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CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

BRUCE JANCIN/ELSEVIER GLOBAL MEDICAL NEWS

Investigational therapies such as inhaled vasoactive intestinal peptide are showing early signs of promise, said Dr. Bernhard Burian.

COPD New-Drug Pipeline Is Beginning to Flow

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Old hands at managing chronic obstructive pulmonary disease using the traditional menu—limited largely to bronchodilators, corticosteroids, oxygen, immunization, and advice to quit smoking—may be stunned to learn that the COPD drug development pipeline is now filled to an unprecedented degree.

The procession of potential new agents is arriving just in time. It is estimated that COPD will be the third-leading cause of death worldwide by the year 2020.

The first wave of new products to reach pharmacy shelves will be improved versions of existing drugs rather than totally new drug classes. Earlier along in the development process are entirely new and promising drug classes addressing novel potential pathophysiologic targets in COPD, Dr. Stephen C. Lazarus said at a satellite symposium sponsored by Sepracor and held in conjunction with the annual meeting of the American College of Chest Physicians.

Fixed-dose combination therapy has been amply shown to be more effective than either agent alone at reducing COPD exacerbations and improving lung function; the increased drug cost is more than offset by the benefits. Formoterol and tiotropium is a combination close to gaining marketing approval. Formoterol

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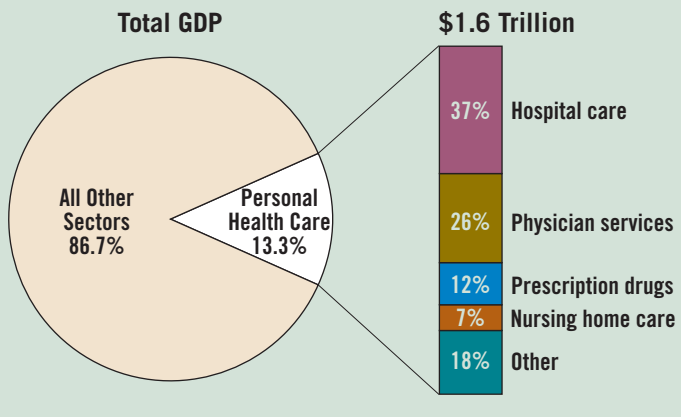
VITAL SIGNS

Personal Health Care Expenditures as a Percentage of Gross Domestic Product, 2004



Source: Centers for Medicare and Medicaid Services

ELSEVIER GLOBAL MEDICAL NEWS

Bronchoscopic Innovations Show Potential for COPD

Procedures target lung volume reduction.

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Pulmonologists are developing a variety of innovative bronchoscopic procedures to achieve nonsurgical lung volume reduction as treatment for advanced emphysema—and hoping to reinvent their specialty along the way.

The goal is to capitalize upon the functional and mortality benefits documented with lung volume reduction (LVR) surgery in a subset of participants in the NIH-sponsored National Emphysema Treatment Trial—but without the associated hefty perioperative mortality, major morbidity, and expense.

If the bronchoscopic innovations prove successful, they could transform the field of respiratory medicine, much as percutaneous angioplasty and stenting have revolutionized cardiology, speakers predicted at the annual meeting of the American College of Chest Physicians.

Planning is underway for large multicenter randomized trials of novel investigational bronchoscopic LVR procedures that have successfully passed the pilot study phase of development. Among them are insertion of one-way valves into pockets of diseased lung tissue, biologic tissue destruction with induction of scarring, and stent placement to create decompression of hyperinflated diseased lungs.

"I have this dream that you'll go into the recovery room and you'll be sweating with scrubs on and the cardiologist is going to come in and say, 'Wow, I had a tough case—I put three stents in,' and you'll say, 'Well, I had a tougher one—I put in seven valves,' or 'put in six stents.' Maybe we'll be able to induce physiologic changes and gain time for these patients," said Dr. Bartolome Celli, FCCP, professor of medicine at Tufts University, Boston.

Dr. Daniel H. Sterman, FCCP,

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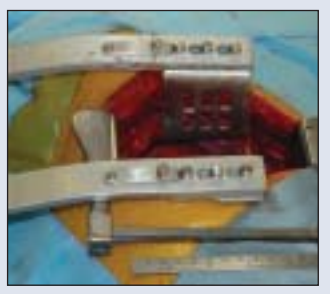
INSIDE



RF Ablation Promising in Lung Cancer

BY BRUCE JANCIN
Elsevier Global Medical News

ROME — Two-year cancer-specific survival following percutaneous radiofrequency ablation of inoperable non–small-cell lung cancer was 92% in a multinational pilot study, Dr. Riccardo Lencioni reported at the annual meeting of the Cardiovascular and Interventional Radiological Society of Europe.

"That's impressive. It's better than what's currently quoted for radiation therapy," observed Dr. Lencioni, professor of radiology at the University of Pisa (Italy).

Based upon these results from the Radiofrequency Ablation of Pulmonary Tumors Response Evaluation (RAPTURE) trial, planning is underway for a definitive, randomized controlled trial, he added.

Lung cancer is the No. 1 cause of cancer mortality, accounting for more than 160,000 deaths per year in the United States. At present, the only reliably effective treatment is surgical resection, with a 5-year survival rate of 70%. Unfortunately, 70%-85% of lung cancer patients have unresectable tumors or are inoperable because of comorbid disease. This has been the driving force behind interest in percutaneous radiofrequency ablation (RFA).

RAPTURE is an ongoing, single-arm prospective study involving RFA performed under conscious sedation with CT guidance in 106 patients with 186 biopsy-proven lung cancer tumors up to 3.5 cm in size. None of the participants was a surgical candidate. Of the 106 patients, 33 presented with

See **RF Ablation** • *page 2*

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Statins May Slow Decline of Lung Function in Smokers

Drug therapy cuts hospital visits by COPD patients.

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Statin therapy may slow the decline in lung function in smokers and ex-smokers with chronic lung disease, Dr. Walid G. Younis said at the annual meeting of the American College of Chest Physicians.

This preliminary finding from a retrospective observational study raises the intriguing possibility that statins might be able to slow the progression of chronic obstructive pulmonary disease (COPD) or restrictive lung disease in smokers and former smokers, noted Dr. Younis of the University of Oklahoma, Oklahoma City.

The most likely mechanism of statin therapy's benefits involves anti-inflammatory effects.
DR. YOUNIS

He reported on 182 current and 303 ex-smokers, mean age 66 years, who were being followed at the Oklahoma City Veterans Hospital. Half were on statin therapy—predominantly simvastatin—for primary or secondary cardiovascular prevention. A total of 319 patients had COPD, 99 patients had restrictive fibrotic lung disease, and the rest had normal lung function.

The mean baseline forced expiratory volume in 1 second (FEV_1) was 57% of the predicted value. During nearly 3 years of follow-up, FEV_1 declined by 88 mL/year in patients not on a statin but by only 12 mL/year in those who were. Moreover, forced vital capacity fell by 125 mL/year in patients not on a statin while actually increasing by 22 mL/year in those on statin therapy. Equally robust benefits were noted in statin users regardless of whether they were current or ex-smokers.

The rate of respiratory-related hospitalizations and emergency department visits during the study period was 35% lower in COPD patients on a statin. However, statin therapy had no impact on rates in patients with restrictive lung disease.

The most likely mechanism of statin therapy's benefits on lung function involves anti-inflammatory effects. Statins decrease blood levels of inflammatory cytokines, including interleukin-6 and -8 and tumor necrosis factor–α, which are known to be involved in the pathogenesis of COPD, Dr. Younis said.

"I think this is provocative enough that you should think seriously about doing a well-designed randomized prospective trial," commented Dr. Ronald F. Grossman, FCCP, professor of medicine at the University of Toronto. ■

IN THIS ISSUE

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RAPTURE Study Results Analyzed

RF Ablation • *from page 1*

non–small-cell lung cancer (NSCLC), 53 had metastases of colorectal cancer (CRC) to the lung, and 20 had lung metastases from other sites.

Two-year overall survival was 48% among patients with NSCLC and 62% in those with CRC metastases. "Of course, these figures may not look so exciting," Dr. Lencioni conceded. "But remember, we started this trial with patients who truly had no other treatment options. This was last-resort therapy."

'We started this trial with patients who truly had no other treatment options. This was last-resort therapy.'
DR. LENCIONI

Moreover, most of the NSCLC patients were long-time smokers and they had high mortality rates due to cardiovascular causes and chronic obstructive pulmonary disease during follow-up. The 2-year cancer-specific survival—that is, freedom from cancer-related mortality—was far more impressive at 92% in the NSCLC group and 82% in patients with CRC metastases, he continued.

In terms of the technical procedural success of RFA, Dr. Lencioni noted that 93% of treated tumors showed no regrowth at the 3-month follow-up CT.

At the 15-month follow-up, the local tumor control rate was 88%. That's higher than reported in many series involving RFA of tumors in the liver and other sites. The likely explanation is that physical energy used for thermal destruction of tissue is particularly efficient when the target is a solid tumor surrounded by air, the radiologist said.

The 30-day mortality in RAPTURE was 0%. One-quarter of patients experienced pneumothorax as a result of the procedure. There were four cases of pleural effusion requiring draining, two cases of pneumonia, and one of atelectasis.

"RAPTURE is an important study," Dr. Luigi Solbiati commented in his Andreas Gruentzig Lecture. "It shows the only significant complication of RFA for lung cancer is pneumothorax—and honestly, it's not a significant complication from a clinical point of view because only about 20% of these pneumothoraxes require aspiration and a chest tube," said Dr. Solbiati, professor of diagnostic imaging at the University of Milan.

Dr. Lencioni noted that small-scale reports of favorable experiences with RFA in lung cancer are starting to come in from centers not involved in the RAPTURE study.

For example, University of Pittsburgh surgeons reported that 15 of 18 treated patients were alive at 14 months' follow-up, with a mean progression-free interval of 17.6 months in the 9 patients with stage I disease (J. Thorac. Cardiovasc. Surg. 2005;129:639-44). And French investigators reported an 18-month overall survival of 71% in 60 treated patients (Radiology 2006;240:587-96).

RAPTURE was funded by RITA Medical Systems Inc., which makes the expandable electrodes used in the study. ■

Dr. Gerard Silvestri, FCCP, comments: *One of the vexing problems in early-stage lung cancer is facing a patient with potentially curable stage I disease and discovering that they are medically inoperable. The results published above are exciting but must be interpreted with caution, as the numbers are small and the long-term outcomes are uncertain. What is needed now are larger trials to confirm these findings and define the patient population that will benefit the most. Studies are needed to compare this treatment to standard therapy. Finally, these patients should be evaluated by a thoracic surgeon to assure that they cannot be offered lung-sparing surgery.*

CHEST PHYSICIAN

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

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References: 1. CHANTIX [package insert]. New York, NY: Pfizer Inc; 2006. **2.** Center for Drug Evaluation and Research. Approval package for: application number NDA 21-928: statistical review(s). Food and Drug Administration Web site. Available at: http://www.fda.gov/cder/foi/nda/2006/021928_s000_Chantix_StatR.pdf. Accessed August 25, 2006. **3.** Gonzales D, Rennard SI, Nides M, et al, for the Varenicline Phase 3 Study Group. Varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. *JAMA*. 2006;296:47-55. **4.** Jorenby DE, Hays JT, Rigotti NA, et al, for the Varenicline Phase 3 Study Group. Efficacy of varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *JAMA*. 2006;296:56-63.

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Subjects were provided with an educational booklet on smoking cessation and received up to 10 minutes of smoking cessation counseling at each clinic visit in accordance with Agency for Healthcare Research and Quality guidelines.[1]

VTE Prophylaxis Deficient in Most At-Risk Patients

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Only one-third of U.S. medical inpatients at increased risk for venous thromboembolism receive appropriate prophylaxis as recommended by American College of Chest Physicians guidelines, according to a large study.

About half of the remaining two-thirds of at-risk patients receive suboptimal venous thromboembolism (VTE) prophylaxis. The other half receives none at all, Dr. Alpesh Amin said at the annual meeting of the ACCP.

He reported on 196,104 medical patients at 227 U.S. hospitals participating in the Premier's Perspective national inpatient administrative database. The study period was January 2002 through September 2005.

All of the nearly 200,000 patients were at least 40 years old, hospitalized for a minimum of 6 days, possessed at least one risk factor for VTE, and were without contraindications to anticoagulation.

The most common admitting diagnosis was severe lung disease, followed by heart failure, cancer, and acute myocardial infarction.

The appropriateness of thromboprophylaxis was determined by comparing daily use of mechanical compression devices and/or anticoagulants with what was recommended for patients in a given risk category in the ACCP guidelines. To be deemed appropriate, preventive therapy had to be in accord with the recommendations in terms of prophylaxis type and duration as well as daily dosage.

Nearly 62% of patients received some form of VTE prophylaxis. However, only 33.9% received appropriate prophylaxis in keeping with ACCP guidelines, which since the mid-1980s have been the acknowledged gold standard, according to Dr. Amin, professor and vice chair of medicine and head of the hospitalist program at the University of California, Irvine.

The highest rate of appropriate VTE prophylaxis—49%—occurred in the nearly 9,000 patients hospitalized for ischemic stroke. Among MI patients, 43% received appropriate prophylaxis, as did 40% with heart failure, 31% with lung disease, and 27% with cancer.

VTE has become an increasingly high-visibility issue in recent years. It has been estimated to cause 300,000 deaths per year—about the same as acute MI, and more than breast cancer, HIV, liver disease, and accidents combined. An effort is underway to incorporate VTE prophylaxis rates into core hospital quality performance measures starting in 2008. March is now national Deep Venous Thrombosis Awareness Month. Airlines make an effort to educate passengers about the problem on long international flights.

The low rate of adherence to VTE prophylaxis 'is a significant concern for us across the nation.'
DR. AMIN

To see if this increased public attention to VTE has been accompanied by a temporal trend for improved rates of appropriate prophylaxis, the investigators analyzed nearly 3 years of quarterly data. They found the rate increased over time, but only modestly, from nearly 30% in early 2002 to 40% in late 2005.

The low rate of adherence to VTE prophylaxis "is a significant concern for us across the nation," Dr. Amin said.

They also analyzed the data by geography, payment type, bed size, rural versus urban hospitals, teaching versus nonteaching hospitals, and whether patients were admitted through the emergency department or by a referring physician.

"Only about one-third got appropriate prophylaxis no matter how you broke it down. We couldn't find one area where we were doing a wonderful job in terms of prophylaxis. There's more to do," he said.

The investigators are currently preparing individual performance reports for each of the 227 participating hospitals to use in their quality improvement programs. They are also reanalyzing the data to see how prophylaxis rates correlate with outcomes.

In addition, they are updating their results by incorporating adherence rates to the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy guidelines. In the initial study, the investigators used the sixth version of the guidelines, which was the newest version for most of the study period. ■

Statins, Angiotensin-II Receptor Blockers Curbed Sepsis Deaths

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Being on a statin and/or angiotensin-II receptor blocker at the time of hospitalization for sepsis is associated with significantly reduced 30-day mortality, Dr. Eric Mortensen said at the annual meeting of the American College of Chest Physicians.

This observation from a large retrospective cohort study raises an intriguing hypothesis: Perhaps starting septic patients on one or both medications at the time of admission could reduce mortality, added Dr. Mortensen of the South Texas Veterans Healthcare System, San Antonio.

Statin users had a 55% reduction in relative risk of 30-day mortality; ARB patients had a 61% reduction.
DR. MORTENSEN

He reported on 3,018 patients in the national Veterans Affairs administrative database hospitalized for sepsis during 2000. In all, 99% were male, with a mean age of 74 years. Their 30-day all-cause mortality was 27%.

At admission, 16% of patients were on a statin, 35% were on an angiotensin-converting enzyme (ACE) inhibitor, and 4% were on an angiotensin-II receptor blocker (ARB). After adjustment for potential confounders, including comorbidities, demographic variables, and use of other medications, statin users had a 55% reduction in relative risk of 30-day mortality. Patients on an ARB had a 61% risk reduction, compared with those not on an ARB. However, outpatient ACE inhibitor therapy had no effect on mortality.

Dr. Mortensen noted that both statins and ARBs have immunomodulatory properties that make a survival benefit in septic patients plausible. Simvastatin and losartan were the most frequently prescribed agents in this VA cohort.

Audience members cautioned that the results could be explained by the healthy user effect—the notion that statin and ARB users may have other health-promoting behaviors enabling them to better survive sepsis. Dr. Mortensen agreed, adding that only a prospective randomized trial can rule that out. He and his coworkers are planning a pilot study. ■

Septic Shock May Trigger Brain Atrophy in Survivors

BARCELONA — Septic shock with prolonged mechanical ventilation may take a toll on the brain, both functionally and physiologically.

Three years after patients survived an episode of severe septic shock, their brains showed more central atrophy than did the brains of matched, healthy controls. Survivors also were more likely to have cognitive impairment than were controls, Dr. Robertus Bisschops said at the annual congress of the European Society of Intensive Care Medicine.

Dr. Bisschops of the University Medical Center Utrecht, the Netherlands, examined the effect of severe sepsis on cognition and brain structure in 14 patients who had survived the illness and 42 healthy age-matched controls. The sepsis survivors (mean age 58 years at the time of MRI) had been mechanically ventilated during their illness for a mean of 3 weeks.

All subjects took a battery of 10 neuropsychological tests, including a depression scale and an intelligence quotient test; cognitive dysfunction was defined as abnormal results on three or more tests.

Three of the survivors were depressed; most of the surviviors (94%) had abnormal results on one neuropsychological test; 65% had abnormal results on two tests; and 29% had abnormal results on three tests, meeting the criteria for cognitive dysfunction.

White matter lesions occurred in 65% of the patients—not significantly different from among controls. However, survivors did have a significantly increased bicaudate ratio than did controls (0.54 vs. 0.43), indicating central brain atrophy. The bicaudate ratio in cognitively impaired patients tended to be higher, though not significantly higher, than it was in survivors with normal cognitive function.

Survivors also had slightly, but not significantly, higher sulcal grades than did controls (mean 3 vs. 2). Higher sulcal grades are associated with decreased cognitive functioning, Dr. Bisschops said.

—Michele G. Sullivan

Spirometry Vastly Underutilized in COPD Management

BY PATRICE WENDLING
Elsevier Global Medical News

TUCSON, ARIZ. — Few patients with chronic obstructive pulmonary disease receive spirometry, recommended medication combinations, and stage-appropriate therapy, results of a retrospective analysis of 200 outpatients demonstrated.

Instead, investigators noted the premature use of inhaled steroids and an early indication for oxygen use prior to maximizing other stage treatments, Dr. Pompeyo Chavez and Dr. Navkiran Shokar reported in a poster at the annual meeting of the North American Primary Care Research Group.

Obstacles to stage-appropriate therapy include money and low spirometry utilization.
DR. CHAVEZ

A third of patients were diagnosed on clinical grounds, even though the 1998 Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations established spirometry as the diagnostic standard.

The investigators reviewed the records of 200 randomly selected patients attending a university-affiliated family medicine clinic for chronic obstructive pulmonary disease (COPD) over a 1-year period. Each hospital chart was reviewed for spirometry results going back 10 years.

The patients' mean age was 65 years (range 41-91 years); 104 patients were female, 144 were Caucasian, 45 were African American, and 11 were Hispanic. A total of 128 patients had public insurance, 41 had private insurance, 10 had mixed insurance, 17 were indigent-care patients, and 4 patients had no insurance.

The prevalence of smoking (45%) in these patients was significantly higher than in the general population (20%-25%), reported the authors, both with the family medicine department at the University of Texas, Galveston. Physicians did well in counseling and offering alternative regimens (68%).

Only 117 patients (59%) had spirometry performed in the previous 10 years. Spirometry confirmed a COPD diagnosis in 102 patients (87%), and did not confirm in 15 patients (13%).

Within 3 months of spirometry, the results were mentioned in 71 cases (61%), severity was noted in 43 cases (37%), and medication was changed in only 48 cases (41%).

Low spirometry use may have occurred because patients had to be referred to a pulmonary laboratory in the institution for testing, and because results may not be followed correctly when patients don't always return to the same physician at the clinic, Dr. Chavez said in an interview. In 102 patients whose COPD stage was known from spirometry, 9 were stage 1, 36 were stage 2, 48 were stage 3, and 9 were stage 4.

Stage-appropriate therapy, based on GOLD criteria, was used in 3 stage 1 patients (33%), in 2 stage 2 patients (5.5%), in 13 stage 3 patients (27%), and in 3 stage 4 patients (33%).

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Although spirometry is considered the diagnostic standard, only 59% of patients received such testing in the past decade.

Overall, 45% of patients received medication combinations not recommended by GOLD criteria, and 22% received medications that were not stage-appropriate combinations according to the criteria, he said.

Short-acting bronchodilators, which are appropriate for all stages of COPD, were used by most (93.5%) patients. Inhaled steroids and oxygen, which are reserved for severe or very severe COPD patients, were used by 42% and 17% of such patients, respectively.

Obstacles to stage-appropriate therapy include money, low spirometry utilization, and lack of awareness of GOLD criteria, Dr. Chavez said. "If spirometry were readily available in the office, I think we'd be more prone to use it," he said. "In Europe they do. There's no research on this in the United States, but my guess is they always refer, which might be a barrier." ■

Dr. Jeffrey Hawkins, FCCP, comments: *This is an interesting look at general medical patients in a family medicine clinic. It may well represent the broader population of all nonspecialty medical care and validate the continued need for ongoing education of our medical colleagues. We should be advocates for the use of basic spirometry and the clinical usefulness of using the therapeutic recommendations of the GOLD guidelines.*

Studies Test Valves, Biologics

Bronchoscopic • *from page 1*

said that although LVR surgery didn't increase survival in the 180-patient National Emphysema Treatment Trial as a whole, it did improve survival, pulmonary functional capacity, and health status in the subset of participants with heterogeneous, predominantly upper lobe emphysema and poor exercise capacity (N. Engl. J. Med. 2003;348:2059-73).

The price of surgical LVR was steep: a 30-day mortality of about 5%, close to 50% major morbidity, and lengthy hospitalization. This has prompted intense research interest in developing procedures to reduce the volume of hyperinflated diseased lung without actually cutting out tissue, added Dr. Sterman, an interventional pulmonologist at the University of Pennsylvania, Philadelphia. He disclosed that he has been a consultant and a member of the scientific advisory committee for Spiration Inc.

He was lead investigator in a multicenter U.S. pilot study of Spiration Inc.'s Intrabronchial Valve (IBV), a one-way valve allowing air to escape from diseased portions of the lung, enabling the lungs to work more efficiently. Five hundred twenty IBV valves were implanted in the upper lobes of 75 emphysema patients in the nonrandomized study, which typically involved an overnight hospital stay.

Forty-six patients benefited, showing significantly improved general and disease-specific health status and reduced oxygen consumption with up to 1 year of follow-up. Complications in this subgroup were limited to one case of bronchospasm and one flare of COPD.

Follow-up CT scans at 3 and 6 months showed significant reduction in the volume of the upper lobes of the responders, compared with their lower lobes, which increased in both volume and vascularity. This suggests the clinical benefits resulted at least in part from a redirection of ventilation and perfusion to the relatively spared lower lung segment, he explained.

The IBV allows air to escape from diseased portions of the lung, enabling it to work more efficiently.
DR. STERMAN

Biologic LVR has one advantage over other good ideas: 'There's no foreign body left inside.'
DR. CELLI

Responders were younger than 75 years old, had fewer lung segments treated, and didn't have any valves placed in the lingula. The findings will be incorporated into the upcoming large randomized trial.

Dr. Celli reported on 15 patients who have undergone a total of 21 biologic LVR treatment sessions involving instillation of a biodegradable agent. "It has one advantage compared to the other good ideas out there: There's no foreign body left inside the individual," the physician noted.

The procedure, being developed by Aeris Therapeutics Inc., is definitely safe, said Dr. Celli, who has received research funding from the company. The only associated adverse events have been the minor sort common with flexible bronchoscopy. All patients were by protocol discharged the day after the procedure, but most could have gone home the same day, he said.

As for efficacy, early results look promising; but it will take many more patients and longer follow-up to know for sure, Dr. Celli added.

The treatment concept involves identifying diseased areas of lung, then instilling the biologic agent to induce atelectasis and shrink the volume so that much healthier but compressed lung tissue is allowed to expand.

A dose-response effect was apparent. The patients who have shown clinically meaningful improvements in vital capacity and exercise capacity were the ones who received the most extensive treatment: bilateral therapy targeting up to 10% of total lung volume. Future clinical trials may target 20%-30%.

The biologic procedure's safety lends itself to repeat sessions as additional areas of lung deteriorate. One appealing but as yet untested strategy: perform biologic LVR, measure lung function, then decide if the patient needs to come back in a few weeks for further LVR to optimize results.

The patient with the best response to treatment to date is swimming for exercise and still going strong 14 months after treatment. To physicians familiar with severe COPD, that's nothing short of miraculous, he said. But investigators haven't figured out why he's doing so well while some others who underwent extensive treatment didn't have major responses.

Nonetheless, the future of nonsurgical interventions looks bright for patients with severe COPD, who traditionally have had few options other than the faint prospect of lung transplantation. Dr. Celli offered a final bit of advice to his fellow chest physicians: "Go learn bronchoscopy." ■

Dr. Robert Cerfolio, FCCP, comments: *The future of nonsurgical methods to provide lung volume type procedures for patients with heterogenous emphysema is bright. Celli and colleagues have presented another way besides one-way valves. The data may be immature, but the promise of this technology is high.*

Pages 8a—8b◊

Bronchial Thermoplasty May Cut Asthma Exacerbations

The investigational outpatient procedure shows promise for long-term improvement in quality of life.

BY BRUCE JANCIN
Elsevier Global Medical News

SALT LAKE CITY — Bronchial thermoplasty is an innovative outpatient procedure showing potential as a long-term nondrug treatment for asthma, Dr. Michel Laviolette said at the annual meeting of the American College of Chest Physicians.

The investigational procedure, performed through a standard flexible bronchoscope, resulted in a significant decrease in asthma exacerbations and improved asthma-related quality of life, compared with medical management, in the yearlong, randomized, 108-patient, multicenter Asthma Intervention Research (AIR) trial, reported Dr. Laviolette of Laval University, Quebec City. Asthmatx Inc., which is developing bronchial thermoplasty using its Alair catheter system, funded the study.

Bronchial thermoplasty involves the use of catheter-delivered radiofrequency energy to thermally ablate airway smooth muscle. Over the course of three half-hour sessions, interventional pulmonologists treat all reachable 3- to 10-mm-diameter airways distal to the main stem bronchi, sparing only the right middle lobe.

In dog studies, there is almost no residual smooth muscle mass after bronchial thermoplasty.

Based upon the encouraging results of the AIR trial, AIR2 is now under way. It is a 300-patient international randomized trial featuring a sham procedure in controls.

Dr. Laviolette explained that AIR trial participants were randomized to standard management with inhaled corticosteroids and long-acting β-agonists, or standard management plus bronchial thermoplasty.

All subjects had moderate to severe persistent asthma.

During 1 year of follow-up, the bronchial thermoplasty group experienced a 40% increase in the number of symptom-free days over baseline, which was significantly better than the 13.7% increase in controls. The mean number of puffs of rescue medication required per week dropped by 90% in the thermoplasty group, compared with 10% in controls. Exacerbation rates during a 2-week destabilization period without long-acting β-agonists were 50% lower, compared with baseline in the bronchial thermoplasty group, but not significantly different than at baseline in the control group.

IN A YEARLONG STUDY OF 108 PATIENTS, THERMOPLASTY LED TO A SIGNIFICANT DROP IN ASTHMA EXACERBATIONS, COMPARED WITH DRUG THERAPY.

In addition, thermoplasty recipients scored significantly better than controls on the Asthma Quality of Life Questionnaire and Asthma Control Questionnaire.

There was no significant difference between the two groups in forced expiratory volume in one second (FEV_1) at 1 year.

In terms of safety, bronchial thermoplasty was associated with a transient worsening of asthma symptoms and airway irritation that typically started the day after treatment and resolved within a week. There were 407 such adverse respiratory events—including dyspnea, cough, wheezing, and night awakening—in the thermoplasty group, compared with 106 such events in the control group. Sixty-nine percent of the events were classified as mild and only 3% as severe in nature.

There were no lingering or unexpected adverse events; between 1 week and 1 year post treatment, there were three respiratory-related hospitalizations in each study group.

Long-term safety and efficacy data are needed, and the treatment is considered experimental.

When asked how long the benefits last, Dr. Laviolette replied that in dog studies, a favorable response to the methacholine challenge test persists at 3 years and counting.

Follow-up in asthma patients isn't as long yet, but improvement is retained at the 2-year mark.

Dr. Laviolette declared that he has no financial relationship with Asthmatx. ■

New Drugs Are on the Horizon

Pipeline • *from page 1*

plus an inhaled corticosteroid is in the wings as well, predicted Dr. Lazarus, professor of medicine and director of the chest faculty practice at the University of California, San Francisco.

Here's what else is on the horizon for the treatment of COPD:

▶ **New β_2-agonists.** The new ones have in common the convenience and improved adherence achieved through once-daily dosing. Arformoterol is the (R,R)-isomer of formoterol. It avoids the potentially proinflammatory effects of the parent drug's S-isomer. It is already marketed as a nebulized solution.

Indacaterol is a once-daily long-acting β-agonist that brought substantial improvement in forced expiratory volume in 1 second (FEV_1) in a recently presented but as yet unpublished randomized trial involving 635 patients with moderate to severe COPD.

Several other once-daily agents are early enough in development that they haven't been assigned names. Also in the pipeline is tulobuterol patch therapy, a novel way to achieve long-acting bronchodilation, Dr. Lazarus said at the satellite symposium.

▶ **Anticholinergics.** Here again, the emphasis is on developing once-daily drugs with long duration of action.

Glycopyrrolate is not a new drug, but it is being developed as a nebulized solution for asthma and COPD. It blocks methacholine-induced bronchoconstriction for about 30 hours. In addition, a couple of new anticholinergics are in the pipeline.

▶ **Phosphodiesterase E4 inhibitors.** They target the inflammation that is a hallmark of COPD. They reduce the activity of neutrophils, macrophages, and CD8+ T-lymphocytes while also decreasing expression of tumor necrosis factor–α and other inflammatory mediators. Clinically, they may reduce COPD exacerbations and improve FEV_1, more so in patients with severe than moderate COPD.

GlaxoSmithKline Inc. has received an "approvable" letter from the Food and Drug Administration for its twice-daily cilomilast (Ariflo). Altana AG's once-daily roflumilast is well into phase III clinical trials. Tetomilast is far earlier along.

Because the anti-inflammatory profile of the PDE4 inhibitors differs from that of corticosteroids, there is research interest in using the two together. Ongoing trials are assessing the role of the PDE4 inhibitors as stand-alone vs. combination therapy, Dr. Nicola A. Hanania, FCCP, said at a satellite symposium sponsored by Altana.

Dr. Lazarus, however, isn't convinced the new PDE4 inhibitors are going to have a major impact.

"They're certainly more specific than the old PDE inhibitors like theophylline, but the bugaboo still seems to be side effects, primarily gastrointestinal," he said. "The data on these agents suggest their efficacy has to be counterbalanced by the high prevalence of GI upset and diarrhea. I'm not terribly optimistic about these in the future."

Dr. Hanania disagreed, pointing out that patients didn't discontinue PDE4 therapy because of GI side effects in the large phase III trials. The GI side effects usually are manageable and are confined largely to the first 3 weeks, added Dr. Hanania of Baylor College of Medicine, Houston.

▶ **Antioxidants.** Oxidative stress is clearly key in COPD. Enthusiasm ran high regarding the therapeutic potential of oral N-acetylcysteine to turn off the oxidative process and interrupt the inflammatory cascade—at least until the large Bronchitis Randomized on NAC Cost-Utility Study (BRONCUS) reported negative results (Lancet 2005;365:1552-60). Critics of the study argue the dose was far too low. Also in the antioxidant pipeline for COPD, albeit in the preclinical stage, are superoxide dismutase analogs.

▶ **Anticytokine therapy.** TNF-α plays a key role in perpetuating the neutrophilic inflammatory response in COPD, so it seems logical that an agent such as infliximab or etanercept would be useful. But Dr. Hanania was a coinvestigator in a recently completed 300-patient trial in which anticytokine therapy showed a disappointing lack of benefit.

An antibody to another inflammatory cytokine important in COPD—interleukin-8—is now in clinical trials. "I think there's some potential for this," Dr. Lazarus said.

▶ **Inhaled vasoactive intestinal peptide.** VIP is known to have anti-inflammatory, bronchodilator, and vasodilator properties. At the ACCP meeting, Dr. Bernhard Burian presented preliminary data from the first 25 patients to complete the ongoing 6-month double-blind placebo-controlled VIP-COPD trial. Participants inhaled 200 mcg of aerosolized VIP or placebo four times daily for 3 months, followed by another 3 months of VIP for all.

The study code isn't broken yet, so the most interesting results—VIP vs. placebo—are still to come. But the group as a whole showed significantly improved exercise capacity and quality of life scores along with stable blood gas exchange and essentially no side effects, said Dr. Burian of the Medical University of Vienna.

The short half-life of VIP in the airways because of protease degradation has been "a huge problem," he added, but the Vienna group has identified several protease-resistant long-acting VIP analogs for use in future clinical trials.

▶ **Histone deacetylase activators.** These drugs are being developed in an effort to partially reverse the corticosteroid resistance that plays such an important role in COPD.

Histone deacetylase figures centrally in the mechanism by which steroids turn off inflammation, and in smokers, the enzyme is downregulated. Interestingly, the PDE inhibitor theophylline upregulates histone deacetylase.

▶ **Protease inhibitors.** Matrix metalloproteinases, cathepsins, and neutrophil elastase are produced by neutrophils and macrophages and are an important part of the COPD inflammatory process. Specific inhibitors of these proteases are relatively early in development.

▶ **Statins, macrolide antibiotics, and epidermal growth factor receptor inhibitors.** What these drug classes have in common is that none was developed for use in COPD, but all have demonstrated intriguing preliminary suggestions of efficacy now being followed up in more definitive trials.

For example, a large year-long study is looking at the use of low-dose macrolide antibiotic therapy as a means of reducing COPD exacerbations, not through an antimicrobial effect but via the macrolide's systemic anti-inflammatory effect. Epidermal growth factor receptor inhibitors are being studied as a means of downregulating mucus hypersecretion in COPD.

Dr. Hanania disclosed that he has received grants for clinical research from Altana and GlaxoSmithKline, and has served as a consultant to GlaxoSmithKline.

Dr. Lazarus has no research grants from or any other form of financial relationship with any pharmaceutical company. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

BY DR. MARK J. ROSEN, FCCP

PRESIDENT'S REPORT

Behind the Scenes at CHEST 2006

From all reports, CHEST 2006 was a major success. Attendance was among the highest of any of our annual meetings, and participants consistently praised the range and quality of the presentations, the expertise of the speakers, and the delivery of important and useful new information that relates directly to the practice of pulmonary, critical care, and sleep medicine. The mission of the ACCP is to promote the prevention and treatment of diseases of the chest through leadership, education, research, and communication; I think we can all be proud that this meeting served our mission well.

To the casual observer, and probably to most who attend, our annual meetings are executed almost flawlessly, and ACCP staff and members make it all look easy. We should appreciate the enormous effort that it takes to organize a meeting of this size and scope with consistent success. Orchestrating over 350 sessions, with more than 700 faculty requires months of preparation and coordination by scores of people working in the background. The planning process that collects relevant topics, organizes them into effective educational formats, and recruits the best faculty takes months of hard work by the NetWorks and the Program Planning Committee. The annual meeting is also one of the most important ongoing projects for each person on the College staff, and work on the 2007 meeting starts long before the 2006 meeting is over. Each meeting is the direct result of continuous and intense effort by ACCP executive staff and the education, marketing, finance, membership, health affairs, operations, and publications groups and The CHEST Foundation. Around 65 staff members attended CHEST 2006 to work very long hours to keep things moving, troubleshoot inevitable last-minute problems, and, at the end, make it all look easy.

The annual meeting is also a convenient venue where we conduct much of the ongoing business of the College. The Board of Regents, Executive Committee, NetWorks, Governors, Pulmonary/Critical Care training program directors, and major committees all meet and plan for the next year. The ACCP enjoys excellent collaborative relationships with a number of other organizations, and the annual meeting is where we move these agendas forward. At CHEST 2006, ACCP leadership met with representatives of the American Thoracic Society, Canadian Thoracic Society, American Association of Critical-Care Nurses, Society of Critical Care Medicine, European Respiratory Society, Asian Pacific Society of Respirology, Society of Thoracic Surgery, National Association of Medical Directors of Respiratory Care, and professional societies from Greece, Portugal, Brazil, and France. In these sessions, we assessed what we have accomplished together and planned for future efforts in education, policy, and advocacy.

Over the last few years, I have grown increasingly appreciative of the complexity of the ACCP as an organization that serves its mission and membership and in awe of the talents and accomplishments of our staff. I am also delighted that the Nominations Committee named Dr. James A. L. Mathers, Jr., FCCP, to be the ACCP President, 2008-2009. Jim brings a wealth of experience in leadership in the ACCP, The CHEST Foundation, and NAMDRC, along with special expertise in healthcare legislation, regulations, and practice administration. ACCP Presidents of the past, present, and future work as a team, and Jim will surely make an outstanding and unique contribution to our ongoing work. We all look forward to working with him. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

EDUCATION INSIGHTS

Reflections on CHEST 2006 QI Programs

BY SANDRA ZELMAN LEWIS, PHD
ACCP Research Analyst

One of the major goals of the ACCP's participation in healthcare quality improvement (QI) is to aid ACCP members with QI efforts in their own practices and institutions. Members who attended CHEST 2006 in Salt Lake City were treated to several opportunities to learn about the national movement and how it will influence their daily practice.

The highlight was the CHEST 2006 Keynote Opening Session, an interactive discussion on "Quality Improvement, Performance Measures, and Pay for Performance: Why You Should Care." Distinguished leaders from the National Quality Forum (NQF), Centers for Medicare and Medicaid Services (CMS), American Medical Association Physician Consortium for Performance Improvement (AMA-PCPI), and American Board of Internal Medicine (ABIM) participated in an informative panel discussion moderated by the Chair of the Quality Improvement Committee (QIC), Dr. Michael Baumann, FCCP. This address touched on the development and endorsement process for performance measures and emerging trends in pay for performance, value-based competition, and how quality is incorporated into the maintenance of board certification.

These themes and others were discussed in two half-day postgraduate courses on "The Use of Evidence-Based Medicine and Practice for the Clinician" followed by "Providing Excellence in Chest Medicine: How Does the Physician Incorporate Quality Improvement and Performance Measures?" These courses analyzed how performance measures are used by third-party payers, realized QI initiatives in private practice, and how chest physicians can use performance measures in their own practices.

Other sessions offered at CHEST 2006 included: Evidence-Based Guidelines and Performance Measures: A Survival Guide for Clinicians; Accidents and Errors—When Things Go Wrong, jointly sponsored by AACN, ATS, SCCM, and ACCP; Best Clinical Practice Guidelines: How Do We Get From the Clinical Guidelines to Individual Best Practices; and a town hall meeting with the Centers for Medicare and Medicaid Services.

Provide feedback on this year's sessions at whyyoushouldcare@chestnet.org. Check www.chestnet.org for the debut of the Quality Improvement Committee's Web pages, accessed from the Education drop-down menu. For questions on QI efforts at the ACCP, contact Sandra Zelman Lewis, PhD, at slewis@chestnet.org. ■

This Month in *CHEST*: Editor's Picks

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

- **The Inescapable Relevance of Bioethics for the Practicing Clinician.** *Dr. Joseph A. Carrese, MPH; and Dr. Jeremy Sugarman, MPH*
- **Drawing Impairment Predicts Mortality in Severe COPD.** *Dr. Raffaele Antonelli-Incalzi, et al*
- **Is Methamphetamine Use Associated With Idiopathic Pulmonary Arterial Hypertension?** *Dr. Kelly M. Chin, et al*
- **Risk Factors for Extubation Failure in Patients Following a Successful Spontaneous Breathing Trial.** *Dr. Fernando Frutos-Vivar, et al*
- **Lung Function and Ischemic Stroke Incidence: The Atherosclerosis Risk in Communities Study.** *Dr. Atsushi Hozawa, et al*
- **Enhancement of Treatment Completion for Latent Tuberculosis Infection With 4 Months of Rifampin.** *Dr. Alfred A. Lardizabal, et al*

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AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

INSIDE ACCP

The Operations Division: Delivering Service

BY DONALD JONES
Vice President, ACCP Operations

The Operations Division is usually the invisible contributor to many of the initiatives of the American College of Chest Physicians.

The product of the Operations Division is SERVICE. A combination of many services provides an infrastructure for the ACCP to conduct its daily business, as well as provide an infrastructure for the future.

The infrastructure is divided into the physical building and the technology behind the operations of the ACCP.

Requests for assistance with purchasing, mailings, shipping, receiving, computer hardware, software issues, and the work environment are addressed by the Operations staff daily.

One of the Operations responsibilities is the maintenance of the ACCP's Northbrook office building. Last year, the Operations Division managed a $1.2 million renovation project to provide more office space and a more efficient floor plan for the various departments.

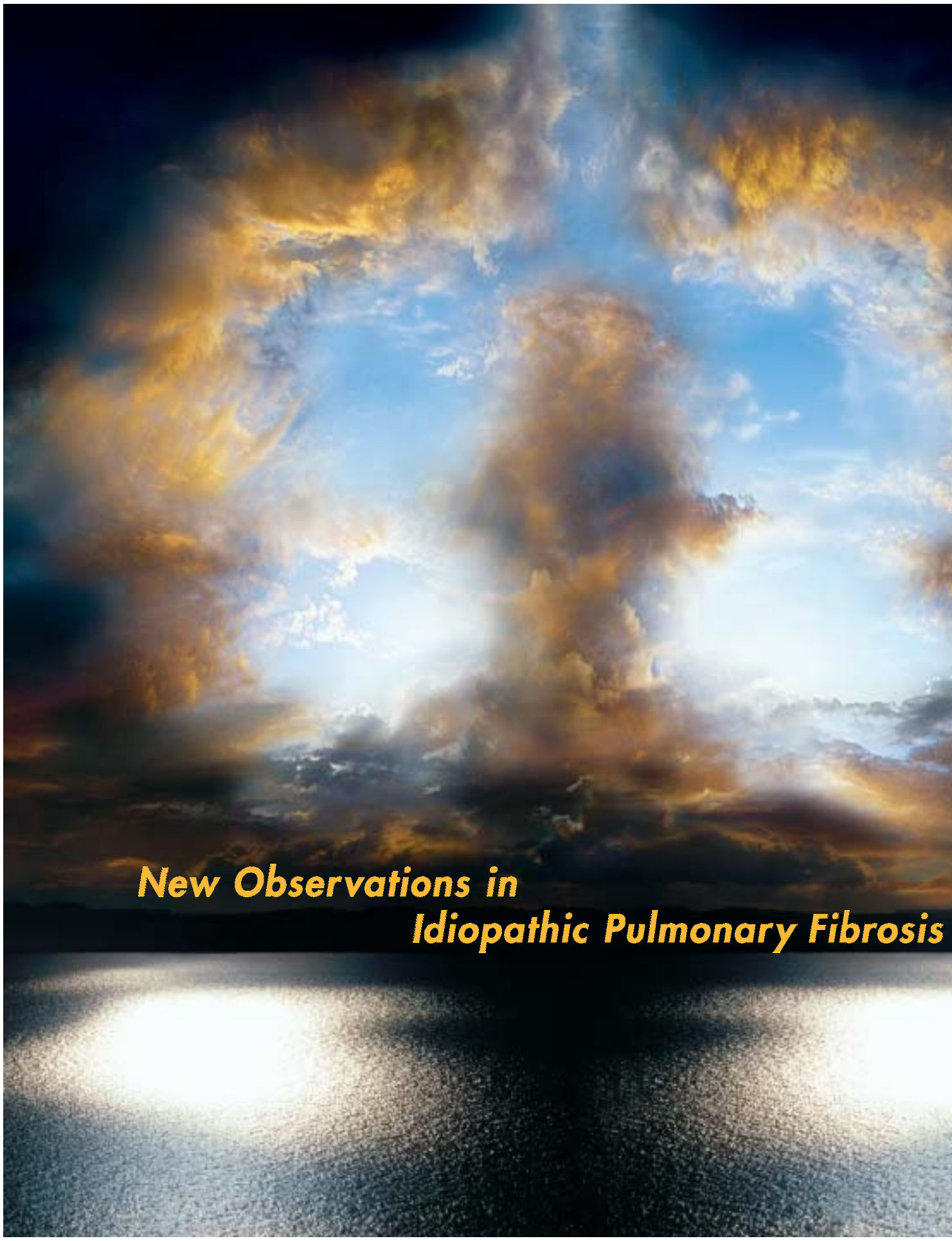
The goal of Operations is to provide a safe and professional environment for the staff to conduct business.

The technical side of the Operations Division is usually involved with many of the other divisions strategic initiatives.

These initiatives usually take advantage of the new technologies enabled by the continued evolution of the Internet. Some examples of these new Web-based applications are e-membership; an online membership application; award applications for The CHEST Foundation; and an entirely new system for the Education Division, which provides for the online submission of education topics and the review, grading, and acceptance of these topics; and faculty disclosure submissions.

All of these new systems provide a much more integrated approach that results in greater productivity for the staff and ACCP members.

In 1995, the Operations Division secured the URL, chestnet.org, and the Web site has been in a continuous



ACCP PRODUCT OF THE MONTH

SLEEP 2: Study Lessons on CD

Use this interactive CD program to study the diagnostic tools used in sleep medicine. This updated second edition features 51 case-based questions to mirror clinical experiences, enhance learning through immediate feedback, and offer references for further study SLEEP 2 complements the first SLEEP CD by covering additional topics and a wider range of diagnostic techniques. Product #6633. Order online at the ACCP Store: www.chestnet.org, or call (800) 343-2227.

NEWS FROM THE COLLEGE

redesign and enhancement cycle ever since.

Every division utilizes this Web site by providing updated information to post or requesting assistance with how best to utilize the Web as a marketing channel or to provide a new service. This is a great resource to find current information about events or products available from the College.

The Operations infrastructure of the ACCP is heavily based on technology.

The role of the technology infrastructure is to meet the day to day business requirements, as well as align the technology with the future strategic direction of the ACCP.

The ACCP has used technology as a catalyst for change in organizational restructuring, process consolidation, and new services to the constituents of the ACCP.

A look at the past and comparing it with today will highlight the challenges of this responsibility.

In the early 1990s, the College was a much simpler and smaller organization, with an annual budget of ~$7 million, a staff of ~45, and an annual meeting budget of ~$2.5 to ~$3 million dollars.

Today, the ACCP has an annual operating budget of almost three times that amount, a staff of ~76, an annual meeting budget of ~$5 to $6 million dollars, plus a much more active membership—thanks to the introduction of ACCP NetWorks.

The technology landscape has changed tremendously since the 1990s, as well.

The introduction of the Web has enabled the ACCP to offer many more services and products directly to the members.

This new business model of self-service to the constituents of the College allows for 24/7 service to individuals around the world.

The self-service model is gaining momentum, as evidenced by the continued increase in the self purchase of registration for ACCP educational courses.

About 45 % of all registrants are purchasing these directly through the Web without any assistance from the staff.

With the support of leadership, our CEO, and the American College of Chest Physicians members we serve, we will continue to expand and increase products and services online.

All of the services are provided by a very dedicated and talented team of 12 individuals who are technologically very savvy and possess a great service-oriented attitude. ■

Coding Updates Webinar

Hear them live—the new coding updates for 2007. Ask questions, and understand how to appropriately document to ensure you are getting paid for all the services you provide. Join the ACCP Webinar "Coding and Documentation: Update 2007" on Monday, Jan. 29, at 11:30 am (CST).

More information is available at www.chestnet.org/education/online/webinar/ or call Joyce Bruno at (847) 498-8120.

COMING IN JANUARY...

Chicago Hosts CHEST 2007

Look for a wrap-up of the highlights from CHEST 2006 in next month's issue of *CHEST Physician*—plus an exciting glimpse of CHEST 2007 in Chicago, October 20-25, 2007!

Pulmonary Perspectives

Postthrombotic Syndrome: A Need for Attention

Despite major progress over the past 30 years in the diagnosis, prevention, and treatment of venous thromboembolic disease, relatively little remains known about its most common sequela, the postthrombotic syndrome (PTS), also known as the postphlebitic syndrome. It receives little attention in reviews or textbooks.

This lack of attention contrasts with the significant morbidity associated with PTS. Its costs are high in terms of direct costs of care and indirect costs in days lost from work, disability, and diminished quality of life (Kahn et al. *Ann Intern Med* 2002; 162:1144; Kahn et al. *J Thromb Haemost* 2004; 2:21). In the past several years, prospective randomized studies and reviews have provided new insights into the clinical picture of PTS and have highlighted the need for more information. The purpose of this *Perspective* is to provide a review of what we know and what we need to know about PTS, with a view toward renewed interest among pulmonologists, internists, and general practitioners.

THE LACK OF ATTENTION CONTRASTS WITH THE SIGNIFICANT MORBIDITY ASSOCIATED WITH PTS. ITS COSTS ARE HIGH IN TERMS OF DIRECT COSTS OF CARE AND INDIRECT COSTS.

Definition and Epidemiology

PTS is a syndrome that occurs after symptomatic or asymptomatic deep venous thrombosis (DVT). Its manifestations are those of venous insufficiency. Aching pain, heaviness, itching, tingling, and cramps in the affected limb are common. Physical findings may include pretibial edema, hyperpigmentation, eczematous changes, venous ectasia, redness, induration, and ulceration. Although PTS had been thought to be a late sequela of DVT, prospective studies have shown that most cases develop within the first 2 years after an acute episode of DVT (Prandoni et al. *Ann Intern Med* 1996; 125;1; Prandoni et al. *Ann Intern Med* 2004; 141;249).

While the reported incidence of PTS has ranged from 20 to 100%, the incidence has probably declined with the advent of improved detection and prophylaxis of DVT. The incidence now appears to range from 20 to 50%, with severe disease in 5 to 10% (Kahn. *J Thromb Thrombolysis* 2006; 21:41). Variations in incidence may be related to differences in population risk factors, diagnostic criteria, and prophylaxis.

Pathophysiology, Etiology, and Risk Factors

Relatively little is known about the pathophysiology of PTS. DVT is thought to damage venous valves with subsequent venous incompetence and venous hypertension. Popliteal reflux, in particular, has been associated with development of PTS with or without residual thrombus (Prandoni et al. *J Thromb Haemost* 2005; 3:401). It is important to note that PTS may occasionally occur in the absence of demonstrable venous abnormalities and that significant venous abnormalities may be present post-DVT without the development of PTS (Johnson et al. *J Vasc Surg* 1995; 21:307). These findings suggest that other factors may be involved, such as damage to the microcirculation or the lymphatic circulation.

The only clearly demonstrated risk factor for PTS is ipsilateral recurrent DVT, which is associated with a 3-fold to 10-fold increased risk (Kahn. *Curr Opin Pulm Med* 2006; 12:299). Other implicated risk factors include older age, obesity, and subtherapeutic oral anticoagulation during the acute episode of DVT (Prandoni et al. *Semin Thromb Hemost* 2006; 32:744). Curiously, factor V Leiden and prothrombin mutations do not appear to be associated with increased risk, despite the increased risk of thrombotic disease with these mutations.

Diagnosis

The diagnosis of PTS is largely a clinical one. There is no gold standard and no definitive objective measurement.

The diagnosis can be made with reasonable certainty if there is a history of DVT and the clinical features of PTS described above are present. Since PTS can occur after asymptomatic DVT (Wille-Jorgensen et al. *Thromb Haemost* 2005; 93:236), the diagnosis may need objective testing in the absence of a history of DVT. If clinical signs are present without a history of DVT, a finding of uncompressible popliteal or common femoral veins on compression ultrasonography can confirm the presence of residual clot and establish the diagnosis of PTS. If compression ultrasonography is normal, Doppler ultrasound to assess valve competency is indicated. If both studies are normal, the diagnosis of PTS is unlikely, even in the presence of symptoms. Two diagnostic caveats are that the diagnosis of PTS should not be made without clinical symptoms or too soon after the acute episode of DVT, because the early associated swelling and pain of acute DVT may subside in 3 to 6 months without the development of PTS.

Prevention

Because recurrent ipsilateral DVT is a known risk factor for PTS, prophylaxis to prevent DVT and good anticoagulation to prevent recurrence are basic preventive measures. The appropriate duration of anticoagulation has long been in question, but a recent study suggests that an elevated D-dimer 1 month after discontinuation of oral anticoagulation is associated with an increased risk of recurrent disease (Palareti et al. *N Engl J Med* 2006; 355:1780). Other studies have found that elevated D-dimer levels, in association with residual thrombosis, predict recurrence. If recurrent disease can be reduced by appropriate duration of anticoagulation, such a change may also effect the development of PTS.

Other possible prophylactic measures include early mobilization after the acute episode of DVT (Partsch et al. *Int Angiol* 2004; 23:206) and prolonged use of compression stockings after the initial episode. Two studies have found that use of compression stockings for 2 years after the initial episode of DVT can decrease the incidence of PTS by 50% (Brandjes et al. *Lancet* 1997; 349:759; Prandoni et al. *Ann Intern Med* 2004; 141:249), although a study of compression stockings using sham compression stockings as a control found no effect of compression on the development of PTS (Ginsberg et al. *Ann Intern Med* 2001; 161:2105). Despite the negative findings of the only sham controlled trial, antithrombotic guidelines recommend the prolonged use of compression stockings following an acute episode of DVT (Buller et al. *Chest* 2004; 126(suppl):401S).

The role of thrombolytic therapy remains controversial. Thrombolysis hastens the return of venous patency after acute DVT, but it does not clearly result in a lower incidence of PTS and is associated with a higher complication rate, mainly bleeding (Forster et al. *Curr Opin Hematol* 2002; 9:437).

Treatment

The treatment of PTS is even more problematic. Treatments are the same as those used for primary venous insufficiency, but they are usually less effective for PTS. Therapies include the use of compression stockings, intermittent compression pumps, leg elevation, topical treatment of ulcers, medications such as horse chestnut seed extract or hydroxyethyl rutosides, and sometimes surgery (Pesavento et al. *Semin Thromb Hemost* 2006; 32:744). Diuretics do not appear to be useful for the edema of PTS. In general, the prognosis is better for patients whose symptoms become worse quickly than for those whose symptoms progress more slowly.

What We Need To Know

We are in need of a much greater understanding of the pathophysiology and etiology of PTS.

Understanding the roles of microcirculation, inflammation, and injury in the development of this syndrome may help develop more effective treatments. More information about patients at risk may help target preventive strategies. Specific markers of disease would also be important in the diagnosis of the condition. More prospective randomized controlled trials of therapies, including thrombolytics and compression, with appropriate controls to determine best therapies, best prophylactic measures, and duration of therapies are needed. Lastly, a much greater awareness of this important cause of disability is crucial to the consistent application of currently known preventive measures. Patients also need to be aware of the syndrome and cautioned to seek help if it develops. ■

Dr. Deborah Shure, Master FCCP
Editor, Pulmonary Perspectives
Miami, FL

Editorial Comment

This is Dr. Deborah Shure's final article as Editor of *Pulmonary Perspectives*. She leaves a 15-year legacy of editorial leadership, intelligence, wit, and a gift for making the difficult understandable. Her commitment to science and truth is legendary. She has enhanced the lives of many pulmonologists as teacher, mentor, and friend. And I, for one, am ever grateful.

Dr. Aymarah M. Robles, FCCP
Deputy Editor

Remarks From the Editor and Deputy Editor

As the outgoing Editor after 15 years and Deputy Editor after 5 years, we are grateful to have shepherded *Pulmonary Perspectives* for so long and have many to thank—the past Editorial Board members, the contributors, the readers who have made such generous comments about the quality and usefulness of *Perspectives*, and, most particularly, Pam Goorsky, our in-house editor extraordinaire. Her professionalism, effectiveness, graciousness, and good humor are beyond measure.

Our philosophy for *Perspectives* has been to provide opinions on interesting topics from experts in the field without the constraints of the traditional journal format. Along with our readers, we have learned a great deal with each issue. We hope that the incoming Editor and Deputy Editor will find the experience as rewarding as we have.

Dr. Deborah Shure, Master FCCP, Editor
Dr. Aymarah M. Robles, FCCP,
Deputy Editor

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AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Status Asthmaticus in the Pediatric ICU

There are few studies that critically examine treatment of severe asthma exacerbations in the PICU.

Asthma exacerbations are one of the most common causes of hospitalization in children.

Although there have been considerable advances in our understanding of its pathophysiology and an array of treatment options, asthma remains a potentially fatal disease with significant morbidity. While overall hospitalization for asthma is decreasing in children, the incidence of severe status asthmaticus requiring pediatric ICU (PICU) admission appears to be increasing.

Despite a large amount of ongoing research regarding the management of children with asthma, there are few studies that critically examine the treatment of severe asthma exacerbations in the PICU.

Large prospective clinical trials are difficult, due to the relatively small numbers of children admitted to the PICU with asthma and the wide variability in treatment practice between regions and among institutions (Bratton et al. *J Pediatr* 2005; 147:355).

As a result, treatment for refractory asthma exacerbations is generally determined by personal experience, anecdotal evidence, and the results of small clinical studies.

Defining rigorous outcome measures is also difficult in pediatric patients with asthma. Critically ill children, due to their age and developmental level, are frequently unable to reliably perform tests that are used to assess pulmonary function in adult patients with asthma exacerbations, such as spirometry and peak flow testing (van der Windt et al. *J Clin Epidemiol* 1994; 47:635).

Clinical asthma scores, derived from combinations of physical findings, have been developed in an effort to quantify severity of illness in these children. The lack of reliable and reproducible measures of pulmonary function in critically ill children is a significant barrier to clinical trials in this population.

First-line care for the treatment of pediatric asthma exacerbations includes oxygen, systemic corticosteroids, and aerosolized ß2-agonists. In children unresponsive to these treatments, PICU admission is necessary for additional therapies and closer monitoring of respiratory status. Several second-line therapies are available, a combination of which is used in the PICU for the treatment of status asthmaticus.

β_2-Adrenergic Receptor Agonists

Additional β_2-adrenergic receptor agonists, delivered either by aerosol or IV, are frequently the next step in the treatment of pediatric status asthmaticus incompletely responsive to initial therapy. Continuously delivered albuterol is generally preferred in children and has been found to reduce hospitalizations and improve pulmonary function when compared with intermittent aerosol treatments (Camargo et al. *Cochrane Database Syst Rev* 2003; 4:CD001115). Relatively high doses of continuous albuterol (20 to 30 mg/h) are routinely used to treat acute bronchospasm in children, and undiluted albuterol aerosols have even been used in certain clinical situations (Gutglass et al. *Pediatrics* 2000; 105:e67). These therapies are generally well tolerated, with a minimum of cardiac side effects, in pediatric patients (Chiang et al. *J Pediatr* 2000; 137:73).

In children with severe airway obstruction, IV β_2-adrenergic receptor agonists are used to overcome problems with drug delivery.

Terbutaline, the only IV β_2-agonist available in the United States, has been shown to improve pulmonary function and gas exchange and to shorten PICU length of stay when titrated according to clinical asthma score (Carroll et al. *Pediatr Pulmonol* 2006; 41:350). In this prospective study, children with status asthmaticus incompletely responsive to inhaled β_2-agonists were treated with IV terbutaline according to a protocol that titrated the terbutaline dose based on their severity of illness. These children had significantly shorter PICU length of stay, shorter hospital length of stay, and reduced hospital charges when compared with children treated with IV terbutaline prior to initiation of the protocol. Dosing ranges of up to 4 µg/kg/min of IV terbutaline have been used in children with status asthmaticus.

Anticholinergics

Aerosolized anticholinergic medications, such as ipratropium, are effective bronchodilators and another mainstay in the treatment of children admitted to the PICU with status asthmaticus.

The combination of ipratropium and β_2-adrenergic receptor agonist therapy has been well shown to improve pulmonary function and to reduce hospitalization, with particular benefit in critically ill children (Schuh et al. *J Pediatr* 1995; 126:639). Aerosolized ipratropium has minimal side effects at the usual dosage of 250 to 500 µg every 6 h.

Magnesium

The efficacy of magnesium for the treatment of children with acute asthma exacerbations is controversial. Magnesium, when delivered IV, has shown acute bronchodilatory effects and may reduce the inflammatory response in asthma. However, systematic reviews of the literature have not demonstrated the effectiveness of the routine administration of high-dose magnesium (Rowe et al. *Ann Emerg Med* 2000; 36:181). As a result, magnesium remains an unproven therapy in children admitted to the PICU with status asthmaticus.

Critical Care Institute
American College of Chest Physicians

Heliox

Heliox, a blend of helium and oxygen, reduces airway resistance and may be a therapeutic option for severe refractory asthma in children. Studies have found a reduction in dyspnea, improved gas exchange, and improved pulmonary function in some patients.

However, a randomized, controlled trial in children (Carter et al. *Chest* 1996; 109:1256) and a systematic review of the literature failed to demonstrate significant beneficial effect (Ho et al. *Chest* 2003; 123:882). In addition, to significantly lower the density of the inhaled gas, helium needs to comprise 60 to 80% of the mixture, prohibiting its use in many hypoxemic children with status asthmaticus.

Methylxanthines

Aminophylline and theophylline were at one time the primary therapy for acute asthma exacerbations. Recently, these medications have fallen out of favor due to their narrow therapeutic range, higher incidence of side effects, and decreased effectiveness compared with sympathomimetic therapy (McFadden et al. *Am J Respir Crit Care Med* 2003; 168:740). In the PICU, however, methylxanthines may continue to play a role in those children incompletely responsive to higher dose β_2-adrenergic receptor agonist and anticholinergic therapy.

Endotracheal Intubation and Mechanical Ventilation

If a patient does not respond to aggressive medical therapy, endotracheal intubation and mechanical ventilation may be necessary. However, identifying which children may benefit from mechanical ventilation is challenging.

Although potentially life-saving, endotracheal intubation and mechanical ventilation can aggravate bronchospasm, worsen underlying dynamic hyperinflation, and are associated with a relatively high incidence (10 to 26%) of serious adverse effects in children with asthma (Werner et al. *Chest* 2001; 119:1913). In addition, modest degrees of hypercarbia are generally well-tolerated in nonintubated children with status asthmaticus (Roberts et al. *Crit Care Med* 2002; 30:581).

Because of the risks involved with this intervention, aggressive medical therapy is encouraged prior to endotracheal intubation.

Noninvasive Positive Pressure Ventilation

The success of noninvasive positive pressure ventilation (NPPV) in treating acute exacerbations of other chronic obstructive diseases has led to the interest in the use of NPPV for the treatment of asthma.

NPPV has shown some benefit in the treatment of asthma exacerbations in adults, improving gas exchange and respiratory function in some patients (Meduri et al. *Chest* 1996; 110:767). In another small case series of children admitted to the PICU with status asthmaticus (Carroll et al. *Ann Allergy Asthma Immunol* 2006; 96:454), NPPV improved subjective and objective markers of pulmonary function and was well-tolerated for several days without the need for significant amounts of sedative medications. Staff familiarity with NPPV, combined with nonpharmacologic methods of relaxation and distraction, is important to sustain tolerance in this population.

Conclusion

Treatment of status asthmaticus in children admitted to the PICU is frequently subjective and includes a combination of second-line therapies. Few controlled studies that examine the efficacy of treatments received in the PICU exist and, as a result, there are few truly evidence-based treatment strategies.

Barriers to clinical trials include the relatively small numbers of children admitted to the PICU with status asthmaticus, the wide variability in treatment strategies, and lack of rigorous outcome measures. Improving outcomes in this population will require strategies to overcome these barriers in future studies. ■

Dr. Christopher L. Carroll, FCCP
Assistant Professor, Pediatric Critical Care
Connecticut Children's Medical Center
Hartford, CT

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

PRACTICE MANAGEMENT UPDATE

On-site Practice Management Consultations

Some members took advantage of a new service at CHEST 2006 provided by the Practice Management Department. Diane Krier-Morrow, MBA, MPH, CCS-P, coding and reimbursement consultant to the College, provided one-on-one consultations on any practice management issue of interest to attendees.

Twenty-five College members participated in these consultations and were pleased to speak with someone on issues of interest to their particular practice situation. The discussions were as varied as the types of practice situations that exist. A sampling follows:

► A solo practitioner from Tennessee wanting to expand his practice.

► A California physician in pulmonary and sleep medicine, a couple years before retirement, wanting to revise his templates for evaluation and management coding with discussion of patient history documentation, promised to develop a practice compliance plan.

► A cardiothoracic surgeon from Georgia who had not looked at his surgical payments on selected procedures in years and was concerned with the significant drop in payments. Relevant CPT thoracoscopy codes on AMA's CodeManager were reviewed, and it was explained that nationally, ACCP represents pulmonary, critical care, and sleep medicine through the AMA CPT and RUC processes. He was referred to the Society of Thoracic Surgeons, which represents him nationally on coding and reimbursement issues. There is a thoracic surgery chapter in the new ACCP 2007 coding book.

► A number of physicians from the Private Practice Leadership Program were interested in talking individually about the new 2007 diagnostic and procedure codes presented at their Saturday session.

► Two pediatric pulmonologists were very interested in talking about the new sleep apnea codes, CPT **94774-94777**.

► A fellow stopped by to ask some basic coding questions, such as what is ICD-9-CM diagnostic and CPT procedural coding. Diane spoke with the Private Practice NetWork and suggested that a program be developed for fellows before they begin their practices. This is being investigated for CHEST 2007.

Check the 2007 edition of *Appropriate Coding for Critical Care Services and Pulmonary Medicine* for details on the new procedure and service codes.

Most importantly, there are new ventilation management codes, **94002-94005** for CPT 2007. Also, the 6-minute walk test and oximetry were added to the parenthetical for simple pulmonary stress testing in CPT **94620**.

In the allergy section, a new code for expired nitric oxide is **95012**. We believe that this PFT will require modifier **25** on the evaluation management service if provided on the same day, because that code is in the allergy section of CPT.

There are new sleep apnea codes, CPT **94774-94777**. Additionally, there is a new code for surfactant administration, **94610** and **99363-4** for anticoagulant. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

NETWORKS

Two New Guidelines Being Produced

Pulmonary Physiology, Function, and Rehabilitation

Two years ago, the Pulmonary Function, Physiology, and Rehabilitation NetWork began work on an update of the 1997 Evidence-Based Guidelines for Pulmonary Rehabilitation.

Several members of the ACCP were selected by the Health and Science Policy Committee and appointed by the College to work with several members of the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) on the project. The committee worked with Carla Herrerias, ACCP Clinical Research Analyst, to research the literature and put together the updated version of the guidelines. The newly developed ACCP grading system for guidelines was used in the process (*Chest* 2006; 129:174-181).

The document is in its final draft form and is undergoing review by the AACVPR and the ACCP boards for suggestions and final approval.

The updated version of the guidelines evaluated those topics reviewed in the 1997 guidelines, including various components (*eg*, lower and upper extremity training, inspiratory muscle training) and outcomes (*eg*, dyspnea, health-related quality of life, healthcare utilization) associated with pulmonary rehabilitation. In the updated version, there was also evaluation of other components associated with rehabilitation, including psychosocial intervention; long-term maintenance; nutrition; rehabilitation for diseases other than COPD; and adjunctive therapies, including supplemental oxygen therapy and anabolic steroids.

This project involved the collaboration of two organizations that are intimately involved in providing pulmonary rehabilitation for patients with chronic lung disease and should help us optimize provisions of rehabilitative services for patients.

Thoracic Oncology

More than 50 Thoracic Oncology NetWork members serve on the panel that has been actively describing the evidence and developing recommendations for the Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition).

Additional members were recently involved in reviewing chapters from these guidelines, which are expected to be published in 2007.

The primary focus of the NetWork in the next year will be the promotion of the guidelines through programs and sessions at CHEST 2007, development of implementation tools, and other marketing efforts.

Also, watch for the debut of the new Web pages for this NetWork. The Web pages will feature clinical content, NetWork projects, and other NetWork activities.

For further information or to learn more about the Thoracic Oncology NetWork, contact Sandra Zelman Lewis, PhD, staff liaison, via e-mail at slewis@chestnet.org. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

Happy 10th Birthday to NLHEP!

BY DENNIS E. DOHERTY, MD, FCCP
Chairman of NLHEP
AND GRETCHEN LAWRENCE, BA, RRT
Program Associate for NLHEP

As a result of a pivotal meeting on the state of COPD in 1996, the National Lung Health Education Program (NLHEP) was created.[1] Goals for the organization have not changed: to increase awareness of COPD to the community and to health-care professionals; and to support the use of spirometry in the primary care physician (PCP) office to establish an earlier diagnosis of this under-appreciated disease.

Educational materials have been developed and revised over the past 10 years, among them "Save Your Breath America," a booklet written in easy-to-understand language for COPD patients and their families.

A new professional booklet, "Long Term Oxygen Therapy: History, Scientific Foundations, and Emerging Technologies," a product of the 6th Oxygen Consensus Conference, was released in October.

In the past 2 months, over 10,000 of these two booklets alone have been distributed in time for Respiratory Care Week and National COPD Month.

A REVIEW OF NLHEP'S EFFORTS CLEARLY SHOWS THAT THIS ORGANIZATION IS AS DEDICATED TO ITS GOALS AS IT WAS WHEN IT FORMED 10 YEARS AGO.

The battle cry of NLHEP, "Test Your Lungs—Know Your Numbers," emphasizes earlier detection of COPD via routine use of spirometry in primary care offices.

This concept was reinforced in 2004 when NLHEP launched the Spirometer Review Process (SRP)—an evidence-based evaluation tool using a list of required features that are easy for manufacturers to incorporate into their office spirometry systems—and make it easier for PCPs to use these simple devices to obtain the only three numbers needed to make the diagnosis of COPD, the FEV_1 and FEV_6 expressed as a percent of predicted (based on age, height, and gender), and the FEV_1/FEV_6 ratio.[2]

The most recent addition to NLHEP's educational arsenal are the COPD awareness posters, with all 13 available now in Spanish.

These colorful posters represent all ages, ethnic groups, and both genders and are intended for display where patients go for health care—the PCP office, the ED, outpatient clinics, and health fairs. These posters and much more information can be found on the NLHEP Web site (www.nlhep.org).

NLHEP turns 10 this year, and a review of its efforts clearly shows that this organization is as dedicated to its goals as it was when it was formed 10 years ago—and NLHEP continues to be an active participant in the fight to increase awareness of COPD across the United States.

Several ACCP Fellows serve on the Executive Board, and Dr. Robert M. Rogers, FCCP, is the ACCP representative to the board.

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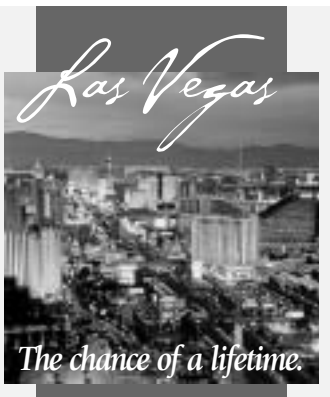
2. Ferguson GT, Enright PL, Buist AS, et al. Office spirometry for lung health assessment in adults: a consensus statement for the National Lung Health Education Program. Chest 2000; 117:1146-1161

CLASSIFIEDS

PROFESSIONAL OPPORTUNITIES

HAWAII ISLANDS OF SUN, SURF & ALOHA

Straub Clinic & Hospital, 150-physician multi-specialty group with a 159-bed hospital, is seeking a fellowship trained BC pulmonologist with expertise in pulmonary hypertension, interstitial lung disease, and interventional bronchoscopy. This out-patient based position in our Chest Diseases Clinic is at the same location as our hospital for in-patient care. Straub is part of Hawaii Pacific Health, one of the largest healthcare systems in the state, providing tertiary, specialty, and acute care services. Benefits include relocation allowance and professional liability insurance. Combine a professional career with the recreational activities, cultural diversity, superb lifestyle and excellent climate year-round. Visit www.straubhealth.org Send CV to: Ellen Kaye, Physician Recruitment Coordinator, Straub Clinic & Hospital, 888 South King Street, Honolulu, HI 96813; email ekaye@straub.net fax: (808) 522-4006; phone: (800) 5-STRAUB (578-7282)



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PULMONARY/ CRITICAL CARE FACULTY

Additional pulmonary/critical care faculty members are sought for a growing section at Washington Hospital Center. WHC is a 907-bed not-for-profit teaching hospital located in downtown Washington, DC. The pulmonary/critical care section is responsible for a busy ICU, IMC, inpatient and outpatient consultation service, and respiratory therapy. An integrated pulmonary/critical care fellowship program has been developed with NIH. In addition to clinical and teaching responsibilities an interest in research is expected. Address inquiries, along with CV, to Gene Colice, MD, Director, Section of Pulmonary, Critical Care & Respiratory Services, Washington Hospital Center, 110 Irving Street, NW, Room 2A68; Tel #202-877-7856; Fax #202-291-0386.

Have questions on classifieds?
Call Rhonda Beamer 443-512-8899 Ext 106 for more information.

Parents and Children Disagree on Asthma Impact

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SAN FRANCISCO — A physician who relies on parent reports to assess the effects of asthma on a child's physical and emotional health may be getting only part of the story, according to findings presented in a poster at the annual meeting of the Pediatric Academic Societies.

Separate interviews with 414 children (aged 7-16 years) and one of their parents showed that parents and children often disagree about the impact of asthma, sociologist Lynn M. Olson, Ph.D., reported.

Dr. Olson, director of the department of research at the American Academy of Pediatrics in Elk Grove Village, Ill., found that children in all age groups tended to describe their physical health as worse than was reported in their parents' accounts.

"We found in each of the age groups, children were more likely to report more symptoms and worse health than did the parents," she said in an interview at the meeting, which was sponsored by the American Pediatric Society, Society for Pediatric Research, Ambulatory Pediatric Association, and American Academy of Pediatrics.

On questions of emotional health, however, adolescents were significantly less likely than parents to report a negative impact.

Dr. Olson said the study was part of a larger investigation sponsored by the National Heart, Lung, and Blood Institute that looked into children's ability to report on their own asthma health status.

Most children in the study, 61%, used a prescribed controller of asthma symptoms 5 or more days a week. Some 53% of parents described their child's condition as "moderate/severe." The population was diverse (including 46% African American, 37% white, and 11% Hispanic families), with 42% of family incomes less than $30,000 annually.

Each parent-and-child pair completed adult and child versions of the Child Health Survey for Asthma. The survey contained questions about physical activities and asthma impact during the previous 2 weeks. Answers were computed in scores of 1-100, with higher scores signaling better health.

Under physical health, only 70% of parents and children agreed on whether the child had difficulty sleeping. Agreement was little better for questions relating to cough (73%), limits on strenuous activities (73%), and limits on sports/running outside (78%).

Agreement improved slightly when the pairs were asked about wheezing with a cold (80%), wheezing without a cold (81%), cold won't go away (81%), shortness of breath (82%), tight chest (83%), limits on moderate activities (83%), and limits in gym class (86%).

Parents and children were most likely to agree on asthma's impact on limits on mild activities (93%). They disagreed more, however, on emotional impact issues.

The lowest level of agreement, 69%, regarded frustration with asthma treatments and frustration with activity limits. Just 70% concurred when asked about the child being frustrated with having asthma and asthma causing family stress.

When Dr. Olson and her coinvestigators stratified the direction of difference by age group, children aged 7-9 years reported lower scores overall than did the parents (79.5 vs. 83.3 for physical health and 73.1 vs. 77.3 for emotional health). These differences were not statistically significant, however.

Children aged 10-12 years reported significantly worse scores for physical health, compared with their parents (80.5 vs. 86.2), but there was a trend to better child scores for emotional health (80.6 vs. 78.8) in this age group.

Adolescents aged 13-16 years reported an overall score of 77.3 for physical health, while their parents scored them at 83.7. They rated their emotional health at 79.3, but their parents gave this the lowest score: 69.1. Both differences were significant.

"When you look at the way questions are asked [and] messages are delivered, the target audience is the parent. Rarely is the audience considered to be the child," she said. "Whenever possible in research and in practice, we should be considering asking both the parents and the child." ■

Dr. LeRoy M. Graham, FCCP, comments: *Specific inquiry of children regarding disease impact is an important component of clinical assessment in determining disease severity and in the formulation of effective management plans. As many, if not most, children are directly responsible for taking their medications, such inquiry may enhance adherence by establishing relevant goals of therapy.*

Sleep-Related Breathing Disorder, Depression Linked

BY DIANA MAHONEY
Elsevier Global Medical News

Individuals with sleep-related breathing disorder are at an increased risk for developing depression, and the likelihood of developing depression is directly related to the severity of the breathing disorder, a longitudinal study has demonstrated.

Because sleep-related breathing disorder and depression have both been independently associated with substantial morbidity, impairment, and disability, Paul E. Peppard, Ph.D., and his colleagues at the University of Wisconsin, Madison, designed a population-based epidemiological study to look for a link between the two conditions.

The investigators evaluated 788 men and 620 women participating in the ongoing Wisconsin Sleep Cohort Study.

All of the patients underwent between one and four overnight in-laboratory polysomnography evaluations and clinical assessments that included body mass index, medical history, and interviews to determine the nature and frequency of sleep problems, daily activities, and medication use (Arch. Intern. Med. 2006;166:1709-15).

All of the participants completed the 20-item self-reporting Zung depression scale to assess depressive symptoms.

The scale ranges from 25 to 100; scores between 50 and 59 indicate mild depression, and scores of 60 or higher indicate moderate to severe depression.

Two sleep-related items on the Zung scale—"I have trouble sleeping through the night" and "I get tired for no reason"—were excluded because of their potential for creating an inherent association between sleep-related breathing disorder and depression, according to the authors.

For the investigation, the severity of sleep-related breathing disorder was categorized based on apnea-hypopnea index (AHI) cutoff points.

No events in 1 hour indicated no sleep-related breathing disorder, 1-4 events indicated minimal sleep-related breathing disorder, 5-14 events indicated mild sleep-related breathing disorder, and 15 or more events indicated moderate or worse sleep-related breathing disorder.

After investigators had controlled for age, body mass index, alcoholic drink consumption, and history of cardiovascular disease, an increase in sleep-related breathing disorder level to the next higher category was associated with a 1.8-fold increase in the odds for developing depression, compared with an unchanged sleep-related breathing disorder level.

CLINICIANS SHOULD BE AWARE OF THE INCREASED LIKELIHOOD OF THE CO-OCCURRENCE OF THE TWO CONDITIONS.

The odds of developing depression for participants with minimal, mild, or moderate or worse sleep-related breathing disorder, compared with participants who had no sleep-related breathing disorder, were 1.6-fold, twofold, and 2.6-fold greater, respectively, in adjusted models that combined longitudinal and cross-sectional associations.

Further adjustments for symptoms of sleep-related breathing disorder—including insomnia, daytime sleepiness, fatigue, and polysomnographic features such as sleep efficiency and percentage of time in slow-wave sleep—did not alter the associations.

That suggests that these items are not strong explanatory factors.

The use of hypnotic agents or benzodiazepines, or the presence of comorbid conditions such as diabetes also did not alter the associations.

In addition, there was no evidence of important interactions between sleep-related breathing disorder, depression, gender, age, or comorbid conditions.

Given the association of sleep-related breathing disorder with depression, clinicians should be aware of the increased likelihood of the co-occurrence of these two conditions in patients diagnosed with either condition independently.

In addition, suboptimal mental health should be added to the list of potential multiple adverse outcomes associated with sleep-related breathing disorder.

In addition, patients should be evaluated and treated accordingly, the authors wrote. ■

Video-Assisted Thoracoscopic Surgery Cuts Pneumonia

BY MITCHEL L. ZOLER
Elsevier Global Medical News

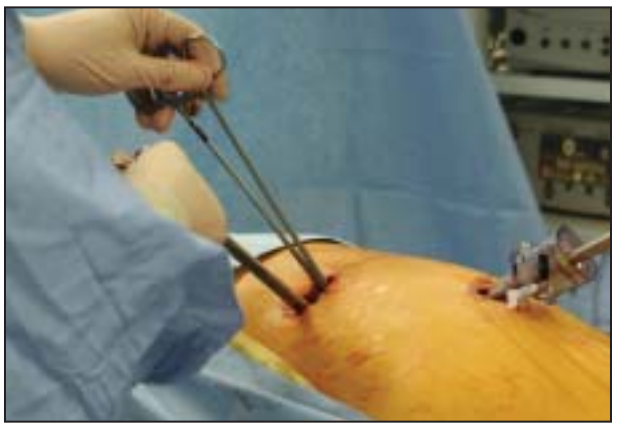
CHICAGO — Video-assisted thoracoscopic surgery was associated with a lower risk of pneumonia compared with conventional thoracotomy for patients undergoing lobectomy, according to a review of 147 patients with non–small-cell lung cancer.

Until now, video-assisted thoracoscopic surgery (VATS) has had questionable value compared with open thoracotomy, but the new findings indicate that VATS causes less morbidity than does conventional surgery, Dr. Bryan Whitson said at the annual clinical congress of the American College of Surgeons.

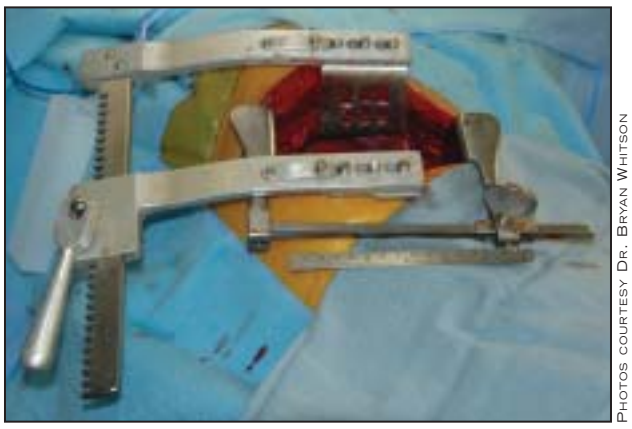
All other outcomes were roughly similar between the two methods.

The study reviewed patients who underwent lobectomy for clinical stage I non–small-cell lung cancer at the University of Minnesota, Minneapolis, from January 1998 to June 2005. Thoracotomy was used exclusively until 2001, when VATS was introduced. Both methods were used while VATS was introduced, said Dr. Whitson, a surgeon at the university.

The review included 88 patients treated by thoracotomy and 59 treated with VATS. In general, the two groups were similar with respect to age, gender, and incidence of comorbidities such as diabetes, coronary disease, and chronic obstructive pulmonary disease. The VATS patients had a significantly higher prevalence of hypertension, chronic renal insufficiency, and history of other cancers at the time of their surgery. Pathologic staging during surgery showed that 92% of the VATS group and 83% of the thoracotomy group actually had stage I disease.



The VATS technique uses a minimal access incision. At right is the video camera.



Traditional thoracotomy resulted in a six times higher incidence of pneumonia than the VATS technique.

PHOTOS COURTESY DR. BRYAN WHITSON

The only notable difference in outcomes between the two groups was in the incidence of pneumonia during the 30 days after surgery: 19.3% in the thoracotomy patients compared with 3.4% in the VATS patients, a significant difference, Dr. Whitson said.

Patients treated with VATS showed a trend toward a shorter hospital stay than did the thoracotomy patients (mean 6.4 days vs. 7.7 days), as well as a slightly longer intensive care stay (1.2 days vs. 0.5 days).

Other measures were similar, including the incidence of postoperative myocardial infarction, incidence of reoperations, and total survival. At an average of 4 years after surgery, the survival rate was 72% for the VATS group and 66% for the thoracotomy group.

VATS is taking off as an alternative to thoracotomy, commented Dr. Zane Hammoud, a surgeon at Indiana University in Indianapolis. But surgeons are still looking for the right indications, he added. ■

Dr. Robert Cerfolio, FCCP, comments: *Although some argue that the oncologic effectiveness of VATS remains unproven, there is clearly a trend toward performing VATS lobectomy for patients with non–small-cell lung cancer. This article provides further evidence for its continued use in properly selected patients.*

New NCQA Measures to Focus on Quality of Care

BY JANE ANDERSON
Elsevier Global Medical News

The National Committee for Quality Assurance is finalizing new performance measures that will look at quality of care all the way down to the physician group and even the individual physician level.

The measures, which will form the foundation of a new Health Employer Data and Information Set (HEDIS), could require physicians to begin reporting some quality data to health plans directly.

The draft ambulatory care quality measures were released for public comment in October. Final measures are expected before the end of the year, according to an NCQA spokesman.

"This is a big change," said Dr. Bruce Bagley, medical director for quality improvement at the American Academy of Family Physicians (AAFP) and a member of the NCQA committee that approved the draft measures. "Physicians now will begin to report some data from their clinical records, such as 'Why I didn't give an indicated medication.' "

HEDIS, which measures quality of care, is the main tool that health plans use to track and report on their performance to payers.

Until now, HEDIS has used administrative claims data "almost exclusively" to measure quality at the health plan level, said Dr. Bagley. Now, "NCQA has rewritten these specifications so that it's possible to drive the measures down to the physician level."

The draft measures are designed to allow health plans to report on physician performance for their networks. They include six prevention measures, such as breast cancer screening and influenza vaccination rates, as well as measures that address care for coronary artery disease, depression, and asthma. Measures addressing overuse and misuse of health care services also are part of the proposed HEDIS addition.

The measures include detailed technical specifications and implementation methods, such as appropriate sample sizing, for use by health plans.

The draft measures are not new, Dr. Bagley pointed out. They were included in the National Quality Forum–endorsed National Voluntary Consensus Standards for Physician-Focused Ambulatory Care, and the AQA (formerly the Ambulatory Care Quality Alliance) adopted these measures as part of its Recommended Starter Set of Clinical Performance Measures for Ambulatory Care.

"We see these [measures] as supplementing a number of national and regional physician-level measurement efforts that are already underway," said NCQA spokesman Jeff Van Ness. Because NCQA included detailed instructions for implementation, "this lowers the hurdle for plans to begin to move and implement these among physicians," he said.

Nonetheless, Dr. Bagley said, once these measures are made part of HEDIS, physician groups and individual physicians will need to develop methods to collect the necessary information without resorting to retrospective chart audits.

"We're promoting prospective data collection," such as checklists that can be filled out at the time of the patient visit, he said.

Mr. Van Ness said that most of the comments NCQA has collected on the draft measures have come from large national health plans. He declined to provide information on the content of the comments, citing privacy concerns. ■

Dr. Michael Baumann, FCCP, comments: *The development and dissemination of performance measures for the outpatient and inpatient arena are an area physicians must continue to watch closely. There may be many unintended consequences that need to be monitored more closely in order to provide a fair and equitable process for physicians while continuing to improve care for our patients.*

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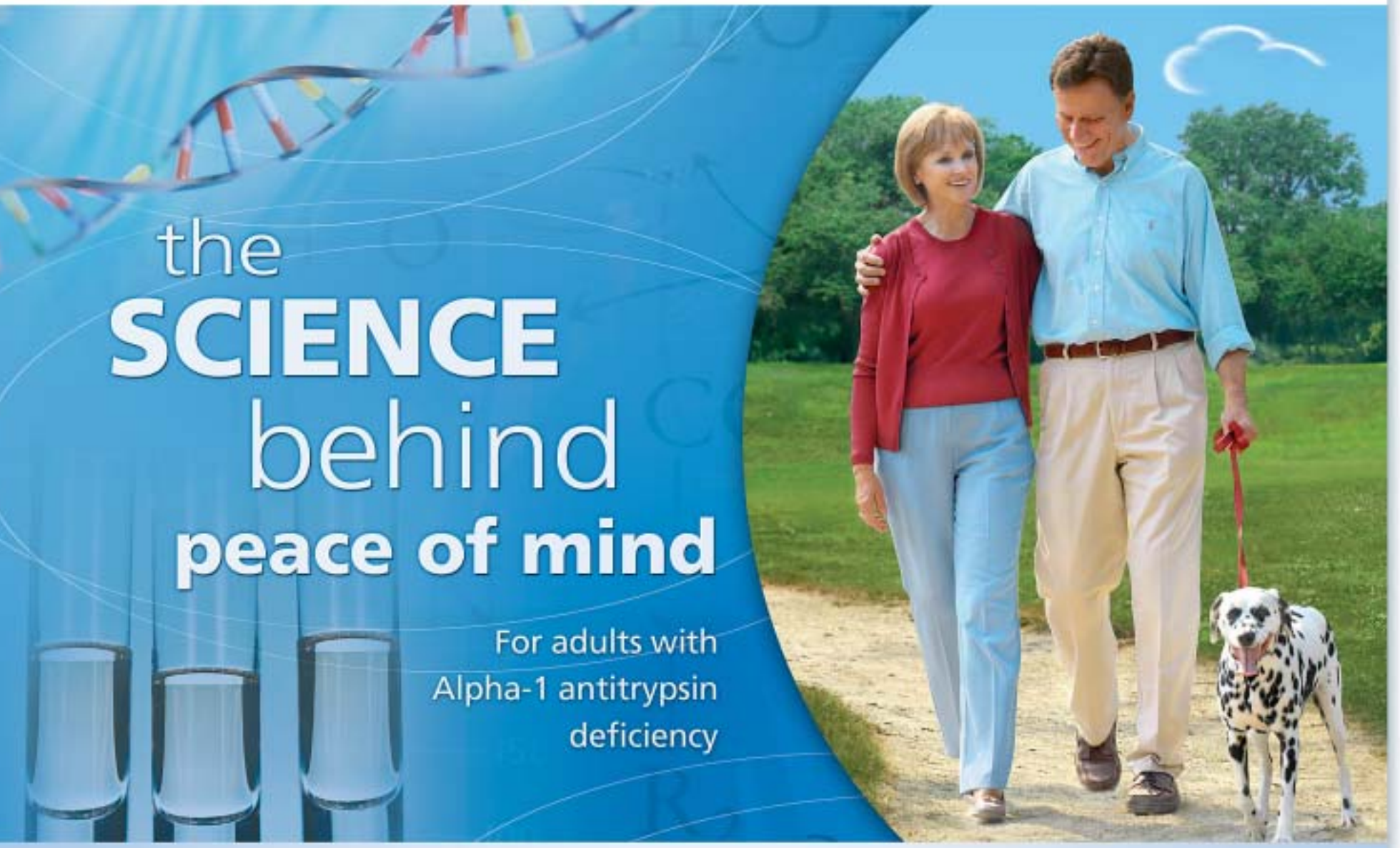

Zemaira® — The next generation in purity for Alpha-1 augmentation therapy

- **Pure** — The only Alpha-1 augmentation therapy approved by the FDA as highly purified (lot release specification, ≥94% purity)*,[1-3]
- **Effective** — **Three times fewer** COPD exacerbations than with Prolastin®†
- **Well tolerated** — **Six times fewer** infusion-related adverse events than with Prolastin®‡
- **Fast** — **Half or less** the infusion time of other augmentation therapies§,[1-3]

Zemaira® is indicated for chronic augmentation and maintenance therapy for adults with alpha$_1$-proteinase inhibitor (A_1-PI) deficiency and emphysema.

Clinical data demonstrating the long-term effects of chronic augmentation therapy with Zemaira® are not available.

As with other Alpha-1 therapies, Zemaira® may not be appropriate for the following adult individuals as they may experience severe reactions, including anaphylaxis: individuals with a known hypersensitivity and/or history of anaphylaxis or severe systemic reaction to A_1-PI products or their components and individuals with selective IgA deficiencies who have known antibodies against IgA.

In clinical studies, the following treatment-related adverse events were reported in 1% of subjects: asthenia, injection-site pain, dizziness, headache, paresthesia, and pruritus.

Zemaira® is derived from human plasma. As with all plasma-derived products, the risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

For more information, call **1-866-ZEMAIRA (1-866-936-2472),** or visit **www.Zemaira.com.**

Zemaira®
alpha$_1$-proteinase inhibitor (Human)
Unmatched purity. Uncompromised care.

Please see brief summary of full prescribing information on following page.

* Shelf life purity specification is ≥90%

† In a retrospective analysis in the pivotal clinical trial, Zemaira® patients were three times less likely to experience exacerbations of their COPD than Prolastin® patients

‡ No clinically significant differences were detected between the treatment groups

§ Based on recommended dosage as stated in the product package inserts of 60 mg/kg body weight at the infusion rate of 0.08 mL/kg/min