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Courtesy Dr. Michele Carbone

"Erionite is a very hazardous substance, and we should not wait for disease to occur to start taking actions," one researcher said.

Will Erionite Be the Next Asbestos?

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO – Exposure to erionite, a fibrous, cancer-causing mineral that is more lethal than asbestos, is becoming a public health hazard in the United States.

Although erionite was originally thought to be a peculiarity of Turkey, naturally occurring deposits have been identified throughout the western United States. A new study shows that concentrations of airborne erionite in Dunn County, North Dakota, equal or exceed those in Boyali, a Turkish village with a 6.25% mesothelioma-related mortality rate.

Moreover, the study found no significant difference in the physical characteristics or biological activity of erionite from North Dakota and that from Cappadocia, Turkey, where in some villages 50% of all deaths are due to mesothelioma. Turkish homes made of stone laced with erionite from nearby mountains have been tagged as "houses of death" by residents resettled with the help of the Turkish Ministry of Health and researchers.

"We have a unique opportunity to implement novel prevention and early detection programs in erionite-rich regions of the United States, similar to what has been done in Turkey," researcher Dr. Michele Carbone said at the Chicago Multidisciplinary Symposium in Thoracic Oncology, where he presented the new study.

Erionite-contaminated gravel has been used in North Dakota for 2-3 decades to pave more than 300 miles of roads, including school bus routes, parking lots, and other public areas. The North Dakota Department of

See **Erionite** • *page 6*

Drug Resistance Triggers Lung Ca Transformation

Adenocarcinoma shifted to SCLC.

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO – A small study provides compelling data that both the genotype and phenotype of non–small cell lung cancers can transform as part of acquired resistance to tyrosine kinase inhibitors.

Repeat tumor biopsies revealed that the histologic diagnosis of the tumor shifted from adenocarcinoma to small cell lung cancer (SCLC) in 14% of 37 consecutive patients with epidermal growth factor receptor (EGFR)–mutant non–small cell lung cancer (NSCLC) and acquired tyrosine kinase inhibitor (TKI) resistance, Dr. Lecia Sequist said during the plenary session at the Chicago Multidisciplinary Symposium in Thoracic Oncology.

The original L858R mutation or E 19 deletion was retained in all cases but, in one patient, an additional PIK3CA mutation was seen only when the tumor shifted to SCLC.

Although other groups have documented sporadic case reports of transformation, Dr. Sequist called the 14% transformation rate remarkable. "I think this points to a broader conceptual model of acquired resistance, and we need to think very carefully about doing more repeat biopsies in patients," she said.

EGFR-mutant NSCLC is highly sensitive to EGFR TKI therapy, but acquired resistance develops at about 9-12 months due to T790M mutations in half of patients and MET amplification in 10%-15%. Elucidating the remaining mechanisms of drug resistance is of great clinical and scientific significance, said Dr. Sequist of Massachusetts General Hospital Cancer Center, Boston.

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INSIDE

Passive Smoking Increases BP in Kids

BY SHARON WORCESTER
Elsevier Global Medical News

Parental smoking was an independent risk factor for elevated systolic blood pressure in 4,236 preschool children who were part of a blood pressure screening project in Germany.

Current cigarette smoking was reported by 29% of fathers and 21% of mothers of the children in the study, and both parents reported smoking in 12% of cases. Children who had a parent who smoked were significantly more likely to have higher systolic blood pressure, even after adjusting for risk factors such as body mass index, parental hypertension, and birth weight, Dr. Giacomo D. Simonetti of the University of Heidelberg (Germany), and his colleagues reported.

Having a parent who was a smoker increased the likelihood of having a systolic blood pressure in the top 15% of the population by 21%, the investigators found (Circulation

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New Fungal Infection Guidelines Include Novel Agents

BY DIANA MAHONEY
Elsevier Global Medical News

The choice of treatment for the management of adult pulmonary fungal infections should be based on diagnostic findings and individual risk factors, according to a new policy statement issued by the American Thoracic Society. "In most cases, treatment of fungal infections must be based on the causative fungus, the severity of disease, and the clinical features of each patient," the authors wrote.

The policy statement provides organism- and infection-site specific guidelines for therapy, including dosing recommendations, and incorporates the range of novel antifungal medications, such as the extended-spectrum triazoles and echinocandins, that have been introduced since the previous guidelines were published in 1988, according to Dr. Andrew Limper, FCCP, of the Mayo Clinic in Rochester, Minn., and his colleagues on the American Thoracic Society (ATS) Fungal Infections Working Group.

In particular, the recommendations outline the management of endemic mycoses, including histoplasmosis, sporotrichosis, blastomycosis, and coccidioidomycosis; fungal infections with increased prevalence in immune-compromised and critically ill patients, including cryptococcosis, aspergillosis, candidiasis, and *Pneumocystis* pneumonia; and rare and emerging fungal infections, such as zygomycoses, hyalohyphomycoses, the phaeohyphomycoses, and infections related to *Trichosporon* species (Am. J. Respir. Crit. Care. Med. 2011; 183:96-128).

Endemic Mycoses

The guidelines recommend treatment with itraconazole for mild to moderate histoplasmosis, sporotrichosis, and blastomycosis, and treatment with amphotericin B for severe disease (followed by itraconazole in patients with sporotrichosis).

Patients with severe histoplasmosis with diffuse pulmonary infiltrates and critically ill patients with severe pulmonary blastomycosis may require systemic steroid therapy, as well.

Further, for patients with pulmonary blastomycosis and concomitant CNS involvement, combination therapy with liposomal amphotericin B (vs. amphotericin B deoxycholate) and fluconazole "should be considered due to theoretic better CNS penetration," the authors of the guidelines wrote.

Antifungal therapy is not recommended for primary pulmonary coccidioidomycosis in immunocompetent patients who have no risk factors for dissemination, while patients with disseminated infection should be treated with an extended-spectrum triazole, according to the guidelines, which also specify that critically ill patients with disseminated paracoccidioidomycosis should be treated initially with amphotericin B, followed by ketoconazole, itraconazole, or sulfadiazine.

Immunocompromised Patients

The treatment options for fungal infections in patients with compromised immune systems, including transplant patients, those being treated for autoimmune inflammatory conditions, and HIV-infected patients, include oral trimethoprim and sulfamethoxazole, oral primaquine plus clindamycin, or oral atovaquone for mild to moderate *Pneumocystis* pneumonia. Patients with moderate to severe disease should be given trimethoprim, sulfamethoxazole, and possibly prednisone, the guidelines recommend.

Emerging Fungal Infections

"The management of emerging or rare fungi is supported by limited evidence-based studies with no randomized, blinded comparative studies," the authors wrote, noting that treatment recommendations are thus based on clinical experience and in vitro susceptibility testing. Because the majority of affected patients are immunocompromised, "a primary strategy for management of these infections with underlying diseases is to maximally reduce immunosuppressive drugs, provide immunostimulants, and/or rapidly control the underlying diseases or conditions, such as HIV infection, diabetes, and/or chemotherapy-induced neutropenia," they stated.

Secondarily, particularly in the angioinvasive zygomycoses, necrotic tissues, cysts, or true abscesses should be debulked or debrided, they emphasized.

The third management strategy includes specific antifungal recommendations, such as amphotericin B for zygomycosis; voriconazole, posaconazole, or lipid formulations of amphotericin B for fusariosis; voriconazole or posaconazole for scedosporiosis; itraconazole, voriconazole, or posaconazole for phaeohyphomycoses; and, possibly, voriconazole, posaconazole, or itraconazole for trichosporonis and *Paecilomyces* infections.

"The exact dosing and duration of treatment for these emerging, rare infections are not precise, and consultation with an expert in infectious disease regarding these clinical decisions should be considered," the authors stressed.

THE TRIAZOLES AND ECHINOCANDINS HAVE BEEN INTRODUCED SINCE THE PREVIOUS GUIDELINES WERE PUBLISHED IN 1988.

The policy statement also includes recommendations for the treatment of *Candida* and *Aspergillus* infections, which are becoming increasingly common in the intensive care unit, the authors stated. For candidemia, the guidelines recommend that all existing central venous catheters should be removed, if possible, or a new placement site should be obtained and initial antifungal treatment should be with fluconazole, an amphotericin B formulation, an echinocandin, or a combination of fluconazole and amphotericin. With respect to *Aspergillus* infections, the guidelines recommend intravenous voriconazole or liposomal amphotericin B for invasive pulmonary aspergillosis; voriconazole or itraconazole for mild to moderate chronic necrotizing aspergillosis; and liposomal amphotericin B or intravenous voriconazole for severe chronic necrotizing aspergillosis.

The authors reported financial relationships with AlphaMed Pharmaceuticals, Pfizer, Ortho-McNeil, MiraBella Technologies, AstraZeneca, GlaxoSmithKline, Bayer, Novartis, Aradigm, Astellas, Enzon, Merck, and Schering-Plough. ■

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CHEST PHYSICIAN

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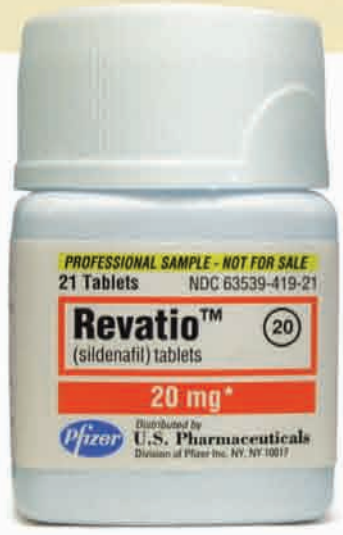

Indication

REVATIO is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability and delay clinical worsening. Delay in clinical worsening was demonstrated when REVATIO was added to background epoprostenol therapy. The efficacy of REVATIO has not been adequately evaluated in patients taking bosentan concurrently.

Important Safety Information

Do not use REVATIO in patients taking organic nitrates in any form, either regularly or intermittently. Consistent with its known effects on the nitric oxide/cGMP pathway, sildenafil was shown to potentiate the hypotensive effects of nitrates.

Before starting REVATIO, physicians should carefully consider whether their patients with underlying conditions could be adversely affected by the mild and transient vasodilatory effects of REVATIO on blood pressure. Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD) and administration of REVATIO to these patients is not recommended. Should signs of pulmonary edema occur when sildenafil is administered, the possibility of associated PVOD should be considered.

Caution is advised when PDE5 inhibitors, such as REVATIO, are administered with α-blockers as both are vasodilators with blood pressure lowering effects.

In PAH patients, the concomitant use of vitamin K antagonists and REVATIO resulted in a greater incidence of reports of bleeding (primarily epistaxis) versus placebo. The incidence of epistaxis was higher in patients with PAH secondary to CTD (sildenafil 13%, placebo 0%) than in PPH patients (sildenafil 3%, placebo 2%).

Co-administration of REVATIO with potent CYP3A4 inhibitors, eg, ketoconazole, itraconazole, and ritonavir, is not recommended as serum concentrations of sildenafil substantially increase. Co-administration of REVATIO with CYP3A4 inducers, including bosentan; and more potent inducers such as barbiturates, carbamazepine, phenytoin, efavirenz, nevirapine, rifampin, and rifabutin, may alter plasma levels of either or both medications. Dosage adjustment may be necessary.

Non-arteritic anterior ischemic optic neuropathy (NAION) has been reported post-marketing in temporal association with the use of PDE5 inhibitors for the treatment of erectile dysfunction, including sildenafil. It is not possible to determine if these events are related to PDE5 inhibitors or to other factors. Physicians should advise patients to seek immediate medical attention in the event of sudden loss of vision while taking PDE5 inhibitors, including REVATIO.

Sudden decrease or loss of hearing has been reported in temporal association with the intake of PDE5 inhibitors, including REVATIO. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors. Physicians should advise patients to seek prompt medical attention in the event of sudden decrease or loss of hearing while taking PDE5 inhibitors, including REVATIO.

REVATIO should be used with caution in patients with anatomical deformation of the penis or patients who have conditions which may predispose them to priapism.

REVATIO contains sildenafil, the same active ingredient found in VIAGRA®. Combinations of REVATIO with VIAGRA or other PDE5 inhibitors have not been studied. Patients taking REVATIO should not take VIAGRA or other PDE5 inhibitors.

Patients with the following characteristics did not participate in the preapproval clinical trial: patients who have suffered a myocardial infarction, stroke, or life-threatening arrhythmia within the last 6 months, unstable angina, hypertension (BP >170/110), retinitis pigmentosa, or patients on bosentan. The safety of REVATIO is unknown in patients with bleeding disorders and patients with active peptic ulceration. In these patients, physicians should prescribe REVATIO with caution.

The most common side effects of REVATIO (placebo-subtracted) were epistaxis (8%), headache (7%), dyspepsia (6%), flushing (6%), and insomnia (6%). Adverse events of REVATIO injection were similar to those seen with oral tablets.

The most common side effects of REVATIO (placebo-subtracted) as an adjunct to intravenous epoprostenol were headache (23%), edema (14%), dyspepsia (14%), pain in extremity (11%), diarrhea (7%), nausea (7%), and nasal congestion (7%).

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COPD in Acute MI Patients Spells Trouble

BY BRUCE JANCIN
Elsevier Global Medical News

CHICAGO – Chronic obstructive pulmonary disease is a powerful risk factor for in-hospital mortality or cardiogenic shock in patients with ST-elevation MI, a large retrospective study showed.

The clinical inference is that the reduced cardiopulmonary reserve imposed by COPD – a disease often marked by pulmonary hypertension and right ventricular dysfunction – renders the circulatory system less capable of coping with the effects of an MI, Dr. Kohei Wakabayashi said at the annual scientific sessions of the American Heart Association.

Of 3,249 patients who underwent emergent percutaneous coronary intervention for STEMI at Washington (D.C.) Hospital Center, 365 had known COPD. Their rate of in-hospital mortality or cardiogenic shock (24%) was substantially greater than in patients with no COPD (14%).

Patients with COPD were significantly older, were more often smokers and women, and had a higher prevalence of chronic renal insufficiency, hypertension, and diabetes. In a multivariate logistic regression analysis adjusted for these factors, COPD emerged as the single strongest independent predictor of in-hospital mortality or cardiogenic shock in patients undergoing PCI for STEMI, with an associated 83% increased risk, said Dr. Wakabayashi of the center. ■

COMMENTARY

Dr. Darcy Marciniuk, FCCP, comments: Preexisting COPD is associated with significant negative outcomes in the setting of acute MI. This research builds on our prior understanding of the negative association between COPD and the long-term prognosis of stable ischemic heart disease.

Total Maximum EHR Incentive Payment Amounts

Calendar year	First calendar year for which an eligible professional receives incentive payment				2015 and subsequent years
	2011	2012	2013	2014	
2011	$18,000	—	—	—	—
2012	$12,000	$18,000	—	—	—
2013	$8,000	$12,000	$15,000	—	—
2014	$4,000	$8,000	$12,000	$12,000	—
2015	$2,000	$4,000	$8,000	$8,000	$0
2016	—	$2,000	$4,000	$4,000	$0
Total	**$44,000**	**$44,000**	**$39,000**	**$24,000**	**$0**

Note: Incentives were mandated in 2009 by the HITECH Act.
Source: Centers for Medicare and Medicaid Services

Registration Opens for EHR Incentive Programs

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

ELSEVIER GLOBAL MEDICAL NEWS

A new federal initiative offering bonus payments to physicians who successfully implement electronic health records launched Jan. 3, and early signs indicate it could help spur adoption of the technology.

Officials in the Office of the National Coordinator for Health Information Technology recently released two surveys showing that more than 40% of office-based physicians and 80% of hospitals plan to seek federal incentives for the adoption and use of EHRs under Medicare and Medicaid.

The incentive programs, which launched at the start of the year, offer payments to physicians for using health information technology (HIT) to improve patient care. The federal government recently issued regulations detailing how physicians and hospitals can meet standards for so-called "meaningful use" of the technology. Physicians who meet the criteria are eligible to receive up to $44,000 over 5 years under the Medicare program or $63,750 in 6 years under the Medicaid program. Eligible hospitals could receive millions of dollars, according to the Centers for Medicare and Medicaid Services (CMS).

The survey of office-based physicians, conducted by the Centers for Disease Control and Prevention, found that 41% plan to achieve meaningful use and seek federal incentive payments. Of those, about 80% said that they plan to enroll during first stage of the program, this year or next.

A separate survey, conducted by the American Hospital Association, found that 81% of hospitals plan to achieve meaningful use and apply for incentive payments, with about 65% enrolling in the same time frame.

While the federal government has promoted these incentives for more than a year, it was uncertain whether physicians would choose to participate.

Dr. Steven Waldren, director of the Center for Health IT at the American Academy of Family Physicians, said most physicians will be able to meet the current thresholds for functions like electronic prescribing, which are outlined in the meaningful use criteria. The greater challenge will come in capturing and reporting that data to the government, he said.

Dr. Waldren recommended that physicians seek out the Regional Extension Centers set up by the federal government. These centers have been established around the country and are specifically charged with aiding small practices and those working in underserved areas.

The financial incentives seem to be helping physicians who were "on the fence," move in the direction of purchasing a system, said Dr. Michael S. Barr, a senior vice president at the American College of Physicians.

The success of the program can't be judged until figures are available on how many physicians met the stage 1 meaningful use standards, said Dr. Barr, who also serves on the Health IT Policy Committee's meaningful use workgroup. As quality measures become more robust, the data should also show whether the program has resulted in improvements in clinical quality of care, Dr. Barr said. ■

Mineral Poses Lung Risk

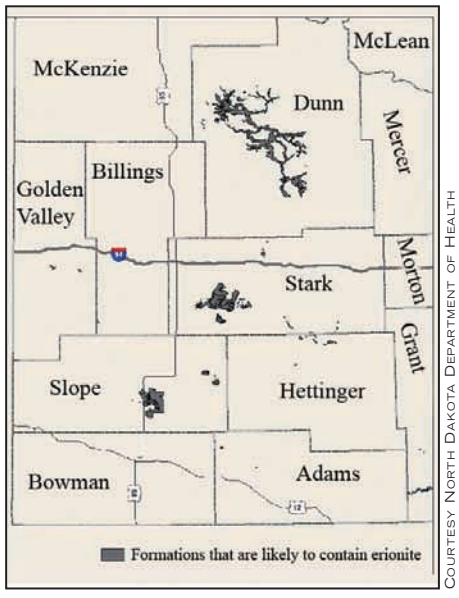
Erionite • *from page 1*

Health became aware of the health problem in 2006, and the following year recommended discontinuing use of erionite-containing gravel for roads and testing for erionite prior to new or continued gravel mining. The recommendations slowed the use of erionite-containing gravel in North Dakota, but it continues to be shipped outside the state, said Dr. Carbone, director of the Cancer Research Center of Hawaii and professor and chair of pathology at the University of Hawaii, both in Honolulu.

After a baseball field with erionite-containing gravel was closed in 2008 in the tiny town of Killdeer, N.D., the Associated Press quoted a state legislator as telling state and federal officials they were making a "mountain out of a molehill with what little data you have" and that taxpayers were having a "tough time trying to swallow this." One resident said she used the bright white gravel on her flower beds, while an area rancher said concerns over erionite were "one of those sky-is-falling kinds of deals."

Part of the battle over public opinion may be due to timing. No increase in mesotheliomas has been observed in Dunn County, but we are just now approaching the latency period where cancers would begin to develop, Dr. Carbone said. "We are in the same situation we were in the United States in the '20s and '30s with asbestos, and hopefully we will not repeat the same mistakes when danger was ignored until many people died of mesothelioma," he said, pointing out that mesothelioma kills about 3,000 Americans each year.

Dr. Carbone drew a parallel between Dunn County and Libby, Mont., where vermiculite containing asbestiform amphiboles was mined from 1920 to 1990 and given free of charge for insulation and to build driveways and ball fields. In 2004, researchers at the Center for Asbestos Related Disease in Libby identified accelerated loss of lung function in 94 of 123 miners, family members, and residents (Am. J. Med. 2004;46:219-25) and more recently reported on 11 new cases of mesothelioma in people with environmental exposure to contamination in the community, surrounding forest, and the Kootenai River and railroad tracks used to haul the vermiculite (Am. J. Med. 2008;51:877-80). The authors conclude that "an epidemic of mesothelioma can likely be expected from this type of asbestos contamination over the next 20-plus years."



Courtesy North Dakota Department of Health

Deposits of erionite are common in Dunn County, N.D., where it is used for gravel.

Despite prior identification of asbestos in the mine and illness among workers, the situation went unnoticed and unaddressed by health authorities for over a decade until a Seattle Times newspaper article appeared in November 1999, noted Dr. Aubrey K. Miller, a researcher and senior medical adviser with the National Institute of Environmental Health Sciences in Bethesda, Md.

'Hopefully we will not repeat the same mistakes [as with asbestos] when danger was ignored until many people died.'

DR. CARBONE

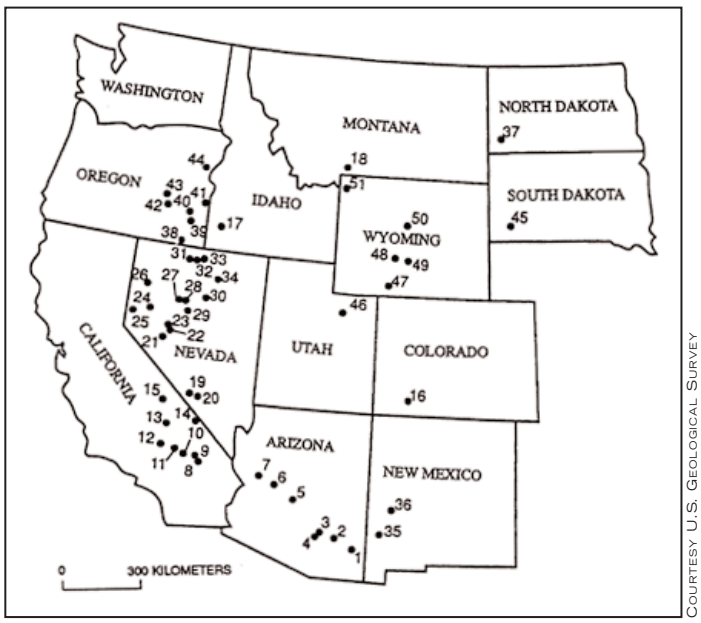
"Thus, individuals in North Dakota should be concerned," he said in an interview. "Erionite is a very hazardous substance, and we should not wait for disease to occur to start taking actions to protect public health. There is no excuse based on our current knowledge to play a wait-and-see game."

Lung screening was offered to Dunn County residents exposed to erionite, but only 34 residents, including gravel pit and road maintenance workers, enrolled in the study. A significant increase in interstitial changes above background prevalence was observed on high-resolution computed tomography in 17.6% of residents, compared with 1.5% for male urban transportation workers with low cumulative asbestos fiber exposure, Dr. Carbone said.

Transmission electron microscopy (TEM) revealed higher total concentrations of erionite fibers in air samples taken street-side in Dunn County (mean 0.108 structures per cubic centimeter [s/cc]) than from samples taken from the streets of five Turkish villages including Boyali (mean 0.00 s/cc), he said. Total TEM erionite concentrations were also higher indoors in Dunn County than in Boyali (mean 0.175 s/cc versus 0.043 s/cc).

Research in Turkey has shown that increased industrialization significantly increases airborne particulates, an observation that is particularly worrisome since oil production activity has increased road traffic in Dunn County and development has grown in states such as Nevada, where erionite deposits are far more common than in North Dakota.

Equally worrisome is that, unlike asbestos, erionite has no current health benchmarks nor is it regulated by the U.S. Environmental Protection Agency or other agencies, Dr. Miller said. "The horse is out of the barn for some, but I think we can do a lot more to protect others," he said. "You can't ban a natural substance, but I'd certainly like to see contaminated materials and disturbance of problem areas managed more effectively."



Courtesy U.S. Geological Survey

The western United States has widespread deposits of erionite, which is linked to increased risk of mesothelioma.

Dr. Carbone stressed the need to reduce erionite exposure, but is also working to isolate mesothelioma-susceptibility genes that might help to explain the pathogenesis of the disease and to identify high-risk patients for early treatment.

The U.S. Early Detection Research Network, a branch of the National Cancer Institute, has funded a clinical trial that is prospectively evaluating osteopontin and mesothelin as early markers for the detection of mesothelioma. The 800-patient trial is expected to begin in 2011 and to be completed sometime in 2014, said Dr. Carbone, its coprincipal investigator together with thoracic surgeon Dr. Harvey I. Pass, professor and chief of the thoracic surgery division at New York University's Langone Medical Center in New York City.

Dr. Carbone and his team are also looking to identify some point in the evolution of mesothelioma process that is vulnerable to intervention. Dr. Haining Yang, now also at the University of Hawaii Cancer Center, was the first author of a previous report that tumor necrois factor–alpha inhibits asbestos-induced cytotoxicity via a nuclear factor-kappa B-dependent mechanism that increases the percentage of human mesothelial cells that survive asbestos exposure, thus increasing the pool of asbestos-damaged cells susceptible to malignant transformation (Proc. Natl. Acad. Sci. USA 2006; 103:10397-402).

When the investigators looked at tissue culture, North Dakota, Oregon, and Turkish erionite were found to induce high-mobility group protein B1 (HMGB1) and TNF-alpha release from human mesothelial cells and macrophages, Dr. Yang and colleagues also reported. When coupled with chronic inflammation of the peritoneum and pleura, HMGB1 and TNF-alpha release have been linked to malignant mesothelioma in mice and in humans (Proc. Natl. Acad. Sci. USA 2010;107:12611-6).

Dr. Carbone called for a larger, more detailed epidemiologic survey of the health implications of erionite in North Dakota, as was performed for Libby, Mont., and said that it should include mine and road workers with direct exposure as well as adults and children with environmental exposure.

This survey also should include correlative studies that exploit recent findings regarding biomarkers involved in fiber carcinogenesis, as is being done in Libby, he said.

The study was partially funded by a National Cancer Institute investigator grant.

Dr. Carbone and Dr. Miller reported no conflicts of interest. Coauthors reported funding from Rosetta Genomics, Celera, Soma Logic, and SourceMDX, and one reported having a leadership role in the American College of Radiology Imaging Network. ■

Allegra Now Available OTC

Beginning on March 4, Allegra (fexofenadine hydrochloride) allergy relief products will be available without a prescription.

Sanofi-Aventis announced that the U.S. Food and Drug Administration has approved over-the-counter status for Allegra 12- and 24-hour tablets for patients aged 12 years and older, Children's Allegra 12-hour tablets and orally disintegrating tablets for children aged 6 years and older, and Allegra liquid for children aged 2 years and older.

According to the company, the FDA also approved behind-the-counter sale of Allegra-D 24-hour and 12-hour extended-release tablets, which include the decongestant pseudoephedrine, for patients older than 12 years.

The approval for OTC Allegra is for the same rhinitis indication as the prescription version.

According to its Web site, Allegra will be "the only over-the-counter allergy brand without a drowsiness warning."

The nonprescription Allegra products will be the same strength as the prescription drugs, which have been sold for nearly 15 years. The prescription adult dose is 60 mg, twice daily.

–Elizabeth Crawford
"The Pink Sheet"

CHEST PHYSICIAN and *"The Pink Sheet"* are published by Elsevier.

More Dangerous Form of Plaque Linked to OSA

BY RICHARD HYER
Elsevier Global Medical News

CHICAGO – Patients with obstructive sleep apnea have more active atherosclerotic disease with a greater degree of vessel involvement and more vulnerable plaque than do patients without the disease, according to a retrospective matched cohort study presented at the annual meeting of the Radiological Society of North America.

"We found that those folks who have obstructive sleep apnea have the more dangerous form of plaque," said Dr. U. Joseph Schoepf of the Medical University of South Carolina, Charleston, at a press briefing.

VITALS

Major Finding: Coronary CT angiography reveals a higher prevalence of stenotic coronary artery disease and more extensive vessel involvement in patients with obstructive sleep apnea than in those without OSA.

Data Source: A retrospective study of 95 obese patients, 49 with obstructive sleep apnea and 46 without.

Disclosures: The study was not funded, and Dr. Schoepf made no disclosures relevant to the study. His general disclosures are that he has served on the speakers bureau of and/or received research grants from the Bracco Group, General Electric, and Bayer AG. He also has served on the Siemens AG Medical Advisory Board.

"This is the first time that a noninvasive test, namely coronary CT angiography, has been applied to this, to actually demonstrate it. The clinical relevance is that we have a noninvasive tool at hand that allows us potentially to care better for our patients who have that disease."

Patients with obstructive sleep apnea (OSA) repeatedly stop breathing during sleep due to airway collapse. It is a disease of obesity, and 30% of Americans are obese, Dr. Schoepf said.

Diminishing the oxygen supply exposes the cardiovascular system to oxidative stress, and may render vessel linings more vulnerable to the formation of atherosclerosis. OSA has been linked to coronary artery disease, he noted.

Computed tomography is the only noninvasive test that can directly evaluate cardiac vessel patency and analyze the composition of atherosclerotic lesions on vessel walls, Dr. Schoepf said. Therefore, it was used to study the association between OSA and coronary artery disease.

Investigators performed a retrospective search for patients who had undergone CT of the heart and polysomnogram assessment for suspected OSA.

One observer measured coronary artery calcium, known informally as hard plaque. Two observers in consensus analyzed heart CT data for the presence and degree of coronary artery narrowing or blockages.

The presence and extent of noncalcified or "soft" plaque, also known as vulnerable plaque, were also evaluated. Noncalcified plaque frequently causes acute cardiac events such as heart attack and unstable angina.

The retrospective search revealed 97 patients who had undergone both heart CT for atypical chest pain or prior equivocal test, as well as a polysomnogram. (Two patients were excluded because their polysomnogram was performed more than 36 months before or after the date of their cardiac CT.)

The mean apnea-hypopnea index score in this patient cohort was 27.5 (moderate).

Of the 95 remaining patients, 49 (23 women, mean age 61 years, average body mass index 33 kg/m^2) had documented obstructive sleep apnea by polysomnogram.

The other 46 patients (24 women, mean age 60 years, average body mass index 30 kg/m^2) were found not to have obstructive sleep apnea by polysomnogram.

The investigators found no significant difference in age, gender, body mass index, or cardiovascular risk factors between the two groups.

Agatson calcium scores (which are a measure of hard plaque) were not significantly different between the two groups (mean score 272 for the group with OSA versus 241 for those without OSA, $P = .5$).

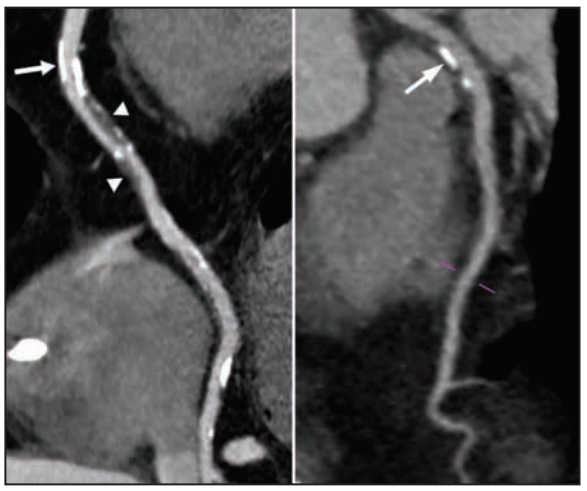
The presence of any type of narrowing in the heart vessels was found to correlate with the presence of obstructive sleep apnea (P less than .0001).

The total number of heart vessels with any narrowing was also found to correlate with the presence of obstructive sleep apnea ($P = .0008$).

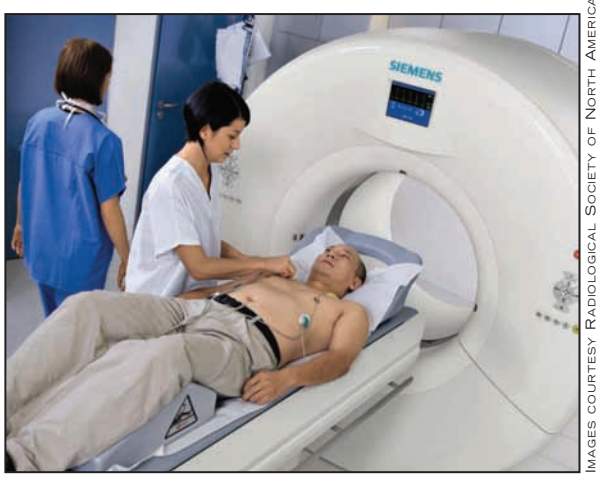
In addition, the degree of narrowing in the highest grade of lesion correlated with obstructive sleep apnea ($P = .0013$).

The presence of noncalcified plaque (soft or vulnerable plaque) had a significant correlation with the presence of obstructive sleep apnea in this study, Dr. Schoepf said.

If the study's findings are sustained by larger prospective trials in the future, cardiac CT could emerge as a useful noninvasive tool for investigating the relationship between obstructive sleep apnea and coronary artery disease, he concluded. ■



CT angiograms of heart vessels show calcified plaque (arrows, both images) and soft plaque (arrowheads, left image) in a patient with OSA.



IMAGES COURTESY RADIOLOGICAL SOCIETY OF NORTH AMERICA

Coronary CT angiography revealed the presence of soft plaque and narrowing in the heart vessels of patients with obstructive sleep apnea.

Phrenic Nerve Stimulation Shows Early Promise in CSA

BY BRUCE JANCIN
Elsevier Global Medical News

CHICAGO – First-in-man results of a fully implantable system for chronic phrenic nerve stimulation for treatment of central sleep apnea in heart failure patients showed significant improvements in the periodic breathing pattern that were sustained and even enhanced during 1 month of therapy, a study has shown.

Participants in this small pilot study were recipients of the RespiCardia system, which consists of a fully implantable pulse generator and transvenous stimulation lead, Dr. William T. Abraham reported at the annual scientific sessions of the American Heart Association.

In the study's acute phase, 13 heart failure patients with central sleep apnea (CSA) marked by Cheyne-Stokes breathing with oxygen desaturation, central apneic episodes, and disrupted sleep architecture underwent two overnight sleep studies. On one night, patients received no treatment. On the other night, they received phrenic nerve stimulation with the generator remaining outside the body.

Three patients then underwent implantation of the full RespiCardia system. After a month-long healing period during which the system remained off, they returned for two overnight sleep studies: the first with the system off, the second with it switched on for the first time. A month later they were back in the sleep lab for another overnight study – this time to assess the effects of 1 month of treatment, explained Dr. Abraham, professor of internal medicine, physiology, and cell biology and director of the cardiovascular medicine division at Ohio State University, Columbus.

The acute benefits observed in the 13 patients during a single night of therapy, compared with no treatment, were replicated in the 3 patients with the implanted system – and those benefits were even greater after a month of treatment. For example, the mean apnea-hypopnea index at baseline was 34.3 events per hour of sleep, compared with 18.9 during the first night of treatment and 12.0 after 1 month of phrenic nerve stimulation. Similarly, the other respiratory parameter assessed in the study – the CSA index – improved from 18.0 episodes per hour at baseline to 4.3 on the first night of treatment and 0.5 after a month of chronic phrenic nerve stimulation.

Nocturnal oxygen desaturation also improved markedly, as shown by mean 5% oxygen desaturation index scores of 35.4 at baseline, 20.0 on the first night of therapy, and 12.4 after 1 month.

Sleep architecture as reflected in the arousal index improved from a mean of 20.1 arousal episodes per hour at baseline to 8.0 on night 1 and 7.6 after 1 month of therapy.

The pulse generator can be implanted in either the right or left pectoral location, depending on whether a heart failure patient has another device already in place. The stimulation lead is placed in the pericardiophrenic vein. An optional transthoracic impedance sensing lead can be placed in the azygos vein to monitor respiration.

Dr. Abraham said the next step in the development of the RespiCardia system is to determine whether the improvements in oxygenation, sleep architecture, and central apneic episodes seen in this preliminary month-long study are maintained in larger numbers of patients over longer periods, and more importantly whether these sleep-lab benefits translate into improved heart failure status and quality of life.

He said that he serves as a modestly compensated consultant to Cardiac Concepts, which sponsored these studies and is developing the RespiCardia system. ■

Microscopic Invasion May Predict Lung Ca Survival

BY PATRICE WENDLING
Elsevier Global Medical News

VITALS

Major Finding: Five-year overall survival was 50% for patients with microscopic vascular invasion vs. 66% for those without MVI.

Data Source: Retrospective analysis of 514 patients with early non–small cell lung cancer.

Disclosures: Dr. Ruffini, his coauthors, and Dr. Socinski have no relevant financial conflicts.

CHICAGO – New data suggest that microscopic vascular invasion may be a more powerful prognosticator in early lung cancer than are the tumor size–based categories suggested in the new TNM staging system.

Researchers used histologic and immunohistochemical techniques to identify microscopic vascular invasion (MVI), or the presence of neoplastic structures inside the lumen of a vessel, in one-third (154) of 512 patients with resected, pathologically staged T1a to T3 node-negative non–small cell lung cancer (NSCLC). The 2009 edition of the tumor, node, metastasis (TNM) staging system for lung tumors was used.

MVI was significantly correlated with the presence of tumor-infiltrating lymphocytes (odds ratio 1.65, $P = .03$), adenocarcinoma histology (OR 1.32, $P = .003$), and increased tumor size (OR 1.13, $P = .009$).

Five-year overall survival was significantly lower for patients with MVI at 50% vs. those without MVI at 66% ($P = .001$), Dr. Enrico Ruffini said at the Chicago Multidisciplinary Symposium in Thoracic Oncology.

The difference in survival remained significant even in those with squamous cell carcinoma (45% vs. 61%, $P = .05$), although it was more pronounced in those with adenocarcinoma (56% vs. 70%, $P = .03$). "Microscopic vascular invasion is a significant independent negative prognostic factor," he said.

When patients with pT1a-T2b tumors were stratified by T-size category, the presence of MVI resulted in a one-category upstaging for each T category, said Dr. Ruffini of the division of thoracic surgery at the University of Torino (Italy). For example, T1a patients with MVI had a prognosis similar to that of patients with T1b tumors without MVI. The number of T3 cases was too small to stratify.

T size was prognostic of survival in the MVI-negative patients ($P = .03$) but was not a statistically significant factor in MVI-positive patients ($P = .9$), indicating that MVI is indeed a more powerful prognosticator, he said.

The 2009 TNM stresses the importance of tumor size as a major prognostic factor, but no TNM edition has so far included MVI as a major determinant in the staging of NSCLC.

In a multivariate survival analysis that included age, sex, histology, grading, T-size determinant, MVI, perineural invasion, and tumor-infiltrating lymphocytes, MVI was a stronger prognostic indicator (hazard ratio 1.43, $P = .02$) than was T-size determinant (HR 1.06, $P = .06$), Dr. Ruffini said.

Invited discussant Dr. Mark Socinski pointed out that 88% of patients in the analysis had 5 cm or smaller tumors, a category of patients in whom adjuvant therapy has been discouraged. He highlighted a recent meta-analysis of 4,584 NSCLC patients in five cisplatin-based adjuvant chemotherapy trials that showed an overall significant survival benefit of 4% at 5 years, but also a potentially negative effect in resected stage 1A disease (Ann. Oncol. 2010;Suppl. 7:vii196-8).

"We need to make sure [MVI] is easily reproducible amongst pathologists, and we also clearly need to demonstrate that adjuvant therapy can overcome the biologic impact of this histopathologic finding," said Dr. Socinski of the Lineberger Comprehensive Cancer Center at the University of North Carolina, Chapel Hill.

COMMENTARY

Dr. Richard Fischel, FCCP, comments: This paper describes a very interesting and potentially clinically significant finding. The authors found that microscopic vascular invasion in resected lung cancers had a closer correlation with overall survival than did tumor size used in the TNM staging system. While it remains to be seen if this information can lead to improved treatment regimens for these selected patients, the opportunity to make an impact would appear to exist and will hopefully lead to further study in this area.

Dr. Ruffini said study limitations included retrospective design, an outcome measure of overall survival rather than disease-free survival, and the long study period of January 1998 to August 2008. Prospective validation of MVI is underway using the International Association for the Study of Lung Cancer database, he said.

Median tumor size among the 512 patients was 3.4 cm, with 164 classified as having T1a (less than 2 cm) tumors, 123 T1b (2-3 cm), 164 T2a (3-5 cm), 50 T2b (5-7 cm), and 11 T3 (over 7 cm) tumors. ■

TKI Therapy Changed Histology

Drug Resistance • *from page 1*

Although rebiopsy is not common practice, invited discussant Dr. Mark Socinski said it should be on the clinicians' radar because it can alter the therapeutic course of refractory disease and arguably the clinical benefit.

"I think the message here is to consider rebiopsy more often in selected patients until we have a better understanding of this one disease we call non–small lung cancer that we realize is an incredibly heterogeneous disease," said Dr. Socinski, director of the multidisciplinary thoracic oncology program at the Lineberger Comprehensive Cancer Center at the University of North Carolina–Chapel Hill.

Among the five patients whose cancer transformed, two maintained a slow, indolent course after SCLC transformation, while three had a change around the time of their biopsy to an explosive growth pattern more clinically reminiscent of SCLC, Dr. Sequist said. Four patients were treated with SCLC-like chemotherapy regimens, and three responded with marked partial responses.

Longitudinal data from fluorescent in situ hybridization analysis for MET and EGFR gene copy number suggest that the resistant tumor is distinct from the original tumor and that MET amplification lies in a distinct subpopulation of the cell and is selected out under pressure from TKI therapy, she said.

Multiple biopsies over time also identified a waxing and waning of genotypic and phenotypic findings in response to selective pressure of TKI therapy. This pattern was most pronounced in a case that transformed from EGFR TKI-sensitive adenocarcinoma to resistant SCLC while on erlotinib (Tarceva) for more than 1 year, switched back to TKI-sensitive adenocarcinoma following treatment with chemotherapy and radiation and a 9- to 10-month break from erlotinib, and then after a very successful but short-lived response to erlotinib, shifted back to SCLC a second time upon clinical resistance.

"It's showing us that if you do repeat biopsies, it can direct patients toward clinical trials that they have a higher likelihood of benefiting from," said Dr. Sequist. "It's a really a nice thing to be able to offer patients."

The population comprised 15 men and 22 women. All patients, median age 60 years, had clinically responded to either gefitinib (Iressa) or erlotinib, with a median of 18.4 months of initial EGFR TKI therapy (range 4-69 months). The majority, or 81%, remained on TKI at the time of repeat biopsy. Repeat biopsy showed T790m mutations in 49%, PIK3CA in 5%, MET amplification in 5%, and an unknown mechanism in 30%, reported Dr. Sequist at the symposium, cosponsored by the American Society of Clinical Oncology, American Society for Radiation Oncology, International Association for the Study of Lung Cancer, and University of Chicago.

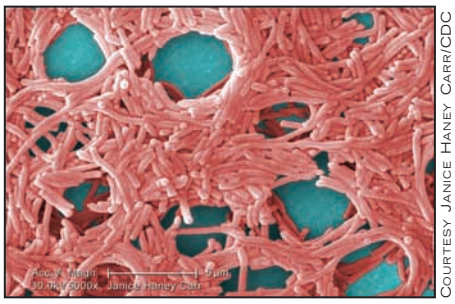
Dr. Sequist and Dr. Socinski disclosed no relevant conflicts. Two coauthors have submitted a patent for genotyping methods. ■

Anti-TNF-Alpha Timing, Type Linked to *L. pneumophila*

BY DIANA MAHONEY
Elsevier Global Medical News

BOSTON – The risk of Legionnaires' disease associated with tumor necrosis factor–alpha antagonist therapy is greatest during the first year of treatment and is significantly higher for patients receiving adalimumab or infliximab compared with etanercept, according to a study reported at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Using data from the RATIO registry, Dr. Fanny Lanternier of the Necker Hospital for Sick Children in Paris and colleagues conducted an incidence and risk factor study to investigate the relationship between the three drugs included in the registry – adalimumab, infliximab, and etanercept – and *Legionella pneumophila* infection, which they previously reported in patients receiving anti–tumor necrosis factor–alpha (anti-TNF-alpha) treatment. The prospective French RATIO (Research Axed on Tolerance of Biotherapies) registry was designed to collect information on opportunistic and severe bacterial infections and lymphoma in patients treated with anti-TNF-alpha agents. The researchers used the French population as the reference for the incidence analysis, and they conducted a case-control study – with four anti-TNF-alpha–treated controls per case – to investigate the risk of newly diagnosed cases of *L. pneumophila* infection. Mean patient age was 53 years.



COURTESY JANICE HANEY CARR/CDC

Risk of *L. pneumophila* infection is greatest during first year of treatment with adalimumab or infliximab.

From Feb. 1, 2004, to Jan. 1, 2007, the RATIO registry received reports of 27 cases of laboratory-confirmed *L. pneumophila* infection. "The overall annual incidence rate of infection for patients on anti-TNF-alpha therapy, adjusted for age and sex, was 47/100,000 patients per year, which represents a 13-fold increased risk, compared with the reference population," Dr. Lanternier reported. When evaluated by agent, the standardized incidence risk was significantly higher, at 22.3, for patients taking infliximab or adalimumab – both anti-TNF-alpha monoclonal antibody agents – compared with 3.0 for patients taking etanercept, which is a soluble TNF-alpha receptor therapy, she said at the meeting, which was sponsored by the American Society for Microbiology.

Similarly, in the case-control analysis, exposure to adalimumab or infliximab vs. etanercept was an independent risk factor for *L. pneumophila* infection, as was the first year of anti-TNF-alpha treatment, Dr. Lanternier said.

Compared with patients with *L. pneumophila* infection in the French population, anti-TNF-alpha–treated patients with the infection were younger and had a markedly lower infection-related mortality rate at 3.7% vs. the 10%-20% observed in the population not treated with anti-TNF-alpha drugs, said Dr. Lanternier, attributing the difference to the probability that the immunosuppressed patients are more closely monitored.

In a separate study, Dr. Alfred F. Sorbello, medical officer for the U.S. Food and Drug Administration, reported an association between *L. pneumophila* infection-mortality and onset of the infection within 90 days of initiating anti-TNF-alpha therapy in patients of younger mean age receiving concomitant steroids or methotrexate. This finding was based on a review of reports on 21 of 80 patients to the FDA Adverse Event Reporting System between 1999 and 2010. Although the results are limited by the small number of patients included in the analysis because of missing data, lack of randomization, and underreporting, they do suggest a key role for TNF-alpha in host defense against *L. pneumophila*. ■

COMMENTARY

Dr. Marcos Restrepo, FCCP, comments: French investigators reported very similar data from the RATIO registry in 2006 (Clin. Infect. Dis. 2006;43:e95-e100). However, the additional information from the FDA is very interesting, and this article included further cases since the initial 2004 cases. I would recommend to clinicians that every time they see patients receiving anti-TNF-alpha medications with pneumonia, they should consider *Legionella* and treat according to the community-acquired pneumonia guidelines with appropriate atypical coverage that includes *Legionella*.

Evidence for Smoking–Severe RA Link Strengthened

'As a heavy smoker, you are almost two times more likely to develop RA.'

BY JENNIE SMITH
Elsevier Global Medical News

Smoking is implicated in more than a third of cases of the most severe and common form of rheumatoid arthritis, researchers in Sweden have found, and in one in five cases of RA overall.

Results from a population-based study strengthened the growing body of evidence that links smoking with development of anti–citrullinated protein/peptide antibody (ACPA)–positive rheumatoid arthritis. In a dose-response manner, the link became stronger with heavier smoking, regardless of allele status.

The investigators, led by Henrik Källberg, Ph.D., of the Karolinska Institute in Stockholm, determined the excess fraction of RA cases attributable to smoking to be 20%, regardless of the presence of known genetic risk factors, which comprise single or dual copies of the HLA-DRB1 shared epitope.

Smoking was estimated to be responsible for 35% of ACPA-positive cases (31% for women and 42% for men), and for each copy of the HLA-DRB1 shared epitope (SE) that was found, smoking was dose-dependently associated with an increased risk of ACPA-positive RA. In people with two copies of the HLA-DRB1 SE, 55% of ACPA-positive RA was attributable to smoking, Dr. Källberg and colleagues found (Ann. Rheum. Dis. 2010 [doi:10.1136/ard.2009.120899]).

Dr. Källberg and colleagues also found an increased risk of developing RA (OR, 1.9; 95% confidence interval, 1.1-3.5) among heavy smokers without any genetic risk factors. "That was one really interesting finding," Dr. Källberg said in an interview. "As a heavy smoker, you are almost two times more likely to develop RA" even without the HLA-DRB1 SE alleles, he said.

For their research, Dr. Källberg and colleagues collected blood samples and questionnaire information from 1,205 people who were diagnosed with RA according to the American College of Rheumatology's 1987 criteria, as well as 872 healthy controls matched for age, sex, and geographic location. The cases were part of the Swedish EIRA (Epidemiological Investigation of Rheumatoid Arthritis) cohort study.

The questionnaires solicited information on past and current smoking, thereby allowing investigators to classify each subject by smoking history (current and former smokers of 0-9, 10-19, and 20 pack-years, with 1 pack-year defined as equaling 20 cigarettes per day for 1 year). The investigators tested blood samples for ACPA status and the presence of genotyped SE alleles.

The investigators calculated the odds ratios of developing RA associated with different smoking levels and SE alleles, together with 95% confidence intervals, by using logistic regression models.

The interaction between smoking and the presence of SE alleles was evaluated as a departure from additive effects, and was estimated by calculating the attributable proportion due to interaction.

For former light and moderate smokers, the risk of developing RA declined and approached never-smoker levels the longer the person had not smoked since quitting. Former heavy smokers, however, continued to see elevated risk, even decades after quitting.

The dose-dependent association with smoking was "not a total surprise. We knew from earlier studies that there was some sort of relationship with the amount," Dr. Källberg said. "We just didn't expect it to be so clear cut."

The fact that ex–heavy smokers continued to see elevated risk does not mean that smokers shouldn't quit, Dr. Källberg said. "To some degree, the damage may be done, but we actually find that you gain something by quitting smoking. Quitting smoking can affect how well you respond to treatment."

Although smoking's presence in RA is smaller than in lung cancer, it is "similar to that seen for ischemic heart disease," the investigators wrote in their analysis. Furthermore, cardiovascular disease is associated with RA and is the major cause of premature death in people with RA, according to the investigators.

Dr. Källberg and colleagues noted that some other factors, such as air pollution, alcohol consumption, and hormonal differences could affect the smoking-RA interaction among populations. However, they wrote, they were confident – based on the age, sex, and residential matching of controls and cases within the same population – that their methodology was strong.

Dr. Källberg and colleagues' study was funded by grants from the Swedish government; the insurance company AFA; the European Union; the Flight Attendant Medical Research Institute; National Institutes of Health; and the COMBINE (Controlling Chronic Inflammatory Diseases With Combined Efforts) project. Neither Dr. Källberg nor any of his colleagues declared any conflicts of interest. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: The research presented by Dr. Källberg and team regarding the increased incidence of rheumatoid arthritis and heavy smoking provides additional confirmation of this association, which has been suspected from prior research. The group found an increased RA risk in smokers even without apparent genetic risk factors. Heavy smoking not only increased the risk of RA, but also affected response to therapy. Yet another reason to encourage those who haven't heard the message to stop smoking.

Hypothyroidism Risk Rises With Recent Smoking Cessation

BY MICHELE G. SULLIVAN
Elsevier Global Medical News

VITALS

Major Finding: Smokers may face an elevated risk of hypothyroidism in the first 2 years after they quit using tobacco.

Data Source: In a case-control study of 140 patients with new-onset autoimmune hypothyroidism and 560 controls, patients who had recently stopped smoking were more than five times as likely to have the disorder as never-smokers, or those who had stopped smoking more than 2 years before.

Disclosures: Dr. Carle said he had no potential financial conflicts.

PARIS – Smokers who have recently kicked the habit could face a significant increase in the risk of developing new-onset hypothyroidism.

The risk is greatest within the first 2 years of quitting, when it can run as high as five times the risk of someone who has never smoked, or who has been tobacco-free for more than 2 years.

There's no obvious explanation for the phenomenon, Dr. Allan Carle said at the International Thyroid Meeting. However, he said, a 2007 study suggests that current smokers actually have a significantly lower risk of developing hypothyroidism but an increased risk of hyperthyroidism (Arch. Intern. Med. 2007;167:1428-32).

"Perhaps quitting causes come kind of rebound effect, with changes in antithyroid antibodies," said Dr. Carle of the Aalborg Hospital, Denmark. But his case-control study could only observe the phenomenon – not uncover its possible cause.

He and his associates compared 140 patients with incident autoimmune overt hypothyroidism, extracted from a population-based study, to 560 age- and sex-matched controls from the same population.

All the subjects provided information on their smoking status, including daily and overall tobacco intake, years of smoking, pack-years of smoking, and – if they were past smokers – the time since quitting. Clinical measurements included autoantibodies to thyroid peroxidase (TPOAb) and thyroglobulin (TgAb); thyroid function; and a thyroid ultrasound exam. Possible relationships were examined in both univariate and multivariate models that controlled for confounding.

The investigators used the group of never-smokers as the reference group. The risk of hypothyroidism among current smokers and those who had quit more than 2 years before the study was not significantly different from the risk among never-smokers. There were also no significant relationships between new hypothyroidism and the duration or magnitude of smoking.

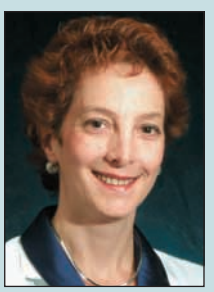
However, among subjects who had quit within the past 2 years, the risk of new hypothyroidism was significantly increased. Those who had quit within the past 1 year were 5.6 times as likely as never-smokers to develop the disorder; those who had quit 1-2 years before were 5 times as likely to develop it.

The risk of new-onset hypothyroidism dropped back to the reference range for those who had quit smoking 3-10 years before the study (odds ratio 0.85).

"Recent quitters were also more hypothyroid than other study subjects who had hypothyroidism," Dr. Carle said. Those who had quit within the past 2 years had a median total T4 level of 20 nmol/L, compared with 40 nmol/L in never-smokers with the disorder, and a median thyroid-stimulating hormone level of 82 mU/L vs. 49 mU/L.

"Looking at these data, we can say that in this series, 13% of new-onset hypothyroidism was associated with smoking withdrawal," Dr. Carle said. Because of this association, he recommended thyroid testing for all patients who report recent smoking cessation, "especially in those who have any complaints of symptoms." ■

COMMENTARY



Dr. Jeana O'Brien, FCCP, comments: The association of new-onset hypothyroidism in smokers who have recently quit is without any known cause at this time. Although further studies may help determine the etiology, at present, the importance of this information is primarily to increase the level of suspicion for hypothyroidism in those with suggestive signs or symptoms. Additional studies would be useful to confirm this finding.

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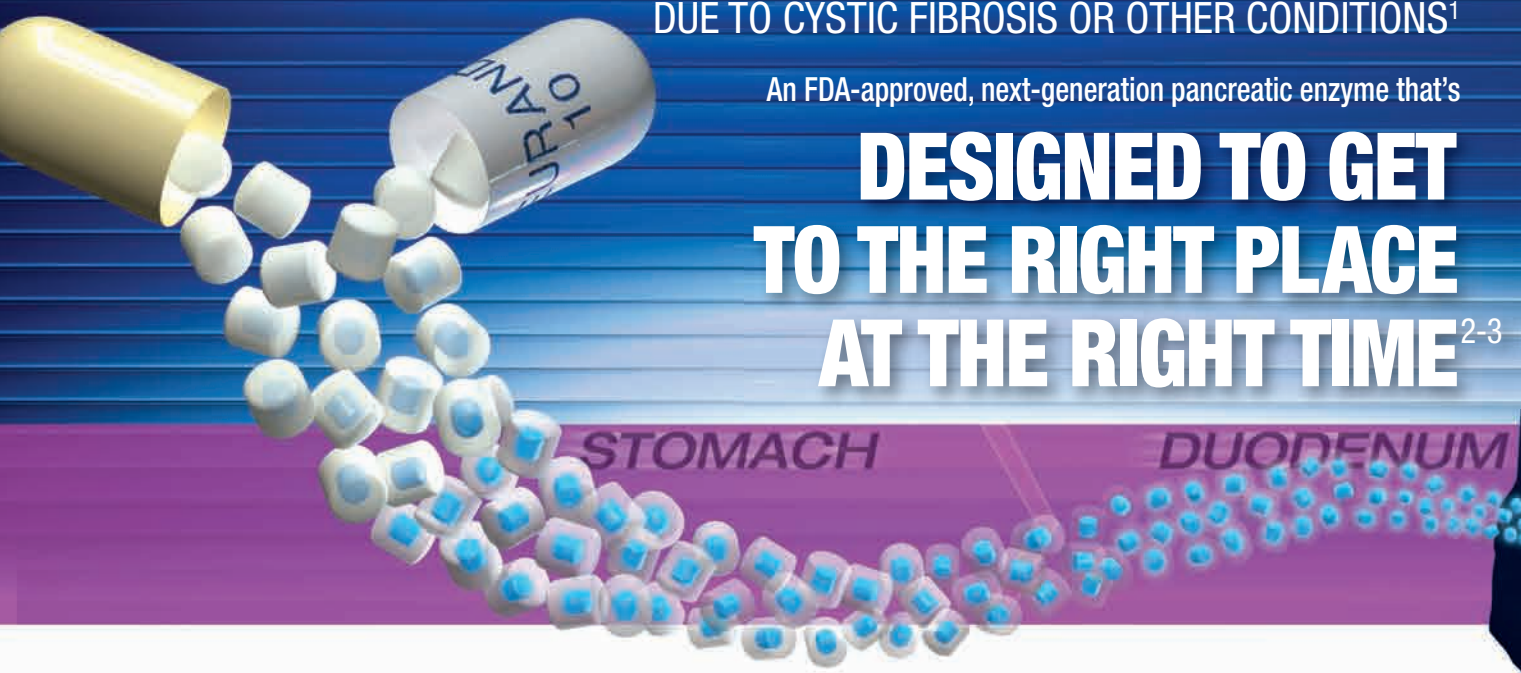

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*Reports were subjective and recorded in a daily diary form.[4]

References: 1. ZENPEP [package insert]. Yardley, PA: Eurand Pharmaceuticals, Inc.; 2010. **2.** Data on file MED-0151, Eurand Pharmaceuticals, Inc., Yardley, PA. **3.** Data on file MED-0152, Eurand Pharmaceuticals, Inc., Yardley, PA. **4.** Wooldridge JL, Heubi JE, Amaro-Galvez R, et al. EUR-1008 pancreatic enzyme replacement is safe and effective in patients with cystic fibrosis and pancreatic insufficiency. *J Cyst Fibros*. 2009;8(6):405-417.

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Pulmonary Pathologies Abound in RA Population

BY SUSAN LONDON
Elsevier Global Medical News

VANCOUVER, B.C. – Chest physicians must consider a slew of diagnostic possibilities when evaluating patients with rheumatoid arthritis who have developed pulmonary abnormalities, according to Dr. Kevin R. Flaherty, FCCP.

"We have to keep in mind all the different things that can go wrong in these patients when we are trying to treat them: Is this progression of the underlying disease? Is this a complication of the therapy? Or is this the development of something new, like a cancer, that's now causing the patient's symptoms?" he said to attendees of CHEST 2010, the annual meeting of the American College of Chest Physicians.

Pulmonary Manifestations of RA

"The lung is a common site for extra-articular rheumatoid arthritis," noted Dr. Flaherty, who is a pulmonologist and associate professor at the University of Michigan Health System in Ann Arbor. Of the many pulmonary manifestations of RA, interstitial lung disease causes the greatest morbidity and mortality.

The lifetime risk of interstitial lung disease is nearly 8% in patients with RA, compared with 1% in the general population (Arthritis Rheum. 2010;62:1583-91). And this disease confers a poor prognosis, with a near tripling of the risk of death and with a median survival after diagnosis of only about 2.5 years.

High-resolution CT (HRCT) and pulmonary function testing appear to be useful for identifying interstitial lung disease early in its course, Dr. Flaherty said.

For example, among patients within 2 years of an RA diagnosis, 44% have been found to have HRCT, pulmonary function test, and other abnormalities consistent with interstitial lung disease in the absence of symptoms (Am. J. Respir. Crit. Care Med. 1997;156:528-35).

"The [HRCT] features were mild – reticular thickening, ground glass, and not much honeycombing – suggesting maybe that we might be able to impact the disease, because I think once you get to honeycomb lung and end-stage fibrosis, our ability to impact this disease is likely to be lower," he said.

Another study among patients with recent-onset RA found abnormalities on HRCT but normal results on pulmonary function tests (Scand. J. Rheumatol. 2007; 36:338-44), "suggesting that symptoms and pulmonary screening are not going to be as sensitive as HRCT screening."

'What we are really begging for are some prospective, well-done clinical trials' of potential treatments.

DR. FLAHERTY

As for which patients to screen for interstitial lung disease, the predictors of abnormal pulmonary function testing in the RA population are respiratory symptoms, smoking, anti–cyclic citrullinated peptide positivity, and use of prednisone (Arthritis Res. Ther. 2010;12:R104).

HRCT appears to be more sensitive than pulmonary function testing for detecting disease progression (Arch. Intern. Med. 2008;168:159-66). And carbon monoxide diffusing capacity at diagnosis is the best predictor of progression (Ann. Rheum. Dis. 2002;61:517-21).

"We are starting … to see data emerging that really mirrors what we see in idiopathic lung disease, that the histopathology and the CT appearance can help us in terms of stratifying patients for risk of subsequent mortality," Dr. Flaherty said.

For example, a study of patients with RA-associated interstitial lung disease found 50% mortality in those with a usual interstitial pneumonia (UIP) histology, compared with none in those with a nonspecific interstitial pneumonia (NSIP) histology after a similar median follow-up of about 4 years (Chest 2005;127:2019-27).

A honeycomb pattern on HRCT was found only in the UIP group, suggesting that this radiographic pattern is a good surrogate for this histology, Dr. Flaherty noted. And indeed, patients having a definite UIP radiographic appearance have poorer survival (Eur. Respir. J. 2010;35:1322-8).

Continued on following page

Less Therapy May Be Better in Pulmonary Sarcoidosis

BY SUSAN LONDON
Elsevier Global Medical News

VANCOUVER, B.C. – Management of pulmonary sarcoidosis is moving away from hard clinical targets and toward patients' self-reported well-being and goals, said Dr. Daniel A. Culver, FCCP, a pulmonologist at the Cleveland Clinic.

Physicians may treat sarcoidosis for a variety of reasons, and research is helping to sort out which of them are valid, he said at CHEST 2010, the annual meeting of the American College of Chest Physicians.

One reason might be to improve radiographic or physiologic parameters. In particular, the Scadding stage of a patient's chest x-ray at presentation has been used for about 50 years to estimate prognosis and the need for treatment.

"But in fact there are a number of pieces of data coming out now that suggest that the chest x-ray may not be the most ideal way to measure how things are going to go for patients," he commented.

In one study, for example, half of patients with pulmonary sarcoidosis were rated as having a better chest x-ray during an exacerbation as compared with before, despite their worsening symptoms and spirometry (Respirology 2008;13:97-102).

Another reason for undertaking treatment might be to improve patients' symptoms, according to Dr. Culver. A recent review has described a so-called sarcoidosis penumbra, a collection of disease-related issues that affect patients' well-being but are often not well captured by tests (Semin. Respir. Crit. Care Med. 2010;31:501-18). For instance, two in every three patients have depression, and one in six has sleep apnea.

"This took us a long time as sarcoidologists to recognize, that it's not the x-ray and vital capacity that the patients care about," but rather their ability to function and enjoy life, he said. "Going forward ... for both immunosuppressive therapy and the treatment of sarcoidosis in general, we are going to see it more focused on patient-centered outcomes and quality of life rather than things that we'd all like to measure, like the vital capacity."

'If the symptoms are relatively mild or modest ... observation is completely reasonable.'

DR. CULVER

Another reason that physicians may treat sarcoidosis is to alter the natural history of the disease and prevent fibrosis. But "most sarcoidosis will resolve within the first 5 years, at least radiologically," Dr. Culver noted, and current evidence suggests treatment does little to alter this.

In one study, 39% of patients with stage 2 or 3 disease on chest x-ray had neither progression nor improvement during a 6-month period. When these stable patients were assigned either to immediate treatment with a fairly aggressive regimen of prednisolone or to as-needed treatment only if spirometry showed deterioration, just 19% of the latter group required treatment during the next 5 years (Thorax 1996;51:238-47).

"If you can hold off on treating, you may be able to prevent side effects from medicines … and still have a patient who has their disease spontaneously resolve," he commented.

That said, the as-needed treatment group had a smaller improvement in forced vital capacity (FVC), and there were some other potentially important differences in outcomes between groups.

"Right now, we don't think that steroid therapy given preemptively has a tremendous impact on the natural history of the disease," Dr. Culver said. "This is probably the best study that addresses this question, but this doesn't necessarily resolve the issue."

Finally, physicians may initiate treatment for sarcoidosis because they feel compelled to do something, according to Dr. Culver. "But the evidence for this [practice] really is not very strong, despite the fact that steroids have been used for about 60 years now."

A recently proposed algorithm for treating pulmonary sarcoidosis draws on all of these accumulated data and recommends symptom assessment as a first step (Semin. Respir. Crit. Care Med. 2010;31:501-18).

"If the symptoms are relatively mild or modest – and this requires a discussion with the patient – then I think observation is completely reasonable," Dr. Culver said.

In more severe cases, the algorithm proposes short-course, moderate-dose therapy with prednisone 20-30 mg daily for 3-4 weeks, as supported by several studies, including a recent one among patients with acute exacerbations (Am. J. Med. Sci. 2010;339:1-4). "Be less aggressive with your steroid dosing," he recommended. "You can really get away with shorter courses, with lower doses than we have been using in the past."

For patients who have a good response, the goal is to taper to 10 mg daily or less, a practice endorsed by a Delphi consensus study of sarcoidosis management (Respir. Med. 2010;104:717-23).

When patients have an inadequate response to prednisone or are unable to reduce the dosage to 10 mg daily, the algorithm suggests adding an immune modulator (methotrexate, azathioprine, leflunomide, or mycophenolate).

There have been few head-to-head comparisons of these agents, although methotrexate is by far the agent preferred by U.S. physicians treating sarcoidosis, partly because it has been the best studied. "That's the drug that we use as our second-line agent," he noted. "The reason that we like methotrexate is it seems to work pretty well, it's pretty inexpensive and pretty reliable, and it's not hard to get through the insurance company."

Data from his institution show that leflunomide also works well. A review of 40 patients with pulmonary sarcoidosis found they had an improvement in FVC within 6 months of starting this drug, as well as a reduction in average prednisone dose to 5 mg daily. "We have really moved leflunomide to the next agent in our algorithm after methotrexate," he said.

Infliximab is the only agent that has been shown to be efficacious in a double-blind, randomized controlled trial of patients with sarcoidosis, Dr. Culver said.

In unselected patients, infliximab is associated with just a 2.5% improvement in percent predicted FVC (Clin. Chest Med. 2008;29:533-48, ix-x) – or about that seen with steroids. But among those with more severe lung disease (an FVC of less than 69%), there is a roughly 3.25% improvement. The improvement was 6% in the randomized trial (Sarcoidosis Vasc. Diffuse Lung Dis. 2006;23:201-8). "We think for patients failing cytotoxic agents that infliximab is a nice option," Dr. Culver said.

And studies are helping to identify which patients are most likely to benefit from infliximab: those who have had disease for more than 2 years, have worse dyspnea (a Medical Research Council dyspnea score of at least 2), lower FVC, poorer quality of life (assessed with the St. George's Respiratory Questionnaire), reticulonodular changes on chest x-ray, or an elevated C-reactive protein level.

Dr. Culver advised physicians to establish the goals of treatment and to remember the chronic nature of sarcoidosis. "Think about treating your patient longitudinally, because remember, you are not treating this as if it's an infection, you are treating this as if it's hypertension that needs to be controlled in the long term."

Dr. Culver reported having affiliations with the biotechnology and pharmaceutical companies Centocor (manufacturer of infliximab), Takeda, and Actelion. ■

COMMENTARY

Dr. Darcy Marciniuk, FCCP, comments: It has become clear that the chest radiograph shouldn't be the sole target for therapy in sarcoidosis. We should assess and value various clinical end points, including the symptoms experienced by the patient. As highlighted by Dr. Culver, there are therapeutic options available to the clinician, but sometimes the best therapy is no therapy coupled with close observation.

Continued from previous page

Rigorous studies are lacking when it comes to treating interstitial lung disease in the RA population, he said. Case reports, case series, and retrospective analyses have assessed many immunomodulating and immunosuppressive agents, but "what we are really begging for are some prospective, well-done clinical trials to help us sort all of these potential treatments out."

Pulmonary Side Effects of RA Therapy

Pneumonitis is often a concern in patients using methotrexate to treat RA. But with low-dose therapy, only 3% of patients develop this complication after a mean treatment duration of 23 months (Chest 1996;109:933-8). Only a small number of patients develop methotrexate toxicity, Dr. Flaherty pointed out.

Anti–tumor necrosis factor (TNF) agents such as infliximab have been associated with pulmonary adverse effects and complications, including infection, atypical presentation of tuberculosis, and pulmonary fibrosis.

Some reports have also raised concern that anti-TNF agents may hasten progression of interstitial lung disease in patients with RA and thus increase mortality. "The data on that are still out," Dr. Flaherty said. Evidence thus far suggests that mortality in patients treated with these agents is similar to that in their counterparts treated with traditional disease-modifying antirheumatic drugs (Ann. Rheum. Dis. 2010;69:1086-91).

Rituximab has been linked to severe infections in RA patients, most of which (40%) are pulmonary (Arthritis Rheum. 2010;62:2625-32). Just one infection was opportunistic; most were bacterial.

Pulmonary Cancers

Patients with RA have increased risk of lung cancer (standardized incidence ratio, 1.63) as well as for another malignancy that can involve the lung, lymphoma (Arthritis Res. Ther. 2008;10:R45), as a result of their underlying disease, long-term immunosuppression, or both.

Treatment with biologic agents has not been associated with a significantly elevated risk of lung cancer among patients with RA, Dr. Flaherty said. But treatment with methotrexate has, with the incidence of lung cancer among methotrexate users about triple that of the general population (Arthritis Rheum. 2008;59:794-9).

"So as we are seeing [patients] with pulmonary manifestations, we have to keep in mind their risk of cancers as well," he recommended.

Dr. Flaherty had no disclosures. ■

COMMENTARY

Dr. Darcy Marciniuk, FCCP, comments: Rheumatoid arthritis patients with pulmonary involvement truly test the clinical skills and expertise of pulmonologists.

Involvement related to the underlying disease is varied and can be significant, and is added to by complications of therapy and malignancies. Dr. Flaherty reminds us that a thorough clinical, physiologic, and radiographic assessment assist in their management.

Endosonography Helps ID Thoracotomy Candidates

BY MARY ANN MOON
Elsevier Global Medical News

For patients with suspected non–small cell lung cancer, adding endosonography before surgical staging improves detection of mediastinal nodal metastases, thus reducing unnecessary thoracotomies by more than half, a study has shown.

In addition, because endosonography is minimally invasive, adding this step doesn't raise the rate of complications for staging procedures, said Dr. Jouke T. Annema of Leiden (the Netherlands) University Medical Center and associates.

The researchers compared surgical staging alone to endosonography followed by surgical staging because "at present it is not known whether initial mediastinal tissue staging of lung cancer by endosonography improves the detection of nodal metastases." Failure to detect such metastases during staging results in patients undergoing thoracotomy for tumor resection, only to have the thoracotomy aborted when unresectable or metastatic lung disease is discovered (JAMA 2010;304:2245-52).

The investigators randomized 241 patients suspected of having resectable NSCLC, who were treated at four tertiary referral centers in Belgium, the Netherlands, and the United Kingdom. The patients were assigned to surgical staging alone, which is the current standard of care (118 subjects), or to endosonography followed by surgical staging (123 subjects).

The sensitivity of surgical staging alone was 79%. This improved to 94% when endosonography was combined with surgical staging, Dr. Annema and colleagues said.

Mediastinal nodal metastases were found in 41 of 118 patients (35%) by surgical staging alone, compared with 62 of 123 patients (50%) by the combined approach. This means that there were 21 unnecessary thoracotomies with surgical staging alone, for a rate of 18%, compared with 9 with the combined approach, for a rate of 7%.

The complication rate was 6% for surgical staging, compared with 1% for endosonography.

These findings show that endosonography improves the sensitivity of surgical staging, halves the rate of unnecessary thoracotomy, and has a low complication rate. Because it also does not require general anesthesia and has been shown in previous studies to be cost effective as well as preferred by patients, "endosonography should be the first step for mediastinal nodal staging," the investigators said.

They added that all of the staging procedures in this study were performed in specialty centers by highly trained and experienced interventionists, so the applicability of the study findings to other settings is limited.

VITALS

Major Finding: Performing endosonography to detect mediastinal node metastases before conducting surgical staging identifies more patients with metastases than does surgical staging alone, sparing them from further unneeded thoracotomy.

Data Source: A multicenter randomized clinical trial involving 241 consecutive patients with suspected non–small cell lung cancer treated between 2007 and 2009.

Disclosures: This study was supported in part by Hitachi Medical Systems, COOK, Olympus, the Zorgprogramma Oncologie Gent, the U.K. National Health Service R & D Health Technology Assessment Program, and the National Institute for Health Research Cambridge Biomedical Research Centre.

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COMMENTARY

Dr. Richard Fischel, FCCP, comments: The authors address a very important aspect regarding staging of lung cancer using endosonography, also known as EBUS or endobronchial ultrasound. They describe prethoracotomy staging to help avoid unnecessary thoracotomies, which is an important concept in the treatment of lung cancer. The data do indicate that adding EBUS to the preoperative staging protocol is beneficial, resulting in improved sensitivity for the detection of metastatic disease. It is very likely that preop EBUS may become the standard of care in lung cancer surgery; however, at this time mediastinoscopy remains the gold standard.

NETWORKS
Blast Lung, Home Care Equipment, Fibrosis

Disaster Response

Blast Lung Injury

An understanding of blast injury and its effect on lungs is critical for all pulmonologists and critical care specialists in the 21st century. Recently, a bomb explosion ripped through the busiest airport in Moscow, resulting in casualties: 31 dead and over 130 injured. Previous bomb explosions on trains since 1995 have killed several people and injured many individuals. These include bomb explosions on trains in Paris (1995), Moscow (1996), Sri Lanka (1996), Manila (2000), Angola (2001), Chechnya (2003), Madrid (2004), London (2005), Mumbai, India (2006), and Panipat, India (2007).

Many of the terrorist acts across the world have increased the awareness of injuries from explosive detonations that release energy at supersonic speeds from the epicenter of the blast. This blast event contributes to primary blast injuries that often affect the head, ear, abdomen, and lung. Secondary injuries may also occur as a result of bomb fragments and other debris that are thrown out. It can also result in tertiary injuries to the individual if he or she gets thrown out from the blast, resulting in head injuries and bone fractures. Other blast-related injuries that are not due to the above three mechanisms are referred to as quaternary injuries, and they include burns and exacerbation of previous medical conditions.

Blast lung injury is one of the major causes of morbidity and mortality among the victims of explosion. The incidence of pulmonary blast injury varies from 17% to 63%. There is tissue damage from the pressure changes, and the severity depends on factors such as the explosive used, intensity of the blast wave, its duration, and the proximity of the victim to the epicenter of blast. Pulmonary contusion, hemorrhage, and edema are seen from parenchymal and vascular damage. Blast lung can be associated also with pneumothoraces, hemothoraces, bronchopleural fistula, air/fat embolization, and other pleural and parenchymal injuries. Body armor may not protect against blast lung injury. Pulmonary symptoms may include cough, dyspnea, chest pain, and hemoptysis. On physical examination, apnea, tachypnea, cyanosis, cough, wheezing, and/or decreased breath sounds may be present. Blast lung is suspected when patients present with respiratory difficulty and hypoxemia without external chest injury. The key aspects of management are maintaining oxygenation, careful fluid resuscitation, addressing pneumo/hemothoraces, and initiating mechanical ventilation for respiratory failure.

Dr. Angeline A. Lazarus, FCCP
Vice-Chair

Home Care

CMS Competitive Bidding Program: What the Pulmonologist Should Know

It was hoped that the Medicare Modernization Act would reduce costs and improve access to home care medical equipment through a competitive bidding process. Centers for Medicare & Medicaid Services (CMS) accepted bids covering respiratory home care equipment for nine areas (Cincinnati, Cleveland, Charlotte, Dallas, Kansas City, Miami, Orlando, Pittsburgh, and Riverside, CA) starting January 2011. To obtain a list of vendors, access the medicare.gov site, and the Resource Locator will allow matching of patient zip code and the appropriate approved vendor. Current patients using oxygen/PAP, whose suppliers have not been contracted under the competitive bidding program, have the option to continue renting with their current providers as "grandfathered suppliers." When traveling, patients will need to use contracted suppliers when they are in an area that is covered under the competitive bidding program.

Each contracted supplier is required to list the manufacturers and products they provide. Physicians should be specific when prescribing, including giving reasons that a product should be used. Not all approved providers are able to provide all products; it is possible that a patient could require multiple providers. In-home training is not a mandated component of the bidding process. If physicians would like patients to have education in the home, they will need to be very specific when scripting.

This is a dramatic change in how home respiratory care is provided. Physicians should document complications if access to care is limited or if patient care is affected. The program will be expanded to an additional 91 cities starting in January 2013. Now is the time for caregivers, durable medical providers, and Medicare to learn and correct problems, as delivery of home care moves to this new model.

Dr. Lisa Wolfe, FCCP
Vice-Chair

Interstitial and Diffuse Lung Disease

Recent Advances in the Epidemiology of Pulmonary Fibrosis

Following is a summary of my presentation given at the Interstitial and Diffuse Lung Disease NetWork Open Meeting at CHEST 2010. To view the slide presentation, please visit www.chestnet.org/accp/presentations/network-special-presentations-chest-2010.

Prior epidemiologic investigations of idiopathic pulmonary fibrosis (IPF) have been limited due to its relative rarity. However, the evaluation of death certificate data provides an opportunity to investigate pulmonary fibrosis (PF) from an epidemiologic perspective in order to identify trends in disease-associated mortality and to better understand the burden of disease. Using data from the US Multiple Cause-of-Death Mortality Database (Centers for Disease Control and Prevention, National Center for Health Statistics, www.cdc.gov/nchs), our group recently reported that mortality rates from PF have significantly increased from 1992 to 2003 in both men (28.4%) and women (41.3%), and are predicted to continue to rise into the future (Olson et al. *Am J Respir Crit Care Med*. 2007;176[3]:277). Our results parallel the data from other recent epidemiologic investigations that indicate the incidence of disease is also increasing (Coultas et al. *Am J Respir Crit Care Med*. 1994;150[4]:967; Rhagu et al. *Am J Respir Crit Care Med*. 2006;174[7]:810; Gribbin et al. *Thorax*. 2006;61[11]:980). At the same time, more patients are dying of the disease itself rather than from comorbid conditions (Olson et al. *Am J Respir Crit Care Med*. 2007;176[3]:277; Mannino et al. *Am J Respir Crit Care Med*. 1996;153[5]:1548; Panos et al. *Am J Med*. 1990;88[4]:396; Martinez et al. *Ann Intern Med*. 2005;142:963). Further, mortality rates from PF, like chronic obstructive lung disease, exhibit significant seasonal variation with a significantly higher number of deaths in the winter (17.1%, *P* less than .0001), followed by spring (12.7%, *P* less than .0001) when compared with summer months, even in the absence of recognized infection (Olson et al. *Chest*. 2009;136[1]:16). These results do not appear to be limited to idiopathic disease, as the prevalence of interstitial lung disease in decedents with rheumatoid arthritis has also increased over time despite an overall decline in RA-associated mortality (Olson et al. *Am J Respir Crit Care Med*. 2010; Sep 17 [Epub ahead of print]). Overall, these trends may represent an increase in the clinical recognition of interstitial lung disease, or perhaps they reflect the lack of effective therapies for lung fibrosis. Regardless of cause, these recent epidemiologic investigations do reveal a rapidly growing problem that deserves further research into the mechanisms of and potential therapies for lung fibrosis.

Dr. Amy Olson
NetWork Member

FROM THE CEO

The State of the College

To: ACCP Members and Other Supporters
From: ACCP Operations Team*
Regarding: The State of the College
Date: February 2011

▶ *A strong financial position.*
▶ *The highest impact factor and ranking in the 75-year history of the* CHEST *journal.*
▶ *The largest number of international attendees at the ACCP annual meeting, CHEST 2010.*
▶ *Launching* OneBreath, *a new initiative of The CHEST Foundation, to inspire people to take care of their lungs and heart and never take their next breath for granted.*

These are just a few of the many accomplishments that your ACCP achieved this past year. The purpose of this *State of the College*, which the Operations Team will prepare annually, is to acknowledge and highlight these successes. It is important to note that none of the accomplishments included here would have been remotely possible without the remarkable dedication of our leadership and staff. We profoundly thank ACCP leaders for the considerable time, knowledge, and expertise that they so generously volunteer and ACCP staff for regularly going the "extra mile."

A series of changes accompanied our successes: some bigger—reassessing the way that the ACCP advocates on behalf of its members and their patients, and some smaller—adopting the Google suite of applications. While change can be difficult, we are resolute in our belief that appropriate changes are essential for the College to stay in the lead in these fast-paced times.

Of course, much work remains to be done. The accomplishments outlined here are first steps in realizing our new vision to be the "global leader in providing education in cardiopulmonary, critical care, and sleep medicine to optimize health and advance patient care." Read on for a glimpse of some of the exciting plans unfolding at the College. We look forward to working with you to further develop and implement these ideas and continue to advance your ACCP, the authority in clinical chest education.

Operations

Our strategic planning began with the environmental snapshot that leaders and staff took of the College and the subsequent *ACCP Strategic Plan 2010 – 2011*. The plan sets ambitious goals that look several years ahead and delineate specific strategies and metrics for measuring our success in achieving these goals. Other crucial documents were revisited and revised, including the bylaws and conflict-of-interest policy for ACCP leaders. Through our strategic planning, we acknowledged our core competency of providing the best clinical education in chest medicine and realigned staff to reflect this common purpose.

Last year, the four ACCP Presidents—President, President-Elect, President-Designate, and Immediate Past President—and the Executive Vice President and CEO, began working together as a team, including participating in weekly conference calls, to enhance the continuity of leadership for the common purpose of realizing the ACCP strategic plan. The "Four Presidents" at that time were Kalpalatha K. Guntupalli, MD, FCCP; David D. Gutterman, MD, FCCP; Suhail Raoof, MBBS, FCCP; and James A. L. Mathers, Jr, MD, FCCP, respectively. The new Four Presidents, including Darcy D. Marciniuk, MD, FCCP, and the EVP/CEO, Paul A. Markowski, CAE, will continue this highly collaborative practice, weaving the themes of each President into the strategic efforts of the College.

Finances

Despite a continued anemic economy, the ACCP maintains a strong financial position. In FY 2009-2010, the ACCP and The CHEST Foundation had total assets of $25,166,791, total liabilities of $8,232,837, and total net assets of $16,933,954. This year, we project a budget surplus of $55,206 before depreciation.

We developed key performance indicators to enhance our budget process and rigorously track our progress in achieving the goals of our strategic plan. The Board of Regents and staff regularly review this statistical snapshot, which includes budget FY 2010-2011, year-to-date actual, along with historical financial, staffing, membership, education, and publications information. Our membership also continues to grow. At the time of this writing, there were 17,956 ACCP members, reflecting a 5% increase since 2008 and a 19% increase (3,440) in total international members.

THIS IS AN EXCITING TIME TO BE AN ACCP MEMBER AND EVEN MORE FULFILLING TO ACTIVELY SHAPE ACCP'S FUTURE. WE INVITE YOU TO DO SO ...

The ACCP assembled an effective development team that succeeded in securing support for projects that are identified in the ACCP strategic plan. This support is in the form of CME and non-CME grants, as well as other activities that generate non-dues revenue. Given the current external environment that makes it more difficult to obtain funding, this success is achieved by the increased cooperation between our development team and other areas of the College.

Recently, the Development Division and Clinical Education, Informatics, and Research Division successfully worked together on a non–small cell lung cancer project for 2011-2012, through an ACCP-led collaborative with the American Society for Clinical Pathology, National Institute for Quality Improvement and Education, The France Foundation, and CECity. This project offers the ACCP an opportunity to improve the knowledge, competency, and performance of interdisciplinary teams that are responsible for the diagnosis, assessment, and personalized care for patients with non–small cell lung cancer.

The Marketing and Public Relations Department has been an integral part of the development and implementation of a COPD project that was funded in 2010. The ACCP-convened COPD Alliance is a campaign to increase awareness of COPD among primary care clinicians and is reaching out to thousands of clinicians throughout the United States.

Education Programs

The ACCP hosted the Guidelines International Network (G-I-N) Conference 2010, the first to be held in the United States. The G-I-N Conference brought together a record number of professionals involved in evidence synthesis, guideline development, implementation, quality improvement, and health policy to integrate knowledge and, ultimately, improve patient outcomes.

We developed and launched the first Pediatric Pulmonary Board Review course and associated e-book study guide in collaboration with the American Academy of Pediatrics (AAP). This first-ever board preparation course in pediatric pulmonology met the increasing education needs of pediatric pulmonologists and, as a result of this joint project, the AAP is working toward the development and implementation of Maintenance of Certification material in 2011.

We developed new models to define the role for and shape of our future advocacy efforts. The Board approved the recommendations of the ACCP Advocacy Task Force, which was charged with determining what the ACCP should accomplish with its advocacy efforts and how those efforts should be organized to maximize impact and value to members, patients, and the College. The task force underscored the importance of the ACCP engaging in effective advocacy and called for a targeted and measurable approach.

We collected, reported, and presented data stemming from the work conducted in the interventional and diagnostic bronchoscopy registries. This work enabled the use of aggregated reports, with collaboration from the US Food and Drug Administration, and initiated the facilitation of an ACCP-led bronchoscopy training project, beginning with a fellowship focus, that includes representation from multiple societies, such as the American Thoracic Society, European Respiratory Society, Society of Thoracic Surgeons, British Thoracic Society, Canadian Thoracic Society, American Association for Bronchology and Interventional Pulmonology, and Association of Pulmonary and Critical Care Medicine Program Directors.

Amidst the idyllic backdrop of Vancouver, British Columbia, nearly 5,000 attendees descended on CHEST 2010 from October 30 to November 4, 2010, with the largest number of international attendees (30%) in the history of the meeting. CHEST 2010 was noteworthy in other ways. We moved toward "paperless" CHEST meetings by making use of electronic communication tools. The ACCP provided 24/7 access to the most current and late-breaking meeting information and, in so doing, saved considerable printing and paper costs.

New at CHEST 2010, we offered robust online meeting planning tools to allow attendees to search sessions, build a daily itinerary, select session handouts, download material to various electronic platforms, as well as select, view, and listen from a menu of on-site broadcasting of multiple sessions simultaneously. Other new features at CHEST 2010 included an earlier meeting start day, postgraduate multipass courses, participation in virtual simulation, education that highlighted global initiatives and the impact upon patient care, and advanced clinical care–focused tracks.

The ACCP also conducted a research study to better understand the factors that motivate chest physicians to register, attend, and recommend the CHEST annual meeting. With these data and knowledge, the ACCP can increase attendance and create the "can't miss" meeting for chest physicians.

Communications

We initiated a major overhaul of our information technology infrastructure and Web presence, including the investigation and development of content and learning management systems, in order 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 the ACCP conducts business.

The *CHEST* journal recently went mobile with full issues available on the iPhone®, iPod touch®, and iPad®. The College also 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® app for ACCP-SEEK. Last summer, *CHEST* reached its highest impact factor (6.36) and ranking (3rd out of 43 respiratory journals) (*2009 Journal Citation Reports*) in its 75-year history, and *CHEST Physician* has the distinction of being the most read news publication in the pulmonary medicine market (Kantar Media Medical/Surgical Readership Study, December 2010).

We launched two new e-newsletters as part of our efforts to enhance communication and transparency. *ACCP*

Continued on following page

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Leadership Update features major initiatives in development at the College, and *ACCP NewsBrief* is a weekly e-newsletter sent to all ACCP members and includes ACCP/Foundation news, as well as news from the health-care industry.

The CHEST Foundation

The CHEST Foundation had a financially and programmatically successful 2009-2010. The Foundation ended the year with $8,038,904 in total assets and almost $6 million in net assets.

The Foundation launched a new branding campaign, Web site, and public-facing program, OneBreath™, Make The Most of It. Its new Web site at onebreath.org captures its mission, using the three pillars of education, care, and community, and is providing a breadth of new resources to ACCP members, their patients, and the public.

The Foundation continued its efforts with its strategic partners through the Patient Safety Collaborative (PSC). The collaborative created a white paper on surgical site infection, developed an online tool kit, and planned a pilot project designed to promote a culture of safety. The work of the PSC was highlighted at a CHEST 2010 session.

The Foundation continued its successful clinical research and humanitarian service awards by conferring almost $600,000 in awards at CHEST 2010. To date, The Foundation has invested $5.7 million in 800 ACCP members' grant projects and pro bono service.

The Foundation also continued its tradition of honoring the volunteer service to The Foundation by leaders of the Board of Trustees. At CHEST 2010, The Foundation celebrated the vast achievements of outgoing Chair, Robert G. Johnson, MD, FCCP, who continues his service as the Chair of the OneBreath initiative.

Looking Ahead

While ACCP leaders and staff have accomplished a great deal this past year, much work remains to be done to be the "global leader in providing education in cardiopulmonary, critical care, and sleep medicine to optimize health and advance patient care." In the coming months, we will reconsider our membership structure, dues, and processes, as well as develop an international strategic plan, focusing on carefully selected and limited geographic regions—the Middle East, Latin America, India, and China—with significant potential.

We also will reassess our communications, with an emphasis on social media, and continue the revamping of our information technology infrastructure and Web presence. Overseeing these and other changes will demand effective leadership, which is why the ACCP will implement an annual Board self-assessment tool and redouble our commitment to leadership development at all levels of member engagement.

The College is first and foremost a membership organization. Consequently, it is imperative that members like you be actively involved. This is an exciting time to be an ACCP member and even more fulfilling to actively shape ACCP's future. We invite you to do so by answering the call for nominations this spring or simply by posting a comment to one of our blogs. Your participation at any level is welcome.

On behalf of the entire ACCP staff, thank you for the honor and pleasure of serving you, your patients, and your ACCP. ■

**The ACCP Operations Team includes the following staff: Paul A. Markowski, CAE, Executive Vice President and CEO; P. Stratton Davies, CPA, Senior Vice President and Chief Financial Officer; Ed Dellert, RN, MBA, CCMEP, Senior Vice President, Clinical Education, Informatics, and Research; Dave Eubanks, EdD, RRT, FCCP(Hon), Senior Vice President, Business and Development; Marilyn Lederer, CPA, Executive Director, The CHEST Foundation; William Rieser, SPHR, CCP, Human Resources Director; Stacy Seiden, MPP, Special Projects Manager; and Stephen Welch, Senior Vice President, Communications.*

New ACCP Presidential Blog

To enhance communication between ACCP leaders and members, the ACCP Presidents have launched a new blog, *From the Presidents*. The inaugural post by ACCP President, Dr. David D. Gutterman, FCCP, explains the vision and goals of the blog and features Dr. Gutterman's call for you to share your ACCP experiences.

From the Presidents will feature regular blogs about the College, medical and health-care issues, the profession, and other member-related topics of interest. In addition to Dr. Gutterman, Dr. Suhail Raoof, FCCP, ACCP President-Elect; Dr. Darcy D. Marciniuk, FCCP, ACCP President-Designate; and Dr. Kalpalatha K. Guntupalli, FCCP, ACCP Immediate Past President, will contribute to the blog.

Here's your chance—post your comments today!

You can view the inaugural blog and add your comments at www.chestnet.org/accp/blogs/introducing-presidents-new-accp-blog. ■

Critical Care Commentary

Vena Cava Filters: A Call to Action

The concept of venous interruption can be traced back to Armand Trousseau's lectures at the Hotel Dieu in Paris in the mid-19th century (Trousseau A. Phlegmasia alba dolens. In: Trousseau A, ed. *Clinique Medicale de l'Hotel-Dieu de Paris*. Paris, France: Balliere, 1865; 654). Although surgical venous interruption was occasionally performed, its invasive nature and attendant morbidity and mortality prevented widespread application. This situation dramatically changed with the introduction of the stainless steel Greenfield filter in 1973, which made percutaneous venous interruption feasible (Greenfield et al. *Surgery*. 1973;73[4]:599). Between 1979 and 1999, the number of vena cava filters (VCF) placed annually in the United States rose 25-fold, from 2,000 to 49,000 (Stein et al. *Arch Intern Med*. 2004;164[14]:1541). With the introduction of optional/retrievable VCF that are easy to insert, the expansion in clinical use of these devices has continued to increase. In 2007, nearly 167,000 VCF were placed in the United States, and it is estimated that annual use will top 259,000 in 2012. This expansion in VCF use has been largely driven by the increasing availability of optional filters and increased use for prophylactic rather than treatment indications (Smouse and Johar. *Endovascular Today*. 2010:74-77; Athanasoulis et al. *Radiology*. 2000;216[1]:54; Kim et al. *J Vasc Interv Radiol*. 2008;19[3]:393). Despite the popularity of these devices, there is surprisingly little scholarship documenting their efficacy. Among 2,503 publications on VCF, only two randomized controlled trials (RCT) have been conducted examining outcomes. In comparison, 252 RCT have been reported for the use of low-molecular-weight heparin for venous thromboembolism (VTE) among 2,265 publications (PubMed search conducted Nov 14, 2010).

Consequently, the appropriate indications for VCF insertion continue to be a subject of considerable debate, in large part due to the limited evidence supporting their utility in the treatment of VTE (Table 1). There is broad support for their application in patients who have acute VTE and contraindications to anticoagulation. Although it did not test the efficacy of VCF in the absence of anticoagulation, the PREPIC study did show that filters reduce the incidence of pulmonary embolism (PE) by 63% (6.2% vs 15.1%, hazard ratio 0.37 [95% CI 0.17-0.79], $P = .008$) in patients who received at least 3 months of anticoagulation therapy (PREPIC Study Group. *Circulation*. 2005;112[3]:416). However, skeptics are much less likely to support filter insertion for other indications, such as failure of anticoagulation, as these patients were excluded from participation in PREPIC (Decousus et al. *N Engl J Med*. 1998;338[7]:409). In these instances, hematologists are more apt to intensify or alter anticoagulant therapy (eg, increase the target INR or switch to an alternative anticoagulant, such as a low-molecular-weight heparin), and look for a potentially correctable etiology for anticoagulation failure (eg, heparin-induced thrombocytopenia, antiphospholipid syndrome, Trousseau syndrome, vascular compression—May-Thurner syndrome, thoracic outlet syndrome, and others), rather than resort to filter placement. In many instances, a VCF may impair rather than enhance local thrombotic control by reducing blood flow proximal to the site of thrombosis. Patients with cancer and idiopathic VTE appear to be at particularly high risk for filter-associated thrombotic complications (PREPIC Study Group. *Circulation*. 2005;112[3]:416).

Although vena cava filters have traditionally been placed in the inferior vena cava (IVC), several recently published papers have examined filter placement in the superior vena cava (SVC) (Usoh et al. *Ann Vasc Surg*. 2009;23[3]:350). While pulmonary embolism does occur from the upper extremity and SVC, the incidence is significantly less than the IVC (Muñoz et al and the RIETE Investigators. *Chest*. 2008;133[1]:143). In addition, the complications of filters in the SVC location can be devastating (Owens et al. *J Vasc Interv Radiol*. 2010;21[6]:779). Placement of filters in the SVC should be considered only in extenuating circumstances.

Data are limited to support the use of VCF for other indications, including chronic thromboembolic pulmonary hypertension (Jamieson and Nomura. *Semin Vasc Surg*. 2000;13[3]:236) and patients with free-floating thrombi (Norris et al. *Arch Surg*. 1985;120[7]:806; Pacouret et al. *Arch Intern Med*. 1997;157[3]:305). Prophylactic VCF are extensively used in surgical patients (trauma, bariatric surgery, and others), despite an absence of high-quality data supporting their utility (Girard et al. *Thromb Res*. 2003;112[5-6]:261; Cherry et al. *J Trauma*. 2008;65[3]:544; Antevil et al. *J Trauma*. 2006;60[1]:35; Rodriguez et al. *J Trauma*. 1996; 40[5]:797; Birkmeyer et al. *Arch Surg*. 2010;252[2]:313; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium, Flum et al. *N Engl J Med*. 2009;361[5]:445).

In addition to concerns about the limited data documenting the effectiveness of filters for many of their indications, there are legitimate reasons to be concerned about the safety profile of VCF. While fatal periprocedural complications are rare (0.12%) (Athanasoulis et al. *Radiology*. 2000;216[1]:54), deep venous thrombosis (35.7% vs 27.5%, HR 1.52 [95% CI 1.02-2.27], $P = .042$) and IVC thrombosis (13% vs 1%; these two patients received IVC filters during follow-up) are common adverse events associated with filter placement (PREPIC Study Group. *Circulation*. 2005;112[3]: 416). Although previous reports have suggested that migration and mechanical failures are infrequent events after filter placement (Hann and Streiff. *Blood Rev*. 2005;19[4]:179; Owens et al. *J Vasc Interv Radiol*. 2010;21[6]:779; Athanasoulis et al. *Radiology*. 2000;216[1]:54), a recent study indicates that this conclusion may need to be revised. Nicholson and colleagues conducted a radiographic surveillance study of strut fracture in 80 recipients of Bard Recovery and Bard G2 filters (Bard Peripheral Vascular; Tempe AZ) at their institution (Nicholson et al. *Arch Intern Med*. 2010;170[20]: 1827). They noted a high rate of filter leg fracture for both devices (13/80, 16%). Seven of 28 (25%) Recovery filters and 6 of 52 (12%) G2 filters suffered strut fracture. In seven patients, these fractures were associated with clinical symptoms, including one sudden death and one episode of cardiac tamponade due to a hemorrhagic pericardial effusion that required emergent cardiac surgery (Nicholson et al. *Arch Intern Med*. 2010;170[20]:1827).

Thus, we are left with a number of questions. Given the risks of thromboembolism posed by the presence of a filter, should all patients with IVC filters receive indefinite anticoagulation? The answer to this question is of significant clinical importance, since the vast majority of optional/retrievable filters remains unretrieved (Mission et al. *J Gen Intern Med*. 2010;25[4]:321; Dabbagh et al. *Thromb Res*. 2010;126[6]:493), and many are placed for controversial or questionable indications (Spencer et al. *Arch Intern Med*. 2010;170[16]:1456). Are the problems noted by Nicholson and colleagues a result of selection bias, or do they represent the tip of a previously unrecognized iceberg? Is this complication unique to the Bard Recovery and Bard G2 filters, or is this experience generalizable to all filters? Are optional/retrievable filters more susceptible to mechanical failures than permanent filter models as a consequence of their design? These and many other outstanding questions regarding VCF warrant further rigorous investigation. In some instances (eg, PE prevention in trauma patients), randomized controlled trials are feasible, while in other circumstances (eg, complications of VCF), prospective cohort studies are a more realistic approach. The important goal is to increase the number and quality of clinical studies of VCF.

Two years ago, the surgeon general, Admiral Steven Galston, MD, issued a call to action to improve efforts on prevention of VTE (www.surgeongeneral.gov/topics/deepvein. Accessed Jan 20, 2011). In this spirit, we believe these recent studies sound a clarion call to action to intensively study VCF to better assess their benefits and risks. They represent a valuable tool in the treatment of VTE, but further information is needed as to when and in whom we should use these devices and what are the short- and long-term complications of their use. We think this research will need to be sponsored and supported at the federal level, as there is little incentive for individual manufacturers to conduct these studies. Although almost 40 years have passed since the introduction of the stainless steel Greenfield filter, many questions remain about the safety and efficacy of these devices. The report of Nicholson and colleagues indicates that a careful reexamination of our clinical use of VCF is urgently needed. ■

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Indications for Vena Cava Filters

Broad Agreement

- Acute VTE with contraindication to anticoagulation

Less Agreement

- Failure of anticoagulation
- Chronic thromboembolic pulmonary hypertension
- Limited cardiopulmonary reserve and acute VTE
- Iliocaval thrombus
- Proximal free-floating thrombus
- Thrombolysis of iliocaval DVT
- Treatment of VTE in cancer patients
- Treatment of VTE in pregnant patients
- VTE prophylaxis in high-risk trauma patients
- VTE prophylaxis in high-risk surgery patients

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From the Desk of the Practice Management Committee

BY ROBERT DEMARCO, MD, FCCP, CHAIR; AND DONNA KNAPP BYBEE, FACMPE, VICE-CHAIR

The Practice Management Committee (PMC), a standing committee of the ACCP, meets regularly to discuss issues related to the business of medicine, as well as proper coding and reimbursement for pulmonary, critical care, and sleep medicine physician practices. In addition to working with the Centers for Medicare & Medicaid Services (CMS) and the AMA/CPT Editorial Panel and the Specialty Society Relative Value Scale Update Committee (RUC) on the development of new CPT codes and the establishment of appropriate physician work values, the ACCP PMC monitors and comments on legislative and regulatory policies relevant to the practice of pulmonary, critical care, and sleep medicine. On December 29, 2010, CMS announced the new CY 2011 Medicare Physician Fee Schedule conversion factor to be $33.9764. The revised conversion factor, effective January 1, 2011, represents a 7.86% reduction from the FY 2010 conversion factor of $36.8729.

The ACCP PMC has been working diligently to analyze the impact of the freeze of the sustainable growth rate (SGR), as well as other changes that CMS has made to physician reimbursement on codes of interest to pulmonary, critical care, and sleep physicians. The SGR freeze was enacted through the Medicare and Medicaid Extenders Act (MMEA) on December 15, 2010, to provide a 0% update (as opposed to the 25% proposed cut) to the Medicare Physician Fee Schedule for claims of services rendered between January 1, 2011, and December 31, 2011. Although the physician fee schedule update will be 0%, changes have been made to the Medicare Economic Index, which was rebased from 2000 to 2006, resulting in increases to the practice expense and malpractice relative value units (RVUs). The decrease in the CY 2011 conversion factor, therefore, negated some of these other reimbursement formula increases.

CMS provided the information to its contractors to implement the final rule in CMS Transmittal 828, available at www.cms.gov/transmittals/downloads/R828OTN.pdf. Overall, these changes result in a 1% loss in reimbursement to the pulmonary community for 2011. The ACCP PMC will continue to work on behalf of its members.

We fully expected cuts to the sleep codes, and really expected the cuts to be greater. For CY 2011, CMS rebased the Medicare Economic Index (MEI) from CY 2000 to 2006, which increased some of the practice expense (PE) and the malpractice relative value units. Sleep physicians were surveyed, and the data were analyzed by the sleep societies, which presented the data to the RUC. A consensus panel of ACCP/ATS/AAN/AASM members conducted the review of the PE inputs for clinical labor, medical supplies, and equipment attributable to each code that was reviewed by the RUC PE subcommittee, and inputs were forwarded to CMS, which made the final decision on RVUs for physician work, PE, and malpractice. The reason for the decreases (and because CMS transitions PE RVUs for existing codes over 4 years, we expect future PE decreases to the existing sleep codes, not to the two new unattended sleep codes, **95800** and **95801**) is because of the economies of scale with performing sleep studies now, compared with the time when the CPT codes were introduced and valued. In other words, sleep technicians are now doing two patients, instead of one, and the analysis of sleep studies is more automated, also saving time. So with decreasing times, these are the resulting values.

The AMA provides an example of the CMS final rule on CPT **99213** that has a 3.34% increase for 2011 (www.ama-assn.org/ama1/pub/upload/mm/399/2011-medicare-phys-payment-rates.pdf). Of importance to pulmonary care in the office/outpatient setting are the increase of 2.3% to CPT **99214** from $99.93 in 2010 to $102.27 in 2011 and the 2% increase to **99215** from $134.95 in 2010 to $137.60 in 2011. These are nationalized payment amounts. Each practice should analyze the frequency of its annual mix of procedures and services. Offsetting increases may balance out the negative impact to sleep physicians.

The newest edition of *Coding for Chest Medicine 2011* is available for purchase at www.chestnet.org.

If you have any questions or concerns, please contact Marla Brichta, ACCP Manager, Health Care Practice and Reimbursement, at mbrichta@chestnet.org. ■

Conversion Factor

December 2010 conversion factor	$36.8729
MMEA "zero percent update"	0.0% (1.000)
CY 2011 RVU budget neutrality adjustment	0.4% (1.0043)
CY 2011 rescaling to match MEI weights budget neutrality adjustment	–8.3% (0.9175)
CY 2011 conversion factor	$33.9764

Sleep CPT Codes

CPT Code	Mod	Descriptor	2010 Payment	2011 Payment	$ Change From 2010 to 2011
95800		Sleep study unattended	NA	$205.56	NA
95800	TC	Sleep study unattended	NA	$147.46	NA
95800	26	Sleep study unattended	NA	$58.10	NA
95801		Sleep study unattended w/analysis	NA	$96.83	NA
95801	TC	Sleep study unattended w/analysis	NA	$45.53	NA
95801	26	Sleep study unattended w/analysis	NA	$51.30	NA
95803		Actigraphy testing	$120.57	$162.41	$41.84
95803	TC	Actigraphy testing	$70.43	$115.52	$45.09
95803	26	Actigraphy testing	$50.15	$46.89	–$3.26
95805		Multiple sleep latency test	$395.65	$410.43	$14.78
95805	TC	Multiple sleep latency test	$302.73	$348.60	$45.87
95805	26	Multiple sleep latency test	$92.92	$61.84	–$31.08
95806		Sleep study unattended & respiratory effort	$204.28	$182.11	–$22.17
95806	TC	Sleep study unattended & respiratory effort	$122.05	$119.26	–$2.79
95806	26	Sleep study unattended & respiratory effort	$82.23	$62.86	–$19.37
95807		Sleep study unattended	$479.35	$469.89	–$9.46
95807	TC	Sleep study unattended	$397.86	$406.70	$8.84
95807	26	Sleep study unattended	$81.49	$63.20	–$18.29
95808		Polysomnograph 1-3 channels	$668.87	$649.63	–$19.24
95808	TC	Polysomnograph 1-3 channels	$537.98	$559.59	$21.61
95808	26	Polysomnograph 1-3 channels	$130.90	$90.04	–$40.86
95810		Polysomnograph 4 or more channels	$769.17	$694.14	–$75.03
95810	TC	Polysomnograph 4 or more channels	$596.60	$568.76	–$27.84
95810	26	Polysomnograph 4 or more channels	$172.57	$125.37	–$47.20
95811		Polysomnography w/CPAP	$848.08	$749.18	–$98.90
95811	TC	Polysomnography w/CPAP	$662.97	$618.03	–$44.94
95811	26	Polysomnography w/CPAP	$185.10	$131.15	–$53.95

Note: 2010 conversion factor was $36.8729; 2011 conversion factor is $33.9764.

Alvin Lever Honored by AACN

The American Association of Critical-Care Nurses (AACN) awarded Alvin Lever, MA, FCCP (Hon.), the Marguerite Rodgers Kinney Award for a Distinguished Career during its 2010 National Teaching Institute & Critical Care Exposition in Washington, DC.

Mr. Lever, the immediate past Executive Vice President and CEO of the ACCP—an important AACN partner—received this Visionary Leadership Award for extraordinary and distinguished career contributions to the AACN mission and vision.

Mr. Lever's creativity and vision led to strategic technology development initiatives at the ACCP that expanded key alliances; leveraged resources effectively; and created new markets, programs, and products. Customization, integration, centralization, and business focus helped to achieve these goals.

Established in 1997 and named for a past AACN president, the Marguerite Rodgers Kinney Award for a Distinguished Career recognizes extraordinary and distinguished professional contributions that further AACN's mission and vision of a healthcare system driven by the needs of patients and families where acute and critical care nurses can make their optimal contribution. Recipients of this Visionary Leadership Award receive a $1,000 gift to the charity of their choice, lifetime membership in AACN, and a crystal replica of the presidential "Vision" icon. ■

OneBreath.org Now Available

The CHEST Foundation's new public education initiative, OneBreath™: Make The Most Of It, integrates The Foundation's programs with the education mission of the ACCP. Living well means breathing well, and OneBreath.org will promote access to prevention tools, tips, and community-based activities that will inspire members, patients, and the public to take care of their lung and heart health.

Traditional CHEST Foundation programs are featured under the pillars of education, care, and community. We invite you to visit OneBreath.org to log in and become an online community member. You can use your ACCP ID as your password to simplify your ACCP online accounts. When you become an online community member, you will have a more personal experience through features that allow you to:

- Update your profile.
- View your giving history.
- Check pledge or recurring gift status.
- Manage your online subscriptions.
- Search the Directory for your ACCP colleagues' contact information.
- Send an e-card when you donate online. These colorful cards are taken from the Love Your Lungs® poster contest winners and promote tobacco prevention.
- Let us know your point of view by participating in online polls and surveys.

Coming soon, watch for our quarterly newsletter, *EXTRAORDINAIR,* as well as a blog, discussion board, and document sharing.

Visit OneBreath.org today, and support our efforts to expand our reach and promote positive health habits and activities for better lung and heart health for everyone. ■

The CHEST Foundation Awards Program 2011

The CHEST Foundation provides funds for volunteer service, leadership, and clinical research through its annual awards program. In 2011, awards are offered in thrombosis, end-of-life care, women's health, geriatrics, COPD, lung cancer, and humanitarian service. The CHEST Foundation offers 1-, 2- ,and 3-year awards to ACCP members' projects that meet the qualifications.

The **Third GlaxoSmithKline Distinguished Scholar in Thrombosis** award is open to ACCP members who are FCCPs. It supports clinical educational projects to improve patient care and is intended for the investigation of issues that are not easily supported through traditional funding. The award grants $150,000 over the course of 3 years to support an ACCP Fellow's thrombosis-related project and/or service that does one or more of the following:

- Investigates alternatives for treatment.
- Educates patients about options for diagnosis and treatment.
- Disseminates new knowledge about diagnosis and treatment.
- Addresses family, legislative, or regulatory issues.
- Defines new mechanisms leading to innovations and improvements in treatment.

The clinical research awards reflect the ACCP's multidisciplinary nature.

Alpha-1 Foundation and The CHEST Foundation Clinical Research Award in COPD and Alpha-1 Antitrypsin (AAT) Deficiency. This 1-year $25,000 award supports research focused on COPD and AAT deficiency. Research projects primarily in usual COPD (not associated with AAT deficiency) are allowed. Projects with a focus on AAT deficiency are encouraged.

The CHEST Foundation and the Respiratory Health Association of Metropolitan Chicago Clinical Research Award in Women's Lung Health. This 1-year $10,000 award supports a clinical research project related to women's lung health, which may include research on gender differences in various lung diseases, such as COPD and lung cancer.

Association of Specialty Professors and The CHEST Foundation of the ACCP Geriatric Development Award. This 2-year $50,000 award supports the career development of junior faculty in the early stages of their research career in geriatrics. To be eligible for this award, you must have first applied for the GEMSSTAR award through the National Institute on Aging and received a fundable score. The deadline to apply for the GEMSSTAR award was Nov 3, 2010.

The CHEST Foundation California Chapter Clinical Research/Medical Education Award. This award supports a 1-year clinical research or medical education project proposed by an ACCP member who lives in California.

OneBreath Clinical Research Award in Lung Cancer. This award is new for 2011. Details will be posted at OneBreath.org.

The CHEST Foundation continues its support of leadership in end-of-life care through the **Roger C. Bone Advances in End-of-Life Care Award.** This 1-year award of $10,000 supports an ACCP member's project that stresses the importance of communication, compassion, and effective listening. The award is given for leadership in end-of-life care—on the international, national, or local level—and does not fund research or provide seed money for new programs or projects.

The **D. Robert McCaffree, MD, Master FCCP Humanitarian Awards** support the volunteer efforts of those who give time and expertise to improve the health of communities around the world. The award provides funds to nonprofit and nongovernmental organizations where ACCP members provide pro bono service. The CHEST Foundation will grant awards in amounts of $5,000 and up to $15,000, to a total of $50,000 in 2011.

The CHEST Foundation Awards Committee encourages ACCP members to take advantage of this important member benefit by applying for an award. Learn more and apply for an award at OneBreath.org. The deadline for all awards is May 4, 2011. ■

FCCP Finds Support for Free Clinic

Dr. Kevin Flaherty, FCCP, is an active ACCP member who serves as a steering committee member of the Interstitial and Diffuse Lung Disease NetWork and contributes on many levels to the College's educational endeavors.

When a colleague made him aware of the D. Robert McCaffree, MD, Master FCCP Humanitarian Awards Program, Dr. Flaherty took this opportunity to help further the medical care of those close to home and applied for the award. The Faith Medical Clinic in Pinckney, MI, where he volunteers his time to care for patients with pulmonary conditions, such as COPD and asthma, was chosen to receive the award support.

The Faith Medical Clinic's mission is to provide free comprehensive medical and dental care to uninsured members of the Pinckney and surrounding communities, regardless of race, religion, or creed. The clinic is the only free medical facility in Livingston County and, therefore, has become the safety net of medical care for 1,200 residents. It offers primary, urgent, and chronic care, as a significant portion of this population has chronic and comorbid diseases. The clinic routinely cares for patients with COPD and asthma.

In addition to caring for patients, Dr. Flaherty supervises the volunteer physician assistants and nurse practitioners.

The clinic opened in December 2007 in the basement of the local fire department. As the economy continued to impact the community, the volume of patients increased. The local county government provided a building in the town of Pinckney when it learned that the clinic provided much-needed medical and urgent care for 1,200 underemployed and uninsured residents.

See the story above for more information about applying for CHEST Foundation awards. ■

Product of the Month

Coding for Chest Medicine 2011

Specialty Medicine. Specialty Codes. For a coding resource as precise and specialized as the medicine you practice, turn to *Coding for Chest Medicine 2011*. The updated 15th edition features chapters on allergy and immunology, bronchoscopy, critical care, consultations, electronic medical records, ICU procedures, malpractice issues, pay for performance, pediatric pulmonary medicine, pulmonary function testing, pulmonary rehabilitation, rapid response teams, sleep medicine services, thoracic surgical procedures, and others.

New codes in 2011 include balloon occlusion, unattended sleep studies, bronchial valve insertion and removal, and acoustic PFT-Category III.

An updated consultation chapter includes information provided on payer-specific billing for consultations, with suggested crosswalks for billing Medicare and other payers that no longer recognize outpatient and inpatient codes. ■

PCCSU Lessons for February

- **Medical Applications of Exhaled Breath Analysis and Testing.** *By Alquam Mashir; Kelly Paschke; Daniel Laskowski, RT; and Dr. Raed A. Dweik, MBBS, FCCP*
- **Osteopenia and Osteoporosis in Lung Disease.** *By Dr. Marilynn A. Prince-Fiocco, FCCP*

PCCSU Pulmonary, Critical Care, Sleep Update

www.chestnet.org/accp/pccsu

Pulmonary Perspectives

Humanitarianism in Haiti

A year after the earthquake in Haiti, health-care providers continue to volunteer in an attempt to fill our Caribbean neighbor's medical void. In recent years, several domestic and international natural disasters have captured the attention of the medical community and the public at large. Yet, the Haitian crisis seems to have received more United States–based medical "help" for multiple reasons, such as the proximity between the two nations; 200 years of cultural connections; longstanding American medical projects in Haiti; the enormity of the disaster; and, most importantly, the dire need of the Haitian people.

The complexities of going into a disaster zone and working in a country with a weak public health system are numerous and need to be examined critically. International nongovernmental organizations (NGOs) and Haitian health-care providers on the ground mobilized immediately after the disaster. They were joined by an avalanche of good samaritans from a geographically diverse group of hospitals, American NGOs, and communities started through social-networking sites like Facebook. The response created a unique dynamic in Jimani, a dusty city in the Dominican Republic that borders Haiti. At the public hospital in Jimani, Dominican physicians worked tirelessly, treating crush injuries in patients flown and driven in from Port-au-Prince. Up the road, at Good Samaritan Hospital, an international crew of health-care providers organized themselves to provide care. Admirably, the outpatient surgical center cared for hundreds of patients and housed volunteers, assisted by an NGO deputized to run the center prior to the storm.

Despite the valiant efforts, there were a few glitches. There were abundant concerns about professionalism. While awaiting helicopter transfer of patients to hospitals in larger Dominican cities, transporters could be found videotaping the process with smartphones while holding stretchers. Some critically ill patients were transferred to facilities too overburdened and underequipped to care for them. Poor coordination occasionally exacerbated the chaos and frenzy of activity. In one instance, an American military helicopter was called to pick up a pediatric patient not authorized to be picked up. The patient's father was devastated that his critically ill son was not going to the American medical ship, and the helicopter made an unnecessary landing at Good Samaritan.

Reaction to the crisis has highlighted the need to increase resources in Haiti and the Dominican Republic to handle disasters and care for the critically ill or injured. Disaster training and preparation should enhance the response and relief effort; untrained volunteers can participate in disaster relief but should not direct it. Interested individuals may consider taking a Fundamentals of Disaster Management course (www.sccm.org/FCCS_and_Training_Courses/FDM/Pages/default.aspx) or receive advanced training in emergency management. These potential pitfalls were well anticipated by the Israeli military in its disaster response. It recognized that ethical dilemmas would exist for the team in Haiti, due to the limited resources. Therefore, it created an ad hoc ethics committee and a realistic triage system to support its staff in making treatment decisions (Merin et al. *N Engl J Med*. 2010;362[11]:e38). Today, limitations persist beyond the disaster's acute phase. Field hospitals run by foreign health-care providers remain, and medical decisions are made daily by individuals who do not normally practice in resource-limited environments, a learning experience for foreign health-care providers and an unnecessarily traumatic one for patients and physicians.

The war in Iraq provides a relevant example of alternative management systems. Cannon and Smith described providing care for critically ill Iraqi pediatric trauma patients and inadvertently winning the "hearts and minds" of the local people around their base in Balad. The airmen intervened because a lack of facilities led to a 70% mortality rate for critically ill patients. Their experience led them to suggest a "landmark" partnership between NGOs and the military to supplement the Iraqi medical system (Cannon and Smith. *Crit Care Med*. 2009;37:2322). The contrast between providing medical care in the Iraqi war effort vs the Haitian humanitarian effort is immense, but there is one important similarity. The military presence, in both situations, substantially improved medical care. Amundson and colleagues described their experience on the hospital ship USNS COMFORT in Haiti where they took care of a diverse group of patients, including the critically ill (Amundson et al. *Ann Intern Med*. 2010;152[11]:733). The USNS COMFORT initially partnered with Project Hope to allow civilian medical personnel aboard. After the ship left, however, the American military had a much more limited partnership with the medical relief effort. NGOs continued to run busy field hospitals, and the military provided supplies, occasional personnel, and technical advice, as able. The lack of an ongoing formal partnership with the military led to a loss of expertise that could have benefited the continuing relief effort. It is our personal belief that the military staying formally involved in the medical process in Haiti could have increased our overall ability to serve our Haitian patients. Yet, not all situations are similar. Many times, it may not be feasible or even in an NGO's best interest to work with the military, but it should be considered.

After the acute and subacute phases of a disaster situation, the most important way to continue to improve medical care is to engage a local resource. In the long term, local organizations understand how to deliver more effective health care to their own populace. Long before the world focused on earthquake-ravaged Haiti, a community center in Petit Gauve, a small city 2 hours outside of Port-au-Prince, provided health care to its local residents in recent years. The Henri Gerard Desgranges Foundation (HGD, hgdfoundation.wordpress.com) has struggled to reopen its school and health clinic after the disaster due to a lack of funding and medical staff. The foundation's lab was destroyed, and fewer Haitian physicians are present, but the patients remain. Between 50 and 200 patients a day are seen at HGD, with specific days focused on obstetrics and pediatrics. The center has had volunteers from the US, Canada, and France rotating in for 1-week to 2-month stints. The contribution of foreigners is commendable, but the clinic's future depends on the ability of Haitian physicians to resume management.

Medical providers who wish to volunteer in Haiti should evaluate whether their money, time, and effort would be better spent in helping existing Haitian resources rebuild rather than going on week-long volunteer missions. A moment of reflection on the personal motivation for a medical mission may profoundly impact the choice to go to a disaster zone. Haitians need our "help," but we must be more discriminating in how we extend our helping hands. ■

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This Month in *CHEST:* Editor's Picks

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

TOPICS IN PRACTICE MANAGEMENT

▶ **Long-term Oxygen Therapy.**
By Dr. K. L. Christopher; and Mr. P. Porte.

▶ **Transtracheal Oxygen Therapy.**
By Dr. K. L. Christopher; and Dr. M. D. Schwartz.

ORIGINAL RESEARCH

▶ **"Triple Therapy" Rather Than "Triple Threat": A Meta-analysis of the Two Antithrombotic Regimens After Stent Implantation in Patients Receiving Long-term Oral Anticoagulant Treatment.**
By Dr. H-J Zhao et al.

▶ **Cysteine: A Potential Biomarker for Obstructive Sleep Apnea.**
By Dr. F. Cintra et al.

Editor's Insight

The recent cholera epidemic brings the fragility of the medical-care system in Haiti and the needs of the Haitian people, in the earthquake's aftermath, back into stark focus. This commentary is a partial reflection of the experiences of the authors. Dr. Puri, an ACCP Affiliate, has traveled to Haiti four times. Dr. Lonergan has also made multiple trips to Haiti, the poorest country in North America. CAPT Dennis Amundson, MC, USN, FCCP, whose work is referenced in this article, is the chair of the ACCP Disaster Response NetWork. We are proud of the humanitarian contributions of our ACCP members and agree that long-term solutions for medical care in Haiti require the input of Haitians and should emphasize sustainability.

–Dr. Marilyn G. Foreman, FCCP

Study Shows Rivaroxaban Valid for VTE Prophylaxis

BY NEIL OSTERWEIL
Elsevier Global Medical News

ORLANDO – The investigational oral anticoagulant rivaroxaban was not inferior to a combination of the low-molecular-weight heparin enoxaparin and a vitamin K antagonist for reducing risk of recurrent deep venous thromboembolism for up to 1 year, reported investigators with the EINSTEIN Acute DVT study.

The EINSTEIN Acute DVT trial compared oral rivaroxaban alone with enoxaparin followed by a vitamin K antagonist for prophylaxis of recurrent VTE or pulmonary embolism in 3,449 patients. Patients received oral rivaroxaban 15 mg twice daily for 3 weeks, followed by 20 mg once daily for 3, 6, or 12 months, said Dr. Harry R. Büller at the annual meeting of the American Society of Hematology.

The EINSTEIN-extension study compared rivaroxaban with placebo in 1,197 patients who had completed 6-12 months of rivaroxaban in the EINSTEIN studies or 6-12 months of a vitamin K antagonist, either in the EINSTEIN studies or in routine care. The primary efficacy end point for both studies was the incidence of recurrent VTE. The primary safety outcome for the acute DVT trial was major bleeding or clinically relevant minor bleeding. The major safety outcome in the extension trial was major bleeding (N. Engl. J. Med. 2010;363:2499-510).

Incidence of major bleeding or clinically relevant nonmajor bleeding was identical in the two groups, at 8.1%. Additionally, rivaroxaban, a factor Xa inhibitor in late-stage clinical development, was superior in efficacy to placebo in a randomized double-blind extension study. VTE or pulmonary embolism recurred in 2.1% of 1,731 patients randomized to rivaroxaban and in 3.0% of 1,718 patients randomized to enoxaparin (Lovenox) followed by either warfarin or acenocoumarol.

In the acute trial, there were 36 VTE events in the rivaroxaban group, compared with 51 in the enoxaparin/vitamin K antagonist group (hazard ratio, 0.68; *P* less than .001). In each group, 8.1% of patients had a recurrent VTE.

In the continuation trial, 8 events occurred in 602 patients (1.3%) treated with rivaroxaban, compared with 42 of 594 (7.1%) treated with the enoxaparin/vitamin K antagonist regimen (HR, 0.18; *P* less than .001). Four major bleeding events occurred in patients treated with rivaroxaban vs. none in those who received placebo.

"This regimen of 15 mg [rivaroxaban] twice a day for the first 3 weeks followed by 20 mg for the remainder period provides clinicians and patients, I think, with an attractive and simple treatment option for venous thrombosis," Dr. Büller of the Academic Medical Center in Amsterdam, the Netherlands, said in a press briefing.

Bayer Schering Pharma and Ortho-McNeil funded both studies. Dr. Büller had no relevant disclosures. Several of his coauthors disclosed receiving financial support from Bayer Schering Pharma, and one is employed by the company. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: This large, open-label trial of VTE prophylaxis compares enoxaparin with rivarozavan, a factor Xa inhibitor. The rate of VTE prevention was comparable between the two drugs without increased incidence of major bleeding. There was a slight trend toward fewer recurrent VTEs in the rivaroxaban group. This provides evidence for a new and potentially useful additional therapy for this complex, frequent medical/surgical dilemma.

Risk Score May Predict Recurrent VTE in Cancer

BY NEIL OSTERWEIL
Elsevier Global Medical News

ORLANDO – Among patients with cancer-associated thrombosis, women and those with lung cancer or a history of at least one venous thromboembolic event are at significantly increased risk for recurrent emboli and may require prophylaxis with low-molecular-weight heparin or more aggressive anticoagulation, investigators have reported.

In contrast, patients with stage I malignancies or breast cancer are at relatively low risk for venous thromboembolism (VTE) recurrence and may need only a vitamin K antagonist such as warfarin to prevent a second event, Dr. Martha L. Louzada said at a press briefing in advance of a presentation at the annual meeting of the American Society of Hematology.

The investigators used the data from a retrospective chart study to develop a risk score for determining the clinical probability of VTE recurrence. Each independent risk predictor variable received a point score relative to the magnitude of risk it imposes. Patients with a score from –3 to 0 are deemed to be at low risk (4.5% chance of recurrence), whereas those with scores from 1 to 3 are considered to be at high risk (19.7% chance of recurrence). They were able to reproduce the rule by applying it to data from two randomized controlled trials that compared a low-molecular-weight heparin with a vitamin K antagonist.

"Our future goal is to prospectively validate this clinical prediction rule to assess further reproducibility and generalizability," Dr. Louzada of the University of Western Ontario in London said at the briefing.

To determine whether VTE prophylaxis strategies should be tailored to meet individual patient characteristics or cancer types, the investigators took a retrospective look at the charts of 543 patients with cancer and VTE who were followed at the thrombosis unit of the Ottawa Hospital from 2002 through 2004 and from 2007 through 2008. The investigators restricted their analysis to those patients who had recurrent VTE within 6 months of beginning anticoagulation therapy. They conducted a univariate analysis to gauge the strength of the association between each potential risk factor and VTE recurrence, and evaluated all likely risk-predictor candidates in a logistic regression model.

In all, 55 patients (10.1%) had a recurrent VTE, but the rates of recurrence were similar between the groups, suggesting that treatment type did not have an effect (recurrence rate 9.5% for vitamin K antagonists, 10.5% for low-molecular-weight heparin).

In the multivariate analysis, the authors identified as significant predictors of increased risk, lung cancer (odds ratio 2.55), a history of prior VTE (OR 2.42), and female gender (OR 1.82). Predictors for decreased risk were stage I malignancies (OR 0.75) and breast cancer (OR 0.46).

"The patient even with breast cancer can have a high risk, because the majority of patients are females and being female is a high-risk predictor, whereas breast cancer is a low risk, so it's going to depend on the stage of malignancy of the patient and also whether the patient has a previous history of venous thrombosis," she said.

The study was internally funded. Dr. Louzada said she had no relevant financial disclosures. ■

Even Preschoolers' BP Affected

Smoking • *from page 1*

2011 Jan. 25 [doi:10.1161/circulationaha.110.958769]).

Other significant correlates of systolic blood pressure were gender, height, BMI, birth weight, gestational hypertension, and parental hypertension. Correlates of diastolic blood pressure were gender, height, BMI, birth weight, and parental hypertension, the investigators said.

"Moreover, systolic and diastolic blood pressure progressively increased with the cumulative number of parent-related risk factors (parental obesity, hypertension, and smoking)," they noted.

The absolute difference in blood pressure between children with no risk factors and those with three risk factors was 3.2 mm Hg for systolic blood pressure, and 2.9 mm Hg for diastolic blood pressure, which corresponds to nearly half of a standard deviation of the blood pressure distribution in the total population, the investigators noted.

Children in the study were aged 4.0 to 7.5 years (mean 5.7 years), and were evaluated between February 2007 and October 2008. Blood pressure was measured in conjunction with a family health and lifestyle survey.

The findings demonstrate that the multifactorial dependency of blood pressure on various influences – including familial, prenatal, and environmental influences – are evident even in early childhood, they said, adding that a unique finding of this study is "the novel evidence for a BP-raising effect of environmental nicotine exposure in children as young as 4-5 years of age."

Although the effects of active and passive tobacco exposure on cardiovascular functions in adults are well known and have been widely demonstrated, the effects of passive tobacco smoke exposure on childhood blood pressure have not been reported previously.

Of note, maternal – but not paternal – cigarette consumption had a quantitative relationship with childhood blood pressure in this study, which may be a result of more at-home smoking among mothers vs. at-work smoking among fathers. Also, the effect size of passive smoking was higher in boys than in girls, raising the question of whether the sex-preferential susceptibility of adolescent and adult males to cardiovascular risk factors also is present in younger children. This may be an interesting field of future research, the investigators suggested.

The findings of this study underscore the potential benefits of implementing strictly smoke-free environments, particularly at home. This may help preserve cardiovascular health in both adults and children, the researchers said.

The potential benefits of a smoke-free environment is supported by several lines of reasoning, including the fact that smoke-free environments have been shown to decrease cardiovascular mortality in nonsmokers, that childhood blood pressure consistently tracks into adult life, and that children whose parents smoke are more likely to become smokers themselves.

Indeed, "comprehensive interventions that seek to reduce the cardiovascular risk burden early in life by promoting lifestyle changes in all family members may prove essential for lowering the cardiovascular disease risk of future generations," the investigators concluded.

This study was funded by the Manfred-Lautenschläger Stiftung, the Reimann-Dubbers Stiftung, the Dietmar-Hopp Stiftung, and the Swiss Society of Hypertension AstraZeneca scholarship awarded to Dr. Simonetti. The investigators reported having no other disclosures. ■

Having a parent who smokes increased the likelihood of high BP by 21%.

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.

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