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Overall, 6,185 patients (64%) of the 9,675 patients studied did not receive any pharmacologic VTE prophylaxis while hospitalized.

Many At-Risk Patients Lack VTE Prophylaxis

BY PATRICE WENDLING
Elsevier Global Medical News

NEW ORLEANS — Nearly two-thirds of 9,675 medical patients at risk for venous thromboembolism received no inpatient pharmacologic prophylaxis, and more than 98% received no outpatient prophylaxis, a retrospective analysis showed.

The analysis is unique in that it assessed both inpatient and outpatient pharmacologic venous thromboembolism (VTE) prophylaxis in medical patients at risk of VTE, Dr. Alpesh N. Amin and his associates reported in a poster at the annual meeting of the American Society of Hematology.

"Further efforts to improve VTE prevention in medical patients are required, with particular emphasis needed on the transition to outpatient prophylaxis," the authors concluded.

Most hospitalized medical patients have at least one risk factor for VTE, with the risk persisting for several weeks following discharge.

In addition to hospitalization for a medical illness, VTE risk factors in the study included age at least 60 years (40.5% of patients), malignancy (28%), and obesity (19%).

Overall, 6,185 patients (64%) did not receive any pharmacologic VTE prophylaxis while hospitalized, reported Dr. Amin, executive director of the hospitalist program and professor and chair of medicine at the University of California at Irvine, and his associates. Lack of thromboprophylaxis was most apparent in patients with cancer, occurring in about 70% of 2,544 patients.

Among the 3,490 patients who did receive pharmacologic VTE prophylaxis, 2,045 received enoxaparin and 1,044 received unfractionated heparin. Enoxaparin was the most commonly prescribed of the prophylactic agents in patients with heart failure, severe lung disease, or infectious disease; heparin was the most commonly prescribed agent in patients with cancer.

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FDA: No Increased Risk of Stroke, MI With Spiriva

HandiHaler safety reviewed in COPD.

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Treatment with the Spiriva HandiHaler, which contains a dry powder formulation of the anticholinergic tiotropium, does not appear to be associated with an increased risk of stroke, myocardial infarction, or cardiovascular death in patients with chronic obstructive pulmonary disease, the Food and Drug Administration announced last month.

The FDA has now completed its safety review of this product "and believes the available data do not support an association between the use of Spiriva HandiHaler and an increased risk for these serious adverse events," according to a statement issued by the agency.

The Spiriva HandiHaler, marketed by Boehringer Ingelheim and Pfizer, was approved in 2004 for the long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. It is administered once daily.

The FDA has been conducting a safety review of the Spiriva HandiHaler since the manufacturer submitted data suggesting that treatment with tiotropium was tied to a small increased risk of stroke, compared with placebo (2 cases per 1,000 treated patients). It announced the review in March 2008.

In October 2008, the agency issued a statement about two published studies that suggested an increased risk of stroke, MI, and death in patients treated with tiotropium.

The latest FDA statement said that a 4-year study

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INSIDE

Gene Signature, NSCLC Outcome Linked

BY SUSAN LONDON
Elsevier Global Medical News

CORONADO, CALIF. — A 93-gene signature is associated with the presence of epidermal growth factor receptor mutations in non–small cell lung cancer and predicts better survival in patients with early-stage disease.

In a study led by Dr. Pierre Saintigny of the University of Texas M.D. Anderson Cancer Center in Houston, researchers performed gene-expression profiling in untreated NSCLC tumors (adenocarcinomas or bronchioalveolar carcinomas) from 95 patients having disease of all stages, with the aim of developing a gene signature associated with EGFR mutations. The patients came from institutions in the United States and Asia.

The researchers then validated the signature in tumors from 99 patients with chemotherapy-refractory NSCLC who were enrolled in the BATTLE (Biomarker-Integrated Approaches of Targeted

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HELP FOR HAITI BLOG

CAPT Dennis Amundson, MC, USN, FCCP, Chair of the ACCP Disaster Response NetWork, has been deployed to the USNS Comfort and is docked near Haiti with a team of doctors and nurses. Read his blog at www.chestnet.org.

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CDC: Only 20% of U.S. Was Vaccinated for H1N1

BY ROBERT FINN
Elsevier Global Medical News

Between 39 million and 80 million individuals in the United States contracted 2009 influenza H1N1 between April 2009 and Dec. 12, 2009, according to data collected by the Centers for Disease Control and Prevention.

The midlevel of the estimated range is 55 million individuals.

Of those infected with H1N1 influenza, an estimated 173,000-362,000 have been hospitalized, and between 7,880 and 16,460 have died, the CDC reported.

About 18 million children 0-17 years of age contracted the virus. Adults 18-64 years of age accounted for another 32 million cases, and there were 5 million cases among individuals 65 years of age and older.

According to the results of two surveys, an estimated 61 million persons (20% of the U.S. population) received the monovalent H1N1 vaccine by Jan. 2, 2010, including 29% of children and 22% of health care personnel (MMWR 2010;59:1-5).

About 28% of the people in the initial target groups and 38% of those in the limited vaccine subset received at least one dose of the vaccine. The initial target groups included pregnant women, persons who live with or care for infants less than 6 months of age, young adults aged 6 months to 24 years, and persons aged 25-64 years with certain medical conditions. The limited vaccine subset included pregnant women, persons who live with or care for infants less than 6 months of age, health care and emergency services personnel, children aged 6 months to 4 years, and children aged 5-18 years with certain medical conditions.

The data came from two telephone surveys: the National 2009 H1N1 Flu Survey (NHFS) and the Behavioral Risk Factor Surveillance System (BRFSS).

At an estimated 33%, the vaccination rate was highest among children 6 months to 4 years of age. The lowest rate, 11%, was found among adults 65 years of age and older.

"The results in this report show that nearly 90% of adults aged [less than] 65 years with medical conditions that increase their risk for influenza-related complications remain unvaccinated," wrote J. A. Singleton and colleagues at the CDC. "Given the increased supply of vaccine, efforts to encourage 2009 H1N1 vaccination among persons at increased risk of … complications should be strengthened."

Pregnant women have been hit hard by H1N1 flu, both in terms of hospitalization rates and mortality, as reported elsewhere. The 38% H1N1 vaccination coverage among pregnant women in this report was higher than the typical rate of 15%-25% seen with seasonal flu vaccination, but the confidence interval of 24%-52% is large.

The surveys also revealed lower vaccination coverage among blacks than whites, similar to the disparities seen in seasonal vaccine coverage. "The finding of lower 2009 H1N1 coverage among black heath care workers … highlights a role for targeted outreach efforts," the investigators wrote. ■

Autopsies Show Distinct H1N1 Lung Damage

BY MIRIAM E. TUCKER
Elsevier Global Medical News

Three distinct histological patterns were found in the lungs of 21 Brazilian patients who died of the novel human influenza A(H1N1) infection in July and August of 2009.

The first-ever autopsy study to examine the systemic human pathology of the novel pandemic H1N1 virus demonstrated that the main pathological changes in the 21 individuals were localized to the lungs, where there was also evidence of ongoing aberrant immune responses, Dr. Thais Mauad and associates reported in the Jan. 1 issue of the American Journal of Respiratory and Critical Care Medicine.

"The cause of death in all patients was extensive involvement of the lungs," said Dr. Mauad of the pathology department at the Hospital das Clinicas, Sao Paulo, and associates.

The 21 patients ranged in age from 1 to 68 years (median 34 years), with most (15, or 71%) between the ages of 30 and 59 years. Twelve patients (57%) were male. Two were children, and one was a pregnant woman. Pre-existing medical conditions were present in 16 patients (76%), including cardiovascular disease (7, or 33%) and cancer (5, 24%). Six patients (29%) were current smokers.

Most patients presented with dyspnea (86%), fever (71%), myalgia (67%), and cough (57%). All had respiratory failure requiring mechanical ventilation. Sixteen (76%) were admitted to intensive care, while the other five died in emergency services, the investigators reported.

All patients had heavy, consolidated lungs that were diffusely edematous with variable degrees of hemorrhage, and all but one had exudative diffuse alveolar damage (DAD). Among the 20 with DAD, three distinct patterns of pulmonary pathological changes were identified: Nine patients had classic exudative DAD without interstitial inflammation, six had severe necrotizing bronchiolitis, and five presented with exudative DAD with an immense hemorrhagic component.

"Our data show that the fatalities were related to extensive diffuse alveolar damage, with variable degrees of pulmonary hemorrhage and necrotizing bronchiolitis," said Dr. Mauad, also of the pathology department at São Paulo (Brazil) University, and associates (Am. J. Respir. Crit. Care Med. 2010;181:1-8).

Evidence of bacterial co-infection was found in 8 (38%) of the 21 patients. Among those were five of the six patients with the necrotizing bronchiolitis pattern, which was characterized by a more severe neutrophil-predominant inflammatory exudate than the others, according to the authors.

Previous reports on the pathology of influenza have suggested that the presence of many neutrophils in lung tissue strongly suggests bacterial co-infection, they noted.

The authors reported that they had no conflicts of interest. ■

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CHEST PHYSICIAN

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Pulmonary Perspectives

Racial Disparities in Lung Cancer

Despite achievements in the reduction of tobacco use in adults, cigarette smoking is a primary contributor to many of the leading causes of death in the United States, such as heart disease, lung cancer, and COPD. Though there have been decreases in cancer death rates in the past 2 decades, racial disparities in cancer mortality persist, particularly in regards to African American men (Table) (DeLancey et al. *Cancer Epidemiol Biomarkers Prev.* 2008:17[11]:2908). According to the American Cancer Society, African Americans continue to bear a disproportionate burden of cancer with the highest mortality of any ethnic group for all cancers combined and for most major cancers. Bronchogenic carcinoma is the second most common cancer in African American men and women. From 2000 to 2003, the average incidence of bronchogenic carcinoma was approximately 40% higher in African American men than in white men. From 2000 to 2003, the average annual death rate for bronchogenic carcinoma was 30% higher in African Americans compared with white subjects. African Americans also have a decreased likelihood of 5-year survival from cancer at all sites, at all stages of diagnosis (American Cancer Society. *Cancer Facts & Figures for African Americans 2007-2008*. Atlanta, GA: American Cancer Society, 2007).

It is well known that risk for lung cancer varies among smokers (Bach et al. *J Natl Can Inst*. 2003;95[6]:470). Despite the fact that African Americans initiate smoking at later ages than white subjects and smoke fewer cigarettes per day (Muscat et al. *Cancer* 2005;103[7]:1420), African American men have higher lung cancer incidence and mortality (Harris et al. *Int J Epidemiol*. 1993;22[4]:592; Alberg et al. *Semin Respir Crit Care Med*. 2008;29[3]:223; Gadgeel et al. *Cancer Metastasis Rev.* 2003;22[1]:39; Jemal et al. *CA Cancer J Clin*. 2009;59[4]:225). The reasons for this greater prevalence and mortality have not been conclusively elucidated. Potential explanations may be biological, genetic, or related to socioeconomic status, where poverty, education, or lack of or insufficient insurance may be factors. Other reported mechanisms include distrust of the medical establishment (Gordon et al. *J Clin Oncol*. 2006;24[6]:904), refusal of operative intervention (McCann et al. *Chest*. 2005; 128[5]:3440), and treatment bias.

Differences in nicotine metabolism and smoking behaviors have been reported between racial groups. It has been demonstrated that African Americans have higher serum cotinine levels per cigarette smoked, slower clearance of cotinine, and higher intake of nicotine per cigarette smoked (Perez-Stable et al. *JAMA*. 1998;280[2]:152). Other studies have documented that African Americans exhibit more loss of lung function per cigarette smoked (Dransfield et al. *Respir Med*. 2006;100[6]:1110).

Disparities in tobacco-related knowledge have been reported. Finney and colleagues analyzed data from the National Cancer Institute's Heath Information National Trends Survey to determine knowledge of smoking risk and cancer prevention. Knowledge of lung cancer mortality was lower among women, older adults, and non-Hispanic blacks (Finney et al. *Nicotine Tob Res*. 2008;10[10]:1559). In an analysis of 4,756 smokers who participated in the 2005 National Health Interview Survey (NHIS), African American and Hispanic smokers had significantly lower odds of being asked about tobacco use, adjusted odds ratio (AOR) = 0.70 and 0.69, respectively; being advised to quit smoking (AOR = 0.72 and 0.64, respectively); or having used a smoking cessation aid in the past year (AOR = 0.6 and 0.59, respectively) (Cokkinides et al. *Am J Prev Med*. 2008:34[5]:404).

When lung cancer is localized at diagnosis, the 5-year relative survival rate for African Americans is 42%, though only 14% of lung cancer cases are diagnosed at this stage (American Cancer Society). Compared with white subjects, African Americans tend to present with lung cancer at a higher stage (Berger et al. *Curr Probl Cancer*. 2007:31[3]:202). In a study of race and sex differences in the receipt of timely and appropriate lung cancer treatment, Shugarman and colleagues analyzed Surveillance Epidemiology and End Result (SEER) data linked to Medicare claims for individuals diagnosed with non-small cell lung cancer. For claims analyzed between 1995 and 1999 in individuals with stage I and stage II cancer, African Americans were 66% less likely to receive timely and appropriate therapy in comparison to white subjects. Compared with white men, African American men were the least likely to receive resection (22 % vs 44%). African Americans were 43% less likely to receive timely surgery, chemotherapy, or radiation for stage III disease and 51% less likely to receive timely chemotherapy for stage IV disease (Shugarman et al. *Medical Care*. 2009;47[7]:774). Farjah and colleagues analyzed SEER data for stage I and stage II lung cancers diagnosed between 1992 and 2002.These authors did not find any statistically significant differences in the racial distribution of cancer stage or histologic findings. In this cohort of 17,739 subjects (89% white and 6% African American), African American patients underwent resection less often, 69% vs 83% ($P < .0001$, [OR 0.43, 95% CI 0.36 - 0.52]) (Farjah et al. *Arch Surg*. 2009;144[1]:14). In surprising contrast to an older series (Bach et al. *N Engl J Med*. 1999:341[16]:1198), the lack of operative intervention did not result in a detectable mortality difference. This unexpected finding was speculated to be due to inadequate risk adjustment or unmeasured patient selection factors, such as intrinsic lung function, which affect outcomes. In areas with unlimited access to medical care, such as military facilities or Veteran's Administration facilities, these large variations in outcome are largely mitigated (Mulligan et al. *Cancer Epidemiol Biomarkers Prev*. 2006;15[1]: 25; Greenwald et al. *Am J Public Health*. 1998;88[11]:1681)

Even for those in high risk groups, there are no consensus guidelines for lung cancer screening (Flenaugh et al. *Clin Chest Med* 2006:27[3]:431; Smith et al. *CA Cancer J Clin* 2009;59[1]:27), though a lung cancer risk prediction model has been developed and validated specifically for African Americans (Etzel et al. *Cancer Prev Res* 2008;1[4]:255). As lung cancer is primarily caused by tobacco smoking, many cases of lung cancer are, therefore, preventable. The prevalence of smoking in African American men was estimated to be 27.6% in 2006 (*MMWR Morb Mortal Wkly Rpt* 2007:56[44]:1157). This exceeds the threshold of 12% or less targeted for reduction in smoking by 2010. Of the 45.3 million adults in the United States who were current smokers in 2006, men (23.9%) were more likely to smoke than women (18%), and African Americans (23%) were more likely to be current smokers than whites (21.9%).

Tobacco smoking, and its risk for lung cancer, is increasingly concentrated in populations with limited resources whose lives and smoking behaviors may be affected by stress, violence, and unemployment (Irvin Vidrine et al. *Curr Oncol Rep*. 2009;11[6]: 475). Adequate education about the risks of cigarette smoking and comprehensive, culturally competent smoking cessation programs targeted to high risk groups need immediate implementation. ■

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Comparison of Lung Cancer Incidence and Death Rates 2000-2003

	African American Rate[a]	Caucasian Rate[a]	Absolute Difference[b]	Rate Ratio[c]
Male				
Cancer incidence rate	112.2	81.7	30.5	1.4
Cancer death rate	97.2	73.4	23.8	1.3
Female				
Cancer incidence rate	53.1	54.7	–1.4	1.0
Cancer death rate	39.8	42.2	–2.4	0.9

[a] Rates are per 100,000 and age-adjusted to 2000 US standard population.
[b] Absolute difference = African American minus Caucasian rate.
[c] Ratios of rates in African Americans divided by those of Caucasians are based on two decimal places.
Source: American Cancer Society. Cancer Facts and Figures for African Americans 2007-2008. Atlanta; 2007.

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

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Commentary

This review on racial disparities in lung cancer by Dr. Marilyn Foreman and colleagues is excellent and quite timely, as our nation is struggling with the difficult task of health reform. Dr. Foreman reminds us that substantial racial disparities continue in the incidence, mortality and risk of lung cancer.

A report from the Agency for Healthcare Research and Quality (AHRQ), the 2006 National Healthcare Disparities Report (www.ahrq.gov/qual/nhdr06/nhdr06.htm. Accessed January 20, 2010), notes that disparities related to race, ethnicity, and socioeconomic status "still pervade the American health care system."

A recent report by the Urban Institute (www.urban.org/publications/411962.html, accessed January 20, 2010) estimated that in 2009, disparities among African Americans, Hispanics, and non-Hispanic whites would cost the health-care system $23.9 billion, and over the 10-year period from 2009 through 2018, the total cost will be $337 billion (including $220 billion for Medicare).

So, in addition to the moral imperative for solving the disparities in health care, there are strong economic imperatives. We must have health reform that is responsive to the health needs of the underserved of this nation.

Dr. Alvin V. Thomas, Jr, FCCP
Past President, ACCP

FDA Turns Down Erlotinib for NSCLC Maintenance

BY LAUREN SMITH
"The Pink Sheet"

GAITHERSBURG, MD. — Erlotinib has been rejected as first-line maintenance, monotherapy treatment in patients with non–small cell lung cancer that is either locally advanced or metastatic and who have not progressed on first-line treatment with platinum-based chemotherapy.

The Oncologic Drugs Advisory Committee voted against approval by 12-1 at a Dec. 16 meeting.

The committee, which advises the Food and Drug Administration, said its main concern was the modest effect seen during the company-sponsored trial as well as the fact that only one trial was used to support the entire supplemental new drug application. Erlotinib is marketed as Tarceva by OSI Pharmaceuticals Inc.

"We were presented with a single study, not two studies," said Dr. Ronald Richardson of the Mayo Clinic, Rochester, Minn. "Not a small, well-designed study plus a larger study with supporting evidence, but a single study with some design flaws showing very modest benefits."

SATURN (Sequential Tarceva in Unresectable NSCLC) is the sole randomized trial, which compared erlotinib with placebo as maintenance treatment in 889 patients with locally advanced or metastatic NSCLC who had not progressed after four cycles of first-line treatment with platinum-based chemotherapy. Treatment was continued until progression, death, or unacceptable toxicity.

The protocol-specified, co-primary end points were progression-free survival (PFS) in all patients and progression free survival in the epidermal growth factor receptor–positive subgroup. However, in April 2005, the FDA indicated that overall survival would be needed demonstrate the value of maintenance targeted therapy.

Although erlotinib proved to be superior to placebo for both co-primary PFS end points, and with the use of the protocol-specified unadjusted log rank test, as well superior to placebo for overall survival in all patients and in the epidermal growth factor receptor (EGFR)–positive subgroup, it was not superior to placebo for overall survival.

"In a setting like this, survival is much more relevant than PFS," said Thomas Fleming, Ph.D., of the University of Washington, Seattle. "PFS can provide important insight on clinical benefit, but survival is very critical in capturing the overall sense of benefit."

Furthermore, the superiority seen for PFS—2.6 months for the placebo arm versus 2.8 months for the Tarceva arms—while statistically significant, was considered "modest at best" by both FDA and committee members. The overall survival, which was not statistically significant, was 11 months for the placebo arm and 12 months for the Tarceva arm.

Members also criticized the trial results in light of already approved therapies for the NSCLC indication, mainly the drug pemetrexed (Alimta). "Once a drug is approved for an indication, the bar is raised for me-too drugs," said Dr. Wyndham Wilson of the National Cancer Institute.

Dr. Michael Link of Stanford (Calif.) University agreed, but acknowledged that it is a difficult decision: "The degree of benefit from the drug is reasonably small, but not so much different than other products that have been approved. I thought the risks were relatively minor …So where do you draw the line here?"

Committee members also argued that the patient subgroup analyses, while on the right track to being important for the progress of personalized medicine, were not well collected and riddled with data discrepancies.

"No. 1, whenever you do maintenance therapy, there will be many people who will have no benefit from the maintenance. That's when biomarkers come into play," Dr. Wilson said. "But due to a variety issues, we don't have definitive biomarkers to identify those patients who will benefit from the maintenance therapy. You have to consider that, just because you don't show a drug has excessive toxicity, you don't want to expose patients unnecessarily to that drug.

"I couldn't agree more that we need to empower people to make wise choices for patients," Dr. Fleming said. "But it comes down to having an evidence-based justification to allow people to make informed choices."

Analysts had previously predicted that the EGFR-negative subgroup, the squamous cell subgroup, and the EGFR wild-type subgroup were at risk for exclusion from the indication. ■

Elsevier Global Medical News and "The Pink Sheet" are published by Elsevier.

Dr. W. Michael Alberts, FCCP, comments: *Maintenance chemotherapy with pemetrexed (or, as some term it, early second-line therapy) has been shown to benefit patients with locally advanced or metastatic nonsquamous lung cancer who do not progress on first-line therapy. Unfortunately, erlotinib does not appear to improve the overall survival when used in this manner.*

Higher H1N1 Mortality Seen In American Indians

BY MIRIAM E. TUCKER
Elsevier Global Medical News

The death rate from 2009 pandemic influenza A(H1N1) is four times higher among American Indians/Alaska Natives than among all other racial or ethnic groups in a study that combined data collected from 12 U.S. states.

Released Dec. 11 by the Centers for Disease Control and Prevention, the study was conducted by a working group comprising agency and state health officials, tribal epidemiology centers, and the Indian Health Service. Data included influenza cases reported during April 15–November 13 from 12 states in which half of all the American Indians/Alaska Natives (AI/AN) live: Alabama, Alaska, Arizona, Michigan, New Mexico, North Dakota, Oklahoma, Oregon, South Dakota, Utah, Washington, and Wyoming.

A total of 426 H1N1 deaths were reported by the 12 states during the study period, of which 9.9% (42) occurred among AI/ANs. By contrast, AI/ANs make up just 3% of the states' population. The overall H1N1-related death rate was 3.7 per 100,000 AI/AN population, compared with just 0.9/100,000 for all other racial/ethnic groups combined, giving a mortality ratio of 4.0, the CDC reported on Dec. 11 in Morbidity and Mortality Weekly Report (2009;58: 1341-4).

By age, the H1N1 mortality rates per 100,000 AI/AN population were 3.5 for infants and toddlers aged 0-4 years, 1.1 for youth aged 5-24 years, 4.2 for adults aged 25-64, and 7.2 for those aged 65 and older. Each of these death rates was higher than those of all other racial and ethnic groups combined, the CDC said.

Reasons for the disparity are not clear, but might relate to the high prevalence of conditions such as diabetes and asthma in the AI/AN population. Among the AI/AN individuals with H1N1-related death, 81% had high-risk conditions, compared with 77.6% of individuals in all other racial/ethnic groups combined. Thirty-one percent of the AI/AN decedents had asthma, versus just 14.1% of all other racial/ethnic groups combined, while the proportions with diabetes were 45.2% vs. 24.0%, respectively.

Health disparities between the AI/AN population and other racial/ethnic groups have been well documented, and the higher mortality among AI/ANs seen in this study is consistent with reports of increased influenza-related morbidity and mortality among indigenous populations in other parts of the world during the current H1N1 pandemic as well as previous pandemics. In fact, the same mortality ratio—a fourfold higher influenza-related death rate—was seen among AI/ANs, compared with the general urban population during the 1918-19 influenza pandemic, the CDC noted. ■

NETWORKS

Disaster Response, Home Care, Diffuse Lung Disease

Special Note

CAPT Dennis Amundson, MC, USN, FCCP, Chair of the ACCP Disaster Response NetWork, has been deployed to the USNS Comfort and is docked near Haiti with a team of doctors and nurses. Patients are brought to the ship by helicopter and triaged. The crew provides basic care and treatment for trauma patients, takes x-rays, and performs surgeries. If necessary, patients are moved to an ICU. Monitor the work of Dr. Amundson and others as he reports his experiences at www.chestnet.org.

Disaster Response

Humanitarian assistance (HA) is "the aid and actions designed to save lives, alleviate suffering, and protect human dignity." HA is also part of many countries' international diplomacy policies. "Health" HA is a major, and growing, part of US international diplomacy.

What Is International Health Diplomacy? "Diplomacy" is "influencing the actions required to create a stable and sustainable society." Pillars of diplomacy include an unbiased press, a basic education system, a stable central government, and a safe environment with adequate food, water, power, sanitation, and basic health care. Unfortunately, the developing world remains a difficult environment in which to perform HA. Our international responses remain fragmented, stove-piped, and fraught with political, personal. and institutional biases. Such an atmosphere makes it difficult for the altruistic health-care worker to negotiate.

In 2005, the Department of Defense (DOD) received a requirement to engage in HA in the world community, creating an environment where both civilian and military health-care workers serve side-by-side in these needy countries. Some collaborations have begun, and, in many cases, these partnerships are viable. In other situations, relationships are strained due to mistrust, misunderstanding, and poor communication. There are many opportunities to participate in HA. However, to be effective and to better understand what types of HA the United States is engaged in requires some scrutiny and information. The well-meaning who want to participate need to get appropriate information to make informed decisions about how best to be involved.

The Disaster Response NetWork is composed of individuals representing agencies and organizations involved in HA, including the Department of Defense, nongovernmental organizations, international organizations, and US government agencies. The Disaster Response NetWork is available to assist those interested in getting involved in HA opportunities and to help individuals make appropriate choices for participation.

Contact Jennifer Nemkovich at networks@chestnet.org for more information.

CAPT Dennis Amundson, MC, USN, FCCP
NetWork Chair

Home Care

Challenges of Noninvasive Positive Pressure Ventilation (NPPV)

Clinicians treating patients with chronic respiratory insufficiency are challenged by both the practice guidelines and the reimbursement criteria. The current state of affairs may well change in 2010, but the present issues are described briefly below. The NAMDRC Consensus Conference took place in February 1998 and the "Clinical Indications for Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure" document was later published in *CHEST* in 1999. The conference was a unique format in that it included academic clinicians, Centers for Medicare and Medicaid Services (CMS) officials, and industry representatives, although only the clinicians provided writing for the publication. The document contained limited evidence-based medicine, but it did lead to the CMS criteria for reimbursement to guide future practice.

Ultimately, several categories of guidelines and reimbursement have been established. The way to approach the categories is to realize they are first guided by the primary diagnosis and not by the subsequent criteria. It is also important to realize that patients who require or are allowed access to a backup rate (**E0471**) obtain nearly twice the monthly reimbursement than those not using a backup rate (**E0470**). Therefore, the use of the **E0471** is more restricted.

These disease categories require the clinician to focus on sleep early in the assessment of the patient. It is necessary to decide on the need and urgency of a sleep study, as well as the design of the sleep study in order to effectively demonstrate the criteria and good response to the respiratory assist device (RAD).

The bottom line is that one needs to know the rules to play the game, but playing the game is not gaming the system—it is simply necessary. Ironically, if the treating clinician determines that the RAD criteria cannot be met, but nocturnal NPPV support is necessary, he or she can always prescribe a portable home ventilator (**E0450**), with a diagnosis of "hypoxic or hypercapnic respiratory failure" and use a volume-targeted ventilator with only a blood gas demonstrating this diagnosis. Although pulmonologists often prescribe this equipment, sleep specialists are more typically familiar with the indications and reimbursement criteria and are readily available to help.

Dr. Peter Gay, FCCP
NetWork Chair

Interstitial and Diffuse Lung Disease

How To Best Handle Preliminary Clinical Trial Results

A patient comes to your office with a press release on pirfenidone for the treatment of interstitial pulmonary fibrosis (IPF). While there is no peer-reviewed publication and no FDA approval, there is also no proven effective pharmacologic therapy for IPF. So how do we, as medical professionals, best handle incomplete information on such a disease?

"Should I be flying to Japan where the drug is approved?" "Does it work?" "When can I get it?" "Should I get it?" This is real life.

Data regarding the safety and efficacy of pirfenidone from the CAPACITY 1 and 2 trials have been disseminated. Indeed, a quick Google search would reveal a number of press releases over the last year. This, of course, adds to the buzz but does not inform or contribute to responsible clinical practice.

The principle of autonomy would hold that clinicians should share as much information as possible with patients so that they may make informed decisions about their own health. However, the existence of unpublished data sets that have not undergone either peer review or FDA review cannot be presented as "medical fact."

In our opinion, the clinician should maintain equipoise with regard to clinical investigations throughout the investigative process that includes a full and fair evaluation of the trial results.

A balanced approach to the data is critically important. As an example, the original data sets from the initial gamma-interferon trials were felt to give a positive signal, and, as a result, use of the drug on an off-label basis ensued. Not until the negative results of the larger INSPIRE trial became known was an unproductive clinical practice discontinued.

CAPACITY 1 and CAPACITY 2 demonstrated discordant results. While CAPACITY 2 showed a statistically significant reduction in the rate of decline in the treatment group as measured by pulmonary function testing, CAPACITY 1 did not show any significant differences between the treatment arm and placebo.

Ultimately, a new drug application with the pertinent data sets has been submitted to the FDA for a "fast track" designation.

While the history of pirfenidone may be shared with patients, the wisest course of action remains to await word from the FDA and counsel patience.

Dr. Imre Noth, FCCP, NetWork Chair;
and
Dr. Stephen Frankel, FCCP, NetWork Vice-Chair

PCCU Lessons for February

www.chestnet.org/accp/pccu

New lessons are now posted on the ACCP Web site on the 1st and 15th of each month.

PCCU
PULMONARY AND CRITICAL CARE UPDATE

- **The Unexpandable Lung.** *By Dr. John T. Huggins; and Dr. Peter Doelken, FCCP*
- **Sleep Deprivation: The Metabolic Costs of Chronic Partial Sleep Loss.** *By Dr. Qanta A. Ahmed, FCCP*

BY PAUL A. MARKOWSKI, CAE

FROM THE CEO
Beginnings

You might have seen or heard my name by now. As the new EVP and CEO of the College, I have been in a constant state of movement—greeting and meeting many of you—our leaders, members, staff, and friends of the American College of Chest Physicians. It has been such an exhilarating experience, since my October 2009 introduction into this position, to have already witnessed so many of the strengths and passions of the organization and the people who surround it. My family and I are excited to be back in this area and have been warmly welcomed by many colleagues and friends.

For the last 4 years, I was the Deputy Executive Vice President and Chief Operating Officer at the American Academy of Otolaryngology – Head and Neck Surgery, in Alexandria, VA. Prior to that position, I worked with the American Medical Association for 15 years, holding such positions as Director of Federation Relations and Advocacy Campaign Manager. I am a lifelong Wisconsin and Chicago-area resident, but after 4 years of Virginia winters, I am learning how soon we forget about the "lake-effect" weather of this Midwestern area. Yet, spring will soon be here, and, with it, the College leadership and staff will be in the midst of an important strategic planning event.

As I indicated, I have met with ACCP leaders, staff, and other stakeholders to garner strategic insights and contributions that will help us map the ACCP course for 2010 and beyond. As one of the new tools we will be using, the "ACCP Environmental Snapshot" has been developed to assist in the successful operation of the College. It is an assessment of the environment, both external and internal, of the ACCP and includes the major opportunities and challenges for the College in 2010 from the perspective of the ACCP staff Executive Team. It also describes some of the immediate steps that the Executive Team has taken to address described priorities within the document.

The staff will require guidance from our Board of Regents and its Executive Committee and has had preliminary targeted strategic discussions with the Committee that will lead to defining the primary strategic questions for our spring planning sessions. Simultaneously, The CHEST Foundation has engaged the services of a consulting group that will do an analysis of the fundraising and outreach potential of The Foundation and prepare a strategic fundraising plan to engage not only our generous membership and their patients but other foundations and socially responsible corporations.

Going forward, the Environmental Snapshot will hopefully assist in prioritization and budgeting for the ACCP in order to successfully and efficiently align our resources. Additionally, we must be vigilant in continuously gathering data that will provide us with the most appropriate and useful information for future decision making.

In the coming weeks, we will be asking members to respond to a carefully crafted member survey that will assist us in our strategic planning and in assessing member needs. The results of the survey will be reviewed and information used to further enhance the Environmental Snapshot to advance the ACCP this year and beyond. Thank you, in advance, for responding to this all-important survey instrument.

I look forward to working with the entire ACCP family to maximize the wonderful talents and opportunities within this organization and bringing the College to its greatest heights. Watch for regular updates from me in *CHEST Physician*. ■

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

Guidelines International Network Conference 2010

August 26-28, 2010 – Conference Dates
August 25, 2010 – Preconference Methodology Courses
Chicago, IL, USA
Host: American College of Chest Physicians

The American College of Chest Physicians (ACCP) is honored to be hosting the Guidelines International Network Conference 2010 (G-I-N Conference 2010) in Chicago, IL, August 25-28, 2010. All ACCP members are invited to attend at reduced member prices. The theme this year, "Integrating Knowledge. Improving Outcomes." is designed to encourage collaboration, networking, and sharing of knowledge and methodologies between professionals in all aspects of evidence-based medicine.

The G-I-N is an international not-for-profit association of organizations and individuals involved in the development and use of clinical practice guidelines. G-I-N supports international collaboration to improve the quality of health care by promoting systematic evidence review, rigorous development of clinical practice guidelines, and application into practice. Founded in 2002, G-I-N has grown to include 93 organization members and partners, representing 38 countries.

Who should attend?

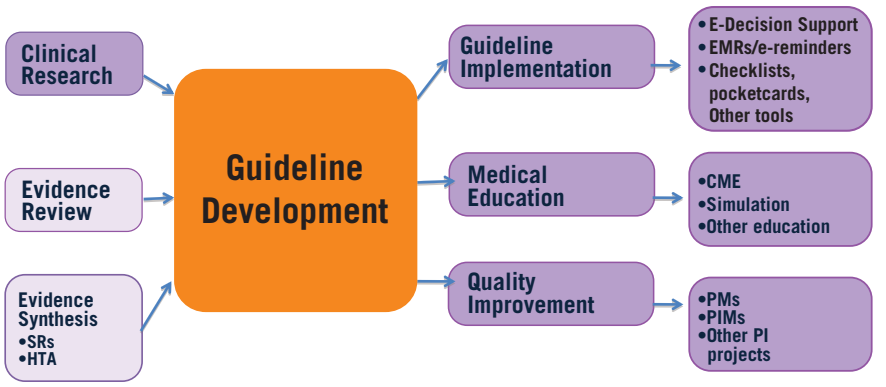
Professionals in the following fields of evidence-based medicine are encouraged to attend conference presentations and participate in interactive workshops:

- Guideline development
- Guideline implementation
- Clinical decision support
- Electronic medical records
- Quality improvement
- Performance measures
- Health insurance payers/purchasers
- Utilization review
- Medical providers and executives
- Public health agencies
- Health policy
- Health-care research
- Evidence synthesis
- Patient care

In addition to the concepts and innovations presented and discussed at the conference, there will be three methodology courses offered the day before the main conference begins.

The **ACCP Guidelines Methodology Course** will inform attendees of the internationally recognized processes employed by the ACCP Health and Science Policy Committee and guideline panels to develop over 20 years of well-known and widely-used guidelines in the prevention, diagnosis, and treatment of venous thromboembolism, lung cancer, pulmonary arterial hypertension, cough, and many other cardiopulmonary conditions. Those in attendance will receive materials to help their organizations model guideline development after the ACCP processes.

G-I-N PUBLIC is a G-I-N Working Group whose main objective is to support effective patient and public involvement in the development and implementation of clinical practice guidelines. The group offers a forum for exchange between patient and public organizations, clinical practice guideline developers, and researchers.



GRADE is both a methodology for assessing the evidence and a grading system for guideline recommendations. The methodology of GRADE has evolved over the years and is now employed by guideline developers and evidence synthesizers all over the world.

Registration for these 1-day courses will be ticketed separately. ACCP members are entitled to reduced prices for the courses and the conference. To register, visit www.GIN2010.org. ■

This Month in *CHEST:* Editor's Picks

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

- **Efficacy and Safety of Low Dose rt-PA for the Treatment of Acute Pulmonary Thromboembolism: A Randomized, Multicenter, Controlled Trial.** *By Dr. C. Wang, et al.*
- **Effects of Pulmonary Rehabilitation in Patients With Restrictive Lung Diseases.** *By Dr. B. Salhi, et al.*

MEDICAL ETHICS
- **"CURVES": A Mnemonic for Determining Medical Decision-Making Capacity and Providing Emergency Treatment in the Acute Setting.** *By Dr. G. V. Chow, et al.*

TRANSPARENCY IN HEALTH CARE
- **Preoperative Briefing in the Operating Room: Shared Cognition, Teamwork, and Patient Safety.** *By Dr. Y. Einav, et al.*

www.chestjournal.org

Hospital Infections Put STEMI Patients at Risk

At least 45% of infected patients were hospitalized for 1 week or more.

BY MITCHEL L. ZOLER
Elsevier Global Medical News

ORLANDO — Infection following acute hospitalization for ST-segment elevation myocardial infarction was linked with prolonged hospitalization and significantly increased risk of death, in a review of more than 11,000 patients in Florida hospitals in 2006.

The incidence of in-hospital infection among the 11,879 patients hospitalized in Florida for ST-segment elevation myocardial infarction (STEMI) was 17%, with more than a third of these patients having two or more infections while hospitalized, Michelle C. Nash and her associates reported in a poster at the annual scientific sessions of the American Heart Association. The most common infections were urinary tract (in 6%), pneumonia (5%), surgical site (4%), and bloodstream (3%). Other infections collectively affected another 4% of the patients.

Among STEMI patients without an infection, 16% had a length of stay of 7 days or more. Among infected patients, the percentage who had an LOS of a week or longer ranged from 45% in patients with surgical site infections to 75% in those with bloodstream infections, said Ms. Nash, a researcher in the department of epidemiology and biostatistics at the University of South Florida in Tampa, and her associates.

In addition, while surgical site and some other infections led to mortality rates nearly identical to the 7% rate in STEMI patients who never developed an infection, other types of infection led to increased in-hospital mortality, such as the 31% rate in patients with bloodstream infections and the 20% rate in those with pneumonia.

In-hospital infections also boosted the risk that STEMI patients would need mechanical ventilation or would develop renal failure or heart failure. "Notably, patients with miscellaneous infections, not those with pneumonia, had the greatest risk for mechanical ventilation" at 25%, compared with 5% in patients who developed pneumonia, the researchers said.

Their analysis also examined clinical features that appeared to be linked with an increased susceptibility to infection. The pattern of factors significantly associated with infection varied depending on infection site.

▶ **Bloodstream infection.** Patients treated with an indwelling arterial or venous catheter and those on dialysis were at increased risk for bloodstream infections. Both of these factors boosted the risk for a bloodstream infection by nearly sevenfold, compared with STEMI patients who did not receive these treatments. Other risk factors included chronic obstructive pulmonary disease (COPD), valve disorders, and blood transfusion, each of which roughly doubled the risk for a bloodstream infection.

▶ **Pneumonia.** Major risk factors for pneumonia included chronic bronchitis, an indwelling arterial or venous catheter, and dialysis, each of which quadrupled the risk. Other significant risk factors included alcohol abuse and COPD—each of which more than doubled the risk—and chronic kidney disease and an operative procedure, which each raised the risk for pneumonia by about 50%.

▶ **Surgical site infection.** Cardiac catheterization and dialysis each raised the rate of surgical site infection by more than 2.5-fold, compared with STEMI patients not receiving these procedures. Other significant risk factors included an indwelling arterial or venous catheter and blood transfusion, which each boosted the risk by 50%-100%. Two factors were found to significantly reduce the rate of surgical site infections: Percutaneous coronary intervention cut the risk by more than a third, and cigarette smoking cut the infection risk by 30%.

▶ **Urinary tract infection.** Female gender had the biggest impact on the risk of urinary tract infections, boosting the risk by nearly 2.5-fold. Dialysis also raised the risk more than twofold. Several other factors significantly raised the risk for urinary tract infection by 47%-94%: COPD, diabetes, chronic kidney disease, an operative procedure, an indwelling arterial or venous catheter, and blood transfusion. In addition, the risk for a urinary tract infection rose by a significant 27% for every 5-year increment in age. Finally, cigarette smoking significantly cut the risk by a third.

Ms. Nash and her associates said that they had no financial support from commercial sources to disclose. ■

VTE Prophylaxis Lacking

VTE • *from page 1*

"Even when pharmacological VTE prophylaxis was provided for the duration of hospitalization, the median length of hospital stay was just 3 days in this study, which falls short of the 6-14 days of VTE prophylaxis provided in clinical trials in medical at-risk patients," Dr. Amin and his associates wrote.

A total of 2,854 patients (29.5%) first received prophylaxis on the last day or next-to-last day of their hospital stay.

In the 30 days following hospital discharge, 98.2% of the medical patients analyzed received no further pharmacologic VTE prophylaxis. Among the 174 medical discharges who did receive outpatient pharmacologic prophylaxis, most received warfarin alone, followed by enoxaparin plus warfarin. Patients with heart failure had the highest level of outpatient prophylaxis within 30 days after discharge (4.8%), and infectious-disease patients had the lowest level (1.1%).

In order to assess pharmacologic VTE prophylaxis, inpatient data from the Premier's Perspective database were cross-matched at the individual patient level with Ingenix LabRx outpatient data from the i3 database (January 2005–December 2007). Patients at least 40 years old and at risk of VTE according to the 2004 American College of Chest Physicians guidelines were included if they had cancer (without surgery), heart failure, severe lung disease, or infectious disease. The data, which came from various payers and types of hospitals in diverse geographical areas, "may not be representative of the U.S. population as a whole," the researchers noted.

The analysis did not include patients undergoing orthopedic surgery, and excluded patients with contraindications to pharmacologic VTE prophylaxis and those without health plan eligibility in the 3 months before hospital admission and 6 months following discharge. The mean age of the patients was 58 years; 67% had managed care, 22% Medicare, 8.8% commercial insurance, and 1.3% Medicaid.

The authors disclosed receiving editorial support from Sanofi-Aventis U.S. in the preparation of the poster, but noted that they were fully responsible for all content and editorial decisions. Coauthors Jay Lin, Ph.D., is an employee of Sanofi-Aventis and Amy Ryan is an employee of Premier Inc. ■

Dr. Jeana O'Brien, FCCP, comments:
This study by Amin, et al. reports on 9,675 patients who met criteria for venous thromboembolism (VTE) prophylaxis and yet did not receive the indicated therapy. The nature of this retrospective review did not allow a thorough assessment of the reasons this occurred. Unfortunately, prior studies have also demonstrated similar gaps between recommendations and practice. While reasons for this are likely complex and varied, this challenge will most certainly require more than additional education. Evidence-based, standardized order sets and computerized physician order entry are systematic approaches that can prompt the clinician in these settings. As CMS encourages hospitals and physicians to move in this direction through the Meaningful Use proposals of the ARRA, we hopefully will see improvements with future analyses.

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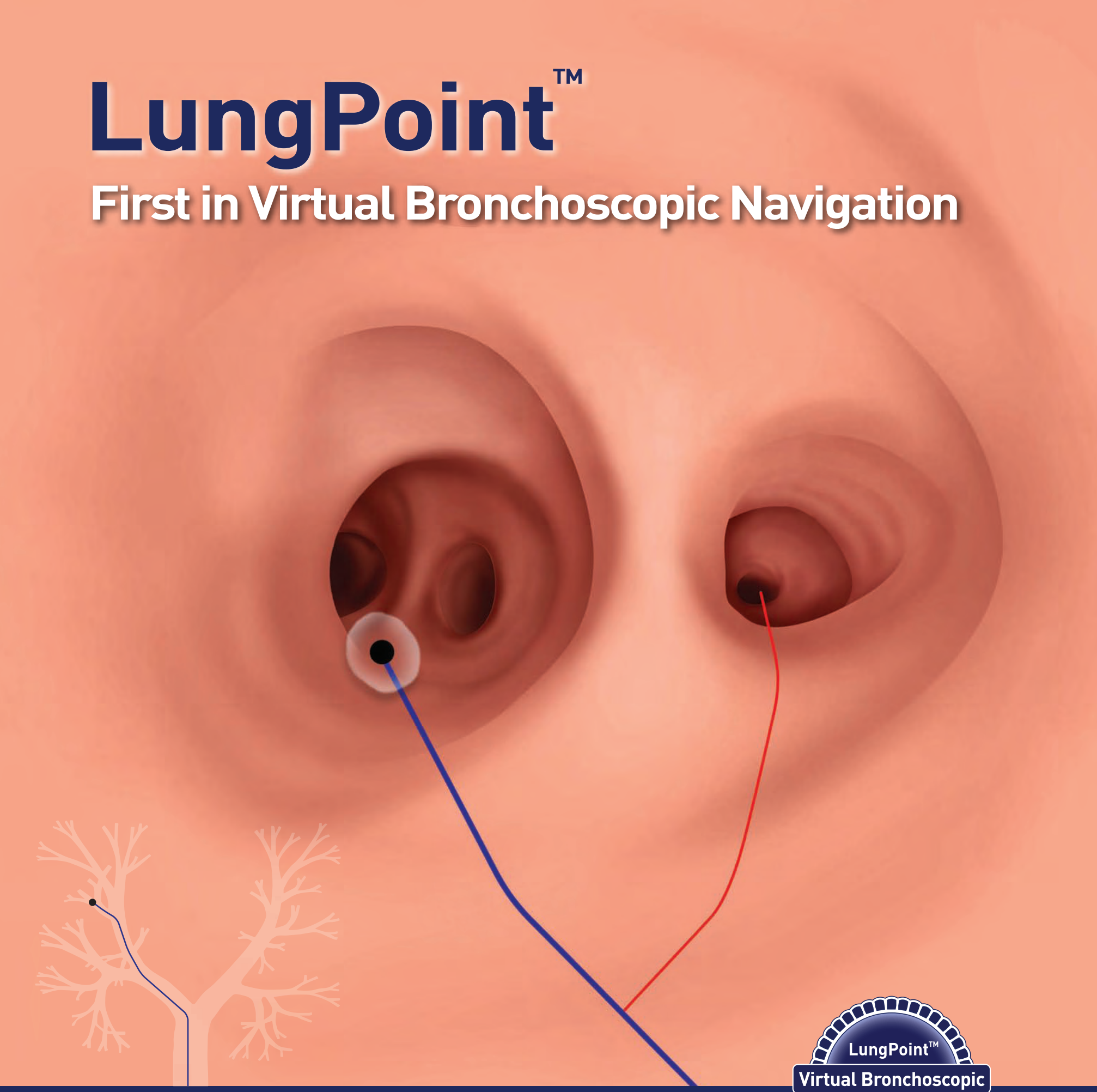

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Gene Polymorphisms Tied to Impaired Lung Function

Carriers have lower FEV_1 values, according to meta-analysis.

BY DIANA MAHONEY
Elsevier Global Medical News

Researchers have identified polymorphisms in nine genetic regions associated with forced expiratory volume in the first second or its ratio to forced vital capacity, a discovery that could provide insights into the pathogenesis of chronic lung disease, according to a meta-analysis reported in Nature Genetics.

"Individuals carrying these polymorphisms will have lower pulmonary function than predicted at a given age, thus placing them at greater risk for developing [chronic obstructive pulmonary disease] and at a greater risk of mortality," the study's authors said.

Dana B. Hancock, Ph.D., of the National Institute of Environmental Health Sciences, Research Triangle Park, N.C., and colleagues conducted a meta-analysis of genomewide association studies for two clinically important lung function measures: forced expiratory volume in the first second (FEV_1) and its ratio to forced vital capacity (FEV_1/FVC).

They identified one genetic locus associated with the former measure and eight loci that were associated with the latter. The loci "include genes with biologically plausible functions, and their identification here encourages future investigations to examine the mechanisms underlying their influence on pulmonary function," the authors wrote (Nat. Genet. 2010; 42:45-52).

For the meta-analysis, the investigators used about 2,534,500 single-nucleotide polymorphisms (SNPs) in 20,890 individuals of European ancestry from four studies within the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium. Those studies, which come from the United States and Europe, included Atherosclerosis Risk in Communities (ARIC), the Cardiovascular Health Study (CHS), the Framingham Heart Study, and the Rotterdam Study.

The researchers adjusted the data for smoking status and quantity (in pack-years), and generated separate subgroup analyses for "ever-smokers" and "never-smokers."

Genetic loci that met genomewide significance were evaluated for replication with the SpiroMeta consortium, an independent consortium having a combined genomewide association study sample size of 20,288 participants of European ancestry, the authors wrote.

The investigators found genomewide significant associations with FEV_1/FVC for SNPs in seven previously unrecognized independent loci, including GPR126, ADAM19, AGER-PPT2, FAM13A, PTCH1, PIDI, and HTR4. Those seven loci include genes that have been linked to accelerated pulmonary function decline, symptomatic asthma, bronchial hyper-responsiveness, and other pulmonary conditions, the investigators noted.

They also confirmed associations with FEV_1/FVC for several SNPs near the gene that encodes the hedgehog interacting protein (HHIP), which plays a crucial role in various embryonic development processes, including the branching morphogenesis of the lung.

Genomewide significant associations with FEV_1 were observed for three genes (INTS12, GSTCD, and NPNT) that have been associated with factors that might lead to lung damage and others that play a role in lung development, the authors stated.

'INDIVIDUALS CARRYING THESE POLYMORPHISMS WILL HAVE LOWER PULMONARY FUNCTION THAN PREDICTED AT A GIVEN AGE.'

All of the identified genetic factors "gave estimated effect sizes consistent with those for well-established risk factors for pulmonary function decline," the authors wrote.

For example, carrying a copy of an implicated allele resulted in an FEV_1 difference ranging from 50 mL to 70 mL, the researchers said. That corresponds to 2.8-3.9 years of age-related decline in pulmonary function and to 1.7-2.3 years of active smoking–related decline, based on established mean declines, the investigators reported.

Further, carrying one copy of an implicated reference allele resulted in an FEV_1/FVC difference ranging from 0.30% to 1%, the researchers wrote, noting that "the lower effect-size estimates are comparable with the mean FEV_1/FVC decline related to secondhand smoking."

Identifying and characterizing functional variants associated with respective polymorphisms will require fine mapping of the regions, according to the authors.

"Understanding the genetic determinants of pulmonary function is paramount in identifying the biological mechanisms that lead to its decline and in ultimately lessening the mortality burden associated with reduced pulmonary function," Dr. Hancock and colleagues explained.

The National Institutes of Health funded the study. The authors did not report any conflicts of interest. ■

Signature for EGFR Mutations

NSCLC • *from page 1*

Therapy for Lung Cancer Elimination) I trial and in 53 NSCLC cell lines.

The development process identified a 93-gene signature associated with EGFR mutation, according to study results reported in a poster at a joint conference of the American Association for Cancer Research and the International Association for the Study of Lung Cancer.

The signature was significantly associated with the presence of EGFR mutations in the development cohort.

DR. SAINTIGNY

The gene signature was significantly associated with the presence of EGFR mutations in the development cohort, in the BATTLE cohort, and in the cell lines.

In addition, the signature correlated with sensitivity of the cell lines to two EGFR inhibitors: erlotinib (Tarceva) and gefitinib (Iressa). Again, the associations were highly significant statistically.

Among 442 patients with early-stage NSCLC of the adenocarcinoma type from the Director's Challenge Consortium (one of the largest cohorts of its type having published gene expression data), patients whose tumors had the gene signature had a reduced risk of death, compared with their counterparts whose tumors lacked the signature (hazard ratio, 0.85; $P = .004$).

Assays testing the association of the signature with sets of genes in various molecular pathways showed two findings that Dr. Saintigny described as striking.

One was an up-regulation of gene sets associated with endocytosis, which might affect regulation of other receptor tyrosine kinases.

The other was down-regulation of gene sets associated with proliferation and mitosis. "That could perhaps explain the good prognosis that is associated with our signature and with EGFR mutation," Dr. Saintigny commented.

"The most exciting thing that is going to happen is we are going to test this signature in the BATTLE trial," he said in an interview, with results expected later this year.

The signature's performance in predicting outcomes will be assessed and compared with that of other predictors, such as EGFR mutation itself and KRAS mutation.

Dr. Saintigny acknowledged that several other EGFR mutation signatures have been reported. "But this one is quite unique because we started from human tumors vs. cell lines," he said.

In addition, accuracy is higher with this one, possibly because a relatively large sample was used for development.

"The most important thing, I think, is to see if this signature brings something else beyond EGFR mutation," he commented.

An unexpected finding was that the signature is also significantly associated with prognosis among patients with wild-type (nonmutated) EGFR.

"So perhaps it brings something [else]; perhaps it identifies EGFR wild-type tumors that behave the same as EGFR mutants," Dr. Saintigny said. "This hypothesis we have to test in clinical trials."

Dr. Saintigny reported that he had no conflicts of interest associated with the study. ■

Dr. W. Michael Alberts, FCCP, comments: *Gene expression profiling is proving to be an especially productive research tool. One may expect continued advances in the use of this information in understanding carcinogenesis and in the design of personalized and targeted therapy.*

Spiriva Review

Risk • *from page 1*

comparing treatment with the Spiriva HandiHaler to placebo in almost 6,000 patients with COPD found no increase in the risk of these outcomes in the treatment arm.

The study was reviewed by the FDA's Pulmonary-Allergy Drugs Advisory Committee in November 2009. In a near unanimous vote, the panel agreed that the data adequately resolve the potential safety concerns for stroke and adverse cardiovascular outcomes associated with the product. ■

A link to the FDA update is available at www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm197429.htm.

Dr. W. Michael Alberts, FCCP, comments: *This information comes as a welcome relief to those patients who benefit from Spiriva (a dry powder formation of tiotropium) and to no lesser degree to those who prescribe this medication.*

Dr. Philip Marcus, MPH, FCCP, comments: *Unfortunately, many of the medications we use for the treatment of COPD carry warnings about potential risks. The latest was the concern about adverse cardiovascular events with tiotropium. It is reassuring that this issue has now been resolved, largely based on the results noted in the UPLIFT study that was published a few months ago.*


temp:101.9F
O2sat:89%
WBC:18.1
MRSA
nosocomial pneumonia
PMNs:80%, bands:15%
creatinine:2.6
CXR:LLL infiltrate

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ZYVOX is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms:

Nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains) or *Streptococcus pneumoniae* (including multidrug-resistant strains [MDRSP]).

Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*. ZYVOX has not been studied in the treatment of decubitus ulcers.

ZYVOX use is contraindicated in patients with known hypersensitivity to linezolid or any of the other product components.

ZYVOX should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g. phenelzine, isocarboxazid) or within 2 weeks of taking any such product.

Unless patients are monitored for potential increases in blood pressure, ZYVOX should not be administered to patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis and/or patients taking any of the following: directly and indirectly acting sympathomimetic, vasopressive, and dopaminergic agents.

Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, ZYVOX should not be administered to patients with carcinoid syndrome and/or patients taking any of the following medications: serotonin reuptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 receptor agonists, meperidine, or buspirone.

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.

ZYVOX is not approved and should not be used for the treatment of patients with catheter-related bloodstream infections or catheter-site infections.

ZYVOX has no clinical activity against Gram-negative pathogens and is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected.

Clostridium difficile associated diarrhea has been reported with use of nearly all antibacterial agents, including ZYVOX, and may range in severity from mild diarrhea to fatal colitis.

Lactic acidosis has been reported with the use of ZYVOX. Patients receiving ZYVOX who develop recurrent nausea, vomiting, unexplained acidosis, or a low bicarbonate level should receive immediate medical evaluation.

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.*

References: 1. Rubinstein E, Cammarata SK, Oliphant TH, Wunderink RG; and Linezolid Nosocomial Pneumonia Study Group. Linezolid (PNU-100766) versus vancomycin in the treatment of hospitalized patients with nosocomial pneumonia: a randomized, double-blind, multicenter study. *Clin Infect Dis.* 2001;32(3):402-412. **2.** Wunderink RG, Cammarata SK, Oliphant TH, Kollef MH; for Linezolid Nosocomial Pneumonia Study Group. Continuation of a randomized, double-blind, multicenter study of linezolid versus vancomycin in the treatment of patients with nosocomial pneumonia. *Clin Ther.* 2003;25(3):980-992. **3.** Boselli E, Breilh D, Rimmelé T, et al. Pharmacokinetics and intrapulmonary concentrations of linezolid administered to critically ill patients with ventilator-associated pneumonia. *Crit Care Med.* 2005;33(7):1529-1533.

Please see brief summary on adjacent pages.

Two Genes Linked to Asthma Susceptibility

BY MARY ANN MOON
Elsevier Global Medical News

Researchers have identified a genetic locus on chromosome 1q31 that is significantly associated with susceptibility to asthma, according to a study published online in the New England Journal of Medicine.

Two candidate genes at this locus were identified in a genomewide association study of North American children of European ancestry, and the findings were replicated in European adults and in North American children of African ancestry, said Patrick M. A. Sleiman, Ph.D., of Children's Hospital at Philadelphia's Center for Applied Genomics and his associates (N. Engl. J. Med. 2009 Dec. 23 [doi:10.1056/NEJMoa0901867]).

The researchers first performed a genomewide association study in 793 children (mean age 7 years) with moderate to severe asthma requiring daily steroid therapy. Controls consisted of 1,988 nonasthmatic children. All the children were Americans of European ancestry.

Eight single-nucleotide polymorphisms (SNPs) were found to be significantly associated with asthma. All of these SNPs mapped to the DENND1B gene or the CRB1 gene at a novel locus on chromosome 1q31. The findings were then replicated in a Northern European cohort of 917 adults who had childhood-onset asthma and 1,546 control subjects.

A cohort of 1,667 African American children with asthma and 2,045 African American children without asthma was then assessed. Again, each of the eight SNPs on chromosome 1q31 was strongly associated with asthma.

The study was supported by an award from the Children's Hospital of Philadelphia, and grants from the state of Pennsylvania, the Lundbeck Foundation, and the National Institutes of Health. No conflicts of interest were reported. ■

PRACTICE MANAGEMENT UPDATE

Boost Your Bottom Line With eRx and PQRI

BY DIANE KRIER-MORROW, MBA, MPH, CCS-P
ACCP Coding and Reimbursement Consultant

With the many practice management changes affecting pulmonary, critical care, and sleep practices in 2010, it is essential that pulmonologists actively participate in the Centers for Medicare & Medicaid Services (CMS) Physician Quality Reporting Initiative (PQRI) and Electronic Prescribing (eRx) incentive program.

PQRI participation will realize a 2% bonus payment on ALL Medicare claims reported in 2010, not just the claims that include the PQRI code(s). Measures are reported only through individual claims-based reporting or registries. The ACCP offers a Medicare-approved registry, PQRI Wizard.

For more pulmonary-specific information, go to www.chestnet.org/downloads/practice/pm/2010_PQRI.pdf.

There is also a 2% bonus payment for electronic prescribing. If you do both, that is a 4% increase!

Claims-Based Reporting eRx

eRx, previously part of PQRI, #125, is now unnumbered and its own Medicare benefit. Go to www.cms.hhs.gov/ERxIncentive for information on the simplified reporting requirements.

► To report electronic prescribing, a qualified eRx system must be adopted. No provider enrollment is required. A qualified eRx system is capable of generating a complete active medication list; selecting medications, printing prescriptions, electronically transmitting prescriptions, and conducting alerts (eg, inappropriate dose, route of administration, drug-drug interactions, allergy concerns, or warnings and caution); providing information on lower costs, therapeutically appropriate alternatives (if any); and providing information on formulary or tiered formulary medications, patient eligibility, and authorization requirements received electronically from the patient's drug plan (if available).

► For prescription(s) generated and transmitted via qualified eRx systems, report HCPCS code **G8553—At least one prescription created during the encounter was generated and transmitted electronically using a qualified eRx system.** This single code replaces **G8443-G8446** published on page 23 in ACCP's *Coding for Chest Medicine 2010*.

► Code **G8553** (called the numerator) must be reported on the same claim form as the denominator codes, for the same beneficiary, same date of service, by the same individual NPI who performed the covered service.

► Denominator codes are report ICD-9-CM diagnosis codes and must include one of the following CPT® Category I or HCPCS codes relevant to pulmonary: New and established office/outpatients **99201-99215**; Nursing facility care, **99304-99316**; Domiciliary, rest home or custodial care, **99324-99337**; Home services, **99341-99350;** and Health and behavior assessment, **96150-96152**, on the same claim form.

► Code **G8553** must be submitted with a line-item charge of zero dollars ($0.00). The charge field cannot be blank. If the system doesn't allow zeroes, use $0.01.

► Claims may NOT be resubmitted for the sole purpose of adding or correcting an eRx code. Faxes do NOT qualify as electronic prescribing. CMS includes a completed sample claim on its Web site.

► During the reporting period (1/1/2010 through 12/31/2010), eligible professionals who generate at least one eRx associated with a patient visit on 25 or more unique events, will be eligible for a 2% incentive payment on ALL Medicare-allowed charges. An additional criterion that at least 10% of Medicare Part B charges consist of the denominator codes is required. ■

The Passing of Two Presidents

Dr. Alan Jay Block, Master FCCP, passed away December 5, 2009, in Gainesville, Florida.

Dr. Block was President of ACCP from 1987 to 1988 and was Editor in Chief of the journal *CHEST* from 1993 to 2005. He served as Professor of Medicine and Anesthesiology and Chief of the Division of Pulmonary and Critical Care at the University of Florida School of Medicine for more than 25 years. He inspired fellows, residents, and medical students for nearly 3 decades with his teaching, his commitment to patient care, and his encyclopedic knowledge of pulmonary and critical care medicine.


DR. ALAN JAY BLOCK, MASTER FCCP

Dr. Block also was a pioneer in the sleep medicine field. At the University of Florida, he was the first inductee into the UF Sleep Medicine Hall of Fame in 2009.

During his years as Editor in Chief of *CHEST*, Dr. Block encouraged international development with special translated print editions in China, Italy, Mexico, Spain, and Turkey, among other countries. He also ushered in technologic advances in the form of online manuscript submission and peer review.

Dr. Al Soffer, Master FCCP, and past Editor in Chief of *CHEST*, once commented on Dr. Block, "Gifted clinician, teacher, author, and investigator. Dr. Jay Block brought all these talents to his role as Editor in Chief of *CHEST*. Under his guidance, *CHEST* became a unique international publication for the dissemination of clinical guidelines and original research."

Dr. Richard Irwin, Master FCCP, and current *CHEST* Editor in Chief, notes, "There is a variety of ways by which the success and quality of medical journals can be measured. These include: circulation, manuscript submissions, quality of publications as reflected by acceptance rate, citation counts and impact factor, and financial health. During Dr. Block's tenure, all of these metrics steadily improved. Under his stewardship, he laid the foundations for the present success of the journal."

Dr. Block is survived by his wife of 48 years, Linda, his daughters, Margo Cook (Tommy) and Allison Jaffe (Paul), three grandchildren, and his brother, Edward (Joanne) Block, MD. ■

Thomas L. Petty, MD, Master FCCP, passed away December 12, 2009, in Denver, Colorado.

Dr. Petty served as Emeritus Professor of Medicine and Anesthesiology at the University of Colorado Health Sciences Center, where he had been a faculty member since 1962.

Dr. Petty's affiliation with the ACCP began in 1969 when he became an FCCP and, later, he served as ACCP President from 1981 to 1982. In 1995, Dr. Petty was named a Master Fellow. In recognition of Dr. Petty's many accomplishments and out of gratitude for his many outstanding contributions, The CHEST Foundation, the philanthropic arm of the ACCP, established the Thomas L. Petty, MD, Master FCCP Endowment in Lung Research in 2007.


DR. THOMAS L. PETTY, MASTER FCCP

Dr. Petty has been widely regarded as the "Father of Pulmonary Medicine," a giant who advanced every significant area in pulmonary disease and many areas in critical care and sleep medicine. A caring and thoughtful patient advocate and physician educator, his friendship was cherished by all who knew him. Dr. Edward C. Rosenow, Master FCCP, notes that "I don't recall ever seeing Tom mad. And he was always so approachable by the young physicians who delighted in being in the presence of a real 'giant'."

Throughout his career, he was credited with a long list of academic and professional accomplishments, such as spearheading the Nocturnal Oxygen Therapy Trials (NOTT) in the mid-1970s and identifying ARDS. Dr. Petty was also the founding chairman of NLHEP. He published more than 750 articles in medical journals and authored or edited more than 40 books or editions. Among his many awards and accolades are the University of Colorado's Silver and Gold Award for Excellence and a place in Colorado's Pulmonary Physicians' Hall of Fame.

Dr. Petty is survived by his wife, Carol, daughter Caryn (Jonathan) Winkler, sons Tom and John (Gina), and eight grandchildren.

View a special tribute video at www.chestfoundation.org. ■

Critical Care Commentary

Caring for ICU Patients and Families Lacking English Proficiency

Effective communication between patients, families, and providers is pivotal to optimal medical care, particularly in the ICU. Accurate information transfer helps ensure that valid informed consent and meaningful histories are obtained and delays in care and errors are minimized. Detailed discussions are key to successful end-of-life care, especially when explaining the patient's illness, prognosis, and treatment options, and when making choices about life-sustaining therapy. Finally, communicating effectively allows caregivers to address patients' and families' concerns, build therapeutic bonds, and foster emotional support (Lilly et al. *Am J Med.* 2000;109[6]:469; Lautrette et al. *N Engl J Med.* 2007;356[5]:469; Curtis and White. *Chest.* 2008;134[4]:835).

Dr. Neil Halpern, FCCP
Section Editor, *Critical Care Commentary*

A rich literature addresses communication shortcomings in the ICU (Abbott et al. *Crit Care Med.* 2001;29[1]:197-201; Azoulay et al. *Crit Care Med.* 2000;28[8]:3044; Nelson et al. *Arch Intern Med.* 2007;167[22]:2509). The families of critically ill patients consistently cite miscommunication as a source of conflict and dissatisfaction. Important family conferences are frequently delayed and responsibilities delegated to junior members of the medical team. Discussions often lack the content necessary for patients and families to make decisions, placing too much emphasis on technical issues but too little on likely outcomes and goals of care. Many families receive inadequate emotional support, which may contribute to psychiatric morbidity (Pochard et al. *Crit Care Med.* 2001;29[10]:1893; Siegel et al. *Crit Care Med.* 2008;36[6]:1722).

A growing number of people living in the United States communicate predominantly in languages other than English, particularly Spanish (www.census.gov/Press-Release/ www/releases/archives/american_community_survey_acs/010601.html). Up to one in five speaks a language besides English at home; of these, 44% speak English "less than very well." Close to 5% of households are "linguistically isolated," meaning that all household members age 14 or older have at least some difficulty with English. Residents aged 65 and older constitute the largest portion of those with limited English proficiency (LEP). Patients and families with LEP are at high risk for suboptimal communication, which may compromise their care unless special steps are taken (Norris et al. *J Palliat Med.* 2005;8[5]:1016).

For many years, ineffective strategies were used to address language barriers. Sometimes little effort was made to communicate with patients with LEP, particularly if interpreters were not available or time constraints precluded finding assistance. Crash courses in "medical Spanish" were offered to foster communication but probably increased the risk of misinterpretation, particularly when conversational subtleties exceeded caregivers' linguistic skills. In many cases, bilingual coworkers and family members were recruited to interpret, the latter increasing the risk of bias if relatives filtered or censored information (Crawley et al. *Ann Intern Med.* 2002; 136[9]:673). Even today, with the widespread availability of professional interpreter services, providers still attempt to "get by" using family members, coworkers, and their own rudimentary language skills to communicate with patients with LEP (Diamond et al. *J Gen Int Med* 2009;24[2]:256). All these approaches increase the risk of miscommunication and suboptimal care.

Trained interpreters can diminish or even eliminate language barrier problems. Regardless of their specific training, medical interpreters possess tested professional language skills, are trained in

Continued on following page

The CHEST Foundation 2010 Awards

An important benefit of ACCP membership is that it offers you an opportunity to apply for one of The CHEST Foundation awards. Whether your area of expertise is research in critical care, lung cancer, women's health, or AAT deficiency and COPD; leadership in end-of-life care; or humanitarian service, The CHEST Foundation offers 1-, 2-, and 3-year awards to ACCP members who meet the qualifications for one of the many awards offered in 2010.

The **Third GlaxoSmithKline Distinguished Scholar in Respiratory Health** award is open to ACCP members who are FCCPs and involved in the area of respiratory health. The successful candidate will have a 3-year opportunity to examine issues that are not easily supported by traditional funding, such as the development of public policy, patient education models, or economic analysis of treatment or care delivery in this patient group. This award grants $150,000 over the course of 3 years for a project or program that relates to the treatment of respiratory disease.

The research awards, granted to ACCP members who submit outstanding research projects in various areas of chest medicine, reflect the multidisciplinary nature of the ACCP. In 2010, The CHEST Foundation will offer a variety of clinical research awards in the areas of geriatric development, lung cancer, COPD and alpha-1 antitrypsin (AAT) Deficiency, and women's lung health. The 2010 research opportunities also reflect the continuing partnerships of The CHEST Foundation with the Association of Specialty Professors, the LUNGevity Foundation, and the Alpha-1 Foundation. **New for 2010** is the partnership with the Respiratory Health Association of Metropolitan Chicago in sponsoring a $10,000, 1-year Clinical Research Award in Women's Lung Health.

Focusing on the important area of critical care, The CHEST Foundation continues to acknowledge outstanding leadership in end-of-life care through the **Roger C. Bone Advances in End-of-Life Care Award**. The year 2010 marks the 10th year that this prestigious award will be granted to an ACCP member involved in palliative and/or end-of-life care. Members of the Palliative and End-of-Life Care NetWork serve on the review committee.

The CHEST Foundation's **D. Robert McCaffree, MD, Master FCCP Humanitarian Awards,** formerly know as **The CHEST Foundation Humanitarian Recognition Awards and Project Development Grants,** support the volunteer efforts of those who generously give their time and medical expertise to improve the health of people living in communities around the world. Since 1998, The CHEST Foundation has awarded almost $1.5 million in awards given to nonprofit and nongovernmental organizations where ACCP members focus their pro bono service. The CHEST Foundation will grant awards in the amounts of $5,000 and up to $15,000 to a total of $50,000 in 2010.

NEW for 2010: All CHEST Foundations awards now use an online-only application process, which is available at http://mc.manuscriptcentral.com/chest2010. Even before an ACCP member logs in to apply, he/she can view the requirements for each award by clicking on the "Instructions & Forms" on the right side of the screen. Each award application provides a description of the award, the applicant qualifications, and the requirements needed before starting the online application process, which requires an ACCP member ID number to log in. Applicants will need to prepare separate Word documents for each section of the online application. Each document (file) is then uploaded and saved as each section of the application is completed. ■

DEADLINE FOR ALL 2010 AWARDS: May 4, 2010

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medical terminology, the ethics of interpreting, and abide by hospital policies and HIPAA. In 2001, the Office of Minority Health released the National Standards on Culturally and Linguistically Appropriate Services (CLAS), which made it the law that health-care institutions provide professional interpretation services to non-English speaking patients (www.omhrc.gov/templates/browse.aspx?lvl=2&lvlID=15). Many hospitals provide trained interpreters in person and have independent departments to facilitate services to patients and families with LEP. When interpreters are not available in person, skilled services can be accessed remotely, for example, using video conferences, wireless speakerphones, and double headset phones. Our hospital uses several companies that provide remote interpreter services when a professional interpreter is not available on-site.

Professional interpreters offer assistance beyond simple translation. For example, interpreters can share insights regarding background factors that influence how patients and families interpret medical issues and decision making. Interpreters are likely to be sensitive to cultural subtleties, such as whether it is appropriate to make direct eye contact during conversation, how gender and age influence communication, and how formal sessions should be. Interpreters are also positioned to identify attitudes and beliefs that caregivers might not otherwise know about, such as opinions about the relationship between medicine and religion, views on the role of patient autonomy, attitudes toward suffering and talking explicitly about death, and the comparative importance of traditional Western vs alternative medical treatments (Norris et al. *J Palliat Med.* 2005;8[5]:1016; Crawley et al. *Ann Intern Med.* 2002;136[9]:673; Kagawa-Singer and Blackhall. *JAMA.* 2001; 286[23]:2993). Some families may consider it their responsibility to shield the patient from the truth, potentially conflicting with the caregiver's impulse to reveal necessary information. In such cases, interpreters should convey the family's preferences to caregivers, allowing the latter to negotiate an approach that respects cultural sensitivities, while still meeting the ethical imperative to honor the patient's wishes. Interpreters may also help identify educational deficits and the need for additional explanation to ensure that medical issues are fully understood. By considering the cultural background of the patient and family with LEP, the health-care team is likely to be more successful at forming bonds, communicating effectively, and minimizing disagreements (Galanti G. *Caring for Patients With Different Cultures*. Philadelphia, PA: University of Pennsylvania Press; 2004).

Focus groups held with professional medical interpreters have generated specific advice for physicians (Norris et al. *J Palliat Med* 2005;8[5]:1016). For example, physicians should meet with interpreters before conferences to ensure the latter are familiar with the issues to be discussed. This may be especially useful during emotionally difficult or complex cases, since it gives the interpreter the opportunity to be prepared to greet the patient or family appropriately or ask questions that may help providers achieve their goals. Interpreters also suggest that many conferences could be enhanced by drawing or showing pictures.

Providers and interpreters should be aware that not all terms and concepts translate directly or reliably. Clinicians' language is often opaque, even to patients and families of similar cultural and ethnic backgrounds, particularly when medical jargon (*eg*, DNR, intubation) is used or vague terms (eg, poor prognosis) are left undefined.

It is important to decide beforehand whether strict verbatim translation should be used or whether the interpreter should be given leeway to compensate for words and phrases that do not translate well. Following conferences, it may be wise for caregivers and interpreters to debrief to ensure there are no persistent misunderstandings or unanswered questions.

Even with professional interpreters, conferences with patients and families with LEP pose special obstacles.

In one study investigating end-of-life conferences that included an interpreter, 55% of all translated speech contained some alteration, including additions, omissions, substitutions, and editorializations (Pham et al. *Chest.* 2008;134[1]:109). Of the alterations, 93% had a negative impact on communication, for example, interfering with information transfer or reducing emotional support and rapport.

Another study found that, compared with conferences that did not require interpretation, those using an interpreter had less clinician speech and fewer expressions of support for the family (Thornton et al. *Crit Care Med.* 2009;37[1]:89).

In our experience, even when communication is adequate, clinicians are often frustrated by their inability to relate directly to patients and families. For example, clinicians sometimes find the interpreter's voice distracting and lacking emotion. Some clinicians feel excluded from the dialog when patients or families speak directly to the interpreter. To address this, it may be helpful to ensure that interpreters do not interfere with the line of vision between caregivers and the patients and families, allowing direct eye contact if desired and appropriate.

Every interaction, no matter how short, offers patients and families the opportunity to express concerns, ask questions, and receive information and emotional support. The use of professional interpreters should not be limited to formal family meetings or circumstances when informed consent is required. As much as possible, interpreters' assistance should be sought for every session, even for short, routine visits to the patient's room.

Ensuring good communication between clinicians and patients and families with LEP imposes special challenges. Potential pitfalls need to be acknowledged, including the risk of miscommunication, cultural misinterpretation, and difficulty building rapport. Fortunately, the widespread availability and skills of professional interpreters allow clinicians to overcome these obstacles in many, if not most, ways.

By fostering communication and shedding light on important cultural factors, professional interpreters provide an indispensable service that greatly improves the quality of medical care provided to patients and families lacking English proficiency. ■

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