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CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

TIM QUILL

Critically ill patients who received epoetin alfa were no less likely to receive a red cell transfusion, said Dr. Howard Corwin, FCCP.

Results Mixed for Epoetin in Critically Ill

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Treatment with epoetin alfa reduced mortality in trauma patients but did not decrease the need for red cell transfusions and was associated with an increased risk of thrombotic vascular events in a prospective, randomized study of 1,460 critically ill surgical, medical, or trauma patients admitted to intensive care units.

Patients who received weekly injections of epoetin alfa for up to 3 weeks were no less likely to receive a red cell transfusion than those who received placebo, but they were at an increased risk of thrombotic events. Treatment was associated with lower mortality, however, particularly among trauma patients, reported Dr. Howard Corwin, FCCP, of the Dartmouth-Hitchcock Medical Center, Lebanon, N.H., and his associates (N. Engl. J. Med. 2007;357:965-76).

The patients in the study were treated at 115 U.S. medical centers between December 2003 and June 2006. They received weekly subcutaneous injections of epoetin alfa (40,000 U) or placebo, weekly, for a maximum of 3 weeks. The injections started within 48 and 96 hours of admission to the intensive care unit, and the patients were followed for 140 days. All patients were age 18 years or older; the mean age was 50 years.

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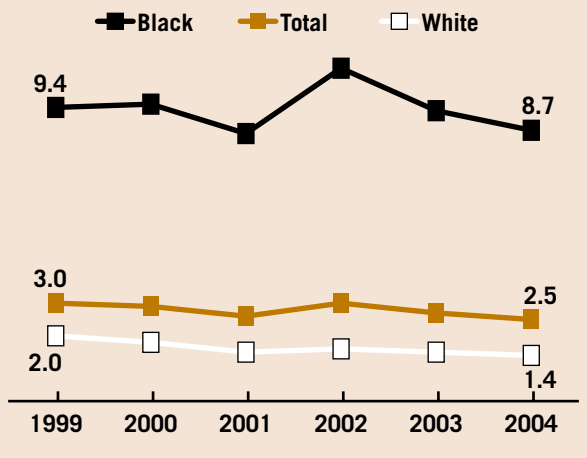
VITAL SIGNS

Disparities in Asthma Deaths in Children

(mean mortality rate per 1,000,000 children aged 0-17 years)



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ELSEVIER GLOBAL MEDICAL NEWS

COPD's Global Toll Is Far Greater Than Commonly Assumed

Study uncovers unexpected prevalence.

BY JONATHAN GARDNER
Elsevier Global Medical News

The burden of chronic obstructive pulmonary disease is underestimated worldwide, and there are higher levels and more advanced forms of the disease than have been reported, according to an international study documenting prevalence.

Researchers found that smoking and advanced age increased the likelihood of developing chronic obstructive pulmonary disease (COPD), but reported that the prevalence of COPD in people who have never smoked, as well as in younger patients, suggests that other factors—such as tuberculosis and exposure to particulates and fumes through occupation or the use of biomass fuels—may also play a role (Lancet 2007;370:741-50).

The study, from sites in 12 countries involving 9,425 subjects aged 40 years or older who were tested by spirometry, found an overall prevalence of 10% for stage II or higher COPD (12% for men, and 9% for women), wrote Dr. A. Sonia Buist of Oregon Health and Science University, Portland, and her colleagues.

The sites were Adana, Turkey; Bergen, Norway; Cape Town, South Africa; Guangzhou, China; Hannover, Germany; Krakow, Poland; Lexington, Ky.; Manila, Philippines; Reykjavik, Iceland; Salzburg, Austria; Sydney, Australia; and Vancouver, B.C., Canada.

Across the sites, the likelihood of developing stage II COPD increased for smokers, with an odds ratio of 1.2 for each additional 10 pack-years (defined as the number of packs per day over the course of a year) the study found. For each additional 10 years of age, the odds ratio of developing stage II COPD was 1.94, the researchers wrote.

Past reviews of COPD data worldwide have found lower

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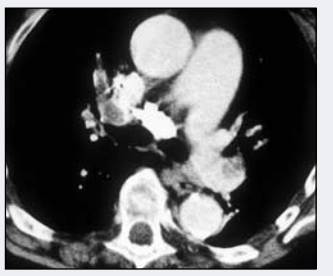
INSIDE



Sleep Duration Linked to Mortality Risk

BY TIMOTHY F. KIRN
Elsevier Global Medical News

Both too much sleep and not enough sleep appear to be associated with increased mortality, according to a new longitudinal study.

Sleeping less than 6 hours per night or more than 9 hours per night was associated with almost twice the mortality risk of sleeping 6-8 hours per night, according to an analysis of sleep data from a prospective cohort study of more than 10,000 British civil servants.

The findings were recently presented at a meeting of the British Sleep Society, and the research article has been accepted for publication in the journal Sleep (www.journalsleep.org/Accepted.aspx).

The investigators found that a decrease in the amount of time slept was associated with increased mortality from cardiovascular causes. Furthermore, an increase in sleep time was associated with an excess of mortality from all other causes, according to Jane Ferrie, Ph.D., of University College London, and her colleagues.

Previous studies have reported a U-shaped relationship between time sleeping and mortality, the investigators said. What has not been looked at by a sleep study before is the effect a change in sleep patterns might have.

The researchers examined sleep data collected from British civil service employees aged 35-55 years who were enrolled beginning in 1985 in a long-term study known as Whitehall II. Baseline sleep duration data were

See **Sleep Duration** • *page 17*

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COPD Burden Assessed

Global Toll • *from page 1*

prevalence rates, ranging between 0.6% and 4% in men and 0.2% and 3.2% in women, although "the general perception is that these estimates are not accurate," according to Dr. E.F.M. Wouters, FCCP, of University Hospital Maastricht (the Netherlands) in an accompanying commentary. "Further quantification of the burden of COPD is, therefore, crucial" for public health planning, Dr. Wouters added.

The researchers wrote that their findings suggest that international public health officials need to prepare for a higher disease burden in the future. "Our estimates of the overall prevalence and staging of COPD are consistently higher than these figures, which accord with claims that COPD has generally been underestimated in the past," they said.

The authors found that the prevalence of stage II or higher COPD was greatest Cape Town (22% among men and 17% among women). Men in Cape Town also had the highest proportion of subjects who had smoked 20 or more pack-years (34%), but Cape Town women were only third in that ranking.

Researchers cautioned that the small number of subjects at each test site (minimum 300 men and 300 women) prevented within-site analysis because of the low absolute number of COPD patients at each site. In addition, they noted that Lexington, Ky., and Vancouver, B.C., had low response rates because they recruited patients through random-digit dialing, a weakness that could have introduced some bias.

A second Lancet study on the risk of COPD from passive smoking in China found that adults at the highest exposure levels have increased odds of developing COPD, according to Peng Yin of the University of Birmingham (England) and colleagues (Lancet 2007;370:751-7).

The survey of 6,497 members of a Guangzhou, China, community social and welfare association for people older than age 50 years found significantly elevated odds of COPD among subjects who never smoked if they were exposed to more than 40 hours a week of passive smoke for more than 5 years at home (adjusted odds ratio 1.6), work (OR 1.5), or combined work and home (OR 1.48).

"This study adds fuel to the controversy, showing that passive smoking might also have a role," wrote Dr. Ana B. Menezes and Dr. Pedro C. Hallal of the Universidade Federal de Pelotas (Brazil) in an accompanying commentary. ■

Routine ICU Epo Use Not Supported

Epoetin • *from page 1*

The proportion of patients who received a red cell transfusion between days 1 and 29, the primary end point, was 46% among those who received epoetin and 48% among those who received placebo. The mean number of red cell units transfused per patient between days 1 and 42, a secondary end point, also was similar among those on epoetin (4.5 U) and those on placebo (4.3 U).

The change in hemoglobin concentration from baseline, another secondary end point, increased significantly more among those on epoetin at day 29, when it was 1.6 g/dL higher, compared with 1.2 g/dL higher among those on placebo, a significant difference. The absolute hemoglobin value at day 29—11.2 g/dL versus 10.8 g/dL—was also significantly higher among those on epoetin. But at day 42, the differences in hemoglobin concentrations between the two groups were no longer significantly different.

At day 29, mortality in the overall population was significantly lower among those on epoetin (8.5%) than among those on placebo (11.4%). Among the trauma patients, mortality was 3.5% among those treated with epoetin and 6.6% among those on placebo, also a significant difference. Mortality followed a similar pattern at 140 days. The mortality difference was the most important finding of the study, the authors said.

Among those on epoetin alfa, the incidence of thrombotic vascular events through 140 days was significantly higher among those who received three doses of epoetin (23%, compared with 16% for those who received three placebo doses). A greater proportion of patients who received one and two doses of epoetin had thrombotic events, compared with those who received one and two doses of placebo, but those differences were not significant.

The study hypothesis was that the use of epoetin alfa would improve clinical outcomes by preventing adverse events with red blood cell transfusions, but "this was clearly not the case," the authors said, and pointed out that mortality was reduced, despite the lack of an effect on transfusions.

On the basis of available data, "we believe that epoetin alfa could benefit trauma patients remaining in an ICU for more than 48 hours," who have hemoglobin concentrations under 12 g/dL and no history of thrombotic disease, and who meet other inclusion criteria of their study.

Until more studies are done, the data suggest that epoetin alfa should not be used in a patient who has not spent at least 48 hours in the ICU, they added.

In an editorial, Dr. Deborah Cook and Dr. Mark Crowther, of the department of medicine at St. Joseph's Healthcare, McMaster University, Hamilton, Ont., said that it was "tantalizing but premature" to suggest that treatment with epoetin alfa could save the lives of trauma patients who have hemoglobin concentrations below 12 g/dL, have been in the ICU for at least 48 hours, and have no renal insufficiency or history of venous thromboembolism.

The absolute difference in the number of trauma patients who had died at day 29 and 140 was small, "and is insufficient to provide support for the routine use of erythropoietin in practice," they wrote (N. Engl. J. Med. 2007;357:1037-9).

The Procrit brand of epoetin alfa was used in the study. Four of the study authors were from Johnson & Johnson Pharmaceutical Research and Development, which sponsored the study. Several of the authors disclosed that they received consulting and/or lecture fees from Ortho Biotech and/or Johnson & Johnson Pharmaceutical Research and Development. Drs. Cook and Crowther reported no ties to the manufacturer. ■

Dr. Stephen Pastores, FCCP, comments: *Given that epoetin alfa did not reduce the incidence of red cell transfusion (in the context of a restrictive transfusion strategy) and its association with an increased risk of thrombotic events, the routine use of epoetin alfa cannot be recommended in the critically ill. Furthermore, the finding of a decreased mortality among trauma patients treated with epoetin alfa must be interpreted cautiously, because of the small absolute difference in the number of deaths between the placebo group and the epoetin alfa group.*

IN THIS ISSUE

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Predictive Markers Useful in Scleroderma Lung Disease

BY NANCY WALSH
Elsevier Global Medical News

BARCELONA — Following three serum markers of disease activity could provide a simple, noninvasive means of monitoring the efficacy of cyclophosphamide in patients with systemic sclerosis who develop interstitial pneumonia, according to the results of a new study.

Interstitial pneumonia develops in more than 50% of patients with systemic sclerosis and is the major cause of death in this condition. Findings from a double-blind trial of cyclophosphamide plus corticosteroids demonstrated significant benefits in improving scleroderma lung disease (N. Engl. J. Med. 2006;354:2655-66).

However, thus far no means of monitoring treatment response have been established, according to Dr. Chihiro Tanaka of Kanazawa (Japan) University.

Serum levels of surfactant protein-A (SP-A) and SP-D have been reported to reflect disease activity in interstitial lung diseases such as idiopathic pulmonary fibrosis and pulmonary proteinosis, Dr. Tanaka wrote in a poster session at the annual European College of Rheumatology.

Surfactants are proteins secreted by type II alveolar cells that help maintain the elasticity of pulmonary tissue. SP-D also plays an important role in the innate immune system in the lungs (J. Rheumatol. 2004;31:1112-20).

The third marker, KL-6, is a glycoprotein antigen expressed primarily on type II pneumocytes in the alveoli and on respiratory bronchiolar epithelial cells. Elevations of this antigen have been observed in multiple types of interstitial lung diseases, including idiopathic interstitial pneumonia, hypersensitivity pneumonia, and sarcoidosis.

Concentrations of KL-6 also have been shown to be higher among patients with systemic sclerosis who have pulmonary fibrosis, compared with scleroderma patients without lung involvement (J. Rheumatol. 2000;27:930-4).

In Dr. Tanaka's study, 16 adult patients with systemic sclerosis and interstitial pneumonia each underwent six monthly cycles of cyclophosphamide pulses in doses of 15 mg/kg, plus oral prednisolone, 10-30 mg/day.

They were classified as having active interstitial pneumonia based on analysis of bronchoalveolar lavage fluid and high-resolution computed tomography (HRCT). Response to treatment also was evaluated by HRCT, and the findings correlated with serum levels of SP-A, SP-D, and KL-6.

The 10 patients who showed improvements on HRCT after six cycles of cyclophosphamide also showed decreases in KL-6 and SP-A, Dr. Tanaka noted.

Among the four patients whose HRCT findings did not change following treatment, serum levels of KL-6, SP-D, and SP-A also did not change.

TAKEN TOGETHER, THESE THREE MARKERS COULD PROVIDE A WAY OF EVALUATING RESPONSE TO CYCLOPHOSPHAMIDE TREATMENT.

In the two patients whose HRCT findings worsened, serum levels of KL-6 and SP-D increased rapidly until the third cycle, while SP-A levels did not change.

Taken together, these three markers could provide a way of evaluating response to cyclophosphamide treatment that is less expensive and noninvasive, compared with HRCT and bronchoalveolar lavage, he concluded. SP-D may prove to be the most sensitive, he added.

Possible mechanisms for the elevation of these markers in patients with scleroderma-associated lung disease include increases in total numbers of type II cells and increased secretion by each type II cell, as well as increased leak from the airspace into the interstitium and decreased clearance from the vascular compartment (Eur. Respir. J. 2002;19:439-46). ■

Dr. Susan Harding, FCCP, comments: *These preliminary data need to be supported with a large cohort. The Scleroderma Lung Study examined the effect of 1 year of oral cyclophosphamide on scleroderma lung disease, showing a limited beneficial effect (N. Engl. J. Med. 2006;354:2655-66). Tashkin and colleagues recently reported their outcomes at 2 years, showing continued beneficial effects on pulmonary function through 18 months, which then dissipated (Am. J. Respir. Crit. Care Med. 2007; Aug 23, ePub ahead of publication). Maybe the investigators of the Scleroderma Lung Study could carefully examine these biomarkers' ability to predict improved pulmonary function in these patients with cytoxan. Meanwhile, polymorphisms impacting the transcription of connective tissue growth factor (CTGF) was a risk factor for fibrosing alveolitis in scleroderma patients (N. Engl. J. Med. 2007;257:1215-20), giving us new insight into the pathogenesis and potential new targets for treatment of this life-threatening disease.*

Idraparinux Was Effective For DVT, but Not for PE

BY MARY ANN MOON
Elsevier Global Medical News

The synthetic pentasaccharide idraparinux was as effective as standard anticoagulant treatment in preventing short-term recurrences of deep vein thrombosis but not short-term recurrences of pulmonary embolism in a worldwide clinical trial comparing the two approaches.

When idraparinux therapy was extended for a further 6 months, it prevented long-term recurrences of both types of thromboembolism, but raised the risk of hemorrhage to such a degree that the net clinical benefit was deemed "marginal," researchers said.

Idraparinux is a long-acting inhibitor of activated factor X with a substantially longer half-life than the related anticoagulant fondaparinux. Its advantage over standard anticoagulation therapy in venous thromboembolism (VTE) is that it is administered in once-weekly subcutaneous injections at a fixed dose that doesn't require any adjustment or laboratory monitoring.

Dr. Harry R. Buller of the University of Amsterdam and his associates in the van Gogh studies, evaluated idraparinux for VTE at 145 medical centers in 25 countries. The studies were funded by the drug's manufacturer, Sanofi-Aventis.

The first report involved two parallel randomized open-label trials comparing the efficacy and safety of idraparinux with those of standard anticoagulant therapy in patients with deep vein thrombosis (2,904 subjects) or pulmonary embolism (2,215 subjects). The patients were treated for 3-6 months.

For the DVT patients, the incidence of recurrent thromboembolism was similar with idraparinux as with standard therapy. However, the drug's efficacy was inferior to that of standard therapy for PE. "This difference in efficacy was due to an excess of early fatal and nonfatal recurrences of PE and was associated with an increase in total mortality," Dr. Buller and his associates said (N. Engl. J. Med. 2007;357:1094-104).

"A plausible explanation for the observed differences is lacking, especially since many patients with DVT probably had concurrent asymptomatic PE," they noted.

Adverse bleeding event rates with idraparinux were similar to or lower than those with standard therapy.

"Another factor that was not specifically addressed in these two trials, but which should be considered in evaluating the risks and benefits of idraparinux, is the absence of a specific antidote for this anticoagulant that could be administered during bleeding. … [This] is a particular liability for an agent with such a long duration of action," the van Gogh investigators pointed out.

In the second report, Dr. Buller and his associates evaluated an additional 6 months of prophylaxis using idraparinux compared with placebo. The 1,215 subjects were followed for a further 3-6 months after discontinuing the drug.

Idraparinux reduced the frequency of recurrent thromboembolism to 1%, compared with nearly 4% for placebo, for a relative risk reduction of 73%. However, there was an excess of major bleeding episodes, including fatal hemorrhages, with the drug—an overall rate of nearly 3%, compared with no such episodes in the placebo group.

"These observations suggest a prolonged risk of hemorrhage in patients treated with idraparinux for more than 6 months," the investigators said (N. Engl. J. Med. 2007;357:1105-12).

This trial "showed the efficacy of idraparinux during a 6-month extended treatment period, at the expense of an increased risk of bleeding. We conclude that the net clinical benefit of such treatment is marginal," they noted. ■

PAH Drug Sitaxsentan Faces Uncertain Approval Future in United States

The manufacturer of sitaxsentan continues to pursue U.S. approval of the endothelin receptor antagonist for treating pulmonary arterial hypertension, after receiving its third notice from the Food and Drug Administration that the supporting application lacked evidence of effectiveness.

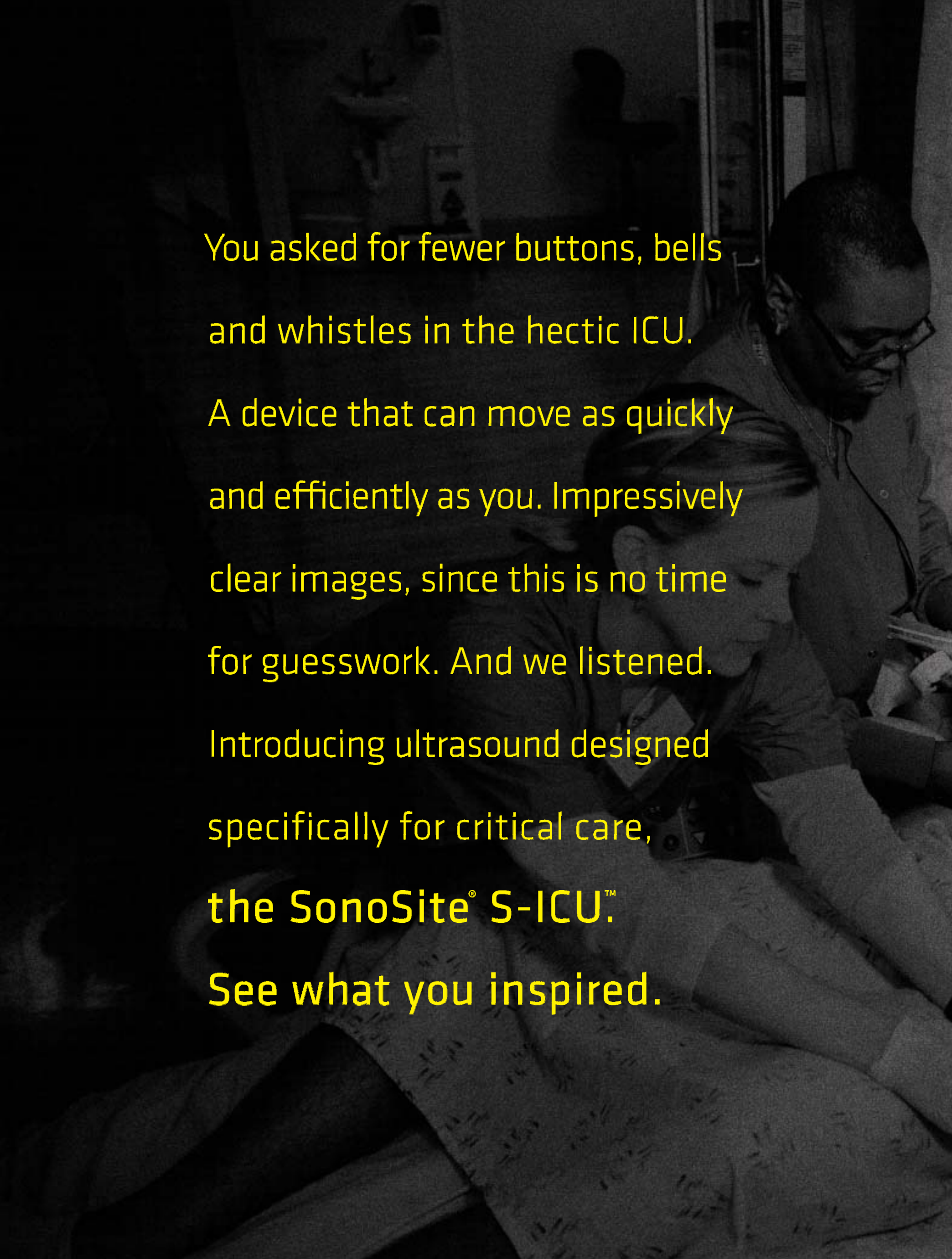
The FDA has been reviewing sitaxsentan for treating pulmonary arterial hypertension (PAH). But in June, manufacturer Encysive announced that it had received a third "approvable" letter for the drug from the FDA, stating that the drug's effectiveness had not been demonstrated, but that there was some evidence of improved exercise tolerance and that the company should conduct another trial.

In response to the company's subsequent request for a formal dispute resolution on the new drug application (NDA), the FDA reviewer "agreed with the decision of the Division of Cardiovascular and Renal Products that, while the data provided in the NDA are suggestive of the effectiveness of [sitaxsentan], it did not provide the substantial evidence of effectiveness needed for approval," the company announced in September. The reviewer encouraged the company to conduct another study to show the drug's effectiveness in exercise capacity, as measured by the change in 6-minute walk distance.

The company is working with outside clinical and statistical experts to develop another phase III study protocol, "so we can move ahead quickly with a new trial if it is ultimately required for approval in the United States," George Cole, president and chief executive officer of Encysive, said in a statement. "We continue to believe that the issue raised by the FDA was sufficiently addressed in the NDA." Sitaxsentan is approved for treating PAH in Europe, Canada, and Australia.

If approved, sitaxsentan would be the seventh drug approved by the FDA for treating PAH; the sixth was the endothelin receptor antagonist ambrisentan (Letairis) approved by the FDA in June.

—Elizabeth Mechcatie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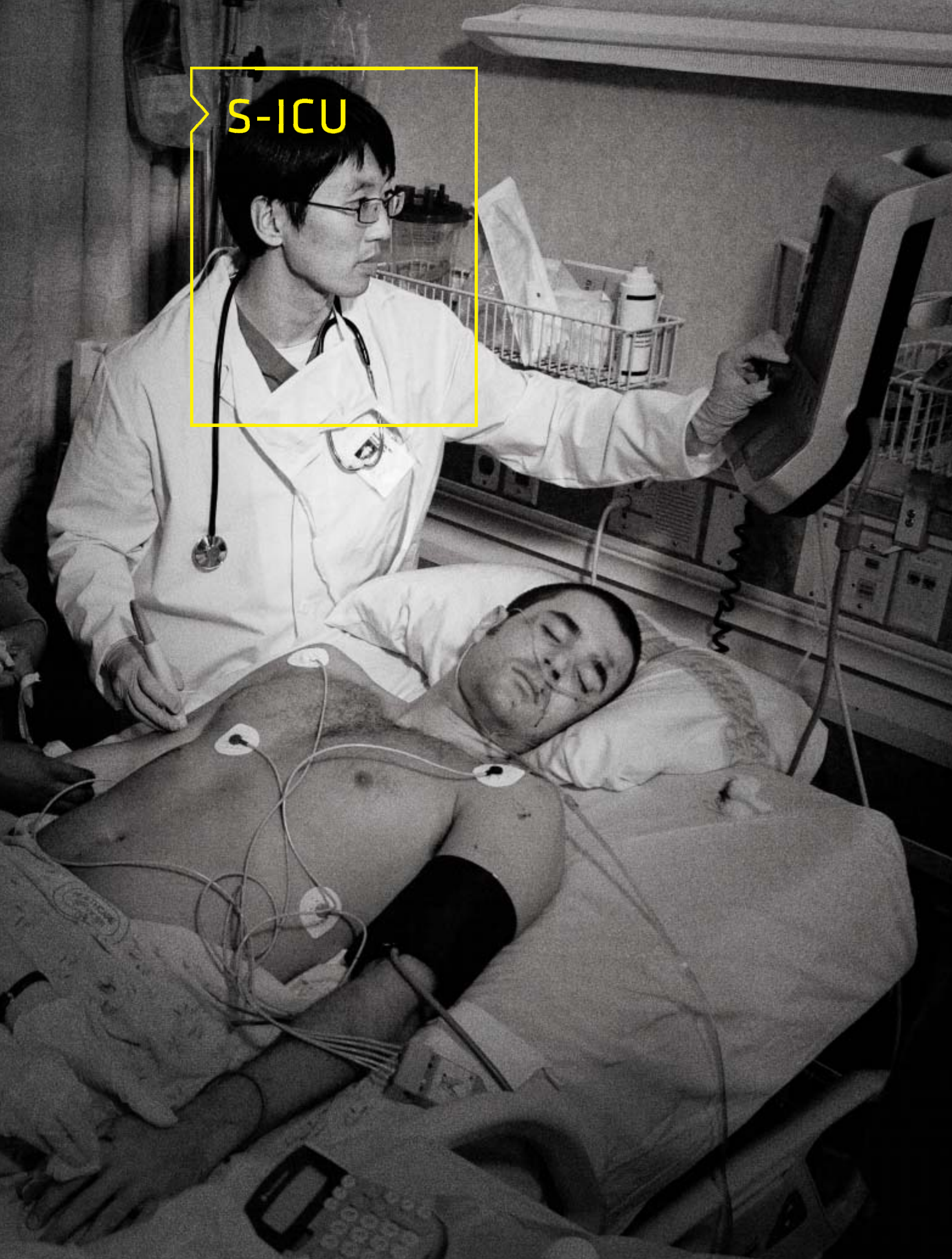
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Pulmonary Perspectives

New Guidelines for the Diagnosis and Management of Asthma—Will They Improve Care of Patients With Asthma?

"The Expert Panel recommends the use of multifaceted, clinician education programs that reinforce guidelines-based asthma care and are based on interactive learning strategies" (Evidence B). This quote from the section of the full report titled "Education for a Partnership in Asthma Care" highlights a discussion of the evidence supporting improvement and standardization in the quality of care given to people with asthma. An extensive literature search from 1997 through 2006 was undertaken to identify studies that focused on methods of implementing guideline-based practice. The process of implementation is designed to change the behavior of clinicians. Reasons for lack of adherence to guidelines were shown in an observational study (Cabana et al. *Arch Pediatr Adolesc Med* 2001;115:1057) that identified the barriers to pediatricians' adherence to asthma guidelines. Lack of time, lack of educational resources, lack of support staff, lack of feeling competent in educating patients with asthma, and, what they considered to be a major barrier, lack of reimbursement were all cited as reasons for not adopting guideline-directed care. The review of the literature identified that multifaceted clinician education programs based on interactive learning strategies can improve quality of care and patient outcomes. If the multifaceted, tailored intervention to the audience is not undertaken, the standard "guideline" talk, with or without feedback, is unlikely to promote change in general practice care.

Interactive learning strategies present a promising venue for moving forward to both improve and standardize care for all patients with asthma but require clinicians to participate in programs designed to enhance their skills in communicating with patients with asthma. In addition, the report recommends documenting the discussion with the patient, as well as the level of the patient's asthma control, at every visit. Search of the literature identified a lack of documentation of the content of medical visits for asthma, including a lack of information necessary to assess either asthma severity or asthma control.

The release of the first National Asthma Education and Prevention Program (NAEPP) clinical practice guideline in 1991 opened the door to a focused approach to evaluation and management of patients with asthma. To help health-care professionals bridge the gap between current knowledge and practice, the NAEPP of the National Heart, Lung, and Blood Institute (NHLBI) convened Expert Panels to prepare asthma guidelines. The charge to all three panels has been the same; develop a report that would provide a general approach to diagnosing and managing asthma based on current science. This third report, Expert Panel Report (EPR) 3, like the preceding two, is organized around four components of effective asthma management:

1. Use of an objective measure of lung function to assess the severity of asthma and to monitor the course of therapy.
2. Environmental control measures to avoid or eliminate factors that precipitate asthma symptoms or exacerbations.
3. Patient education that fosters a partnership among the patients, his or her family, and clinicians.
4. Comprehensive pharmacologic therapy for long-term management designed to reverse and prevent the airway inflammation characteristic of asthma, as well as pharmacologic therapy to manage asthma exacerbations.

An extensive literature review was conducted in three cycles over an 18-month period (September 2004 to March 2006, with additional major articles included until May 2007). The combined number of titles screened from these three cycles was 15,444, which did not include many titles identified by the panel members. Of these, 1,654 articles serve as a reference resource used to update the guidelines and are available on the NHLBI Web site. Evidence tables were prepared for selected topics to better assess the weight of the evidence. The Expert Panel agreed to specify the level of evidence used to justify the recommendations being made. Panel members only included ranking of evidence for recommendations they made based on the scientific literature reviewed. The system used to describe the level of evidence is as follows (Jadad et al. BMJ 2000; 320: 537):

Evidence Category A: Randomized controlled trials (RCTs), rich body of evidence with substantial numbers of studies with large populations participating.

Evidence Category B: RCTs, limited body of data. Evidence is from end points of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs, or meta-analysis of RCTs.

Evidence Category C: Nonrandomized trials and observational studies.

Evidence Category D: Panel consensus judgment. Clinical literature addressing the subject was insufficient to justify placement in one of the other categories but provision of some guidance was deemed valuable.

In addition to specifying the level of evidence to support any recommendation, the Expert Panel agreed to indicate the strength of the recommendation by using the term "is recommended." When the phrase "should, or may be considered," is used, this indicates the recommendation for application to clinical practice is less strong. This distinction was the panel's effort to address nuances of using the evidence ranking system. The process behind the development of EPR 3: Full Report 2007 included interpretation of the evidence, drafting of summary statements of the literature reviewed, reviewing comments from various external reviewers, and responding to queries raised during public review of a draft version from February through March 2007.

In summary, the process behind the NAEPP "Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma—Full Report 2007" represents the commitment and efforts of the NHLBI/NAEPP to produce evidence-based guidelines that are practical for clinicians to incorporate into their practices.

THIS ASTHMA GUIDELINE IS FOUNDED ON THE CONCEPTS OF SEVERITY AND CONTROL, WITH THE TWO DOMAINS OF IMPAIRMENT AND RISK ACTING AS 'BRIDGES' TO IMPROVED CARE.

Given the 3-year process for development of the new document and the difficulties of implementing asthma guidelines into practice, what is it that forms the foundation of the new document and can these concepts be incorporated into practice? This asthma guideline is founded on the concepts of severity and control, with the two domains of impairment and risk acting as "bridges" to improved care. The functions of assessing and monitoring patients with asthma are closely linked to these concepts of severity, control, and responsiveness to treatment:

Severity: the intrinsic intensity of the disease process. Severity is most easily and directly measured in a patient who is not currently receiving long-term control treatment.

Control: the degree to which the manifestations of asthma (symptoms, functional impairments, and risk of untoward events) are minimized and the goals of therapy are met.

Responsiveness: the ease with which control is achieved by therapy.

It is important to recognize that asthma severity, control, and responsiveness are linked together such that the goals of asthma therapy are identical for all levels of baseline asthma severity: to assist the patient in becoming well-controlled, which will minimize both the patient's impairment in the present and risk in the future.

Both asthma severity and asthma control are bridged by two domains: impairment and risk. Impairment is an assessment of the frequency and intensity of symptoms in the present, as well as the functional limitations that a patient is experiencing now or has recently experienced. Risk is an estimate of the likelihood in the future of either an asthma exacerbation defined as the need for a course of oral systemic corticosteroids, progressive irreversible loss of pulmonary function over time, or adverse response to medications.

The Expert Panel recommends that clinicians classify asthma severity using the domains of current impairment and future risk. Initial assessment of patients who have confirmed asthma begins with the severity classification, because the selection of type, amount, and scheduling of therapy should correspond to their asthma severity classification. This initial assessment of asthma severity should take place once the diagnosis has been confirmed. Assessment of the disease is made on the basis of the patient's recall of symptoms, as well as current spirometry results. No longer is peak flow monitoring encouraged for assisting in the diagnosis of the disease, given the enormous variability of its results. Peak flow may serve as a useful tool for monitoring trends in asthma control over time, especially in patients with moderate to severe asthma that is not well-controlled, patients with a history of severe exacerbations, or in patients who are poor perceivers of their airflow obstruction and worsening asthma symptoms.

Pre- and postbronchodilator spirometry is encouraged when considering the diagnosis; repeated once the patient's condition has stabilized while receiving therapy, which is usually at 3 to 4 months into therapy; during periods of progressive or prolonged loss of asthma control; and, at a minimum, every 1 to 2 years, depending on the patient's asthma control.

The components of current impairment include the following symptoms: daytime symptoms, nighttime awakenings, need for rescue inhalers (short-acting bronchodilators), interference with normal activities (work, school, recreational/athletic endeavors), and quality-of-life assessments. Quality of life assessments include any work or school missed because of asthma, any disturbance in sleep due to asthma, any change in caregivers' activities due to a child's asthma, and any reduction in usual activities. Evaluation of clinical trial data and observational studies has confirmed that the parameters for the impairment domain (symptoms, activity levels, and pulmonary function) reflect increasing gradients of severity, especially in studies of adults.

A closely related and second dimension of severity is the concept of future risk of adverse events, including exacerbations, irreversible loss of pulmonary function, risk of death, and risk of potential adverse response to medications. The assessment of risk in the future requires a careful medical history, observation, and clinician judgment. Although the classification of severity in EPR 3 focuses on the frequency of exacerbations, it is important to note that the severity of disease does not always correlate with intensity of exacerbations, which may vary from mild to life-threatening. Any patient with

Continued on following page

DR. GENE L. COLICE, FCCP
Editor,
Pulmonary Perspectives

AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

PRESIDENT'S REPORT

The President Says 'Farewell'

This is my final column as President of the ACCP, which calls for retrospection, analysis, a look ahead, and some reflection on what it has meant to me personally. One of the things I was told as "President Designate" was, "Mark, you have to have a theme" for the year as President. My first reaction can be summarized delicately here as, "Don't Make the ACCP Worse." The members will have to judge if the College is better, worse, or the same as last year. My "official" and loftier theme was about building teams to improve the College, our profession, and most of all, the care we give to our patients. I believe that we can look back and agree that we moved ahead in many areas, with some extraordinary successes and few backward steps. We also did it with team efforts and despite increasing government and regulatory scrutiny of professional organizations, contracting budgets, and increasing competition from other organizations.

BY DR. MARK J. ROSEN, FCCP

To me, the primary goal of the College is to offer the best education in the world in chest diseases, critical care, and sleep medicine. Here, we accomplished much in the last 2 years. The journal *CHEST* has a new look and new standards about what gets published. As a result, the journal is better than it ever was, and I believe that most of our clinician colleagues would agree that *CHEST* is the most important, relevant, and therefore valuable, peer-reviewed journal in our field. The Health and Science Policy Committee designed and implemented processes for developing evidence-based clinical practice guidelines that are recognized increasingly as the profession's standard. Our board review courses for pulmonary medicine and critical care medicine are already the best anywhere, and, this year, the College offered our second Sleep Medicine Board Review Course. Surpassing all expectations, this "sold out" course had an even higher attendance than the other two board reviews, and the evaluations were consistently outstanding, confirming the College's importance in sleep medicine and education.

The ACCP is on the verge of implementing some bold and innovative strategies to bring us to a different level as an educational organization. At CHEST 2007, we are introducing a new concept that clearly identifies each session's format, where it fits into our overall curriculum, and classifies it by the type of instruction and methodology used. You ask, "So what? I just come to hear good speakers on good topics." So you should, but our new approach will offer a variety of educational methods that provide interactive experiences and simulated clinical environments that are proven to be more effective than standard lectures. Starting with CHEST 2007, all ACCP CME certificates will be issued electronically after the attendee provides the feedback that we need to make these meetings even better. This is not a traditional CME certificate that only reflects the total hours attended. Rather, it also categorizes the hours by instructional methodology and specifies the hours linked to common areas required by state medical licensing requirements.

This year saw major progress in the College's use of simulation technology and instructional methods in our educational programs, and we will soon have a permanent simulation center at ACCP headquarters in Northbrook, IL. There, we will offer programs that will probably provide the most effective educational experiences anywhere. The ACCP embraced the use of ultrasonography in pulmonary and critical care medicine, and we ran our first large, hands-on course this year. It was so well received, that we will conduct similar courses regularly. We will work this year with our expert colleagues from France to develop standards for training in this important field.

Another major component of the College's work is to advocate for our patients and our profession. It was a good year here, too. The Patient-Focused Critical Care Enhancement Act was introduced into the Senate largely as a result of our efforts in collaboration with ATS, SCCM, and AACN. The Capitol Hill Caucus was well-attended and inspiring, as always, and we learned from political insiders more about the enormity of the problems with our "system" of health care and the importance of these issues in the upcoming presidential election. We also emerged with new knowledge that we need to focus our advocacy activities on issues that distinguish our members and our patients from others in medicine. Yes, we need to advocate forcefully to change the Medicare Sustainable Growth Rate formula that is driving physicians away from caring for patients, but we also need to advocate for (among other things) our patients' ability to use portable oxygen concentrators on all commercial airlines and for them to be covered under Medicare and Medicaid for pulmonary rehabilitation services. Our advocacy efforts will be planned and executed increasingly by collaboration among the ACCP Governors, Government Relations Committee, and Practice Management Committee.

The College's international efforts are also expanding. We are increasing our collaboration with the major international professional organizations and some national societies to improve education and patient care. Our international Regents and Governors are calling for more programs outside of North America and an increased role in the operations of the College; in response, we constituted a strategic planning group that will meet soon to plan for these efforts.

The ACCP does many great things, and putting it together involves many disciplines working in complex relationships. All of the College's accomplishments are attributable to the forward thinking and intense effort by teams of ACCP staff and our volunteer members. The individuals who comprise these teams are paragons of commitment, ability, and innovation. We also manage somehow to accomplish this as friends. Speaking for myself, I look forward to every project I work on with others at the College. Dr. Alvin Thomas will assume the challenges, responsibilities, and satisfaction that come with being ACCP President, and I wish him the best.

On reviewing this manuscript, it looks more like a "State of the Union" than a "Farewell to the Troops." Rightly so, because I'm not leaving—working with the College is one of the most fulfilling things that any of us can do. I will stay on to work with all of the wonderful staff and members as long as I can. Starting immediately, and for the next few years, I am delighted to have the opportunity to become more active in the efforts of the Education Committee. See you around. ■

Continued from previous page

asthma, even intermittent asthma, can have a severe exacerbation. This is why the new guideline removed the term "mild" intermittent and replaced it with "intermittent," which should emphasize that patients at any level of severity are at risk for severe, life-threatening exacerbations. The frequency of exacerbations requiring oral systemic corticosteroids has been correlated in observational studies with the designation of persistent, rather than intermittent asthma. Utilizing the frequency and intensity of exacerbations has been incorporated into the classification of severity in this document. For all age groups, the more frequent and intense the exacerbation, the greater the degree of underlying disease severity. All figures on severity in the document include a detailed discussion on this issue in the "note" section of the figure.

Once severity is determined using the domains of impairment and risk during the patient's initial presentation, appropriate medication and other therapeutic interventions are initiated. Classifying severity is emphasized for initiating therapy. The emphasis thereafter for clinical management is changed to the assessment of asthma control. The level of asthma control will be used to monitor and guide all future decisions to either maintain or adjust therapy. This is in sharp contrast to the previous asthma guidelines that raised questions about applying the severity classifications once treatment was established and resulted in placing more emphasis on severity rather than on the ongoing monitoring of whether the goals of asthma therapy were being met. This new guideline, EPR 3, clarifies this important issue.

The level of asthma control (well-controlled, not well-controlled, or very poorly controlled) is the degree to which both dimensions of the manifestations of asthma impairment and risk are minimized by therapeutic intervention. The level of control should be evaluated at all future visits and will determine therapeutic options, including maintaining or adjusting therapy, *ie*, step-up or step-down. Asthma control is defined by both (1) reducing impairment: preventing chronic and troublesome symptoms, decreased use of rescue inhalers, normal or (near) normal pulmonary function, maintaining normal activity levels, and meeting patient and family expectations of and satisfaction with care; and (2) reducing risk: prevent recurrent exacerbations of asthma and minimize need for ED visits or hospitalizations and prevent progressive and irreversible loss of lung function; for children, prevent reduced lung growth and provide optimal pharmacotherapy with minimal or no adverse effects.

There is a great deal more in this new guideline that emphasizes the education for a partnership in asthma care between the clinician, the patient, and the family, with multiple points of care defined as opportunities to educate the patient and family. In addition, there is a strong recommendation for all patients with asthma to have a written asthma action plan that includes instructions for daily management, as well as recognizing and handling worsening asthma, including the self-adjustment of medications in response to acute symptoms or changes in peak flow measurements if being performed.

In the section on medications, there is an extensive discussion on the role of long-acting bronchodilators in persistent asthma. "In the opinion of the Expert Panel, the beneficial effects of LABA in combination therapy for the great majority of patients who require more therapy than low-dose ICS alone to control asthma (i.e., require step 3 care or higher) should be weighed against the increased risk of severe exacerbations, although uncommon, associated with the daily use of LABAs (see discussion in text)." ■

Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma is available at www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm.

Dr. Stuart W. Stoloff
Clinical Professor of Family & Community Medicine
University of Nevada School of Medicine
Reno, NV
Member of Expert Panel Report 3
NIH/NHLBI/NAEPP Guidelines for the Diagnosis and Management of Asthma

NEWS FROM THE COLLEGE

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PRACTICE MANAGEMENT NEWS

Updated Surgery Report

ACS Issues 2007 Edition of *Physicians as Assistants at Surgery*

The American College of Surgeons (ACS) has issued the fourth edition of *Physicians as Assistants at Surgery*, a report developed in cooperation with 22 other surgical specialty organizations.

The report reflects the consensus opinion of the surgical specialties about whether a physician, as an assistant, is required "almost always," "some of the time," or "almost never" for each surgical procedure listed in the American Medical Association's *Current Procedural Terminology® (CPT) 2007*.

Surgeons who are appealing claims denials for these procedures often rely on this resource. Health insurance companies also frequently refer to the report to inform reimbursement policies for assistants at surgery.

As indicated in the report, ACS maintains that health insurers should reimburse all medically necessary services.

An indication that a physician would "almost never" be needed for some procedures does *not* imply that a physician is never needed. ACS acknowledges that it may be necessary to use nonphysicians (*eg*, physician's assistants or surgeon's assistants with additional surgical training, registered nurses with specialized training) to assist in operations, depending on local resources and individual patient needs.

The *Physicians as Assistants at Surgery* report is available on the ACS Web site at www.facs.org/ahp/pubs/2007physasstsurg.pdf. ■

NSF Pickwick Postdoctoral Fellowship Is Now Open

As part of its ongoing commitment to advancing sleep research, the National Sleep Foundation (NSF) is pleased to offer the NSF Pickwick Postdoctoral Fellowship and invite interested candidates to apply!

This fellowship supports researchers pursuing careers in basic, clinical, and applied sleep research.

The application deadline is November 1, 2007. Funding begins July 2008.

Since 1996, the NSF Pickwick Fellowship program has funded more than 30 young investigators who have gone on to have exemplary and thriving research careers.

We encourage you to share this information with potential candidates, colleagues, and others who may be interested.

For more information about the fellowship, visit www.sleepfoundation.org/pickwick, or contact Jessica Steinitz at jsteinitz@sleepfoundation.org. Thank you for your support! ■

National Sleep Foundation

NATIONAL SLEEP FOUNDATION

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2007-08

November 15 - 18, 2007
2007 Pulmonology Update: A joint meeting of the SPOI, SATS, and ACCP
Cape Town, South Africa

November 30 - December 4, 2007
12th Congress of the APSR; 2nd Joint Congress of the APSR/ACCP
Queensland, Australia

December 6 - 9, 2007
Meeting Post-CHEST SBPT/ACCP
Araxa, Brazil

December 7 - 9, 2007
Ultrasonography: Fundamentals in Critical Care
Scottsdale, Arizona

January 10 - 13, 2008
Sleep Medicine 2008
Scottsdale, Arizona

April 4 - 6, 2008
Celebration of Pediatric Pulmonology 2008
Weston, Florida

April 11 - 13, 2008
Ultrasonography: Fundamentals in Critical Care
St. Louis, Missouri

August 22- 25, 2008
ACCP Sleep Medicine Board Review Course
Orlando, Forida

August 22- 26, 2008
ACCP Critical Care Board Review Course
Orlando, Forida

August 27- 31, 2008
ACCP Pulmonary Board Review Course
Orlando, Forida

October 25 - 30, 2008
CHEST 2008
Philadelphia, Pennsylvania

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EducationCalendar

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NEWS FROM THE COLLEGE

ACCP Releases Lung Cancer Guidelines

The American College of Chest Physicians (ACCP) has released new evidence-based lung cancer guidelines in hopes that an updated series of recommendations will assist physicians in achieving the best possible outcomes for their patients. Published as a supplement to the September issue of *CHEST* (www.chestjournal.org), the guidelines cite that there is little evidence to show lung cancer screening impacts mortality in patients, including those who are considered at high risk for the disease, and recommend against use of low-dose computed tomography (LDCT) for general screening of lung cancer.

"Even in high risk populations, current research does not show that lung cancer screening alters mortality outcomes," said Dr. W. Michael Alberts, FCCP, co-chair of the ACCP lung cancer guidelines and Chief Medical Officer, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL. "We hope that one day, we can find a useful and accurate tool for general lung cancer screening, but, at this time, the evidence does not support the use of LDCT screening."

Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition) provides 260 comprehensive recommendations related to lung cancer prevention, screening, diagnosis, staging, and medical and surgical treatments. The guidelines also include new recommendations related to bronchioloalveolar carcinoma (BAC), often seen in nonsmokers, and updated recommendations related to adjuvant chemotherapy after surgical resection and the diagnosis and treatment of solitary pulmonary nodules. Listed below are a few of the new recommendations.

Screening

Due to the lack of supporting evidence, the guidelines recommend against the use of LDCT, chest radiographs, or single or serial sputum cytologic evaluation for lung cancer screening in the general population, including smokers or others at high risk, except in the context of a well-designed clinical trial.

"Population screening for lung cancer is not recommended and may, ultimately, put the patient at risk for further complications," said Dr. Gene L. Colice, FCCP, vice chair of the ACCP lung cancer guidelines and Director, Pulmonary, Critical Care, and Respiratory Services, Washington Hospital Center, Washington, DC. "Nodules are commonly found during screening; however, to determine whether they are cancerous requires additional testing, which is fairly invasive and extensive. This may cause the patient needless risk, both physically and psychologically."

Bronchioloalveolar Carcinoma

For the first time, the guidelines include recommendations on the diagnosis, prognosis, and treatment of BAC. Recommendations suggest that although staging, diagnosis, and treatment are the same for BAC as for other histologic subtypes of non-small cell lung cancer (NSCLC), additional treatment options for patients with BAC exist that may prove to be equivalent, if not more effective, including sublobar resection and the use of epidermal growth factor receptor-targeted agents.

Adjuvant Chemotherapy

Previous recommendations did not support postoperative chemotherapy for Stage I or Stage II NSCLC. However, the new guidelines support the use of platinum-based

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adjuvant chemotherapy for patients with completely resected Stage II NSCLC who have good performance status. The change in the recommendation was prompted by new research showing adjuvant therapy significantly reduced the risk of death in patients with Stage II NSCLC.

Solitary Pulmonary Nodules

The new recommendations outline a specific algorithm for the evaluation and management of solitary pulmonary nodules. They also stress the value of risk factor assessment, the utility of imaging tests, the need to weigh the risks and benefits of different management strategies, and the importance of obtaining patient preferences.

The recommendations were rigorously developed and reviewed by 100 multidisciplinary panel members, including pulmonologists, medical oncologists, radiation oncologists, thoracic surgeons, integrative medicine specialists, oncology nurses, pathologists, health-care researchers, and epidemiologists.

The guidelines were further reviewed and approved by the ACCP Thoracic Oncology NetWork, the Health and Science Policy Committee, the Board of Regents, and external reviewers from the journal *CHEST*. The guidelines have been endorsed by the American Association for Bronchology, American Association for Thoracic Surgery, American College of Surgeons Oncology Group, American Society for Therapeutic Radiology and Oncology, Asian Pacific Society of Respirology, Oncology Nurses Society, The Society of Thoracic Surgeons, and the World Association of Bronchology. ■

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NEWS FROM THE COLLEGE

Be 'Aware' in November of COPD and Lung Cancer

November is designated as both Lung Cancer Awareness Month and COPD Awareness Month, and the ACCP urges you to participate in related activities. These national and international observances offer patients, families, physicians, and health-care advocates a wide range of opportunities to heighten awareness, stress prevention, and help improve patient care and treatment for these diseases.

World COPD Day is held on Wednesday, November 14. This year's theme is "Breathless, not Helpless."

The 31st Annual Great American Smokeout will be celebrated on the following day, Thursday, November 15. The daylong event was first held in 1977 and is sponsored by the American Cancer Society. Its goal is to get smokers to quit by challenging them to remain cigarette-free for 24 hours.

While these two events provide a great opportunity to get involved, remember that the lung cancer and COPD awareness campaigns last all month. The ACCP and The CHEST Foundation have developed a series of products and resources to help you support the fight against lung cancer and COPD. To learn more, visit www.chestnet.org. ■

NEWS FROM THE COLLEGE

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This Month in *CHEST*: Editor's Picks

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

▶ **Association of RBC Transfusion With Mortality in Patients With Acute Lung Injury.** *By Dr. G. Netzer, FCCP, et al*

▶ **Contralateral Recurrence of Primary Spontaneous Pneumothorax.** *By Dr. T-W. Huang, et al*

▶ **Topics in Practice Management: Interfacility Transport of the Critically Ill Pediatric Patient.** *By Dr. S. J. Ajizian; and Dr. T. A. Nakagawa*

▶ **No Difference in Risk for Thrombocytopenia During Treatment of Pulmonary Embolism and Deep Venous Thrombosis With Either Low-Molecular-Weight Heparin or Unfractionated Heparin: A Metaanalysis.** *By Dr. T. A. Morris, FCCP, et al*

▶ **Assessing Future Need for Acute Care in Adult Asthmatics: The Profile of Asthma Risk Study: A Prospective HMO-Based Study.** *By Dr. M. L. Osbourne, FCCP, et al*

www.chestjournal.org

Editor's Note—Watch for It

CHEST Participates in an International Collaboration

The Council of Science Editors has organized a Global Theme Issue on Poverty and Human Development to "raise awareness, stimulate interest, and stimulate research into poverty and human development." *CHEST* is one of over 220 biomedical journals to agree to participate in this endeavor, with a common publication date on or after Monday, October 22, 2007. *CHEST* is publishing in its November issue an editorial that highlights the work of the ACCP and The CHEST Foundation in poverty and human development; special features focus on indoor air pollution and child mortality, socioeconomic status and lung function, and technology in developing countries. *CHEST* also is publishing original research on chronic bronchitis associated with the use of biomass fuel. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

Dr. Petty Tribute at the Making a Difference Awards Dinner

A special reception and tribute are being held in honor of Thomas L. Petty, MD, Master FCCP, at the ninth annual Making a Difference Awards Dinner on Saturday, October 20, 2007, at the Chicago Cultural Center, in Chicago.

The CHEST Foundation, and Platinum Exclusive Sponsor, Boehringer Ingelheim Pharmaceuticals, Inc., is hosting the Thomas L. Petty, MD, Master FCCP VIP Reception, which precedes the dinner.

The private reception is being attended by physicians who were trained by Dr. Petty, as well as upper level donors to the Thomas L. Petty, MD, Master FCCP Endowment in Lung Research and Making a Difference Awards Dinner sponsors at the Bronze Sponsorship level and above.

The tribute paid to Dr. Petty during the Making a Difference Awards Dinner is highlighting Dr. Petty's dedication and accomplishments to further lung health and research and his personal interest in improving patient care.

The Thomas L. Petty, MD, Master FCCP Endowment in Lung Research is The CHEST Foundation's way of continuing to express admiration and appreciation for Dr. Petty's outstanding work.

Your donation to this important endowment fund will support, in perpetuity, lung research and the improvement of care for patients with respiratory diseases.

Visit The Foundation's Web site at www.chestfoundation.org for more information on how to contribute, or contact Teri Ruiz at truiz@chestnet.org or (847) 498-8308. ■

Comings and Goings—CHEST Foundation Board

Six CHEST Foundation board members are rotating off the board this year and are being recognized during The CHEST Foundation's meeting at CHEST 2007 for their exceptional support and service to The Foundation during the past 4 years.

A number of areas within The Foundation have been strengthened by the outstanding work of these Board members, and The Foundation is grateful for their commitment of time and financial resources that will enable The Foundation to build on the momentum they were so much a part of creating.

The Foundation sincerely thanks the following trustees for their service from 2003 to 2007:

- Dr. Joseph P. Lynch III, FCCP
- Dr. Praveen N. Mathur, FCCP
- Dr. Richard A. Matthay, FCCP
- COL John P. Mitchell, MC, USAF, FCCP
- Dr. M. Patricia Rivera, FCCP
- Dr. Jorge E. Sinclair Avila, FCCP

The CHEST Foundation Board of Trustees also welcomes those newly nominated:

- Dr. W. Michael Alberts, FCCP
- Dr. Vera A. DePalo, FCCP
- Dr. Naresh A. Dewan, FCCP
- Dr. Susan Harding, FCCP
- Dr. Darcy D. Marciniuk, FCCP
- Dr. Charlie Strange, FCCP

CT Reading Tips Sharpen Diagnosis in Potential PE

Multidetector CT imaging is a good second test to provide more information.

BY KERRI WACHTER
Elsevier Global Medical News

WASHINGTON — CT imaging can be a useful tool to distinguish pulmonary embolism from other conditions with similar symptoms, provided you're familiar with some of the common pitfalls, Dr. J. Jeffrey Carr, a professor of radiologic sciences and public health sciences at Wake Forest University, Winston-Salem, N.C., said at the annual meeting of the Society of Cardiovascular Computed Tomography.

The symptoms of pulmonary embolism (PE) are well known: a sudden onset of dyspnea, tachypnea, pleuritic chest pain, and fainting, said Dr. Carr. Unfortunately, these symptoms are often common in patients without PE.

D-dimer assays are usually the first test used to diagnose PE. D-dimer is a degradation product produced by plasmin-mediated proteases of cross-linked fibrin, which increases with thrombosis. It's important to know whether your institution uses the latex agglutination assay or the enzyme-linked immunosorbent assay, Dr. Carr explained, because different cut points are used with each test.

"The key thing to realize with the D-dimer is that it's not useful in the inpatient population or for individuals that you think have an intermediate or high risk of pulmonary emboli," said Dr. Carr. Even in a population of patients at low risk, a quarter of the tests will be negative, which means that 75% of patients in this population will have indeterminate results.

Multidetector CT imaging is a good second test to provide more information. In an April 27, 2005, meta-analysis of studies that used a CT to rule out pulmonary embolism, researchers looked at the overall clinical validity. They identified 15 studies involving 3,500 patients (JAMA 2005;293:2012-7). They found that the negative predictive value of CT angiography of the pulmonary arteries was 99.4%. The authors concluded that the clinical validity of CT imaging to rule out PE is similar to that of conventional pulmonary angiography. Of note, this meta-analysis primarily included studies using single-slice CT.

"One of the real advantages … is that CT provides an [alternative diagnosis] in a significant percentage of people who come in to the CT suite," said Dr. Carr. Alternative diagnoses are made using CT in 25%-46% of cases. "That's very valuable, because it allows much more appropriate management."

These diagnoses include pneumonia, malignancies, pleural effusions, esophagitis, pericarditis, aortic dissections, and coronary artery disease. "Even if you don't do cardiac-gated CT in the emergency department but you are using a 64-slice scanner for the evaluation of pulmonary embolism, you will see a remarkable amount of coronary artery disease …that was unidentified simply because of the very high temporal resolution of even the ungated CT scan," said Dr. Carr.

In terms of common PE findings, "typically you're going to see more than one vessel involved; on average, you'll see three emboli somewhere in the pulmonary arterial circulation," said Dr. Carr. It's also common to find large thrombi located in the central or lobar branches.

Most emboli are nonocclusive. "So you'll see the clot kind of dangling there in the pulmonary artery with contrast surrounding it," said Dr. Carr. There is a greater prevalence of clots in the lower lobes because of the greater blood flow to the lower lobes. Most (58%) of PEs identified are in the lower lobes. The clots often end up being long and linear, and typically straddle bifurcations.

When viewed on CT cross-section, the intraluminal filling defect sometimes will have a doughnut-hole appearance. When the vessel in plane is imaged, the railway track appearance is often common. "You'll have a long clot within a vessel. Sometimes these can be completely occluded and you won't get contrast on either side of it, but typically you're going to see contrast on one side or the other," said Dr. Carr.

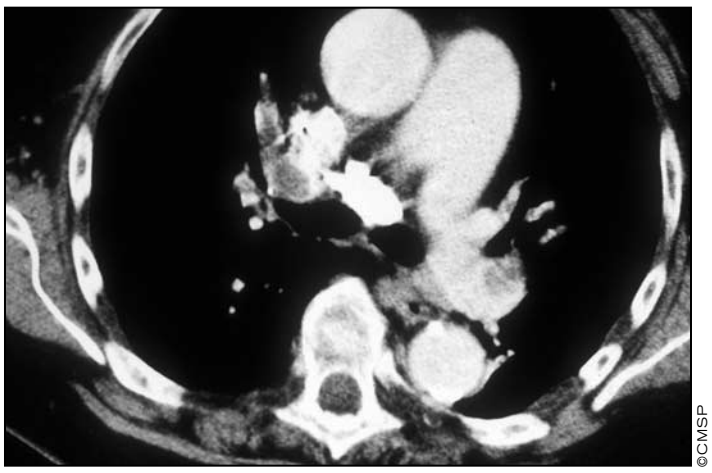
'ONE OF THE REAL ADVANTAGES … IS THAT CT PROVIDES AN [ALTERNATIVE DIAGNOSIS] IN A SIGNIFICANT PERCENTAGE OF PEOPLE WHO COME IN.'

When occlusion is complete, it's common to see the vessel cut off. "You'll be following a blood vessel—the pulmonary artery—and you'll see contrast, which will just disappear from an occlusive clot," said Dr. Carr.

"One of the things that many of us have learned is that there are lung findings associated with pulmonary emboli. Unfortunately, these are not terribly helpful in the diagnosis," said Dr. Carr. Both wedge-shaped opacities and linear bands have been shown to be significant findings in studies, but they are also relatively common in patients without PE. Likewise, pleural effusions and perfusion defects are not diagnostic.

When a CT is viewed, it's very important to view the vessels sequentially by following a vessel down. "If you see one suspected pulmonary [embolus], look at the rest of the pulmonary arteries, because you'll often see two, three, or four others involved in the distribution of the clot," said Dr. Carr.

There are numerous pitfalls to imaging the lungs, cautioned Dr. Carr. Motion defects are chief among these. Patients suspected of PE typically are short of breath and have difficulty holding their breath, which can pose a problem for imaging the lungs. However, the advent of multidetector-row CT has decreased the time necessary for patients to hold their breath.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A CT of the chest shows contrast in the pulmonary vessels and a clot in the right pulmonary artery.

Another key artifact is incomplete opacification of the pulmonary arteries. "You need to beware that you don't have good opacification of the pulmonary arteries and mistakenly call that a pulmonary [embolus]," said Dr. Carr.

Perhaps the largest imaging pitfall for physicians just starting out is a normal lymph node within the lung, said Dr. Carr. Lymph nodes can very closely simulate clots. Lymph nodes can be distinguished by tracing the vessels: Lymph nodes will lie adjacent to vessels, not inside them.

Mucus plugs can also be tricky. The key is to follow the bronchi up and down. "Identify that it's really a bronchus that's occluded and not a pulmonary artery," said Dr. Carr.

Extensive mucoid impaction can also occur. "The key thing is to remember that the bronchi and the pulmonary arteries travel together," said Dr. Carr. Trace these together to ensure you've identified them correctly.

It's also common to mistake the pulmonary vein for the pulmonary artery. Again, trace the vessels up and down. The pulmonary vein will tend to run more horizontally, "so you'll tend to have it in plane," said Dr. Carr.

Dr. Carr disclosed that he had no relevant conflicts of interest. ■

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Sleep Tied to Cardiovascular Risk

Sleep Duration • *from page 1*

available for 9,781 subjects who were interviewed in 1985-1988, while follow-up data were available for 7,729 who were interviewed again in 1992-1993. Mortality data were available through September 2004.

After adjustment for factors such as age, sex, smoking status, body mass index, and cholesterol, those Whitehall II participants who reported sleeping 5 hours or less a night at the first interview had a death hazard ratio of from all causes of 1.24, relative to those who slept 7 hours per night. Those who slept 9 hours or more had a fully adjusted hazard ratio of 1.54.

The fully adjusted hazard ratios of all-cause mortality were slightly higher for those who reported sleep for 5 hours or less and 9 hours or more at the second interview, 1.78 and 1.95, respectively.

The risk of death due to cardiovascular causes was relatively greater for those who slept less after the baseline period than for those who slept more.

Participants whose sleep decreased from 6-8 hours a night at the first interview to less than 6 hours at the second interview had a fully adjusted hazard ratio of mortality from cardiovascular cause of 2.04, compared with 1.22 for those who slept more. Those whose sleep increased from 7-8 hours at the first interview to more than 8 hours at the second interview had a fully adjusted hazard ratio of mortality from noncardiovascular causes of 2.06, compared with 1.44 for those who slept less.

Investigators found a positive association between marital status and sleep duration. Married women were more likely to sleep longer, while married men were more likely to average 7 to 8 hours of sleep per night.

The connection between sleep duration and body mass index wasn't as clear cut. At the Whitehall II study's baseline, higher BMI was associated both with short and long sleep duration in women, but only with short sleep duration in men. By 1992-1993, BMI and sleep duration showed no association in women, but both short and long sleep durations were associated with higher BMI in men.

"Our findings suggest that either a decrease in sleep duration from a regular 6, 7, or 8 hours or an increase from a regular 7 or 8 hours predict all-cause mortality," the authors wrote.

"Patients reporting a decrease in sleep should be regarded as higher risk populations for cardiovascular and all-cause mortality," according to the investigators.

One of the authors holds the Cephalon Chair at Warwick Medical School, Coventry, U.K. None of the other authors had conflicts of interest to declare. ■

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PROFESSIONAL OPPORTUNITIES

Sleep Labs Help in Pediatric Respiratory Disorders

BY CAROLYN SACHS
Elsevier Global Medical News

MAUI, HAWAII — Sleep is a period of vulnerability for the respiratory system, so sleep labs are extremely helpful for dealing with respiratory disorders, Dr. Sally Ward said at a meeting sponsored by the University Children's Medical Group and the American Academy of Pediatrics.

Dr. Ward, head of the division of pediatric pulmonology at Children's Hospital Los Angeles, discussed ways in which polysomnography can be useful in diagnosing or treating a variety of respiratory disorders:

▶ **Obstructive sleep apnea syndrome (OSAS).** "Why bother with a polysomnogram [PSG] in a patient with big tonsils?" Dr. Ward asked. She suggested that a common assumption might be, "They're snoring, they probably have OSAS." Why did the American Academy of Pediatrics say in its practice guidelines that children with symptoms suggestive of OSAS should undergo further testing?

"The presence of obstructive sleep apnea, or the severity, cannot be predicted by history or physical alone," she said. Studies have failed to reveal a relationship between the size of the adenoids and tonsils, and the presence of sleep apnea. And primary snoring, which is more common than is OSAS, is not an indication for surgery, she observed. "It's important that an accurate diagnosis be made in order to prevent unnecessary treatment," and sleep studies help with that process.

Polysomnography also can benefit patients who receive a diagnosis of OSAS and are candidates for surgery. Information about the severity of OSAS affects the pre- and postoperative care and the timing of surgery, Dr. Ward said at the meeting, also sponsored by California Chapter 2 of the AAP. And a PSG provides a basis for comparison in patients who continue to have symptoms after surgery.

Some patients with OSAS who are not amenable to surgery or positive-pressure therapy may be helped by receiving supplemental oxygen during sleep, she said. The procedure can be titrated in a sleep lab to ensure "hitting the target." Patients in this group might include those with craniofacial abnormalities, laryngomalacia, or cerebral palsy.

▶ **Chronic lung disease.** A sleep study can help determine when a baby with chronic lung disease of infancy—bronchopulmonary dysplasia—is able to graduate from wearing oxygen during sleep.

"Using the PSG allows you to choose the proper oxygen level during REM sleep when hypoxia can worsen because of the skeletal muscle atonia. It guides weaning as the conditions may improve, which is usually the case with chronic lung disease of infancy," Dr. Ward explained.

"Children who are graduates from the nursery who are failing to thrive, or who are doing poorly, may be suffering from unsuspected hypoxemia during sleep," she said. A PSG can be useful in that instance.

In older children with chronic lung disease—such as patients with cystic fibrosis—who may have hypoxemia during sleep, "the use of supplemental oxygen has been shown to increase quality of life," Dr. Ward said. "Titrating oxygen during a sleep study in the patient who may have longstanding hypoxemia will allow you to know that you're not decreasing their hypoxic drive with a resulting increase in carbon dioxide."

▶ **Ventilatory muscle weakness.** Children with neuromuscular disease can benefit from a sleep investigation to identify hypoventilation.

These are patients with "a whole host of diagnoses that can involve the respiratory muscles," Dr. Ward said, including spinal muscular atrophy, Duchenne muscular dystrophy, congenital myopathies, myotonic dystrophy, and mitochondrial disorders. They are at risk for chronic respiratory failure, which can be insidious, she said. "It can be just like a slippery slope that can go unnoticed."

▶ **Chronic respiratory failure.** "Given the opportunity, most families in our experience will opt for assisted ventilation for their child as they enter respiratory failure," Dr. Ward said. "It behooves us to try and recognize this issue prior to a crisis, so that elective institution of ventilation can be offered." Because PSGs are very effective at identifying chronic respiratory failure, they can help in managing this transition.

Polysomnography also makes it possible to assess the adequacy of nocturnal ventilation in children who have already been identified as having chronic respiratory failure, and who are technology dependent.

"Ventilatory needs are different during sleep than they are during wakefulness," she said. Once a child is on a ventilator, "using the sleep laboratory can ensure that we're providing normal oxygenation and ventilation during sleep, which is critical to preventing complications and providing these children with good daytime function." ■

NIPPV Didn't Cut Mortality In Acute Pulmonary Edema

BY MITCHEL L. ZOLER
Elsevier Global Medical News

VIENNA — Noninvasive ventilation was safe in helping resolve symptoms in patients with acute cardiogenic pulmonary edema, but the treatment was not lifesaving—it had no effect on mortality in a study with more than 1,000 patients.

"Use [noninvasive ventilation] to relieve patient suffering in the early hours of this illness, but it really only helps the patient in crisis. For the longer term, it doesn't cause harm or benefit," Dr. David Newby said at the annual congress of the European Society of Cardiology.

The study compared both continuous positive airway pressure (CPAP) and noninvasive intermittent positive pressure ventilation (NIPPV) against passive oxygen therapy. Both were equally safe and effective when compared with a standard regimen without high-pressure oxygen.

With 1,069 patients, the 3 Treatments for Cardiogenic Pulmonary Oedema (3CPO) trial is the first large-scale study to test the impact of high-pressure oxygen in this setting, noted Dr. Newby, a professor of cardiology at the University of Edinburgh.

The new study was done at 26 emergency departments in the United Kingdom and was sponsored by England's National Health Service. Patients were enrolled as soon as they arrived at the hospital, and were eligible only if they had acute dyspnea and chest crepitations, were acidotic with an arterial pH of less than 7.35, and were tachypneic with more than 20 breaths per minute. They were randomized to passive oxygen, CPAP administered at an average pressure of 10 cm H_2O, or NIPPV at an average pressure of 14/7 cm H_2O. Therapy was applied for 2 hours. Patients were also treated with nitrates and diuretics.

Treatment with noninvasive ventilation led to small but statistically significant improvements in pulse rate, respiratory rate, and arterial pH, compared with patients in the control group (see table), but the clinical impact of these changes are unclear. In general, however, patients who received either CPAP or NIPPV had more rapid resolution of their dyspnea and other acute symptoms, Dr. Newby said in an interview. Ventilation had no effect on the average length of hospitalization or need for intensive care.

The study's primary end point was the mortality rate at 7 and 30 days after treatment. These rates were very similar for all three treatment groups. Seven-day mortality was 9.8% in 367 patients on standard oxygen, 9.6% for 346 patients on CPAP, and 9.4% for 356 patients on NIPPV. The 30-day mortality rates were 16.7%, 15.4%, and 15.4%, respectively.

The combined rate of death or need for intubation was 11.7% in the control group and 11.1% among the patients on noninvasive ventilation.

Average Levels 1 Hour After Oxygen Therapy for Pulmonary Edema

	Passive oxygen therapy (n = 367)	Noninvasive ventilation (n = 356)
Pulse rate	102 beats per min	96 beats per min
Respiration rate	26 breaths per min	25 breaths per min
Arterial pH	7.30	7.32
Oxygen saturation	94%	93%
Arterial CO_2 partial pressure	6.7 kPa	6.2 kPa

Note: All differences between the two treatment groups are statistically significant.
Source: Dr. Newby

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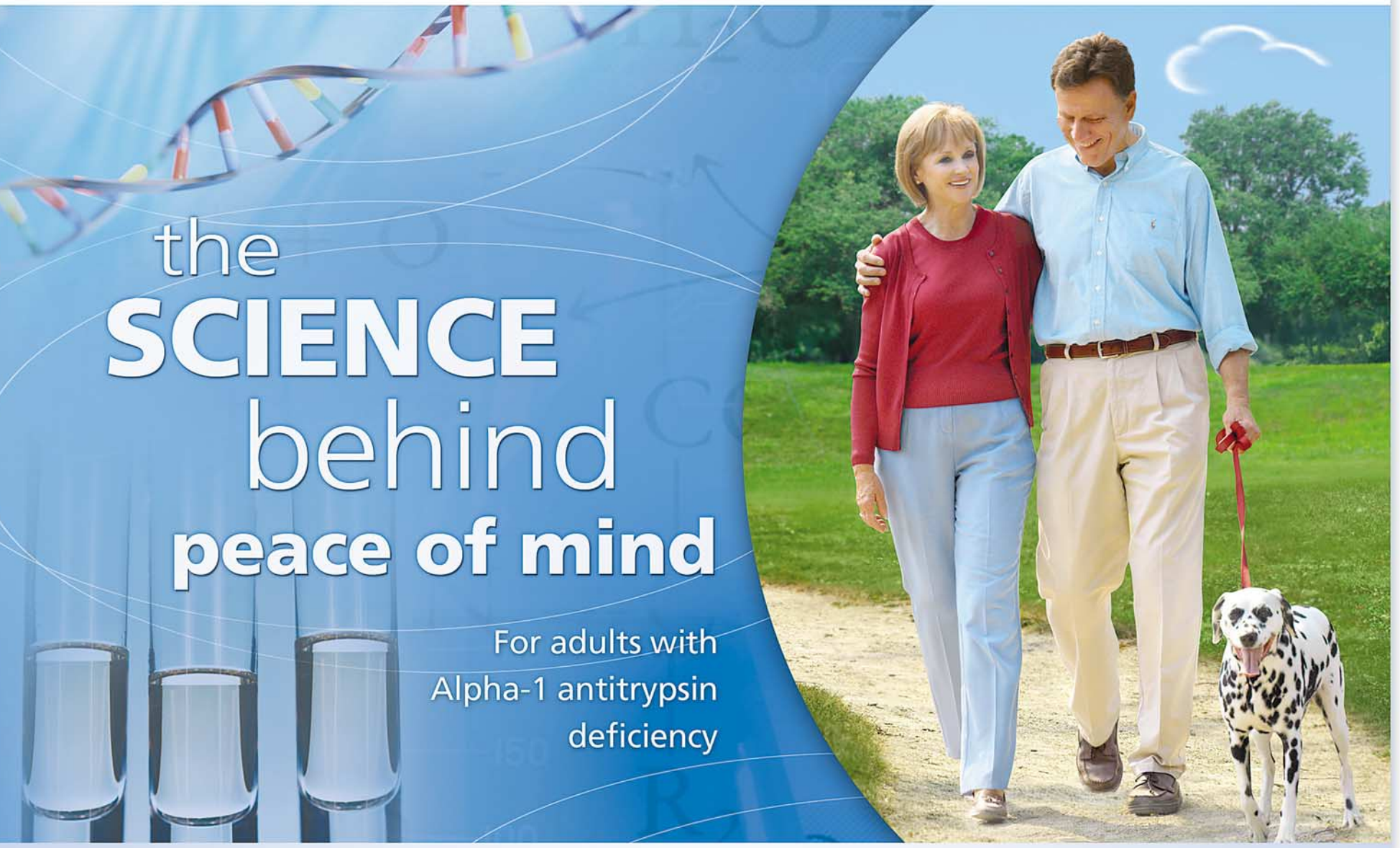

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References: 1. Prolastin® Alpha$_1$-Proteinase Inhibitor (Human), Full Prescribing Information, January 2005. **2.** Aralast™ Alpha$_1$-Proteinase Inhibitor (Human), Full Prescribing Information, August 2005. **3.** Data on file, CSL Behring LLC.

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