a peripheral infiltrate.

LTC William Kelly, MC, USA, FCCP
Chair

Interventional Chest/Diagnostic Procedures

Bronchoscopy is one of the most common procedures performed by chest physicians. The procedure may be uncomfortable, with most patients expressing fear of pain or discomfort and anxiety about complications. There are many examples of the lack of standardization in our daily practice. A pulmonologist at a university hospital routinely gives atropine before bronchoscopy to decrease secretions and dilate the airway, while a colleague at the VA believes that anticholinergic agents are ineffective. Another performs a bronchoscopy on the inpatient ward with topical lidocaine only, while a colleague at another hospital performs bronchoscopy under deep sedation with propofol. Similarly, while one physician prefers nebulized lidocaine 4% for topical anesthesia, another utilizes an atomized solution of tetracaine 1%.

The ACCP Interventional Chest/Diagnostic Procedures NetWork has embarked on the development of a consensus statement (CS) on the use of topical anesthesia, analgesia, and sedation during flexible bronchoscopy based on the best current available data. This CS addresses issues such as performing bronchoscopy with or without sedation, using anticholinergic agents prebronchoscopy, and choosing among various agents and modalities for topical anesthesia, sedation, and analgesia. It is important to realize that a CS represents the collective opinions of a convened expert panel derived by a systematic approach with a traditional literature review as outlined by the ACCP Health and Science Policy Committee recommendations. A CS is not the equivalent of evidence-based practice guidelines and should not be used for performance measurements but rather as a summary of current knowledge and a forum for discussion. ■

Dr Momen M. Wahidi, MBA, FCCP
Vice-Chair

Mandatory Flu Shots Urged for Health Workers

BY JANUARY W. PAYNE
Elsevier Global Medical News

All health care workers should be vaccinated annually against influenza, and doing so should be a condition of new or continued employment, according to a position paper from the Society for Healthcare Epidemiology of America.

This is the first time the organization has recommended mandatory vaccination of all health care workers; and its position was also endorsed by the Infectious Diseases Society of America.

"I am very hopeful that this guideline will encourage the adoption of more mandatory policies at all health care institutions," said Dr. Neil Fishman, president of SHEA and director of health care epidemiology and infection control for the University of Pennsylvania Health System, Philadelphia.

'Influenza vaccination of health care providers is a professional and ethical obligation.'

DR. FISHMAN

A variety of vaccinations already are required at health care facilities, including measles, mumps, and rubella, and some facilities also require vaccination against chickenpox, pertussis, and hepatitis B. "So there are precedents for having vaccines as a condition of employment," Dr. Fishman said.

The hope is that SHEA's new recommendation – published Aug. 31 in the journal Infection Control and Healthcare Epidemiology – will improve the current influenza vaccination rates for health care workers, which now hover in the 30%-40% range, Dr. Fishman said. The recommendation applies to all workers, students, and volunteers in all health care facilities, regardless of whether they have direct patient contact.

Under the SHEA position paper, the only exceptions to the mandatory vaccination policy would be for medical reasons, such as a severe allergy to eggs.

The Centers for Disease Control and Prevention currently recommends that all health care professionals get an annual influenza vaccine and that health care facilities provide the vaccine to its workers with a goal of vaccinating 100% of staff.

Some health facilities and systems already require influenza vaccination as a condition of employment. The University of Pennsylvania Health System, where Dr. Fishman works, has required flu vaccination for its workers since 2009.

Researchers at the Virginia Mason Medical Center, Seattle – believed to be the first in the country to institute mandatory influenza vaccination for its health care workers in 2005 – recently studied their institution's efforts to improve influenza vaccination rates.

They found that in the first year after the mandatory requirement was put in place, 97.6% of the facility's 4,703 health care workers were vaccinated, followed by adherence rates of more than 98% in the following 4 years. Less than 0.7% of the center's workers were exempted from vaccination for medical or religious reasons, and less than 0.2% refused vaccination or left employment (Infect. Control Hosp. Epidemiol. 2010;31:881-8).

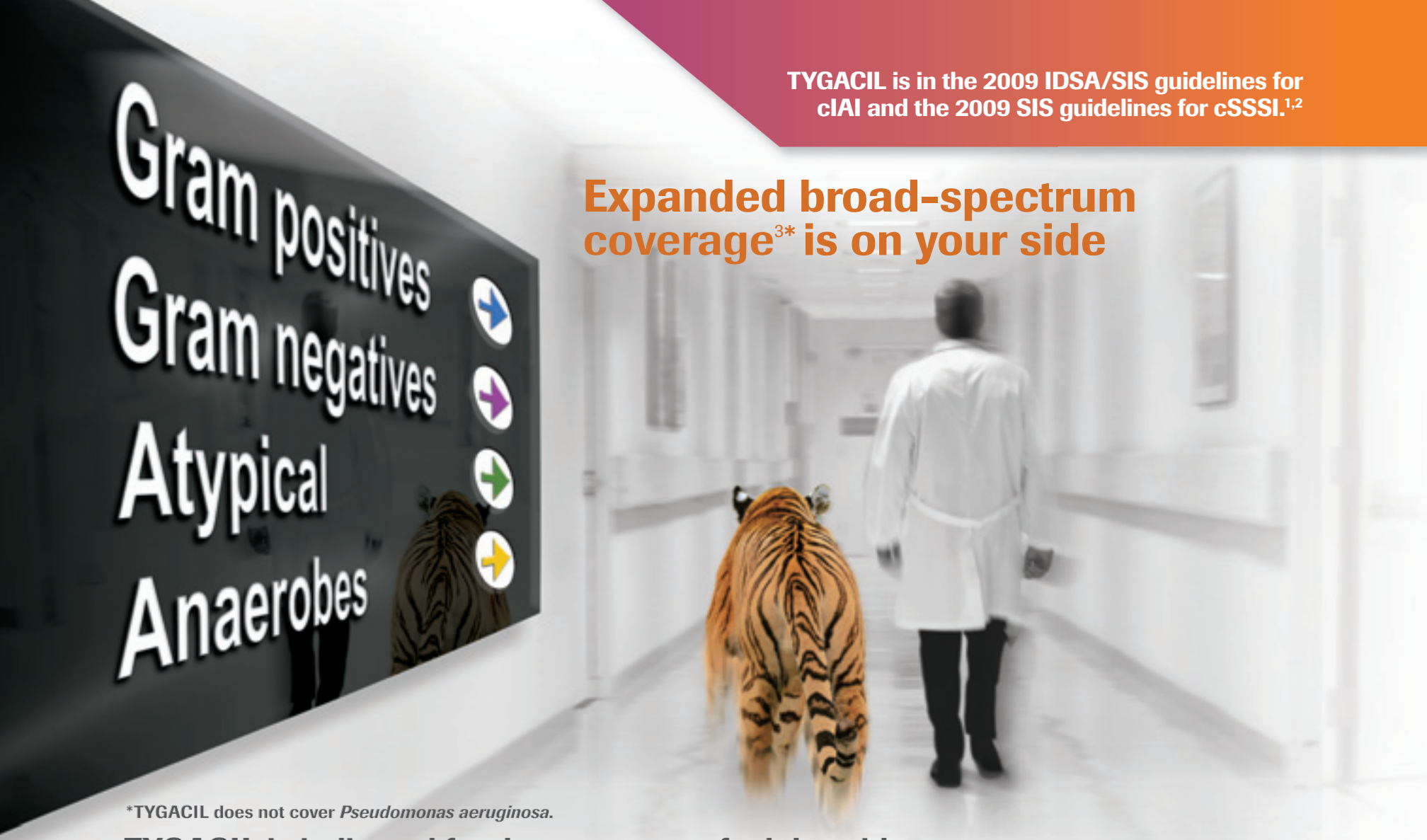
"Influenza vaccination of health care providers is a professional and ethical obligation … to prevent the spread of influenza," Dr. Fishman said.

Dr. Fishman reported no conflicts of interest. The authors of SHEA's position paper reported having served as consultants for or having received honoraria from various companies that make vaccines, influenza diagnostics, and pharmaceuticals. ■

COMMENTARY

Dr. Mark Metersky, FCCP, comments: Hospitals and states that have tried to institute mandatory influenza vaccination for health care workers have faced significant resistance, generally based on ignorance and encouraged by antivaccination fringe groups. This position paper will provide much-needed ammunition for those attempting to institute mandatory vaccination policies.

TYGACIL is in the 2009 IDSA/SIS guidelines for cIAI and the 2009 SIS guidelines for cSSSI.[1,2]



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*TYGACIL does not cover *Pseudomonas aeruginosa*.

TYGACIL is indicated for the treatment of adults with:

- **Complicated skin and skin structure infections** caused by *Escherichia coli, Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus agalactiae, Streptococcus anginosus* grp. (includes *S. anginosus, S. intermedius*, and *S. constellatus*), *Streptococcus pyogenes, Enterobacter cloacae, Klebsiella pneumoniae*, and *Bacteroides fragilis*
- **Complicated intra-abdominal infections** caused by *Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus anginosus* grp. (includes *S. anginosus, S. intermedius*, and *S. constellatus*), *Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Clostridium perfringens*, and *Peptostreptococcus micros*
- **Community-acquired bacterial pneumonia** caused by *Streptococcus pneumoniae* (penicillin-susceptible isolates), including cases with concurrent bacteremia, *Haemophilus influenzae* (beta-lactamase negative isolates), and *Legionella pneumophila*

Important Safety Information

- TYGACIL is contraindicated in patients with known hypersensitivity to tigecycline
- Anaphylaxis/anaphylactoid reactions have been reported with nearly all antibacterial agents, including tigecycline, and may be life-threatening. TYGACIL should be administered with caution in patients with known hypersensitivity to tetracycline-class antibiotics
- Isolated cases of significant hepatic dysfunction and hepatic failure have been reported in patients being treated with tigecycline. Some of these patients were receiving multiple concomitant medications. Patients who develop abnormal liver function tests during tigecycline therapy should be monitored for evidence of worsening hepatic function. Adverse events may occur after the drug has been discontinued
- The safety and efficacy of TYGACIL in patients with hospital-acquired pneumonia have not been established
- **An increase in all-cause mortality has been observed across phase 3 and 4 clinical studies in TYGACIL-treated patients versus comparator-treated patients. The cause of this increase has not been established. This increase in all-cause mortality should be considered when selecting among treatment options**
- **TYGACIL may cause fetal harm when administered to a pregnant woman**
- **The use of TYGACIL during tooth development may cause permanent discoloration of the teeth.** TYGACIL should not be used during tooth development unless other drugs are not likely to be effective or are contraindicated
- Acute pancreatitis, including fatal cases, has occurred in association with tigecycline treatment. Consideration should be given to the cessation of the treatment with tigecycline in cases suspected of having developed pancreatitis
- *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including TYGACIL, and may range in severity from mild diarrhea to fatal colitis
- Monotherapy should be used with caution in patients with clinically apparent intestinal perforation
- TYGACIL is structurally similar to tetracycline-class antibiotics and may have similar adverse effects. Such effects may include: photosensitivity, pseudotumor cerebri, and anti-anabolic action (which has led to increased BUN, azotemia, acidosis, and hyperphosphatemia). As with tetracyclines, pancreatitis has been reported with the use of TYGACIL
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of TYGACIL and other antibacterial drugs, TYGACIL should be used only to treat infections proven or strongly suspected to be caused by susceptible bacteria. As with other antibacterial drugs, use of TYGACIL may result in overgrowth of non-susceptible organisms, including fungi
- The most common adverse reactions (incidence >5%) are nausea, vomiting, diarrhea, abdominal pain, headache, and increased SGPT
- Prothrombin time or other suitable anticoagulant test should be monitored if TYGACIL is administered with warfarin
- Concurrent use of antibacterial drugs with oral contraceptives may render oral contraceptives less effective
- The safety and effectiveness of TYGACIL in patients below age 18 and lactating women have not been established

Please see brief summary of Prescribing Information on adjacent page.

References: 1. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50:133-164. **2.** May AK, Stafford RE, Bulger EM, et al. Treatment of complicated skin and soft tissue infections. *Surg Infect*. 2009;10:467-499. **3.** TYGACIL® (tigecycline) Prescribing Information, Wyeth Pharmaceuticals Inc.

Pfizer

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U.S.News & WORLD REPORT
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Choosing Appropriate Treatment

Mesothelioma • *from page 1*

factors, and the decision is often made at the time of surgery because the preoperative imaging may have underestimated the amount of disease present.

Staging is critical in determining the appropriate procedure, and the merits of each surgical approach have been debated in several recent clinical and registry trials examining individual mortality and morbidity of these procedures at different stages, coupled with the use of a variety of adjuvant therapies. However, many decisions are based on surgical conjecture and bias rather than scientific data.

Evidence shows that PD provides a survival advantage for patients with stage I MPM, which may be accounted for by "lower mortality, lower postoperative adverse events, and greater lung capacity when relapse occurs," according to Dr. Flores. However, he explained, most patients with mesothelioma will present at a stage that requires EPP to eradicate all gross disease. PD can provide an R1 resection in early-stage disease, but as the tumor enlarges and invades the lung, fissures, and costophrenic sulcus, a PD is suboptimal regardless of resection of the pericardium and diaphragm.

There is, however, a critical balance between optimal cytoreduction and morbidity that varies across stages for these two procedures. For stage II disease, there is a "trend toward improved survival for EPP, despite an inherently higher tumor stage than PD," Dr. Flores said.

Stage III disease proved more complex, with similar survival data seen for both EPP and PD. Ultimately, "one should focus on obtaining a complete macroscopic resection based on the extent of tumor" for this stage of disease, choosing the best procedure accordingly, he advised.

For more advanced (stage IV) disease characterized by diffuse chest wall invasion and extensions through the diaphragm to the underlying peritoneum, the situation is much different.

"The tumor may be amenable to EPP, but there will be gross residual tumor left behind in the hemithorax. Because one of the most likely sites of recurrence is the contralateral pleura, the patient is better served by preserving lung function," Dr. Flores explained.

In stage IV disease, PD trended toward better survival, presumably because "when disease spreads to the contralateral lung, PD or debulked patients will be less symptomatic and better functionally able to tolerate systemic therapy because of their greater pulmonary reserve," he said.

"The goal is to remove all gross tumor while preserving as much of the lung as possible. Every patient and clinical situation is unique; therefore, treatment is difficult to generalize. Find an experienced mesothelioma surgeon you trust and leave it in their hands," Dr. Flores said in an interview.

Ultimately, the situation remains complex. Dr. Heyman Luckraz of the New Cross Hospital, Wolverhampton, England, and his colleagues recently reported results with 139 patients. EPP was chosen for clinically fit patients with stage I disease, while patients with advanced disease or who were unfit for EPP underwent PD. "EPP may only have a limited role in diffuse MPM, particularly as neither operative procedure is curative. Ultimately, the place of EPP will only be determined by randomized trial in comparison to PD in stage I disease with both groups receiving adjuvant therapy," the investigators concluded (Eur. J. Cardiothorac. Surg. 2010;37:552-6).

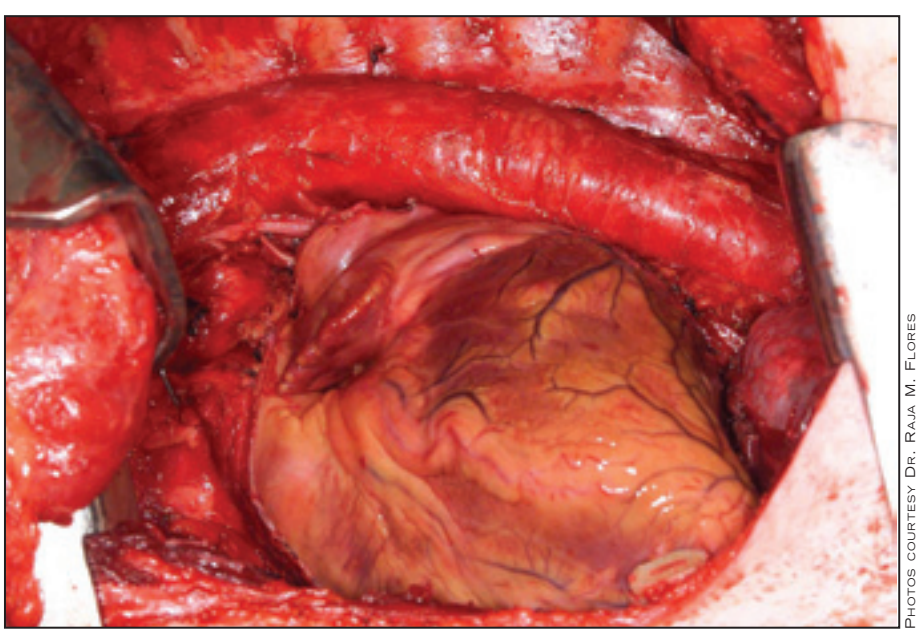
Whether such trials will ever be performed is an open question. Despite the recent Mesothelioma and Radical Surgery (MARS) trial, which demonstrated the possibility of randomizing patients to surgical vs. nonsurgical treatment, there will likely never be a randomized clinical trial powered enough to completely solve the puzzle, according to Dr. Tom Treasure of the University College of London (Eur. J. Cardiothorac. Surg. 2010;37:509-10).

Efforts continue to develop surgical alternatives with less mortality and morbidity than those of the standard EPP and PD procedures. For example, Dr. M.D. Kluger and colleagues at Columbia University, New York, reported the phase I and II results of a recent clinical trial on a two-stage operative cytoreduction procedure coupled with intraperitoneal chemotherapy (Eur. J. Surg. Oncol. 2010; 36:997-1003).

They found that their protocol offered median survival comparable to that of one-stage protocols; rates of morbidity, mortality, and visceral resections were relatively low, and length of stay was relatively short despite the need for two operations.

Ultimately, surgery might be totally immaterial in some cases. In two recent papers, the type of surgery was not found to be predictive of survival. The poor prognosis of sarcomatoid MPM was independent of the extent of surgery, unlike other cell types (Ann. Thorac. Surg. 2010;89:907-11), and the combination of several immunohistochemical markers was found to be the only valid prognostic indicator of survival, including type of surgery (Eur. J. Cardiothorac. Surg. 2010;38:245-53).

None of the authors mentioned in this article had disclosures deemed relevant to their reported research. ■



PHOTOS COURTESY DR. RAJA M. FLORES

A mesothelioma tumor (top) is shown near the heart before surgical resection; en bloc resection (bottom) of lung, pleura, pericardium, diaphragm, and tumor frees the chest of gross disease.

Pages 6a—6b

Critical Care Commentary

Diagnostic Errors in the ICU

Hospitalized patients continue to be harmed by adverse events and medical errors (Leape. *Clin Chim Acta*. 2009;404[1]:2). The contribution to errors by preventable diagnostic errors is underappreciated (Newman-Toker et al. *JAMA*. 2009;301[10]:1060). Studies suggest that the ICU is a particularly high-risk place for diagnostic errors (Shojania et al. *JAMA*. 2003;289[21]:2849), given the ICU's high stress, fast pace, and intense environment.

What Constitutes a Diagnostic Error?

Diagnostic errors occur when diagnoses are wrong, delayed, or missed (Combes et al. *Arch Intern Med*. 2004;164[4]:389; Roosen et al. *Mayo Clin Proc*. 2000;75[6]:562; Pastores et al. *Crit Care*. 2007;11[2]:R48; Maris et al. *Virchows Arch*. 2007;450[3]:329). The error may be discovered in the course of care as new data become available or when the current diagnosis is recognized to be incorrect. However, diagnostic errors are often only revealed by the definitive result of autopsy (Graber et al. *Arch Intern Med*. 2005;165[13]:1493; Pastores et al. *Crit Care*. 2007;11[2]:R48), when it is too late to effect therapy. Life-threatening diseases that go unrecognized and, therefore, untreated, are perhaps the most concerning of these possibilities. However, incorrect diagnoses resulting in unnecessary testing or inappropriate therapy that confers risk, but little or no benefit, may be more ubiquitous (Newman-Toker et al. *JAMA*. 2009;301[10]:1060). Misdiagnoses are usually classified based on their clinical relevance and potential for therapy to have prevented harm. The Goldman (Goldman et al. *N Engl J Med*. 1983;308[17]:1000) or Battle (Battle et al. *JAMA*. 1987;258[3]:339) classification systems are typically used when autopsy recognizes the misdiagnosis. Goldman class I errors are major diagnostic errors in which recognition of the underlying condition before death may have led to different therapeutic options and prolonged survival. Goldman class II errors are major diagnostic errors in which treatment antemortem may not have prolonged survival.

Class I errors have been described in as many as 9% of autopsies in hospitalized patients (5% were considered lethal) (Shojania et al. *JAMA*. 2003;289[21]:2849) and in 6% to 17.5% of ICU patients undergoing postmortem examinations (Maris et al. *Virchows Arch*. 2007;450[3]:329; Pastores et al. *Crit Care*. 2007;11[2]:R48). Class II errors range from 8% to 13% in the ICU. After adjusting for diagnostic improvements over time and declining autopsy rates, analysis suggests that 10% of all hospital deaths involve a major diagnostic error, and 1 in 20 hospital deaths involve potentially preventable class I errors, while as many as 1 in 10 ICU deaths has such an error (Shojania et al. *JAMA*. 2003;289[21]:2849).

Discrepancies found at autopsy create a record of these errors; however, without a definitive test that shows diagnostic errors during life, both lethal and nonlethal diagnostic errors get "lost in the chart." Nonlethal diagnostic errors in the ICU may also affect long-term outcomes, yet this group remains largely undefined and unexplored. An example would be the failure to recognize subclinical status epilepticus that may leave the patient alive but in a persistent vegetative state (Drislane et al. *J Clin Neurophysiol*. 2008;25[4]:181).

Of course, some diagnostic errors may be completely harmless and others may be caught before harm occurs. However, just because a diagnostic error did not cause harm does not mean that it is acceptable or unimportant. To date, almost nothing is known about these incidental errors, but the process by which they occur could provide us with valuable clues on how to implement system strategies that may identify and reduce the harmful ones. Traditional evaluations of care, such as morbidity and mortality conferences or root cause analysis investigations, rarely address near misses.

A Systems-Based Approach

Can we prevent ICU diagnostic errors and their resultant harm? This is a great challenge because we do not yet have a full perspective on the scope of the problem. With that said, we know what does not work. The culture of the ABCDs (accuse, blame, criticize, deny) that commonly surfaces when diagnostic errors occur is often counterproductive, reinforces a culture of "defensive medicine," and fails to address the root causes of the errors and the inherent fallibility in the system. We suggest using systems-based solutions for recognizing and reducing diagnostic errors. While diagnostic errors may result from "thought process" breakdowns in providers, other system-oriented factors, such as data and information management, presentation, integration, and communication, may be vastly more important and are ripe for targeting by systems-based principles.

Systems-based approaches include implementation of comprehensive unit safety programs (CUSPs) to effect culture change and adherence to the principles of safe design – standardization, creation of independent checks (tools such as checklists and staff empowerment encourage staff to speak up when something is not right), and learning from defects – when things go wrong. CUSPs involve all stakeholders (nurses, doctors, administrators, and others) at a local unit level who work proactively to identify risk for patient harm. Such systems interventions have been shown to be very effective at nearly eliminating some adverse events once considered inherent in patients in the ICU (Pronovost et al. *J Crit Care*. 008;23[2]:207; Berenholtz et al. *Crit Care Med*. 2004;32[10]:2014).

"Learning from defect" (LFD) strategies, a second systems-based approach, may also be useful in prevention of diagnostic errors. LFD is a proactive root cause analysis–like strategy that emphasizes not only causal system factors for adverse events but additionally seeks to uncover mitigating factors that may be capitalized upon to improve the system itself and reduce future harm. This strategy is local and streamlined to allow individual units to address their local problems (Pronovost et al. *Jt Comm J Qual Patient Saf*. 2006;32:102).

Creating a Framework for Improvement

What are the root causes of ICU diagnostic errors? We do know that during off-hours, the risk of misdiagnosis goes up (Kollef. *Crit Care Med*. 1991;19[7]:906; Okello et al. *Injury*. 2007;38[1]:112); however, other less-described causal factors, whose contributions remain ill-defined, exist. These may include high-complexity illnesses, alarm fatigue, stress, excessive workload (Donchin et al. *Curr Opin Crit Care*. 2002;8[4]:316), inappropriate staff-to-patient ratios, questionable qualifications of ICU staff physicians (Pronovost et al. *JAMA*. 2002;288[17]:2151), and staffing models that do not fit the particular ICU's needs.

Cognitive and contextual causes that lead to thought-process diagnostic errors may be ascribed to four factors. First, we all have a tendency to focus on the big or pressing problems. The notion that there is a single explanation for a patient's condition ("Occam's razor") doesn't necessarily apply to patients in the ICU who typically have multiple problems on admission or tend to accumulate them during their stay. Our universal approach to the overwhelming problem risks our missing smaller elements, such as a cervical fracture in a patient with polytrauma (Janjua et al. *J Trauma*. 1998;44[6]:1000). Second, critical care physicians are often so busy chasing the "usual suspects" that they can become overly focused. Lack of response to therapy should be considered indicative of a possible misdiagnosis, but patients in the ICU are often so sick that immediate response to treatment is not guaranteed, even with the correct diagnosis. We may become so wedded to the first diagnosis that we cannot easily entertain the possibility that the current diagnosis is incorrect. Third, information is lost to us. We obscure the patient's ability to participate in care (sedation, restraints, intubation) and relay to us whether he or she is experiencing changing or new symptoms. Additionally, physical examination in the ICU has poor sensitivity and specificity (Crowther et al. *Intensive Care Med*. 2005;31[1]:48; Drislane et al. *J Clin Neurophysiol*. 2008;25[4]:181; Hotson et al. *Brain*. 1976;99[4]:673), and laboratory and imaging studies are difficult to interpret (eg, D-dimer levels) (Crowther et al. *Intensive Care Med*. 2005;31[1]:48) or cannot be performed due to logistical or medical challenges (eg, MRI in patients with an automatic implantable cardioverter defibrillator). Fourth, in the ICU, as in many areas of medicine, we are limited in our current scientific understanding or by available diagnostic means. Finally, we may have information overload. The ICU is so complex and inundated with alarms and data that we tend to focus on only the highest perceived threats and may ignore other information that is equally important.

Systems-oriented solutions to address these overburdened situations and reduce ICU errors may need to be generic, such as mandatory staffing by critical care–certified ICU physicians (Pronovost et al. *JAMA*. 2002;288[17]:2151). Others, however, will need to be specific to particular clinical contexts, such as standardization with structured diagnostic algorithms and checklists to ensure cognitive consistency and thoroughness for a particular clinical problem (eg, unexplained hypotension). Additionally, technological solutions to bring order to the chaos of data presentation, integration, and decision analysis in the ICU environment will need to be developed.

Diagnostic errors clearly exist in the ICU, despite the aggressive and organized care that we provide. Diagnostic error type and incidence may vary, but they undoubtedly lead to some level of harm, and all harm should be viewed as a "never should happen event." However, the incidence and harm of ICU misdiagnosis are difficult to quantify and must be addressed more scientifically. To date, misdiagnosis has received too little attention. It's time to more fully define this problem and better diagnose and treat diagnostic errors. ■

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Critical Care Commentary

FROM THE CEO

Year One – Mapping a Future of Unsurpassed Clinical Education

BY PAUL A. MARKOWSKI, CAE

November marks my 1-year anniversary as Executive Vice President and CEO of the ACCP. It has been an exciting 12 months, filled with many changes – big and small – as we work to propel the ACCP "to the next level."

Immediately upon arriving at the ACCP in late October 2009, I was struck by the profound dedication and "can do" spirit of College leaders and staff and their passion for delivering world-class clinical education for chest medicine. The results of a member survey conducted by an outside firm in March suggested that this passion is our greatest strength as an organization. At its strategic planning session in April, the Board determined that, going forward, the College would focus on providing the best clinical education in chest medicine and leveraging appropriate technologies to deliver this content globally to physicians and allied health professionals. We developed the ACCP Strategic Plan 2010 – 2011 to reflect this focus, including the following updated ACCP mission and vision:

Our Mission: To promote the prevention, diagnosis, and treatment of chest diseases through education, communication, and research.

Our Vision: The ACCP is the global leader in providing education in cardiopulmonary, critical care, and sleep medicine to optimize health and advance patient care.

Since the Board approved the strategic plan in June, what has the ACCP done to realize its updated mission and vision and what will this renewed focus on delivering education content in the "information age" mean? With a realigned staff, we initiated a major overhaul of our information technology infrastructure and Web presence, including the development of content and learning management systems, to better serve our members. When this process, which typically takes 18 to 24 months, is complete, the resulting new systems will revolutionize the way that we do business.

We launched the ACCP Board Review e-books on the *CHEST* journal platform to create the www.chestpubs.org site and the first ACCP iPhone®/iPad™/iPod® Touch app for ACCP-SEEK. A *CHEST* app also is in development. Innovations like these have not come at the expense of, but rather go hand-in-hand with, providing exceptional content. This summer, *CHEST* reached its highest impact factor (6.36) – a measure of the average number of citations to articles published in science and social science journals – and ranking (3rd out of 43 respiratory journals) in its 75-year history.

Another highlight was the creation of the COPD Alliance, with the American Academy of Nurse Practitioners, American Academy of Physician Assistants, American College of Osteopathic Family Physicians, American College of Osteopathic Internists, and American Osteopathic Association as participating partners. One of the first action items of this multiyear, multimillion-dollar project will be the development of COPD.org, a shared resource designed to house content on COPD awareness and management.

The Alliance was recently featured in the *ACCP Leadership Update,* one of two e-newsletters launched this summer, as part of our efforts to enhance communication and transparency. *ACCP NewsBrief* is a weekly newsletter sent to all ACCP members and includes ACCP/Foundation news and news from the health-care industry.

As I previously noted here, The CHEST Foundation, in consultation with an outside agency, created a strategic architecture, based on the attributes of The Foundation, in the areas of education, care, and community; a microsite to establish a public face that leverages ACCP and Foundation assets related to patient education about the prevention of chest diseases; and a branding tag line, OneBreath™. The College and The Foundation will work in concert to implement their intersecting strategic plans.

As we take stock of all of the products and services that the College offers, this fall, we turn our attention to the future roles of the NetWorks, advocacy, and global education. After that? Our aspiration is to transform the ACCP into a virtual medical society, where members go online to view a customized dashboard of unsurpassed clinical content in chest medicine. ■

MR. MARKOWSKI *is Executive Vice President and Chief Executive Officer of the American College of Chest Physicians.*

'New Era' of Antithrombotic Tx

Rivaroxaban • *from page 1*

32 countries. All had acute symptomatic DVT but no pulmonary embolism. Participants were randomized to oral rivaroxaban, an investigational direct inhibitor of factor Xa, at 15 mg twice daily for 3 weeks, followed by 20 mg once daily, or to current standard therapy consisting of subcutaneous enoxaparin, typically for about 7 days, followed by warfarin or another vitamin K antagonist at a target international normalization ratio (INR) of 2-3. Treatment duration could be 3, 6, or 12 months at the physician's discretion.

RECURRENT VTE OCCURRED IN 2.1% OF THE RIVAROXABAN GROUP VS. 3.0% ON STANDARD THERAPY.

EINSTEIN-DVT was designed to show whether rivaroxaban is noninferior to standard therapy, which is known to be highly effective, reducing the recurrent venous thromboembolism rate by about 90%, compared with no treatment. But standard therapy is also quite cumbersome because of warfarin's well-known shortcomings, explained Dr. Büller, chairman of vascular medicine at the Academic Medical Center, Amsterdam.

Recurrent venous thromboembolism, the primary study end point, occurred in 2.1% of the rivaroxaban group, compared with 3.0% of those on standard therapy. The resultant 32% relative risk reduction was so robust that it not only established rivaroxaban's noninferiority, it came within a hair's breadth of demonstrating statistically significant superiority for the single-drug regimen, he continued.

The primary safety end point in EINSTEIN-DVT was the combined rate of major bleeding or clinically relevant nonmajor bleeding. This adverse outcome occurred in 8.1% of both groups.

For the prespecified secondary combined end point of recurrent venous thromboembolism or major bleeding, rates were 2.9% in the rivaroxaban arm, compared with 4.2% with standard therapy, for a highly significant 33% reduction in risk.

The rivaroxaban regimen was equally safe and effective regardless of patient age, gender, body mass index, creatinine clearance, or the presence of cancer. Monthly monitoring of liver function tests showed no evidence of hepatotoxicity with the drug. In the standard therapy arm, once patients were off low-molecular-weight heparin and on warfarin they were within the target INR 58% of the time.

'It's time to change' the practice of hospitalizing DVT patients for unfractionated heparin therapy.

DR. BÜLLER

American physicians often initially hospitalize patients with DVT for 5-7 days or more of therapy with unfractionated heparin. Asked to comment on this strategy, Dr. Büller was blunt: "It's time to change."

"I visit the United States often, and I am absolutely surprised that so many physicians there hospitalize their DVT patients for unfractionated heparin. In many other parts of the world, 80%-90% of these patients are treated out of hospital with low-molecular-weight heparin followed by a vitamin K antagonist," he said.

Discussant Dr. Harald Darius, noting that the oral direct thrombin inhibitor dabigatran is widely expected to be the first of the new antithrombins to receive marketing approval for treatment of acute DVT, observed that rivaroxaban's performance in EINSTEIN-DVT appeared to be roughly comparable to that of dabigatran in the RE-COVER trial (N. Engl. J. Med. 2009;361:2342-52). Rivaroxaban had a 2.1% incidence of recurrent venous thromboembolism, while dabigatran at 150 mg twice daily for 6 months had a 2.4% rate. However, dabigatran use was preceded by at least 5 days of subcutaneous low-molecular-weight heparin or intravenous unfractionated heparin, Dr. Darius said.

"I'm quite positive that we're facing a new era of antithrombotic therapy in patients with DVT, but with some questions still to be resolved," he added.

Chief among these questions in his view is the optimal treatment duration using rivaroxaban and the other new agents. Neither EINSTEIN-DVT nor RE-COVER was designed to provide an answer.

"If you look at the guidelines, the treatment duration is extended with every new edition," noted Dr. Darius of Vivantes Hospital, Berlin.

Rivaroxaban is also under development for other potential indications, including stroke prevention in patients with atrial fibrillation, secondary prevention of acute coronary syndrome, treatment of acute pulmonary embolism, and prevention of venous thromboembolism in high-risk hospitalized, medically ill patients.

Dr. Büller disclosed having received research grants and serving as a consultant to Bayer Schering Pharma, which sponsored the EINSTEIN-DVT trial. Dr. Darius declared no financial conflicts. ■

Congestion Does Not Predict Heart Failure Outcomes

BY BRUCE JANCIN
Elsevier Global Medical News

STOCKHOLM – The absence of signs and symptoms of congestion at discharge in patients hospitalized for acute decompensated heart failure does not predict a favorable prognosis, contrary to the conventional wisdom.

A new secondary analysis of the international EVEREST trial provides an important lesson in the everyday management of acute heart failure: "The fact that a patient improves in-hospital with diuretics and other medications is not sufficient. It's not 'mission accomplished,' " Dr. Mihai Gheorghiade said at the annual congress of the European Society of Cardiology.

"There is a dissociation between signs and symptoms of congestion at discharge and outcomes. In spite of having a very low congestion score, the event rate in EVEREST during 10 months of follow-up was astronomical," said Dr. Gheorghiade, professor of medicine and surgery and associate chief of cardiology at Northwestern University, Chicago.

EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan) was a double-blind study that randomized 4,133 patients with worsening heart failure and a left ventricular ejection fraction of 40% or less to the oral vasopressin V2 receptor blocker tolvaptan or placebo within 48 hours of hospitalization.

Standard background therapy in both study arms included diuretics, ACE inhibitor or angiotensin II receptor blocker therapy, a beta-blocker, and an aldosterone antagonist. In the previously reported primary results, tolvaptan proved to have no benefit over placebo during a mean follow-up of 9.9 months (JAMA 2007;297:1319-31).

Dr. Gheorghiade presented a secondary analysis that focused on the 2,061 patients in the placebo group. When these patients were randomized following initial treatment with diuretics, they had a mean congestion score of 4 points based upon their degree of jugular vein distention, rales, and peripheral edema.

'IN SPITE OF HAVING A VERY LOW CONGESTION SCORE, THE EVENT RATE IN EVEREST DURING 10 MONTHS OF FOLLOW-UP WAS ASTRONOMICAL.'

At discharge, patients had lost a mean 2.8 kg of body weight, and 72% had a congestion score of 0 or 1.

Although that appears to be a high rate of short-term treatment success, this large subgroup of patients with minimal or no signs or symptoms of congestion at discharge had a 15% all-cause mortality and a 29% rate of rehospitalization for heart failure during the next 9.9 months.

The adverse event rate was even greater in those with a higher congestion score at discharge. In the overall placebo group, all-cause mortality was 26%, with a 40% rate of rehospitalization for heart failure during follow-up. That is a particularly sobering statistic given that heart failure is the No. 1 reason for hospital admission in the Medicare population.

"We're dealing with a disorder that has an event rate as high as 50%. There is no other medical condition for which patients are hospitalized and are improving with therapy that has a comparable event rate," the cardiologist observed.

The new EVEREST analysis contains an important message for clinical trialists: Using the signs and symptoms of congestion as a key target for treatment during hospitalization as well as the standard end point in acute heart failure studies, as has been common until now, is a recipe for a negative trial result.

"It's very difficult to beat placebo, because placebo plus standard therapy has a tremendous effect on congestion," Dr. Gheorghiade said.

"Looking for new therapies that improve signs and symptoms of congestion in the whole population is a waste of time unless you're dealing with special populations who don't respond to standard therapies, such as patients with low blood pressure," he noted.

Surrogate markers that are better than congestion are needed to guide therapy. One possibility is B-type natriuretic peptide (BNP). The mean BNP at admission in the placebo arm of EVEREST was 1,375 pg/mL. At discharge, BNP was still markedly elevated at 948 pg/mL.

Patients with minimal or no congestion at discharge had a 15% all-cause mortality in the next 9.9 months.

DR. GHEORGHIADE

"The lesson here is that by treating the signs and symptoms of congestion, you can make patients feel much better, but even though they are now able to walk up a flight of stairs, inside, in terms of renal function and BNP, they are still very sick," he said.

Until better treatments for acute heart failure are found, the best thing physicians can do for affected patients is try to identify specific targets amenable to current therapies, such as renal dysfunction or myocardial ischemia, Dr. Gheorghiade concluded.

The EVEREST trial was sponsored by Otsuka. Dr. Gheorghiade has received research grants and/or served as a consultant to Otsuka and numerous other pharmaceutical companies. ■

N.Y. Law Mandates Counseling of Terminally Ill

BY ALICIA AULT
Elsevier Global Medical News

A new law requiring New York physicians to discuss palliative care and end-of-life options with terminally ill patients is well intentioned, but may not do much to change clinical practice or institutional culture, according to some observers in the state.

The New York Palliative Care Information Act was signed into law by Gov. David Paterson (D) in August. Perhaps as a sign that palliative care is being embraced more readily and becoming better understood, it took just 14 months from the time of the bill's introduction in the state Senate (S. 4498 and A. 7617) to its signing.

Even so, "whether or not it will change behavior is a bit of a black box," said Dr. Bradley Flansbaum, director of hospitalist services at Lenox Hill Hospital in New York.

"It's a nice thought, but I don't know how they're going to put it into effect," he said.

Under the law, physicians and nurse practitioners are required to provide a patient who has less than 6 months to live with information and counseling on palliative care and end-of-life options, which would include "the range of options appropriate to the patient, the prognosis, risks and benefits of the various options, and the patient's legal rights to comprehensive pain and symptom management at the end of life."

The physician or nurse practitioner can refer the patient to another provider who is willing to meet the legal statute or who is "professionally qualified" to offer the services.

There is no reimbursement offered for the required services.

COURTESY LENOX HILL HOSPITAL

Will the palliative care law change behavior? That's "a bit of a black box," Dr. Bradley Flansbaum said.

Because it is an amendment to the state's public health law, violations of the new law could result in penalties or fines. It's not clear how it will be enforced or what might trigger the penalties; the health department has until the law's effective date (February 2011) to devise regulations, said David Leven, executive director of Compassion and Choices of New York.

That advocacy group helped devise the proposal and then shepherded it though the legislature, said Mr. Leven. California has a similar statute, but is not as strong because it does not put the onus on physicians, he said.

The organization sought the legislation because even with increased training on end-of-life issues, too few physicians are having conversations with their dying patients, according to Mr. Leven.

That means patients' wishes are not being respected, to the detriment of both patients and the practice of medicine.

The organization also hoped that the law would be a catalyst to improving education in the field of end-of-life care in medical school and at the professional level, he said.

Dr. Wendy Edwards, director of the palliative medicine program at Lenox Hill, said that education would be a key component, but there appeared to be no such formal requirements in the law. About 15 years ago, she was part of a group that attempted to get a bill passed to mandate the teaching of palliative care in medical schools, but it did not get anywhere.

She said she wasn't sure that the new law was the way to increase attention to palliative care, but that it had likely come about as a result of frustration and impatience on the part of palliative specialists.

The law will be positive, however, she said. Palliative care won't just be the standard of care, but will be the law, which gives some backing to hospitals that seek to implement and strengthen their quality of care, and end-of-life care in particular.

But it still will not make it easier for physicians who do not have experience in palliative care, Dr. Edwards said.

"It's a very hard discussion to have; it's not something doctors are trained to do," she noted.

A recent study in non–small cell lung cancer patients found that those who were given palliative care at the time of diagnosis had a better quality of life than did those in standard care (N. Engl. J. Med. 2010;363:733-42). This study may do more to advance the field than does the New York law, Dr. Edwards noted.

Although the Hospice and Palliative Care Association of New York State supported the law, the Medical Society of the State of New York did not. The medical society, which represents a total of 25,000 physicians, opposed the law because of concerns that it would interfere with the way each and every doctor navigates through end-of-life situations with each individual patient, said Elizabeth C. Dears, the society's senior vice president for legislative and regulatory affairs.

Mandating that information be given on palliative care "may undermine the patient's belief and conviction in prevailing against their disease and undercut the confidence in their treating physician," Ms. Dears said.

The medical society also said that physicians are not licensed to provide legal advice in areas such as pain or symptom management.

In addition, physicians may not know what they are supposed to be communicating to patients under certain provisions, while still being subject to penalties.

Although the medical society might object to requiring any such talk, both Dr. Flansbaum and Dr. Edwards said that, realistically, the law should be requiring palliative care to be offered sooner in the disease process. In addition, palliative care should be offered to a broader group of patients, such as those who have chronic life-limiting conditions like heart failure.

"By the time you're invoking palliative care in terminal patients, you're behind the curve," Dr. Flansbaum said. ■

COMMENTARY

Dr. Paul Selecky, FCCP, comments: Like many other well-intended laws, the impact on the delivery of health care may be minimal. Regardless, ACCP members can and should become champions for palliative care in their practice settings, both inpatient and outpatient. We are uniquely qualified because of our training and experience in critical care and the chronic care of lung disease. Invite your colleagues to join you – "build it and they will come." The Palliative and EOL Care NetWork welcomes your involvement in their work to improve the care of our patients. Check the ACCP Web site at www.chestnet.org/accp/networks.

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Spontaneous reports of serotonin syndrome have been reported with the coadministration of ZYVOX and serotonergic agents. If signs or symptoms of serotonin syndrome, such as cognitive dysfunction, hyperpyrexia, hyperreflexia, and incoordination occur, discontinuation of one or both agents should be considered.

Myelosuppression (including anemia, leukopenia, pancytopenia, and thrombocytopenia) has been reported in patients receiving ZYVOX. In cases where the outcome is known, when ZYVOX was discontinued, the affected hematologic parameters returned to pretreatment levels. Complete blood counts should be monitored weekly, particularly in patients who receive ZYVOX for longer than 2 weeks.

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Peripheral and optic neuropathy have been reported primarily in patients treated with ZYVOX for longer than the maximum recommended duration of 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended.

Convulsions have been reported in patients treated with ZYVOX. In some of these cases, a history of seizures or risk factors for seizures was reported.

The most commonly reported adverse events in adults across phase 3 clinical trials were diarrhea, nausea, and headache.

*Methicillin-resistant *Staphylococcus aureus*.

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Please see brief summary on adjacent pages.

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Asthma Admissions Drop After Smoking Ban

BY MARY ANN MOON
Elsevier Global Medical News

Pediatric hospitalizations for asthma decreased by approximately 20% per year after a ban on smoking in enclosed public spaces was enacted in Scotland, said Daniel Mackay, Ph.D., of the University of Glasgow and associates.

Before the legislation was implemented, there was concern that people might transfer their smoking from public areas to their homes, "leading paradoxically to an increase in exposure … among children," they said (N. Engl. J. Med. 2010; 363:1139-45). Such displacement of smoking activity did not occur. Instead, the results support the conclusion of another study that found that a public smoking ban increased voluntary smoking restrictions in homes as well, the authors said.

They used government databases to identify all 21,415 asthma admissions across Scotland from January 2000 through October 2009 for children younger than 15 years. From 2000 until implementation of the smoking ban in 2006, hospital admissions for asthma rose a risk-adjusted average of 4.4% per year.

After the smoking ban was enacted, the risk-adjusted annual rate of pediatric asthma admissions declined 19.5%, a statistically significant difference. The net annual reduction was 15.1% per year. NHS Health Scotland funded the study. The investigators had no conflicts of interest.■

COMMENTARY

Dr. Burt Lesnick, FCCP, comments: This study adds evidence that smoking restrictions in public areas improves the health of nonsmokers. If a clinically significant reduction in pediatric asthma hospitalizations can be achieved with tobacco smoke reductions in public areas, imagine the possible effects if this exposure were reduced in homes.

Bronchodilators Not Needed With 3% Saline?

BY PATRICE WENDLING

Elsevier Global Medical News

MINNEAPOLIS – Hypertonic 3% saline has a low adverse event rate when used without bronchodilators in infants hospitalized for bronchiolitis, according to research presented at a meeting on Pediatric Hospital Medicine.

Three percent saline has emerged as a popular therapy for inpatient bronchiolitis, but is typically coadministered with bronchodilators because of a perceived risk of bronchospasm, Dr. Shawn Ralston, lead author, said in an interview.

There is no evidence to show that 3% saline induces bronchospasm in infants with bronchiolitis or that it is safe when used in the absence of adjunctive bronchodilators.

Studies in asthmatics, however, have shown bronchospasms with the use of hypertonic saline at higher concentrations ranging from 4.5% to 7% with volumes as high as 10-15 cc, she said.

All doses of 3% saline in the current study were 4 mL in volume and nebulized at a 6-L/m flow of oxygen.

There were 444 total doses of 3% saline given to 154 patients aged less than 2 years, hospitalized with acute viral bronchiolitis; 377 doses were given without bronchodilators either 4 hours before or after the saline dose, and 67 were given with concomitant bronchodilators.

Four adverse events occurred in the 377 doses, for an adverse event rate of 1%, Dr. Ralston, a pediatric hospitalist at the University of Texas Health Science Center in San Antonio, reported in a poster at the meeting.

One episode of bronchospasm was reported (0.3% of doses given) in a 6-week-old boy who had received 4 cc of 3% saline. He was stabilized with racemic epinephrine and received a further dose of saline and scheduled albuterol without improvement before transfer to the ICU.

One child experienced coughing during nebulization that resulted in discontinuation of therapy (0.5% of doses given), and two children had excessive coughing that required no intervention.

For comparison, one adverse event each was reported with racemic epinephrine nebulization (3.8% of doses given) and with albuterol administration (0.3% of doses given), Dr. Ralston noted.

FOUR ADVERSE EVENTS OCCURRED IN 377 DOSES OF SALINE, WITH ONE EPISODE OF BRONCHOSPASM REPORTED IN A 6-WEEK-OLD BOY.

Children who received 3% saline were as likely as were those who did not to be given antibiotics (31% vs. 42%) or steroids (6% vs. 15%), and to be transferred to higher levels of care (2.9% vs. 2.3%) or readmitted within 72 hours (1.5% vs. 1.2%).

Dr. Ralston studied 3% saline without bronchodilators "to clarify the questions that remain about its utility, mainly because I believe bronchodilator usage in routine bronchiolitis to be unnecessary and wasteful," she said.

She stressed that the current data cannot be applied to the efficacy of 3% saline and that further trials are needed to evaluate its effectiveness without adjunctive bronchodilators.

"My personal strategy … is not to routinely use any nebulized therapy in the majority of my patients," she said.

Statistical analysis is underway for a large double-blind, randomized trial of nebulized 3% saline vs. normal saline in roughly 700 children up to 24 months of age with viral bronchiolitis, principal investigator Dr. Susan Wu of Children's Hospital Los Angeles, said in an interview. The primary end points are admission rate, length of stay, and change in Respiratory Distress Assessment Instrument score.

Dr. Wu described Dr. Ralston's study as "very exciting because … numerous therapies, including bronchodilators, have been studied showing no effect on important clinical outcomes."

The meeting was sponsored by the Society of Hospital Medicine, American Academy of Pediatrics, and Academic Pediatric Association. Dr. Ralston and coauthors report no financial conflicts. ■

Pulmonary Perspectives

CPR – 50 Years On: Part 1

At Johns Hopkins Hospital 50 years ago, Kouwenhoven and colleagues synthesized nearly a century of clinical and animal investigation and published the first report of treatment of human cardiac arrest with closed chest massage. This technique is now known as cardiopulmonary resuscitation (CPR). Kouwenhoven and colleagues reported 20 cases; all were successfully resuscitated, with 70% leaving the hospital alive. "Anyone anywhere can now initiate cardiac resuscitative procedures. All that is needed are two hands," the authors stated. They described five patients: four with intraoperative events and one with peri-infarction ventricular fibrillation (Kouwenhoven et al. *JAMA*. 1960;173[10]:1064).

The CPR concept promoted by the American Heart Association is the chain of survival consisting of early activation of emergency response, early CPR, early defibrillation when appropriate, and advanced care, primarily advanced cardiac life support (ACLS). Among the more important resuscitation outcomes are return of spontaneous circulation (ROSC), defined as recovery of a palpable pulse any time during CPR, and survival to hospital discharge (STD), particularly neurologically intact survival (Cummins et al. *Circulation*. 1991;84[2]:960).

Epidemiology

Sudden cardiac arrest occurs as many as 500,000 times in the United States annually. Two-thirds of these events occur outside the hospital (OHCA) at a rate of 0.04% to 0.19% per year. More than 60% of these arrests are due to coronary artery disease. About one-quarter of these arrests involve shockable rhythms –ventricular fibrillation or ventricular tachycardia (Lloyd-Jones et al. *Circulation*. 2010;121[7]:e46). The proportion of shockable rhythms has decreased substantially through 4 decades of CPR with recent stabilization (Polentini et al. *Prehosp Emerg Care.* 2006;10[1]:52). Bystanders frequently attempt CPR, but few of these arrests are witnessed. By contrast, almost 80% of in-hospital cardiac arrests (IHCA) are witnessed. Almost half occur in ICU areas. Again, approximately one-quarter of these events involve a shockable rhythm, but only a small fraction result from coronary artery disease (Meaney et al. *Crit Care Med*. 2010;38[1]:101).

Pathophysiology

When effective cardiac action is lost, blood pressure falls precipitously, ultimately decreasing exponentially to a mean static pressure of about 7 mm Hg over 6 to 7 min. Coronary artery flow falls faster than carotid blood flow. Sluggish forward flow dilates the right ventricle (Steen et al. *Resuscitation*. 2003;58[3]:249). The dilated right ventricle presents a significant obstacle to successful resuscitation. Leftward motion of the interventricular septum impairs left ventricular preload and decreases cardiac myocyte length to an ineffective portion of the Frank-Starling curve. Relative equalization of right and left ventricular pressures decreases the gradient for coronary perfusion pressure and flow (Berg et al. *Circulation*. 2005;111[9]:1136).

The immediate goal in CPR is restoration of coronary and cerebral perfusion. Chest compression helps empty the right ventricle into the pulmonary circulation, providing preload to the left ventricle, augmenting the gradient for coronary perfusion. Emptying the left ventricle improves systemic and cerebral perfusion. Effective coronary flow generally requires a perfusion pressure over 20 mm Hg. At this level of coronary perfusion pressure, peak systolic blood pressure is 60 to 80 mm Hg, cardiac output is 25% to 40% of baseline, and there is sufficient cerebral blood flow to avoid anoxic injury (Andreka et al. *Curr Opin Crit Care*. 2006;12[3]:198).

THERE HAS BEEN IMPROVEMENT IN THE RATES OF ROSC FOR RESUSCITATIONS, WITHOUT IMPROVEMENT IN SURVIVAL TO DISCHARGE.

Failure to achieve adequate coronary perfusion pressure will result in pulseless electrical activity (PEA) or asystole, even if a shockable rhythm was initially present.

Although oxygenation is ultimately necessary for successful resuscitation, the application of positive pressure ventilation by rescuers may compromise the ability to generate adequate coronary perfusion. Increased intrathoracic pressure, especially with rapid ventilation rates, has been shown to increase right-sided pressures and decrease coronary perfusion pressure.

Conversely, in animal models, failure to provide oxygen has resulted in poorer outcomes. The best timing and methods for oxygen delivery in CPR remain undetermined (Aufderheide et al. *Circulation*. 2004;109[16]:1960).

Arrest Outcomes

Now, 50 years after Kouwenhoven and colleagues, there has been improvement in the rates of ROSC for out-of-hospital and in-hospital resuscitations, without improvement in survival to discharge. Survival from OHCA is poor (median STD of 4% for all arrests, 8% with attempted resuscitation). Survival varies considerably by geographic location (range, 3% to 16%). Four factors have been identified as important determinants of OHCA survival: witnessed arrest, bystander CPR, a shockable rhythm, and successful ROSC in the field (Sasson et al. *Circ Cardiovasc Qual Outcomes*. 2010;3[1]:63).

In IHCA, there is considerable interhospital variability in the rates of ROSC and STD. Average IHCA ROSC rates approach 50%, with STD approximately 18%. For IHCA, rhythm is more important in determining survival than arrest location (critical or noncritical care setting). Survival of IHCA is lower when the arrest occurs at night or on weekends (Peberdy et al. *JAMA*. 2008;299[7]:785). African-Americans have been reported to have poorer survival rates than Caucasians, attributed to disproportionate care in poorly performing hospitals (Chan et al. *JAMA*. 2009;302[11]:1195). The proportion of successful IHCA resuscitations resulting in STD has decreased over the past 50 years. For both arrest locations, approximately one-third of patients with successful ROSC leave the hospital alive.

The ultimate goal in CPR is to maximize the number of patients leaving the hospital alive and neurologically intact. Improved survival could be achieved by a reduction in the number of cardiac arrests, improving the ROSC rate, and optimization of postarrest care. Variability in ROSC outcomes suggests a potential for improvement in CPR technique. The relatively unchanging percentage of survivors to discharge in both arrest scenarios points to the need for systematic improvements in post–cardiac arrest care.

Prevention

Within a year of the initial description of CPR, as less-favorable outcomes accumulated, the original Johns Hopkins authors recognized that "not all dying patients should have cardiopulmonary resuscitation attempted. Some evaluation should be made before proceeding. The cardiac arrest should be sudden and unexpected. The patient should not be in the terminal stages of … disease, and there should be some possibility of a return to a functional existence" (Jude et al. *JAMA*. 1961;178[11]:1063).

Today, without advance directives, in-hospital CPR is nearly universal. Methods to reliably predict successful resuscitation and individual survival potential are lacking. Even if these were available, selective application of CPR would only improve percentages of ROSC and STD without increasing the actual number of survivors.

End-tidal carbon dioxide (CO_2) reflects the presence of cellular metabolism and sufficient circulation to deliver carbon dioxide to the lungs. End-tidal CO_2 has shown some promise in monitoring the effectiveness of CPR and as a criterion for termination of resuscitative efforts, where one study found that an initial end-tidal CO_2 of less than 10 mm Hg predicted ROSC failure (Grmec et al. *Resuscitation*. 2007; 72[3]:404). However, further research is needed before valid decisions can be made based on this measurement.

Out-of-hospital arrests could be reduced by improved primary and secondary prophylaxis of coronary artery disease. Wider use of beta-adrenergic blockers and implantable defibrillators may have reduced the number of OHCA events but has unintentionally decreased the proportion of shockable rhythms, making successful resuscitation more difficult to achieve (Agarwal et al. *Resuscitation*. 2009;80[11]:1253).

Medical Emergency Teams

Many in-hospital arrests have been associated with 6.5 h (median) of physiologic instability before the arrest event. To effectively treat unstable patients before an arrest occurred, emergency detection and response systems featuring multidisciplinary teams (ie, rapid response teams, medical emergency teams, or intensive care outreach) were developed and deployed. Early studies suggested effectiveness in reducing in-hospital code events with improved mortality outcomes.

The rapid response concept was enthusiastically embraced by The Joint Commission and the Institute for Healthcare Improvement. Subsequent studies report less consistent success. A meta-analysis of the rapid response literature (17 studies and nearly 1.3 million hospital admissions) documents a 33% reduction in arrest events outside of critical care areas without a decrease in hospital mortality. The authors suggested that the lack of mortality benefit may be due to increasing use of do-not-resuscitate orders or a shift of arrest events from hospital floors to critical care areas (Chan et al. *Arch Intern Med*. 2010;170[1]:18).

The weakest link in the rapid response system may be the afferent arm: the ability to recognize and promptly initiate effective treatment of a potential crisis.

A recent expert consensus conference

Continued on following page

Dr Marilyn G. Foreman, FCCP
Editor, *Pulmonary Perspectives*

Dr Loren J. Harris, FCCP
Deputy Editor, *Pulmonary Perspectives*

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cited lack of evidence regarding the predictive value of measures of clinical instability, stating that early warning indices required validation and that the best methods of obtaining and tracking vital signs are, as yet, undetermined.

Conference experts agreed that basic vital signs consisting of blood pressure, heart rate, respiratory rate, temperature, oximetry, and level of consciousness should be measured at least every 12 h (DeVita et al. *Resuscitation*. 2010;81[4]:375). ■

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Editor's Insight

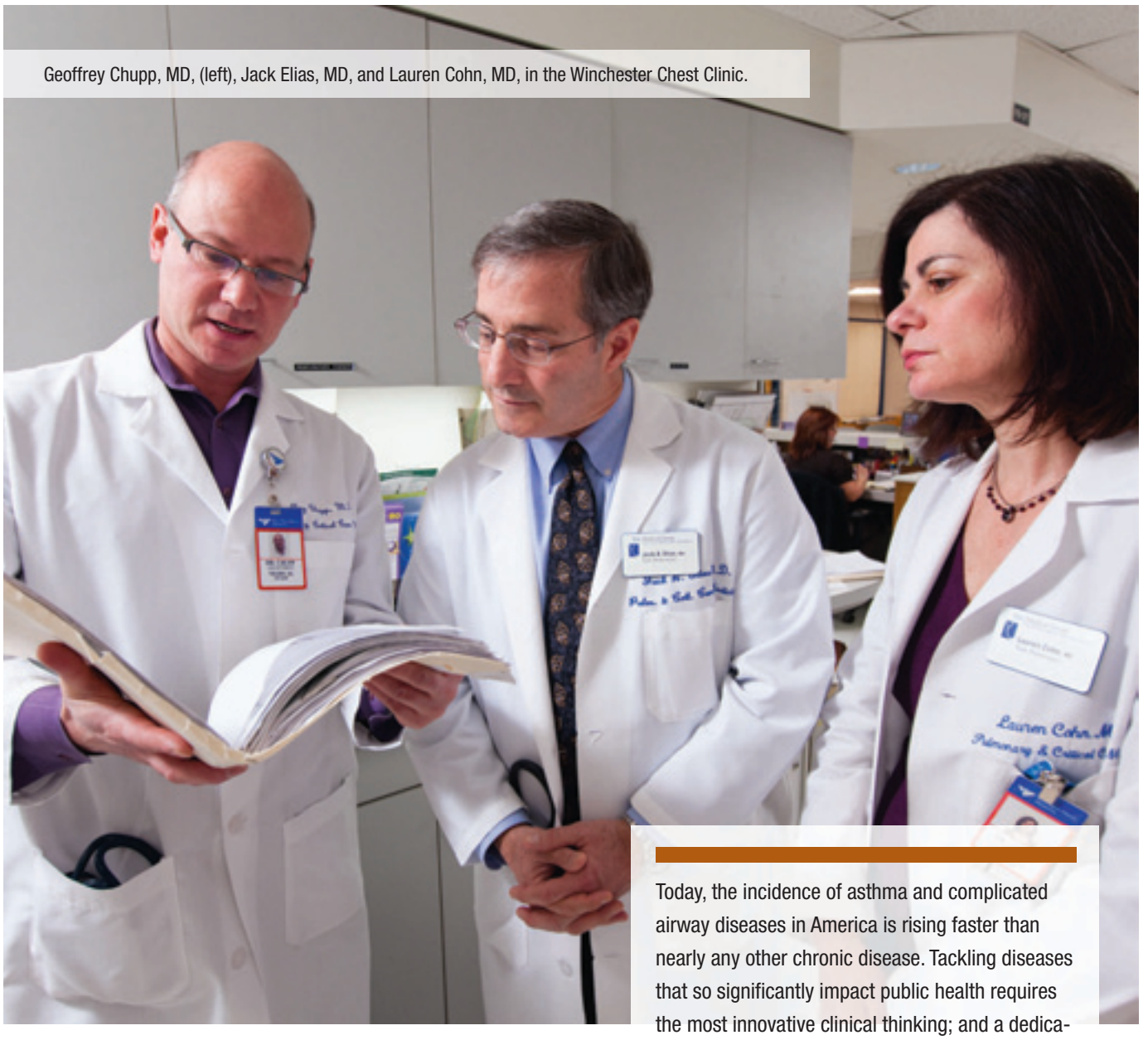
This timely review of cardiopulmonary resuscitation coincides with the imminent release of new guidelines for CPR from the American Heart Association. We look forward to the conclusion of this insightful review in the December Pulmonary Perspectives in *CHEST Physician*.

Traveling With Oxygen: Free ACCP Download

Each year, millions of travelers fly on commercial airlines in the United States and around the globe. As air travel has become more affordable, it has become more accessible for people with serious medical conditions – including lung disease. The Air Carrier Access Act prohibits airlines from discriminating against passengers based on disabilities. While this legislation enhances the freedom of travelers, the varying policies of different airlines concerning the use of portable oxygen can cause confusion among travelers. Adding to the challenge, not all health-care providers are fully informed regarding Federal Aviation Administration regulations and, therefore, are unable to advise their patients adequately.

The Occupational and Environmental Health NetWork of the ACCP has developed a patient education brochure to assist these patients traveling by air with oxygen. This brochure, which is free to download, reviews the effects of altitude and air travel on individuals with lung disease, describes the types of portable oxygen systems that can be used in-flight and while traveling, and provides important tips for patients to consider when planning a trip.

Download the Traveling With Oxygen patient education brochure at www.chestnet.org. ■



Geoffrey Chupp, MD, (left), Jack Elias, MD, and Lauren Cohn, MD, in the Winchester Chest Clinic.

A Successful G-I-N Conference 2010 in Chicago

The American College of Chest Physicians hosted the first US conference for the Guidelines International Network (G-I-N) in August in Chicago. Final attendance broke all previous G-I-N records, with 435 registrants from 30 countries representing North and South America, Europe, Asia, and Oceania. Roughly 40% of the registrants were from the United States.

The conference theme of "Integrating Methods. Improving Outcomes." brought professionals from across the spectrum of evidence-based medicine. The goal was to learn how to integrate collective knowledge into evidence-based practices that can translate clinical research into interventions to improve patient care and outcomes. Attendees ranged from health technology appraisers and evidence reviewers to guideline developers and implementers, as well as those in quality improvement, medical education, and health-care policy.

The 270 submitted abstracts topped previous achievements for both quantity and quality. Dr Dan Ouellette, FCCP, remarked: "I have seldom attended a medical conference with such excellent speakers, such a diverse group of participants, and such well-organized activities and venues."

Five plenary panels composed of 15 invited speakers from around the globe covered the following topics:

- Politics, Media, and Guidelines: A Dangerous Mix?
- Implementation: Bridging the Gap Between Evidence and Action
- Challenges in Managing Conflict of Interest in Guideline Development
- A Seat at the Table: The Effects of Consumer Engagement in Guideline Development
- Rationing or Rationality? Health Economics in National Guidance

There were 14 interactive workshops, 125 presentations over 26 moderated concurrent sessions, and nearly 100 posters. The ACCP Health and Science Policy Committee taught a full-day course on the ACCP guideline methodology, which was attended by 98 guideline developers, varying from novice to very experienced. Another 32 individuals attended a course on using evidence-trained consumers in guideline development.

Eleven nonindustry exhibitors and supporters showcased their products and services, including the Agency for Healthcare Research and Quality, The Cochrane Collaboration, New York Academy of Medicine, several medical specialty societies, registry developers, medical journal publishers, and clinical decision support vendors.

Networking opportunities are very important when G-I-N attendees convene. The social events included a gala on the last night of the conference. Attendees cruised Lake Michigan's Chicago shores on the Odyssey II yacht, topping off a conference that will set the bar high for future G-I-N conferences, including the 2011 meeting in Seoul, South Korea. ■

At an invited plenary session were Kay Dickersin, MA, PhD (Johns Hopkins); Dr Trudy van der Weijden (University of Maastricht); and Dr Theodore G. Ganiats (UC San Diego).

(L-R) Dr Richard Irwin, Master FCCP; Cynthia French, RN; Dr Patricio Escalante, FCCP; and Dr Dan Ouellette, FCCP, enjoyed the gala evening on the Odyssey II yacht.

PHOTOS COURTESY ACCP