VOL. 2 • NO. 12 • DECEMBER 2007

CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

COURTESY DR. SIEGFRIED WIESHAMMER

Patients younger than 60 years had a 20% error rate using dry powder inhalers, versus 42% among those 60 years or older.

To Err Is All Too Human With Powder Inhalers

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — Nearly one-third of patients with asthma or chronic obstructive pulmonary disease incorrectly used their dry powder inhalers in a study of 224 patients reported at the annual meeting of the American College of Chest Physicians.

The error rate increased with age, severity of airway obstruction, and lack of prior training, reported Dr. Siegfried Wieshammer of the Ortenau Hospital Offenburg, Germany, and Jens Dreyhaupt, Ph.D., of the University of Heidelberg, Mannheim, Germany.

Dry powder inhalers, generally marketed as being easy to use, were developed in recent years to overcome the difficulties of using pressurized metered-dose inhalers, which require patients to coordinate actuation of the device with inspiration.

"We conclude that many health care professionals do know how to instruct their patients in inhaler use, but this is not done to the necessary extent," Dr. Wieshammer said. "The current proliferation of inhaler types may become detrimental to the quality of care, because busy doctors don't have sufficient time to become adequately familiar with the strengths, weaknesses, and pitfalls of all these new developments.

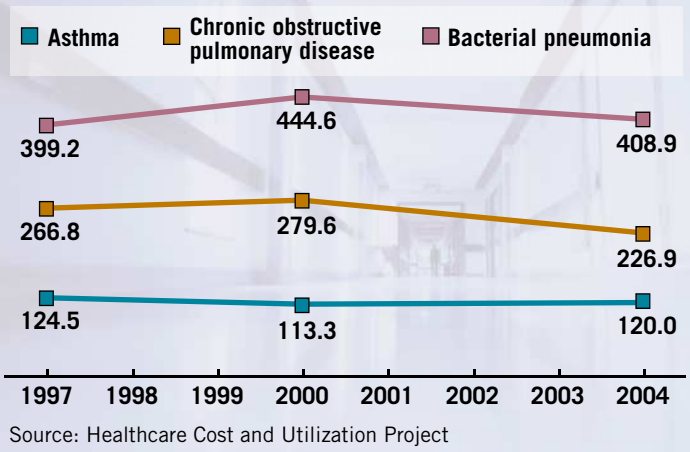
"Doctors should limit their selection to a small number of inhaler types [that have] operating principles they can study in detail,

See **Powder Inhalers** • *page 3*

VITAL SIGNS

Preventable Hospitalizations For Respiratory Conditions

(number of admissions per 100,000 population)



Source: Healthcare Cost and Utilization Project

ELSEVIER GLOBAL MEDICAL NEWS

FDA Panel Backs Label Changes for Antiviral Flu Drugs

Neuropsychiatric events fuel revisions.

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

GAITHERSBURG, MD. — Prompted by concerns about an association between antiviral drugs and neuropsychiatric events in patients with influenza, a closely divided Food and Drug Administration advisory panel voted on Nov. 27 to recommend revised labeling for oseltamivir and zanamivir.

The events have been reported in Japanese children predominantly and include fatalities related to self-injurious behavior. In an 8 to 6 vote on oseltamivir, the FDA's Pediatric Advisory Committee called for a statement making clear that the neuropsychiatric events have been rare, and that they also have been described in patients with influenza who are not on antiviral treatment. The panel's suggested oseltamivir labeling would state that the contribution of the drug in these cases remains unclear. Some panelists said that the abrupt nature of the onset of these events also should be described.

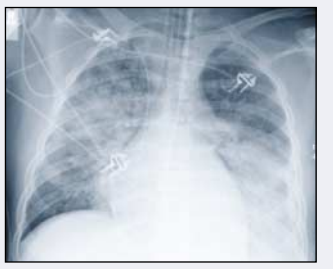
Oseltamivir, marketed as Tamiflu by Hoffmann-La Roche Inc., is an oral neuraminidase inhibitor approved for the treatment and postexposure prophylaxis of influenza in adults and children older than 1 year.

The current label's precautions section includes a statement about postmarketing reports, mostly in Japan, "of self-injury and delirium" associated with oseltamivir in patients with influenza, primarily among pediatric patients. That statement, added in November 2006, says that, "the relative contribution of the drug to these events is not known," and recommends that patients with influenza "should be closely monitored for signs of abnormal behavior throughout the treatment period."

Whether the neuropsychiatric

See **Flu Drugs** • *page 3*

INSIDE



Lung Transplant Value Questioned in CF

BY MARY ANN MOON
Elsevier Global Medical News

Lung transplantation does not improve survival in most children who have cystic fibrosis, suggest data published in the New England Journal of Medicine.

In a study estimating the surgery's survival benefit in 514 children who had CF and who were put on a waiting list for lung transplantation in the United States between 1992 and 2002, the procedure clearly prolonged life expectancy in only five patients—less than 1%, study investigators Dr. Theodore G. Liou of the University of Utah, Salt Lake City, and his associates wrote (N. Engl. J. Med. 2007;357:2143-52).

This "startling" finding has profound implications, Dr. Julian Allen of the Children's Hospital of Philadelphia and Dr. Gary Visner of Children's Hospital, Boston, wrote in an editorial comment accompanying the report.

"Patients with cystic fibrosis and their parents need to be informed that although transplantation may improve quality of life, it may not improve survival. This information is sure to make an already difficult decision more difficult still," and families must receive appropriate social and psychological support to help them make the best choice, they noted (N. Engl. J. Med. 2007;357:2186-8).

One previous study involving 124 children with CF who underwent lung transplant

See **Lung Transplant** • *page 7*

CHEST PHYSICIAN
60 Columbia Rd., Bldg. B
Morristown, NJ 07960
CHANGE SERVICE REQUESTED

Presorted Standard
U.S. Postage
PAID
Permit No. 384
Lebanon Jct. KY

NOW APPROVED!

NEW **DORIBAX™**

doripenem for injection

For more information, please visit **www.doribax.com**

ORTHO-McNEIL, INC.

Panel Wants Revised Labels

Flu Drugs • *from page 1*

events are related to the drug or influenza, it would be useful to include information that reflected "our ongoing uncertainty" and concern about the association, said panelist Dr. Michael Fant of the division of neonatal-perinatal medicine at the University of Texas at Houston.

The public should be made aware that the reports involved behaviors that were infrequent, came on abruptly, and were transient—but occasionally resulted in fatalities, he said. Dr. Fant highlighted one report that he found particularly alarming, in which a 13-year-old Japanese boy taking an antiviral woke up and found himself hanging from a third-floor window with his feet on a 10-cm ledge.

Eleven members of the panel recommended that similar information be added to the label for the other available neuraminidase inhibitor, zanamivir, to reflect similar but fewer reports associated with this drug. The current label for zanamivir, marketed as Relenza by GlaxoSmithKline, lists seizures and syncope as CNS reactions associated with its use.

Neuropsychiatric events also have been reported in patients taking two older antiviral drugs used for the treatment and prophylaxis of influenza: amantadine and rimantadine. Although the panel reviewed these two drugs at the meeting, too, the members unanimously agreed that the information on CNS-related reactions in the labels of these two M2 inhibitors was adequate.

The label for amantadine includes a warning about suicide attempts, personality changes, aggressive behavior, and other CNS reactions in people using the drug. The rimantadine label includes a precaution about ataxia, agitation, and other CNS reactions in clinical trials of the drug.

The FDA usually follows the advice of its advisory panels, which is not binding.

This was the third time since 2005 that the FDA's Pediatric Advisory Committee has met to discuss neuropsychiatric events associated with oseltamivir. A pediatric safety review in 2005 found neuropsychiatric events associated with the drug, mostly in Japan, as well as 12 deaths in Japanese pediatric patients.

By the second meeting, in November 2006, more cases had been identified, still predominantly in Japan, where antivirals are used widely for treating influenza. Most reports fell into the category of delirium with prominent behavioral disturbances, with symptoms typically occurring after one to two doses. As of November 2006, 18 deaths in people aged 17 years or younger had been reported, including 3 characterized by impulsive, abrupt behavior that involved unusually traumatic injuries after one dose of oseltamivir.

Nearly 600 reports of neuropsychiatric events associated with oseltamivir were reported to the FDA's Adverse Event Reporting System (AERS) between October 1999, when the drug was approved, and May 31, 2007. A total of 115 neuropsychiatric events in patients using zanamivir to treat influenza have been reported to AERS between July 1999, when the drug was approved, and Aug. 1, 2007. ■

IN THIS ISSUE

CHEST PHYSICIAN Is Online
CHEST PHYSICIAN is available on the Web at www.chestnet.org/about/publications.

Instruction Cut Inhaler Errors

Powder Inhalers • *from page 1*

so they can teach their patients the optimal use," he added.

The investigators asked 224 newly referred outpatients reporting the use of four common dry powder inhalers (Aerolizer, Diskus, HandiHaler, and Turbuhaler) about the instruction they had received on using their inhaler and to demonstrate their inhalation technique. In all, 24 patients used more than one inhaler. The mean age of the patients was 55 years (range 6-84 years).

At least one essential handling error that made a significant deposition of the medication to the lungs impossible was made in 32% of the 249 examinations. In some cases, patients exhaled into the devices rather than inhaled, which is how the flow of medication to the airways is activated and managed.

Regarding inhaler-specific error rates, Aerolizer had the lowest error rate (9% of 22 visits), followed by Discus (27% of 86 visits), Turbuhaler (35% of 109 visits), and HandiHaler (53% of 32 visits), Dr. Wieshammer said.

The error rate increased significantly with age. Patients aged younger than 60 years had a 20% error rate, whereas those aged 60 years or older had an error rate of 42%. The error rate also increased with the severity of airway obstruction. Dr. Wieshammer speculated that cognitive deficits occurring with the aging process, as well as a COPD-specific cognitive deterioration, make it difficult for older patients with advanced COPD to properly use their inhaler.

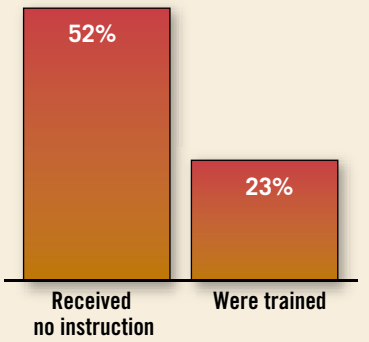
Instruction by medical personal on how to use the inhaler had a major effect on the error rate. Only 23% of trained patients made essential errors, compared with 52% of those who received no instruction, a statistically significant difference. This was somewhat surprising, as a lack of inhaler skills among health care professionals has been repeatedly described, Dr. Wieshammer said.

Using a risk-prediction model, the probability of inhaler misuse was only 9% in the favorable case of an 18-year-old patient with normal lung function and previous instruction who was being treated with Turbuhaler. At the other end of the scale, the probability of ineffective inhalation was 83% in an 80-year-old with moderate to severe obstruction and no prior instruction.

Dr. Wieshammer did not advise against the use of dry powder inhalers in the elderly, but advocated that older patients with advanced COPD should be asked to demonstrate their inhalation technique at every health care encounter. If handling errors can't be eliminated by follow-up training, then a metered-dose inhaler, in combination with a large-volume spacer, might be a valuable treatment alternative in a substantial proportion of these patients, he said.

Dr. Wieshammer disclosed that he has received funds from AstraZeneca Pharmaceuticals LP and GlaxoSmithKline Inc. for arranging educational courses and for speaking engagements in the last 12 months. Dr. Dreyhaupt reported that he has nothing to disclose. ■

Patients Who Made Essential Errors Using Dry Powder Inhalers



Note: Based on a study of 224 patients.
Source: Dr. Wieshammer

AMERICAN COLLEGE OF CHEST PHYSICIANS

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 International Medical News Group and Elsevier Global Medical News. Content for NEWS FROM THE COLLEGE is provided by the American College of Chest Physicians.

The statements and opinions expressed in **CHEST PHYSICIAN** do not necessarily reflect those of the American College of Chest Physicians, or of its officers, regents, members, and employees, or those of the Publisher. The American College of Chest Physicians, its officers, regents, members, and employees, and Elsevier Society News Group, a division of Elsevier Inc., do not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to products, drugs, or services mentioned herein.

Address Changes: Fax changes of address (with old mailing label) to 973-290-8245.

POSTMASTER: Send change of address (with old mailing label) to CHEST PHYSICIAN, 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960.

CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Elsevier Inc., 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250.

ELSEVIER SOCIETY NEWS GROUP, A DIVISION OF INTERNATIONAL MEDICAL NEWS GROUP
President, IMNG Alan J. Imhoff
Director, ESNG Mark Branca
Executive Director, Editorial Mary Jo M. Dales
Executive Editor, IMNG Denise Fulton
Executive Editor, EGMN Kathy Scarbeck
Publication Editor Terry Rudd
Publication Associate Editor Jay C. Cherniak
VP, Medical Education Sylvia H. Reitman
Senior Director, Marketing and Research Janice Theobald
Circulation Analyst Barbara Cavallaro
Executive Director, Operations Jim Chicca
Director, Production and Manufacturing Yvonne Evans
Production Manager Judi Sheffer
Art Director Louise A. Koenig
Display Advertising Manager The Walchli Tauber Group: 443-512-8899, fax 443-512-8909, gary.walchli@wt-group.com, stephen.tauber@wt-group.com
Classified Sales Manager Rhonda Beamer, 443-512-8899, fax 443-512-8909, rhonda.beamer@wt-group.com
ADVERTISING OFFICES 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250
CLASSIFIED ADVERTISING OFFICES The Walchli Tauber Group, 2225 Old Emmorton Rd., Suite 201, Bel Air, MD 21015, 443-512-8899
EDITORIAL OFFICES 5635 Fishers Lane, Suite 6000, Rockville, MD 20852, 240-221-4500, fax 240-221-2541

Prophylactic Steroids Helped 9/11 First Responders

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — Prophylactic inhaled corticosteroids appear to have prevented or reduced lung injury among first responders at the World Trade Center disaster, according to the first study of its kind.

Budesonide taken via Turbuhaler twice daily for 4 weeks beginning 1 week after the attacks of Sept. 11, 2001, reduced respiratory symptoms and improved pulmonary function and quality of life among 158 New York City firefighters, Dr. David Prezant, FCCP, and associates reported in a poster at the annual meeting of the American College of Chest Physicians.

At 2 years after 9/11, treated firefighters had significantly higher vital capacity than controls.
DR. PREZANT

Dr. Prezant called the findings hypothesis generating, although they raise the question as to whether patients exposed to smoke and soot-laden air from the recent California wildfires should be similarly treated.

These findings have to be replicated in a larger group, but they are "intriguing," and health care providers should consider this treatment on a case-by-case basis, Dr. Prezant, codirector of the World Trade Center Medical Monitoring and Treatment Programs, said in an interview.

At 2 years after the 9/11 attacks, treated firefighters had significantly increased vital capacity (220 mL), compared with 158 controls (20 mL) matched for arrival time at the World Trade Center site. Forced expiratory volume at 1 second was improved (91.6% vs. 89.4%), but the difference was not statistically significant.

Quality of life, as measured by St. George's Respiratory Questionnaire, was significantly improved in treated firefighters (21.9 vs. 20.2). The number of respiratory medications prescribed in the 4 weeks prior to the final follow-up visit was also significantly lower among treated firefighters (3 vs. 10), Dr. Prezant and associates reported.

Interestingly, he noted, the number of reported hours wearing respiratory protection in the first week post 9/11 was lower in the treated group than in controls (132 vs. 143 hours). Pulmonary function was normal in both groups. The average age was 43 years in the treated group and 39 years in the untreated group.

"Despite its significant limitations in terms of selection bias and loss of power, [the study] does tell us that there were no significant side effects, there are educational issues that could be easily dealt with, and … there are both statistical and clinical improvements that really warrant this [treatment's] being used in a larger study to confirm these findings," Dr. Prezant told reporters in a press briefing.

"Disasters will occur in the future; fires are always occurring," he said.

"With proper education and planning, we believe this medication is certainly worth its study and has a very good side effect–to-benefit profile."

The steroids were offered free of charge, courtesy of AstraZeneca Pharmaceuticals L.P., to about 11,000 firefighters, but only 2,708 agreed to enroll, and just 158 (6%) completed 4 weeks of treatment.

The most common reasons cited for not enrolling were confusion of corticosteroids with anabolic steroids, and fear of side effects such as osteoporosis.

A common reason for not completing treatment was lack of immediate benefit. Firefighters were told orally and in writing not to expect an immediate effect, but they often used the drug for only 2-3 days, suggesting that a continuous education process is needed, Dr. Prezant said.

While respiratory protection is the primary means of preventing lung injury, first responders often shun it during the stress of an emergency situation, Dr. Prezant noted. ■

Alert Issued on Drug for Helping Smokers Quit

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

The Food and Drug Administration has issued an alert about postmarketing reports of suicidal thoughts, aggressive and erratic behavior, and drowsiness associated with varenicline, the smoking cessation drug marketed as Chantix.

A notice posted Nov. 20 on the FDA's MedWatch site advises health care professionals to monitor patients taking varenicline for behavior and mood changes, and recommends that people taking the drug should contact their physicians if they experience mood or behavior changes, and should be cautious when driving or operating machinery, "until they know how quitting smoking with Chantix may affect them."

Varenicline, a nicotine receptor agonist, was approved by the FDA in 2006, and is taken orally. The notice points out that the review of the drug's safety is ongoing and that the agency is not advising health care providers to stop prescribing the drug.

The FDA is reviewing postmarketing reports of suicidal ideation and occasional suicidal behavior associated with varenicline, recently submitted by the drug's manufacturer, Pfizer Inc., as well as cases recently reported in the popular press and Internet sites, according to the notice.

A preliminary assessment of these reports indicates that many "reflect new-onset of depressed mood, suicidal ideation, and changes in emotion and behavior within days to weeks of initiating Chantix treatment," according to the FDA. Because smoking cessation treatment with or without treatment is associated with nicotine withdrawal symptoms and exacerbation of underlying psychiatric illness, "the role of Chantix in these cases is not clear," although not all the patients in these reports have preexisting psychiatric illnesses and not all had stopped smoking.

The notice also refers to a highly publicized case of erratic behavior that resulted in the death of an individual who was taking varenicline to quit smoking. The FDA is reviewing material submitted by Pfizer in response to a request for information about similar cases. Alcohol and other factors appeared to have played a role in this case.

Reports of people who experienced drowsiness while taking the drug, and of impairment that affected the ability to drive or operate machinery, are also being reviewed by the FDA.

The FDA plans to issue another report when the safety review is completed and when more information or analyses become available.

In the varenicline label, suicidal ideation is listed as a "rare" treatment-emergent adverse effect associated with the drug in clinical trials, and aggression is listed as an "infrequent" adverse event. ■

More information is available at: www.fda.gov/medwatch/safety/2007/safety07.htm#Chantix. Adverse reactions to Chantix should be reported to the FDA's MedWatch program at 800-332-1088 or www.fda.gov/medwatch.

Study Suggests Link Between Iron Deficiency and Idiopathic Cough

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — A small but provocative Italian study suggests that women complaining of chronic idiopathic cough should be evaluated for iron deficiency.

Researchers at the University of Turin (Italy) observed that cough and signs and symptoms of pharyngolaryngitis were improved or resolved after iron supplementation in 16 healthy nonsmoking women who had idiopathic cough and iron deficiency (average serum ferritin 9.4 ng/mL) and mild anemia (hemoglobin 11.6 g/dL).

The women, aged 18-56 years, had no history of atopy, asthma, or other bronchopulmonary diseases, and no evidence of gastroesophageal reflux. All had normal results on lung function tests, lead investigator Dr. Caterina B. Bucca, FCCP, reported at the annual meeting of the American College of Chest Physicians.

The women presented with marked oral redness and soreness, atrophy of oral mucosa and tongue papillae, and angular cheilosis. Nine patients had dysphonia. Exhaled nitric oxide was normal (average 14.9 parts per billion) in all the patients.

Histamine challenge showed bronchial hyperresponsiveness in 4 women, extrathoracic airway hyperresponsiveness in 14 women, and cough hyperresponsiveness in 15 women.

SYMPTOMS IMPROVED AFTER IRON SUPPLEMENTATION IN 16 HEALTHY NONSMOKING WOMEN WHO HAD AN IDIOPATHIC COUGH AND WERE IRON DEFICIENT.

A significant association was observed between PC_5 coughs (the histamine concentration that provokes five coughs) and PC_{25} MIF_{50} (provocative concentration causing a greater than 25% fall in maximal mid-inspiratory flow at 50% of vital capacity), reported Dr. Bucca of the department of biomedical sciences and human oncology at the University of Turin.

After iron supplementation, signs and symptoms of pharyngolaryngitis were resolved in 10 women and improved in 6 women. Significant increases were observed in PC_{20} FEV_1 (provocative concentration causing a 20% drop in forced expiratory volume in 1 second): 18.8 mg/mL to 24.1 mg/mL; significant increases were also seen in PC_{25} MIF_{50} (6.2 mg/mL to 22.2 mg/mL) and in PC_5 coughs (3.8 mg/mL to 17.8 mg/mL).

Dr. Bucca suggested that the tentative explanation of how iron deficiency causes cough is based on the knowledge that iron deficiency impairs immunologic defenses and induces the release of inflammatory cytokines.

"This leads to damage of the airway mucosa, which becomes more permeable to noxious stimuli so that the nervous receptors responsible for the onset of cough are more easily reached by irritants," Dr. Bucca said in an interview.

"Infections of the pharynx and larynx are also favored, so that cough is often associated with painful and inflamed throat and with dysphonia."

Iron deficiency is present in 20% of women in industrialized countries, and in the United States nearly one-third of women have virtually no iron stores. Cough is also more frequent in women than in men.

Dr. Bucca is currently evaluating the nutritional status of all patients who present to her clinic for chronic cough, either idiopathic or associated with diseases of the upper airway, and is planning an epidemiologic study to assess the prevalence of cough and iron deficiency in women of childbearing age. ■

Pages 4a—4b

Adenovirus 14 Tied to Cluster of Hospitalizations

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — During the winter of 2006 and the spring of 2007, adenovirus 14 caused a community outbreak of respiratory disease in Oregon, with a fatality rate of 19%, Dr. Paul Lewis reported at the annual meeting of the Infectious Diseases Society of America.

"This seemed to come out of nowhere," Dr. Lewis, a public health physician with the state of Oregon and a pediatric infectious disease physician with Oregon Health and Science University, Portland, said of the outbreak. "In patients with serious respiratory illness without an identified etiology, clinicians should think about viruses."

The cluster was first identified in the spring of 2007 by his associate, Dr. David Gilbert, who was making rounds in the intensive care unit at Providence Portland Medical Center and thought it was odd that 4 of 13 patients had adenovirus infections, which are typically mild and self-limited.

"When we called other hospitals in the Portland area, we almost fell out of our chairs because they all had seen recent severe and fatal cases of adenovirus," said Dr. Lewis.

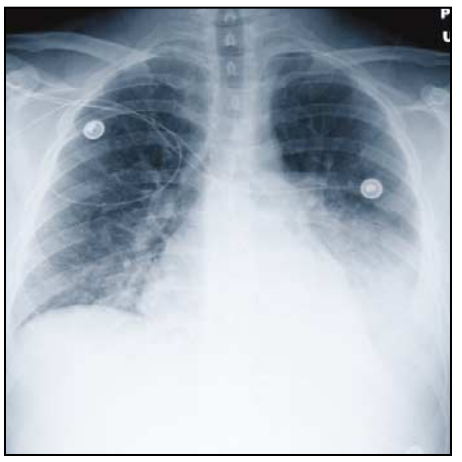
The researchers studied 45 cases of adenovirus that were detected in Oregon medical laboratories between November 2006 and April 2007. The adenovirus isolates were typed by hexon gene sequencing or by a novel adenovirus 14–specific real-time polymerase chain reaction assay.

More than 75% of all adenovirus cases were in male patients. Of the 45 cases, 31 (69%) were adenovirus 14, a serotype first identified in 1953 but seen infrequently and never in outbreaks since that time.

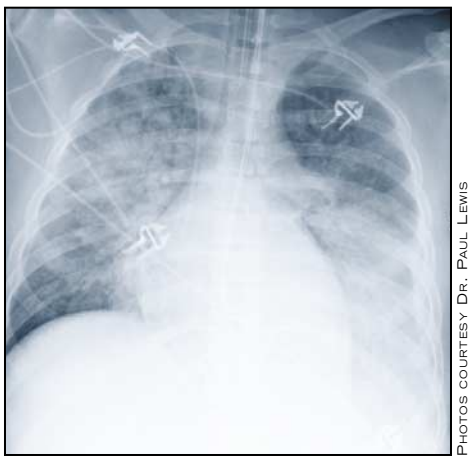
Patients infected with adenovirus 14 were significantly older than patients infected with other adenovirus isolates (a mean of 59 years vs. 1 year, respectively). They also had significantly higher rates of hospitalization (71% vs. 14%, respectively).

Clinical features of patients with adenovirus 14 included fever (84%), tachypnea (77%), hypoxia (48%), and hypotension (43%). Of the 24 chest x-rays obtained, 21 (88%) had abnormal findings; lobar consolidation was the most common pattern.

Dr. Lewis reported that 22 (71%) of the adenovirus 14 patients required hospitalization, and 6 (19%) died. Of the hospitalized patients, 16 (73%) required ICU care, 13 (59%) required mechanical ventilation, and 8 (36%) required blood pressure support with vasopressors.



Lobar consolidation is shown in a patient on day one of hospitalization.



The same patient is shown on day four of hospitalization.

PHOTOS COURTESY DR. PAUL LEWIS

"Infection control was a great concern to hospitals that saw multiple cases," Dr. Lewis said. "Many patients were isolated with [severe acute respiratory syndrome]–like precaution. There was a health care worker at an ICU taking care of one of these patients who was subsequently admitted to that ICU with adenovirus 14," he added. "That's our only known possible case of transmission, but we cannot be sure it was not acquired in the community."

Treatment included "lots of empiric antibiotics." Cidofovir was used in six patients, two of whom died.

Dr. Lewis said that there are 51 known adenovirus serotypes. Types 1, 2, and 5 are nearly universal in children, whereas types 3, 4, and 7 are common in adults. No adenovirus vaccine is currently available in the United States, and previous vaccines developed for the military do not cover adenovirus 14.

He acknowledged certain limitations of the study, including its retrospective design and the potential for testing bias. ■

Asthma Outcomes Reveal Puzzling Racial Disparities

BY JOHN R. BELL
Elsevier Global Medical News

African Americans with moderate to severe asthma who participated in a large prospective study were more likely to visit the emergency department or to be hospitalized than were white patients, even after adjustment for asthma severity, access to care, and socioeconomic status.

The study of 678 adult patients, which was published in Archives of Internal Medicine, found that being African American was associated with a hazard ratio of 1.73 for visits to the emergency department and 2.01 for hospitalizations after controlling for potential.

No significant differences between groups were reported in use of asthma controller medication in the previous 2 weeks. However, African Americans reported using short-acting inhaled beta agonists more than twice as often as did white patients in the previous 3 months (odds ratio 2.22), and their use of other rescue medications was also higher, Dr. Sara E. Erickson of the University of California, San Francisco, and her colleagues wrote.

Asthma monitoring was more prevalent among African Americans, although both whites and blacks had a similar level of exposure to asthma education and similar rates of having seen an asthma specialist in the prior year.

These findings had no clear explanation, the authors said, and the cause of the disparity is likely complex. They acknowledged that their findings might have been confounded by unmeasured socioeconomic factors or comorbid diseases, for which data were not collected. They also suggested that physicians might encourage black patients more often than white patients to seek treatment in the emergency department for their asthma exacerbations or that cultural beliefs about asthma might play a role. Reporting bias was another possibility (Arch. Intern. Med. 2007;167:1846-52).

The investigators assessed a cohort of 524 white and 154 black patients from the Kaiser Permanente of Northern California HMO who had been hospitalized and discharged with asthma as the primary diagnosis or as secondary to acute asthma-related respiratory conditions. They then interviewed each participant via telephone to assess age, sex, race/ethnicity, educational attainment, income, and marital status. The 12-item Short Form General Health Survey was given, as was the Marks Asthma Quality of Life Questionnaire. Socioeconomic status was derived on the basis of geocoding and linkage to Census block group data. ■

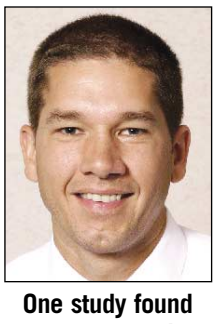
Dr. LeRoy Graham, FCCP, comments: *Mounting evidence continues to document disparities in morbidity and mortality attributable to asthma among African Americans. The fact that simple theories of nonadherence, cultural differences, and lower socioeconomic status fail to explain these disparities mandates the need for further, well-designed, and innovative research in this critical area.*

Collegiate Sports Programs Drop Ball on Asthma Management

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — Most collegiate sports medicine programs surveyed have no asthma management plan in place, even though asthma can result in significant morbidity in young competitive athletes.

A survey of 541 athletic trainers affiliated with National Collegiate Athletic Association sports programs found that only 20% had a specific, written plan for managing asthma exacerbations during practices or games, Dr. Jonathan Parsons and colleagues reported at the annual meeting of the American College of Chest Physicians.



One study found 61 athletes with asthma who died during or after a sporting event from 1993 to 2000.
DR. PARSONS

Written asthma treatment protocols are recommended by the National Athletic Trainers' Association and by the National Asthma Education and Prevention Program, administered by the National Heart, Lung, and Blood Institute.

In all, 61% of responders said their program mandates that albuterol or short-acting β-agonist inhalers be present at all practices, and 59% said such treatment was available at all games.

Because it's not possible to determine when an athlete may have an asthma attack or how severe it may be, having a plan and necessary medication available is essential to improve outcomes, Dr. Parsons, associate director of the Ohio State University asthma center, Columbus, told reporters at a press briefing. He cited a study that identified 61 athletes with asthma who died during or after a sporting event from 1993 to 2000—most of whom were younger than 21 years of age (81%) and had a known history of asthma (91%) (J. Allergy Clin. Immunol. 2004;113:264-7).

Just 17% of NCAA respondents indicated that objective testing is performed when an athlete presents with shortness of breath during exercise. "This likely results in missed diagnoses and inaccurate diagnoses, which exposes athletes to unnecessary medication and unnecessary health morbidity," Dr. Parsons said.

Dr. Parsons and his colleagues recently reported that exercise-induced bronchospasm is relatively common among varsity athletes (39% of 107 athletes), and that symptoms were not predictive of such bronchospasms (Med. Sci. Sports Exerc. 2007;39:1487-92).

A minority of programs (22%) had a pulmonologist as an active or formal member of their sports medicine program. However, when they did, the impact was significant.

Programs with pulmonologists were 2.6 times more likely to have a written protocol for asthma management, 1.6 times more likely to have inhalers available during all practices, and 1.7 times more likely to have inhalers available during all games, differences that were all statistically significant. ■

Study Supports Endobronchial Valves for Emphysema

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO — The Zephyr endobronchial valve significantly improved lung function and exercise capacity in patients with severe emphysema in the first prospective, randomized, multicenter trial to evaluate endobronchial valves.

The device offers patients a minimally invasive and potentially reversible method of lung-volume reduction without the potential risk of significant morbidity associated with open surgical reduction. The unidirectional silicone valve, inserted via fiberoptic bronchoscopy, is designed to block inhaled air from entering diseased portions of the lung while permitting air and fluids to escape during exhalation. The device is limited to investigational use in the United States, but has been sold on a limited basis in Europe and the Asia-Pacific regions.

Results of the VENT (Endobronchial Valve for Emphysema Palliation Trial) indicate that the procedure has an acceptable safety profile, and is particularly effective in patients with complete fissures, effective lobar exclusion, and left-sided disease.

"Most important—and what we are very interested in—is that there was a greater magnitude of effect in prespecified subsets of patients, particularly with respect to technical efficacy and physiologic potential," VENT investigator Dr. Frank C. Sciurba, director of the emphysema research center at the University of Pittsburgh, said at the annual meeting of the American College of Chest Physicians.

Dr. Sciurba was one of five investigators to present data from VENT. The study was conducted at 31 sites from December 2004 to April 2006, and included 321 patients (aged 40-75 years) with severe heterogeneous emphysema, predominantly affecting the upper lobes.

In all, 220 patients were randomized to implantation with Zephyr endobronchial valves (manufactured by Emphasys Medical Inc.) and 101 patients to medical management, defined as maximal medical treatment for stable chronic obstructive pulmonary disease as recommended in the 2001 GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines. Typically, three to four valves were implanted per lobe under moderate sedation. All patients were required to undergo pulmonary rehabilitation before and after surgery.

The study met its coprimary efficacy end points of mean percent change in forced expiratory volume in 1 second (FEV_1) and 6-minute walk test at 6 months. FEV_1 improved by 5.8% in the intervention group, and fell by 0.6% in the control group. The 6-minute walk scores improved by 1.7% in the intervention group, and fell by 4% in the control group. The differences in these outcomes were significant, but were of modest magnitude, said Dr. Sciurba.

He reported that his center received funding to conduct the trial from Emphasys, which sponsored the study.

A 15% improvement in FEV_1 (a predefined measure of a clinically meaningful difference) was achieved by 26.4% of patients in the intervention group, compared with 16% in the control group. Similar increases were observed for 6-minute walk scores (27% vs. 20%).

Secondary end points of quality of life—as measured by the St. George's Respiratory Questionnaire, Modified Medical Research Council Dyspnea Scale scores, and exercise capacity as measured by incremental cycle ergometry—were significantly improved in the intervention group.

Major complications occurred in 6% of patients in the intervention group and in 1% of controls. The difference did not reach statistical significance. Distal pneumonia, which had been a strong theoretical concern before the study, was increased at 6 months in the treatment group, but there was no difference between groups at 12 months, Dr. Sciurba said.

There were eight deaths in the study. One, a massive hemoptysis, was considered procedure related, he said.

Valve expectoration or migration occurred in 6.4% of patients. Valve removal was attempted in 31 patients (14%), primarily because of a lack of efficacy, and was successful in 85 of 87 attempts (98%).

Dr. Sciurba said he was comforted by the fact that the procedure is reversible should patients not achieve the desired results. But he added that, based on analogies from lung-volume reduction surgery, bilateral procedures should result in significantly greater impact than unilateral procedures.

"We believe this procedure is one of several emerging technologies that may eventually prove beneficial to our patients," Dr. Sciurba said in an interview. "My hope is that other minimally invasive technologies will [be proved] to complement these valves and become part of a tool chest for the interventional bronchoscopist to improve lung function and symptoms."

In October 2007, the Food and Drug Administration granted expedited review for a premarket approval application, submitted by Emphasys, requesting approval to market the Zephyr valve in the U.S. ■

Survival Benefit Uncertain

Lung Transplant • *from page 1*

reported a survival benefit, but another by Dr. Liou and his associates showed no survival benefit. This discrepancy generated "heated controversy," the editorialists wrote.

To address these discrepant findings, Dr. Liou's group conducted a new study using data from the Cystic Fibrosis Foundation Patient Registry and from the Organ Procurement and Transplantation Network, which allowed assessment of nearly four times as many patients as were previously studied.

This larger data set afforded the new study greater statistical power.

The investigators identified 514 children with a wide range of lung function and prognoses who were on the waiting list for lung transplantation from 1992 through 2002, which represented "essentially the entire U.S. experience with lung transplantation for CF" during that period.

'SUSTAINED, MULTIDISCIPLINARY CARE RATHER THAN LUNG TRANSPLANTATION IS CENTRAL TO LONGEVITY IN CHILDREN WITH CF.'

A total of 248 underwent transplantation, 120 of whom died after the procedure (median survival 1,037 days). Of the 266 children who did not receive transplants, 141 died.

The researchers performed statistical modeling that accounted for the effects of multiple covariates (*Burkholderia cepacia* infection, age, diabetes status, *Staphylococcus aureus* infection) before and after the procedure to estimate how the surgery would alter each patient's risk of death.

A total of 509 children "did not derive a significant estimated survival benefit." Moreover, most patients (315) "were at significant risk for harm" from the surgery.

"Actuarial survival for lung transplantation for CF has not appreciably changed in the past several years; thus the ability of our model to predict survival outcomes for patients undergoing transplantation after 2002 is likely to be high," the investigators said (N. Engl. J. Med. 2007;357:2143-52).

"We cannot comment on the effect of lung transplantation on the quality of life for children with CF that is so severe that they are considered for this procedure," they noted.

"The results underscore that sustained, multidisciplinary care rather than lung transplantation is central to longevity in children with CF. … Lung transplantation in adulthood, if needed, can be undertaken with a greater probability of increased survival," the researchers added.

In their editorial comment, Dr. Allen and Dr. Visner said the study findings imply that lung transplantation may improve survival only in patients whose predicted 5-year survival is less than 30% or whose predicted median survival is less than 3 years.

"These survival projections are lower than those for many patients who are being referred for transplantation now," they said. ■

Dr. Stephen Rowe, FCCP, comments: *In the most definitive retrospective analysis to date, including the pediatric U.S. lung transplant experience from 1992 to 2002, Liou et al. report no significant benefit of the procedure compared to patients listed but not undergoing transplant.*

Using a proportional hazards model that included a number of covariates, the authors predicted only 5 of 514 subjects to have derived life-preserving benefit by lung transplant, while 315 had a significant risk of harm.

The complexities of appropriate referral for lung transplant are difficult to capture (including quality of life, anticipated time to transplant due to unpredictable waiting lists, etc.), but these data suggest a cautious approach to lung transplant is needed, and frank discussion with families regarding the limited expectation of improved survival.

Perhaps better methods of prioritizing lung transplant recipients will allow allocation of organs to those most likely to attain a survival benefit, particularly until a definitive randomized, controlled trial confirms these findings.

Clearly, the best approach to the care of the CF patient is a comprehensive model that maximizes longevity and quality of life while avoiding the need for transplantation as long as possible.

Study Casts Doubt on Post-Trauma Transfusion Protocol

BY BRUCE JANCIN
Elsevier Global Medical News

COLORADO SPRINGS — Early transfusion of fresh frozen plasma in the resuscitation of patients with early postinjury coagulopathy appears to be independently associated with an increased risk of subsequent multiorgan failure, according to a prospective cohort study of critically injured patients.

Moreover, the increasingly popular practice of delivering units of fresh frozen plasma (FFP) and packed red blood cells (RBC) in a fixed 1:1 ratio also may be counterproductive in patients with early postinjury coagulopathy and shock. This strategy needs to be reexamined, according to Dr. Jeffrey L. Johnson, director of the surgical ICU at Denver Health Medical Center.

He presented his study of the relationship between transfusion and postinjury multiorgan failure (MOF) at the annual meeting of the Western Surgical Association. The study involved 1,415 Denver Health ICU patients who had survived more than 48 hours after they sustained critical injuries during 1992-2004.

Their mean age was 37 years, and all were older than age 15. Blunt trauma was the mechanism of injury in three-quarters of cases. The mean Injury Severity Score was 30. Twenty-four percent of patients developed MOF. Overall 30-day mortality in the study population was 8%.

In an earlier influential 1997 study, the Denver Health group demonstrated a linear relationship between the number of units of red blood cells delivered within the first 12 hours after injury and the risk of subsequent MOF. Those who got more than 20 units had an MOF incidence in excess of 50%. Multiple organ failure is the leading cause of death in the ICU among critically injured trauma patients.

That study helped trigger a widespread change in trauma practice, with greater early use of FFP and less use of red blood cells. But the pendulum may now have swung too far in the other direction, since FFP develops biologically active metabolites during storage that can exacerbate the immunologic dysfunction that can result in MOF, according to Dr. Johnson.

Indeed, when he and his coinvestigators plotted the number of units of FFP given in the first 12 hours against the incidence of MOF in the Denver cohort, they found the odds of MOF increased in a nearly linear fashion after adjustment for patient age and Injury Severity Score. Patients who received 10 U had a sevenfold increased risk.

Patients given 10 U of fresh frozen plasma had a sevenfold higher adjusted risk of multiorgan failure.
DR. JOHNSON

At U.S. trauma centers, FFP is increasingly being delivered together with RBC in a fixed 1:1 ratio. Much of the impetus for this strategy comes from highly favorable reports by U.S. combat surgeons who use this protocol in Iraq and Afghanistan. But when Dr. Johnson and coworkers plotted 30-day survival of the Denver cohort against the ratio of FFP to RBCs administered, they found a U-shaped curve. Mortality was highest at ratios of 1:5 and above, lowest with ratios of 1:2 and 1:3, but also high at 1:1.

They also identified an interaction between the volumes of fresh frozen plasma and red blood cells that were given. The increased risk of MOF associated with FFP was significantly greater in patients who received 6 U of red blood cells or fewer, compared with those who got more. For example, the adjusted risk of MOF was increased nearly sevenfold in patients who got 10 U of FFP but fewer than 6 U of red blood cells, while the risk of MOF attributable to FFP merely doubled in those who received more than 6 U of red blood cells.

In contrast, platelet transfusion was not associated with MOF.

These new findings underscore how little is understood about the early biology of trauma, according to Dr. Johnson.

"Despite the long recognition of this problem, the role of FFP in the treatment of early traumatic coagulopathy remains poorly understood. We do not know what dose to give; we do not know the best timing of FFP delivery; and we do not fully understand the biology, the safety, or the efficacy of plasma in the setting of early coagulopathy," he continued.

Dr. Johnson's study prompted several audience members to vow that they would examine the impact of early use of FFP in a 1:1 ratio with RBC on their own institutional MOF rates. ■

ESA Labels Show Risks for Cancer, Kidney Patients

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

The Food and Drug Administration approved major changes to the labels of erythropoiesis-stimulating agents, addressing serious risks that have been associated with these drugs in patients with cancer or chronic renal failure.

The FDA announced Nov. 8 that it okayed revisions to the boxed warnings and other safety-related changes in the labels of the erythropoiesis-stimulating agents (ESAs). The changes are being made "to make clear recommendations about the safe and effective use of these products and to strengthen the information about the risks that these drugs pose to patients with cancer and to patients with chronic kidney failure," Dr. Richard Pazdur, director of the FDA's division of oncology drug products, said during a press briefing.

ESAs have been associated with an increased risk of tumor progression and lower survival rates when used to treat patients with certain cancers, and an increased risk of serious cardiovascular events in patients with chronic kidney failure.

Three ESAs are approved for use in the United States: two epoetin alfa products, marketed as Epogen and Procrit, and darbepoetin alfa, marketed as Aranesp. All three are approved for treating anemia in patients with chronic kidney failure and for treating anemia caused by chemotherapy in certain patients with cancer. Epogen and Procrit also are approved for use during or shortly after surgery to reduce the need for blood transfusions in patients undergoing major surgery and for treating anemia caused by zidovudine (AZT) treatment in patients with HIV.

This is the fifth time since Procrit and Epogen were approved in 1989 that the ESA labels have been changed to incorporate safety information. The latest changes incorporate recommendations made this year at a meeting of the FDA's oncologic drugs advisory committee in May 2007 and a joint meeting of the FDA's Cardiovascular and Renal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee in September 2007.

The boxed warning for patients with kidney failure treated with ESAs applies to those on dialysis and those not on dialysis. The label now states that the risk of death and serious cardiovascular events, including myocardial infarction, stroke, and heart failure, is greater when ESAs are administered to achieve higher versus lower hemoglobin levels. The warning cites two clinical trials: one study that compared

THE BOXED WARNING FOR PATIENTS WITH KIDNEY FAILURE APPLIES TO BOTH THOSE ON DIALYSIS AND THOSE NOT ON DIALYSIS.

dosing with hemoglobin targets of 13.5 g/dL and 11.3 g/dL, and a second comparing dosing with target levels of 14 g/dL and 12 g/dL.

A separate boxed warning says that dosing in chronic renal failure patients should be individualized to achieve and maintain hemoglobin levels within the range of 10-12 g/dL. "Maintaining higher hemoglobin levels in patients with chronic kidney failure increases the risk for death and for serious cardiovascular reactions," according to the FDA.

In an important change, the label's dosing and administration section contains specific recommendations for dosing adjustments and hemoglobin monitoring in patients with chronic renal failure who do not respond to ESAs with an adequate increase in their hemoglobin levels. In trials, these patients—hyporesponders—appeared to be at greater risk of serious cardiovascular events than were patients with adequate responses.

The label now says that ESA dosages should not be increased in patients who fail to achieve or maintain a hemoglobin level of 10-12 g/dL after 12 weeks of treatment. Treatment should be discontinued in patients who do not achieve hemoglobin levels sufficient to avoid the need for transfusions.

For the ESAs' cancer indication, the boxed warning now includes a list of cancers—including advanced breast, head and neck, lymphoid, and non–small cell lung cancer—in which ESA dosing to a hemoglobin target level of 12 g/dL or more resulted in a reduced survival time or tumor progression. The warning also states that the risk of shortened survival and increased progression "has not been excluded" in patients on chemotherapy when the target level is less than 12 g/dL.

The revised label also emphasizes that ESAs should be used only to treat anemia that patients experience while undergoing myelosuppressive chemotherapy—but not to treat other causes of anemia in people with cancer. In addition, ESAs should be stopped once the chemotherapy course is completed. "These risks should be weighed against the potential for red blood cell transfusions and their associated risks," Dr. Pazdur said.

Quality of life claims also have undergone significant change. The revised label emphasizes that there are no controlled clinical trial data demonstrating that ESAs improve symptoms of anemia, quality of life, fatigue, or patient well-being in patients with cancer, or in patients with HIV on AZT.

For chronic kidney failure patients, the label has been updated to include data on improvements in exercise tolerance and functional ability that have been associated with ESA treatment. But parts of the section on clinical outcomes such as happiness and well-being have been deleted.

FDA officials emphasized that none of the ESAs is approved for treating fatigue or other symptoms of anemia. In cancer patients, ESAs are not approved for treating anemia associated with other cancer-related causes.

It is clear that the achieved hemoglobin value has a definite impact on cardiovascular outcomes in renal failure patients, said Dr. John Jenkins, director of the FDA's Office of New Drugs. But in cancer patients, it is less clear whether the ESA dose or the achieved hemoglobin level affects survival and tumor progression.

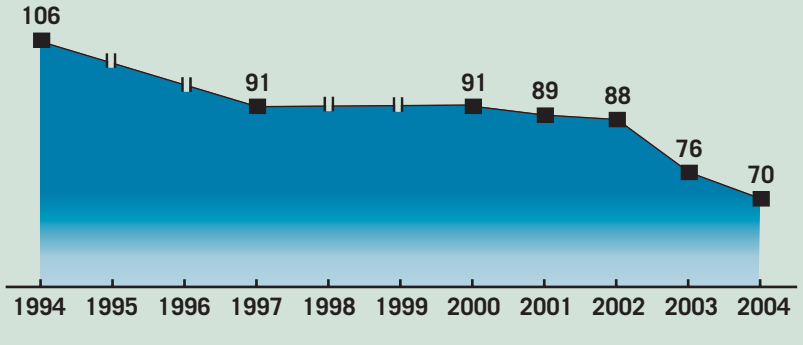
The FDA is working with Amgen to develop a medication guide for patients, which will explain the risks and benefits of ESA treatment. The agency also will work with Amgen on clinical trials of ESA dosing regimens in different types of cancers to learn more about the potential for tumor progression. ■

The FDA issued an alert regarding the changes to the ESA labels, available at www.fda.gov/cder/drug/infopage/RHE/default.htm.

DATA WATCH

Inpatient Mortality from Pneumonia Declining

(per 1,000 admissions)



Source: Healthcare Cost and Utilization Project

ELSEVIER GLOBAL MEDICAL NEWS

Anti-MRSA Program Succeeds Across Institutions

BY BRUCE K. DIXON
Elsevier Global Medical News

CHICAGO — Multisite implementation of a generic hand-hygiene culture-change program can significantly reduce infections caused by methicillin-resistant *Staphylococcus aureus*, according to Dr. M. Lindsay Grayson.

In a landmark study involving six urban and rural Australian hospitals, a centrally organized program encouraging the widespread use of alcohol-based hand rubs halved MRSA bacteremia rates, Dr. Grayson told the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

It is the first large multisite study to demonstrate the benefits of a hand-hygiene culture change, said Dr. Grayson, director of infectious diseases at Austin Health, a provider of tertiary health services in Melbourne, and professorial fellow at the University of Melbourne. In fact, it was a single-institution study at Austin Hospital that set the stage for this expanded study (Med. J. Aust. 2005;183:509-14).

"[In the current study, we] introduced alcohol-based hand rubs and alcohol wipes for [those sharing] equipment, as well as an educational program for health care workers, patients, and patients' relatives," he reported.

The researchers encouraged the culture change with a promotional drive that included coffee-break seminars, quizzes with prizes, a newsletter on hand hygiene, and the attachment of notices to staffers' pay advice slips. They devised slogans to remind people about hand hygiene, and even hired an advertising consultant to maximize the effect of the message.

They also held feedback sessions with senior nurses on sentinel wards to provide them with information on recent outcome data, and conducted medical, surgical, and nursing grand rounds on MRSA. A key component of the program was the development of a computer-based educational package that could be accessed online.

These and other culture change procedures were maintained and used in the 2-year multicenter study of four hospitals in metropolitan Melbourne, and in two regional hospitals. The program was coordinated by staff at Austin Health and the Victorian Quality Council in Melbourne, and funding was provided by the Department of Human Services for the state of Victoria, which backs efforts to control the MRSA "superbug."

The primary outcome measures were rates of hand-hygiene compliance measured at 3- and 6-month intervals, and of MRSA disease—including bacteremia and clinical isolates—per 100 patient discharges measured at 1-month intervals, said Dr. Grayson.

"For all six sites, hand-hygiene compliance rose from 21% at baseline to 47% at 2 years. We identified the same significant improvements in MRSA disease rates that we identified in the single-center Austin study," he said, noting that MRSA bacteremia fell from 0.03 to 0.01 per 100 patient discharges, and clinical isolates fell from 1.12 to 0.8 per 100 discharges.

"We were able to show that during the 2-year program, there were 719 fewer isolates than would have been expected had we not intervened. More importantly, MRSA bacteremia rates were roughly halved, with 60 fewer patients developing bacteremia than we would have otherwise expected," Dr. Grayson said at the meeting, which was sponsored by the American Society for Microbiology.

The results of a cost analysis suggest that the culture change produced a potential savings over the 2-year period of at least $1.5 million. "The program cost roughly $750,000, so this was a 2-to-1 multiplier effect in terms of savings," he said.

"[This study shows] that a coordinated hand-hygiene program that does not involve direct observation can improve compliance in both rural and urban health care settings and bring significant reductions in MRSA infection rates," concluded Dr. Grayson.

A Swiss researcher, Dr. Hugo Sax, said that although such studies show that progress is being made in hand hygiene, optimal rates of compliance will be achieved only if more physicians lead by example.

"We have to address and educate different health care populations with tailored approaches instead of a one-size-fits-all approach," said Dr. Sax, a consulting physician at the University Hospital in Geneva.

But first, physicians must align their own thinking toward patient safety, he said in an interview.

Dr. John M. Boyce, chief of infectious diseases at the Hospital of Saint Raphael in New Haven, Conn., agreed. "The evidence that hand hygiene reduces the spread of MRSA and other organisms is compelling, and we have to convince our physician colleagues that using alcohol hand rubs both before and after each patient visit doesn't slow down their daily routines," he said in an interview.

Pulmonary Perspectives

Automatic Epinephrine Injectors: A Change in Perspective From the Pulmonologists' Standpoint?

Omalizumab treatment and anaphylaxis risk may be the biggest catalyst for this change in perspective.

Automatic epinephrine injectors (AEIs) have long been a staple of the therapeutic armamentarium of the allergist/immunologist (Webb and Leiberman. *Ann Allergy Asthma Immunol* 2006; 97:39). However, as a rule, pulmonologists have not found it necessary to prescribe such injectors for their patients, except perhaps for the severe, "brittle" asthmatic.

With the introduction of immunologic modifiers and monoclonal antibody therapies, especially omalizumab (Xolair; Genentech, Inc./Novartis Pharmaceuticals; South San Francisco, CA), the perspective of the pulmonologist regarding the use of AEIs may be changing. Omalizumab treatment, administered in-office, may be the biggest catalyst for this change in perspective.

The relatively recent "box warning" regarding omalizumab administration prompts consideration of the pulmonologist in this regard. This warning states that, "Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after the administration of Xolair …"

Due to the risk of anaphylaxis, patients should be closely monitored for an appropriate period of time after omalizumab administration, and health-care providers administering omalizumab should be prepared to manage anaphylaxis that can be life-threatening. Patients should also be informed of the signs and symptoms of anaphylaxis and instructed to seek immediate medical care should symptoms occur."

What the warning does not state is that a significant number of the anaphylactic events have occurred long after what would normally be considered "an appropriate observation period." In other words, reactions have occurred after the patient has left the office.

The latest review of the incidence of anaphylactic events related to omalizumab has revealed an incidence of approximately 0.2%—double that which occurred in the premarketing setting (Limb et al. *J Allergy Clin Immunol* 2007; Oct 15, Epub ahead of print).

At the time of this review, there were 124 events in approximately 57,300 patients recorded from June 2003 to December 2006. Some of these events have been life-threatening. Fifteen percent required hospitalization.

What is particularly relevant, in regard to the pulmonologists' consideration of the prescription of an AEI for these patients, is that 41% of these events occurred >2 h after the administration of omalizumab, and 10% occurred >12 h after the drug was given. In other words, a significant number of episodes occurred outside the office.

This observation has prompted the advice that patients should be informed of the signs and symptoms of anaphylaxis and instructed to seek immediate medical care should these signs or symptoms occur. In addition, it has spurred discussion as to whether or not patients receiving omalizumab should be prescribed an AEI.

Indeed, the administration of omalizumab simply highlights the need for consideration of the administration of AEIs. It should be noted that the incidence of anaphylaxis is increasing (Lieberman et al. *Ann Allergy Asthma Immunol* 2006; 97:596).

AS THE LIST OF BIOLOGICAL AGENTS GROWS, WE CAN EXPECT FURTHER INCREASES IN ANAPHYLACTIC EPISODES. THUS, INTEREST IN MANAGING ANAPHYLACTIC EVENTS MAY ALSO INCREASE.

With the increased risks associated with the administration of in-office biological modifiers and monoclonal antibodies, it might be expected that the observations with omalizumab may only be the first in a series of such instances. For example, anaphylactic reactions to α_1-antitrypsin administration have been well-documented.

As the list of biological agents grows, we can expect further increases in anaphylactic episodes. Thus, pulmonologists' interest in management of anaphylactic events, especially in the use of AEIs, may also increase.

Criterion for Administration of Epinephrine for Anaphylaxis

The National Institutes of Health and The Food Allergy and Asthma Network recently convened a panel to define criteria mandating the administration of epinephrine in patients presenting with a possible anaphylactic event.

In the absence of the administration of a known allergen, it was suggested that a two-organ system presentation was required. For example, cutaneous manifestations plus respiratory symptoms, or cutaneous manifestations plus hypotension would normally be necessary.

However, in the presence of a known provocative agent, *eg*, omalizumab, only a single-organ system was needed to prompt the immediate use of epinephrine. For example, a patient manifesting only urticaria, receiving a known provocative agent, would be a candidate for the immediate administration of epinephrine.

Thus, the threshold for the administration of epinephrine in the outpatient setting is lowered in a patient who has been administered a drug, such as omalizumab, that might provoke an anaphylactic event.

PATIENTS SHOULD BE EDUCATED IN THE MANIFESTATIONS OF ANAPHYLAXIS AND PREPARED TO ADMINISTER EPINEPHRINE IMMEDIATELY SHOULD MANIFESTATIONS APPEAR.

It is emphasized, once again, that patients should be educated in the manifestations of anaphylaxis and be prepared to administer epinephrine immediately should any of these manifestations appear. It is well-recognized that the rapid treatment of anaphylaxis with epinephrine can deter fatalities (Lieberman. *Curr Opin Allergy Clin Immunol* 2003; 3:313).

In view of the above observations, the perspective of the pulmonologist on prescribing AEIs to patients may be changing. It would behoove physicians to be familiar with the injectors that are available for use.

AEIs Available in the United States

There are two AEIs available for use in the United States: the EpiPen (Dey, L.P.; Napa, CA) and the Twinject (Verus Pharmaceuticals, Inc.; San Diego, CA). The physician prescribing AEIs needs to be aware of certain principles that are necessary for the successful use of these devices:

▶ **Patients must be trained meticulously in their use.** It is well-known that many physicians prescribing AEIs have not been familiar with the proper technique of administration; therefore, they have instructed patients incorrectly, resulting in improper use in the field.

Also, patients who are not trained properly have been reluctant to use these devices, which dangerously delays therapy (Lieberman. *Curr Opin Allergy Clin Immunol* 2003; 3:313).

▶ **Patients should be prescribed two doses,** because up to 30% of anaphylactic events require two injections. EpiPen is available in a two-pack, and Twinject comes with two injections packaged together. Prescriptions should be written either for an EpiPen two-pack or a Twinject.

▶ **Patients should be instructed as follows:**

Upon the first sign that an allergic event is occurring, administer the epinephrine, and proceed to the nearest medical facility or call 911. If symptoms have not improved within 5 to 10 min, and you have not yet reached the medical facility or you have not yet been visited by emergency medical services, administer the second injection.

From the above, it is clear that the physician prescribing an AEI needs to be familiar with the device chosen. There are differences between these devices.

As noted, the Twinject comes with two doses contained within a single prescribed package. However, the second dose is not delivered as an automatic injection but by the traditional "push plunger-syringe technique." The second dose is a traditionally filled syringe. Therefore, the patient must be instructed in two different techniques.

Both doses of the EpiPen are given by automatic injectors. Both devices are available in 0.3 mg (adult) and 0.15 mg (child) doses.

Summary

There are two contexts in which pulmonologists might consider use of an AEI. One can consider using an injector in the very brittle, severe asthmatic who suffers from acute, life-threatening episodes of bronchoconstriction. One also should consider an AEI in patients who have been administered omalizumab or, for that matter, any drug that may cause anaphylaxis.

Two types of AEIs are available. Regardless of which one is chosen, it is essential that the patient is carefully instructed in the use of the injector and taught to recognize the signs and symptoms of anaphylaxis. The injector should be used in the outpatient setting at the first sign of an anaphylactic event. ■

Dr. Philip Lieberman
Clinical Professor of Medicine and Pediatrics
University of Tennessee, College of Medicine
Memphis, TN

Disclosure: Dr. Leiberman has served on the advisory board and as a consultant for Dey Laboratories and Verus Pharmaceuticals.

Dr. Gene L. Colice, FCCP
Editor,
Pulmonary Perspectives

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

PRESIDENT'S REPORT

Tackling Disparities in Health Care

BY DR. ALVIN V. THOMAS, JR., FCCP

I have decided, with this as my first column for *CHEST Physician*, to give you an idea about who I am and what my goals are for my ACCP presidency.

I am most honored and humbled to be the 70th President of the American College of Chest Physicians.

I am a native of Philadelphia, Pennsylvania, and I am an only child. I am married to Zorita Duckworth-Thomas. I have four children (all adults), eight grandchildren, and one great grandchild. I attended undergraduate school at the University of Pennsylvania, Howard University College of Medicine, and completed my internal medicine and pulmonary fellowship training at the University of Michigan Medical Center. Dr. John G. Weg, Master FCCP, former ACCP president (1980-1981), was Chief of Pulmonary Medicine and my mentor.

I served 2 years after my internship in the United States Air Force and had an exemplary experience. During my second year, I was trained to do surgical anesthesia. That experience gave me particular insight into airway management.

My pulmonary fellowship experience at Michigan was also special. For the first and last time, I worked in a dedicated Respiratory Critical Care Unit with a one-to-one nursing-patient ratio—an unusual experience nowadays!

I then moved from Michigan to Los Angeles to work at the Martin Luther King Jr./Charles Drew Medical Center in the Watts community, a largely minority (Black and Hispanic), poor, and underserved community. It was the first opportunity I had to really work closely with and contribute to the care of underserved patients.

While at the King/Drew Medical Center, I worked closely with Dr. Albert H. Niden, FCCP, Chief of Pulmonary, and grew academically and professionally. Dr. Niden, along with Dr. Ben Burrows, was an early contributor to the COPD literature when he was at the University of Chicago.

While at King/Drew, I also served as program director for the internal medicine residency program. That experience helped me gain a better understanding of the US medical education system, and it substantially strengthened my interpersonal and administrative skills.

After 13 years at King/Drew, I moved back to Howard to serve as Chief of the Pulmonary Division. Because of my experience at Howard, I am more deeply committed to the care of underserved and minority patients, and I am aware of the absolute need for more minority physicians (especially Black and Latino physicians) in academic and community pulmonary, critical care, and sleep medicine.

I feel privileged to be President of the ACCP, a dynamic organization committed to "focused" care of patients and the education of its membership. I am fully supportive of all ACCP programs and intend to use my expertise to help each grow.

Additionally, I am committed to better understanding the issues contributing to disparities in health and health care for the underserved and minority patients with pulmonary, critical care, and sleep-related illnesses and raising awareness of these issues in the College and the pulmonary, critical care, and sleep community, as a whole.

I believe disparity issues must become a part of the "cultural fabric" of the College. Whenever an educational or medical initiative is proposed by a College Institute or NetWork, it should be determined if there are related disparities in health or health care, and these issues should be discussed as part of the overall program submission. Disparity issues should also be a priority in *CHEST* and in the research and advocacy efforts of the College.

The CHEST Foundation has been quite active in supporting programs that are committed to the care of the underserved, and these efforts continue. I am convinced that the commitment of the College to the above issues and other substantial and dynamic programs will make the ACCP even stronger and more successful.

Again, I am most happy to be your 70th President, and I am totally committed to the continued growth and success of our ACCP. ■

ACCP at ERS—Another Big Success!

BY JOYCE BRUNO REITZNER, MBA, MIPH
Senior QI Research Analyst

This year's European Respiratory Society (ERS) meeting provided another excellent opportunity for the ACCP to service its international members and chest physicians around the world. The 2007 ERS Congress was held in Stockholm, Sweden, September 16-19, 2007. Meeting attendance this year exceeded 15,000, with strong representation from Europe, Asia, and the Middle East. Currently, more than 17% of ACCP members are from countries outside the United States and Canada, and many of them attend this meeting.

For more than 10 years, the ACCP has "set up shop" at the annual ERS meeting to provide one-on-one membership service to many of these international members. The ACCP booth also gives these members the opportunity to peruse a variety of educational resources pertinent to their local practice. The most in-demand resources at ERS were the full spectrum of ACCP board review books and CD-ROMs and the ACCP-SEEK series. Aside from servicing members, the ACCP booth provides a venue for international physicians to meet and network with ACCP leadership, colleagues, and other members. If you attend the ERS next year, please be sure to visit the ACCP booth.

This year, the ACCP is providing a new service to the international ACCP membership. The ACCP has unveiled a new online application for international members to seek ACCP endorsement, faculty, or pro bono support for a medical education meeting in their country. The ACCP is accepting proposals for medical education meetings taking place July 1, 2008, through June 30, 2009. The application deadline is December 1, 2007.

For more information, visit www.chestnet.org/education/program/international.php. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

CRITICAL CARE COMMENTARY

Patient Safety in Critical Care

Patient safety has been a growing issue of concern across all lines of medical care. Since the initial Institute of Medicine's report entitled "To Err is Human: Building a Safer Health System," in which there were 1 million adverse events reported, approximately 44,000 to 98,000 patients died from these preventable errors.[1]

In 2001, the Agency for Healthcare Research and Quality (AHRQ) reported that more than 770,000 patients affected by preventable adverse events are injured or die each year from medication errors alone.[2] In 2002, The Commonwealth Fund estimated that 22.8 million people experienced a medical error themselves or through a family member.[3] In March 2002, The Joint Commission implemented a national patient safety initiative.[4] Congress also has joined this effort with resolutions from the US House of Representatives and US Senate moving forward to increase reporting and address patient safety. The American Board of Medical Specialties has expanded its requirements for certification to include competence in providing safe and high quality care. With subsequent follow-up reports, the Institute of Medicine's 2003 report, and The Joint Commission requirements for 2007-2008, safety standards, measures, and goals have been reevaluated and refined. A new science of safety with its own measures and procedures is constantly being reviewed, adapted, and modernized, especially to include the critical care patient.

More than 4 million people are admitted to ICUs in the United States each year. There are approximately 6,000 ICUs across the country caring for about 55,000 people per day. Given the aging population, this number is expected to increase significantly. Critical care beds account for about 10% of all beds, and the annual budget for critical care is about $180 billion, as recently reported. Critical care settings in the hospital are among the most complex. They must manage the charge of maintaining a high tech workplace with all of its competencies and dealing with the hospital's sickest patients in an incredibly stressful environment.

Given the complexity of the patients, the invasive nature of critical care, and the use of drugs and therapies that have significant risks and benefits, it is not surprising that medical errors occur in ICUs at high rates. There is evidence from past reviews to estimate that about 85,000 errors occur every day, and that 25,000 of these errors may have life-threatening potential. In 2005, the August issue of *Critical Care Medicine* published the Critical Care Safety Study by Rothschild and colleagues,[5] which found that adverse events occurred at a rate of 81 per 1000 patient days, and that serious errors occurred at an incidence rate of 150 per 1,000 patient days. After review, the authors concluded that about 45% of these errors could have been prevented. In 2006, the journal *Intensive Care Medicine* published the Sentinel Events Evaluation (SEE) study by Valentin and colleagues.[6] This multinational, multicontinent study revealed that, in 1,913 adult patients, there were 584 events affecting patients in a single 24-h period. The overall incidence rate was 38.8 per 100 patient days, with most errors relating to lines, catheters, and drains; followed by medication errors, equipment failure, and airway and alarm errors.

These patient safety initiatives and the published statistics on adverse events and medical errors take on added meaning in the context of a medical malpractice lawsuit. In a lawsuit, the injured patient ("the plaintiff") must demonstrate that the physician or hospital ("the defendant") had some duty to the patient, breached it, and that the breach of that duty caused harm to the patient. Once the physician-patient relationship is formed, the physician, or hospital where the treatment is rendered, owes a duty to that patient. The duty imposed on a physician or hospital is characterized by the "standard of care" for the applicable discipline or specialty. Thus, under New York law, the plaintiff must prove that there was a deviation from the applicable standard of care, and that the deviation was the proximate cause of the plaintiff's injury.[7]

Critical Care Institute
American College of Chest Physicians

It has been suggested that if the law recognizes a hospital patient's explicit "right to safety," and consequently, a hospital's duty to implement patient-safety measures, hospitals will be more motivated to develop systems to improve patient safety.[8] Currently, a hospital has a duty to safeguard the welfare of its patients but is not "an insurer of patient safety."[9] The scope of a hospital's duty is effectively determined by the risks that are reasonably foreseeable.[10] The statistics cited by Rothschild and colleagues[5] and Valentin and colleagues[6] clearly show that certain medical errors are foreseeable events in the ICU setting. Intensivists, along with their hospital administrators, should be mindful that the patient safety initiatives and guidelines set forth by The Joint Commission may soon set the standard of care. Consequently, any ICU directors or administrators failing to implement patient safety procedures may find themselves, and their hospital, deemed negligent by a jury for their failure to do so.

Despite all of the facts and reported data, patient safety goals are not close to being fulfilled. There appears to be steady progress, with all hospitals and health systems implementing safety goals. However, our measured progress should be greater and more rapid. What are the barriers to our success? Is it the lack of uniformity and the lack of specific measures? Is the cause the complex nature of critical care with all its inherent problems? In any system, to implement change, there must be agreement that a problem exists. With health-care providers, especially those in critical care, it is hard to accept that all is not being done in the best interest of the patients. Indeed, the prevailing attitude seems to be that, while the care provided could always be safer, it is acceptable as it is now. In addition, all involved have to agree on the direction that the solutions take. The more complicated and involved the solutions are, the less chance of implementation. The practitioners also have to agree that the solutions will actually work. There is a growing amount of literature indicating that some of the proposals can yield significant results. There must be agreement that the solutions do not add new adverse effects that could impede care. The newer technologies—electronic medical records, and even computerized physician order entry—have engendered debate and resistance.

Having acknowledged that providing safer critical care is a significant issue, how does a provider start to improve patient outcomes? A culture of safety succeeds only in a multidisciplinary cooperative team environment. These teams must consist of doctors, nurses, residents, managers, and administrators delineating responsibilities for effective communication, monitoring results, and initiating pathways to improve safety. Medical errors are often system errors rather than individual errors, and ending a culture of blame is crucial. Tools used by industry and now in medicine are helpful in changing these attitudes. Failure mode and effects analysis (FMEA), and root cause analysis (RCA) are two of these tools. RCA is generally retrospective and is very effective. FMEA is generally proactive, which appears to be better. After successful implementation in the Veterans Affairs system in 2001, The Joint Commission is incorporating FMEA into its standards. Many interventions have been suggested, including ICU organization (open, closed, or mixed), ICU staffing, work hours, environment, protocols, daily goal sheets, and technologic standards. All have been introduced with varying results.

In the New York City Health and Hospital Corporation (NYCHHC), a critical care collaborative committee representing 11 institutions and the largest public health complex in the country, has been working to improve safety and outcomes. NYCHHC has joined and adapted the Institute for Healthcare Improvement's campaigns, including "Saving 100,000 Lives," "Protecting 5 Million Lives from Harm," and "Surviving Sepsis." Recent publications and presentations (Berlin et al, Venkatram et al. Presented at: American Thoracic Society annual meeting; May 22, 2007; San Diego, CA) have demonstrated that the implementation of daily goal sheets, vent bundles, tight glycemic control, central line bundles, and training videos have decreased events affecting patients significantly, with more reports to follow. In an effort to make safety and quality performance transparent to the general public, safety data are available at www.nyc.gov/hhc. ■

This article is the first in a series discussing possible solutions to patient safety concerns and improvement of patient care and outcomes.

References

1. Kohn LT, Corrigan JM, Donaldson MS, et al. Washington, DC: National Academies Press, 2000

Continued on following page

ACCP Product of the Month: Audio Sessions From CHEST 2007

If you missed the opportunity to listen to an important clinical education session update at CHEST 2007 in Chicago, place your order for audio sessions today. Simply download sessions to your computer, memory stick, or MP3 player to receive information and training resources you can use as a reference or share with your professional team.

To order, visit www.dcprovidersonline.com/accp and click on the "Sessions Available" link. All sessions can be purchased individually. If you need a memory stick for storing the audio sessions, you also may want to purchase the ACCP/DCP memory stick pen. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

Head-of-Bed Monitoring Improves Positioning Compliance

BY MITCHELL G. KAYE, MD, FCCP

Ventilator-associated pneumonia (VAP) is a common medical problem with significant consequences. It complicates the course of almost 30% of patients supported by mechanical ventilation, and it is the leading cause of death among hospital-acquired infections, with a mortality rate that approaches 50%.

Semirecumbent positioning has been shown to decrease the incidence of VAP, yet patients often do not have the head-of-bed (HOB) consistently elevated.

The purpose of this study was to determine whether continuous HOB monitoring using an indicator light increases the amount of time patients supported by mechanical ventilation have the HOB elevated above 30.

This study was performed in a 30-bed ICU at Abbott Northwestern Hospital in Minneapolis, MN. Ninety patients supported by mechanical ventilation were enrolled in this controlled, prospective study.

An electronic sensor attached to the bed frame provided continuous monitoring and recording of HOB angle; whenever HOB was >30, the sensor activated a bright green vertical light and timer on the monitor device.

For the group of control subjects, the light was disabled, the monitor was stored out of view, and the nursing staff was blinded to the time measurements.

For the intervention group, connections to the light were enabled and

Continued from previous page

2. Agency for Healthcare Research and Quality. Reducing and preventing adverse drug events to decrease hospital costs. Research in Action, Issue 1. AHRQ Publication Number 01-0020, March 2001

3. The Commonwealth Fund. New study estimates eight million American families experienced a serious medical or drug error. Published April 15, 2002

4. The Joint Commission. http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/. Accessed November 19, 2007

5. Rothschild JM, Landrigan CP, Cronin JW, et al. The critical care safety study: the incidence and nature of adverse events and serious medical errors in intensive care. *Crit Care Med* 2005; 33:1694-1700

6. Valentin A, Capuzzo M, Guidet B, et al. Patient safety in intensive care: results from the multi-national Sentinel Events Evaluation (SEE) study. *Intensive Care Med* 2006; 32:1591-1598

7. *Amsler v Verrilli*, 119 AD2d 786 (2nd Dept 1986)

8. Annas GJ. The patient's right to safety—improving the quality of care through litigation against hospitals. *N Engl J Med* 2006; 354:2063-2066

9. *NX v Cabrini Medical Center*, 97 NY2d 247, 252 (2002) (citations omitted)

10. Id at 253

Dr. Peter Spiro, FCCP
Assistant Professor of Clinical Medicine
Columbia University College of Physicians and Surgeons
Head, MICU
Harlem Hospital Center
New York, NY

Frances L. Garfinkel, MBA, JD
New York, NY

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

the monitor placed on top of the ventilator, where the light and timer were clearly visible to the nursing staff.

The percentage of time with HOB elevated >30 degrees was significantly greater ($p<0.0001$) in the intervention group, with a median of 81% vs a median of 17% in the group of control subjects.

The efficacy of the monitor device appeared to be related to the indicator light, which was visible from anywhere in the patients' rooms, as well as from outside the room through the doorway or window.

The light served as a visual cue that did not compete with other alarms and provided positive reinforcement to the nursing staff to maintain proper HOB elevation.

Continuous HOB monitoring using an indicator light significantly increases the time patients supported by mechanical ventilation have the HOB elevated >30.

By effectively encouraging and reliably measuring compliance with semi-recumbent positioning, continuous HOB monitoring appears to be a valuable clinical tool in the overall care of patients receiving mechanical ventilation support.

Further research is needed to determine whether continuous HOB monitoring, as part of a comprehensive prevention program, can contribute to a significant decrease in the incidence of VAP. ■

For more information, Dr. Kaye's slide presentation is posted under "Hot Topics" at www.chestnet.org/networks/critical_care/hotTopics.php.

REFERENCES **1.** Gerotziafas GT, Samama MM. Prophylaxis of venous thromboembolism in medical patients. *Curr Opin Pulm Med.* 2004;10:356-365. **2.** Heit JA, Cohen AT, Anderson FA Jr, for the VTE Impact Assessment Group. Estimated annual number of incident and recurrent, nonfatal and fatal VTE in the US [poster]. Presented at the 47th Annual Meeting and Exposition, American Society for Hematology, December 10-13, 2005, Atlanta, GA. [Poster 68] **3.** Murin S, Romano PS, White RH. Comparison of outcomes after hospitalization for deep venous thrombosis or pulmonary embolism. *Thromb Haemost.* 2002;88:407-414. **4.** Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. *Circulation.* 2003;107:I-9–I-16. **5.** American Lung Association. *Chronic Obstructive Pulmonary Disease Fact Sheet.* August 2006. Available at: http://www.lungusa.org/site/pp.aspx?c=dvLUK9O0E&b=35020. Accessed January 8, 2007. **6.** Solucient Inpatient Hospital Statistics, 2006. **7.** Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004;126(suppl):338S-400S. **8.** Fraisse F, Holzapfel L, Coulaud J-M, et al. Nadroparin in the prevention of deep vein thrombosis in acute decompensated COPD. *Am J Respir Crit Care Med.* 2000;161:1109-1114. **9.** Monreal M, Muñoz-Torrero JF, Naraine VS, et al for the RIETE Investigators. Pumonary embolism in patients with chronic obstructive pulmonary disease or congestive heart failure. *Am J Med.* 2006;119:851-858. **10.** Prescott SM, Richards KL, Tikoff G, et al. Venous thromboembolism in decompensated chronic obstructive pulmonary disease. *Am Rev Respir Dis.* 1981;123:32-36. **11.** Solucient Hospital Database, April 2007. **12.** Tillie-Leblond I, Marquette C-H, Perez T, et al. Pulmonary embolism in patients with unexplained exacerbation of chronic obstructive pulmonary disease: prevalence and risk factors. *Ann Intern Med.* 2006;144:390-396. **13.** Stein PD, Beemath A, Meyers FA, Olson RE. Pulmonary embolism and deep venous thrombosis in hospitalized adults with chronic obstructive pulmonary disease. *J Cardiovasc Med.* 2007;8:253-257. **14.** Samama MM, Cohen AT, Darmon J-Y, et al for the Prophylaxis in Medical Patients with Enoxaparin Study Group. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. *N Engl J Med.* 1999;341:793-800. **15.** Alikhan R, Cohen AT, Combe S, et al. Prevention of venous thromboembolism in medical patients with enoxaparin: a subgroup analysis of the MEDENOX study. *Blood Coagul Fibrinolysis.* 2003;14:341-346. **16.** Kleber F-X, Witt C, Vogel G, et al for the THE-PRINCE Study Group. Randomized comparison of enoxaparin with unfractionated heparin for the prevention of venous thromboembolism in medical patients with heart failure or severe respiratory disease. *Am Heart J.* 2003;145:614-621.

Please see a brief summary of prescribing information including boxed WARNING on the next page.

AMERICAN COLLEGE OF CHEST PHYSICIANS®

NEWS FROM THE COLLEGE

EDUCATION INSIGHTS

Databases: Facilitating the Practice of Chest Medicine

BY JOYCE BRUNO REITZNER, MBA, MIPH
Senior QI Research Analyst

Today, many external forces impact the practice of medicine, such as maintenance of certification and state licensure requirements, public reporting of individual physicians' quality of patient care, pay-for-performance and national quality initiatives, and looming reimbursement rate cuts.

While not all physicians feel the effect of these catalysts yet, the catalysts will soon influence the environment where all medicine is practiced. Physicians already touched by these demands are pushed in search of resources to help them seamlessly care for their patients, while fulfilling new and changing requirements. Professional societies are responding to their physician members' needs in a variety of ways. One way these societies are addressing the challenges is to develop

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

clinical databases. These databases acquire, collate, and analyze information to ultimately help physicians fulfill national and local requirements, identify areas where their practice patterns differ from national benchmarks, and determine why.

The concept of clinical databases is not new. The Society of Thoracic Surgeons National Database and National Surgical Quality Improvement Program database, which focus on surgical procedures, have existed for more than a decade, starting in the Veterans Affairs medical system and expanding to the nongovernmental sector. The University HealthSystem Consortium provides its members with the opportunity to participate in a database encompassing clinical and administrative domains. Data quality, aggregation methods, and information use vary across databases. However, the aim of all the databases is to help physicians improve patient care and outcomes while minimizing their practice cost.

Despite this surge in clinical databases, there is a need to capture and aggregate information from pulmonary, critical care, and sleep medicine, while streamlining the reporting burden for individual physicians and enabling them to satisfy pressing administrative requirements to deliver the best quality patient care.

With the guidance of the ACCP Board of Regents, the Quality Improvement Committee has initiated the development of a clinical database for chest medicine physicians for use by ACCP members. In the spring of 2008, the ACCP plans to initiate the pilot phase of the database, which will allow physicians to self-assess competency and practice gaps, benchmark their practice with reliable and clinically relevant information, access more targeted educational interventions, attain maintenance of certification and manage credentialing requirements, and develop local quality improvement programs.

For details about ACCP quality improvement efforts, please contact Joyce Bruno Reitzner, MBA, MIPH, at jbruno@chestnet.org. ■

This Month in *CHEST*: Editor's Picks

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

- **Matrix Metalloproteinase-2 Protein in Lung Periphery Is Related to COPD Progression.** *By Dr. S. Baraldo, et al*
- **Oral or IV Prednisolone in the Treatment of COPD Exacerbations: A Randomized, Controlled, Double-Blind Study.** *By Dr. Y. P. de Jong, et al*
- **Daytime Hypercapnia in Obstructive Sleep Apnea Syndrome.** *By Dr. N. Kawata, et al*
- **Predictors of Rehospitalization and Death After a Severe Exacerbation of COPD.** *By Dr. R. McGhan, et al*
- **Influence of Gender on the Outcome of Severe Sepsis: A Reappraisal.** *By Dr. C. Adrie, et al*
- **American College of Chest Physicians Consensus Statement on the Respiratory and Related Management of Patients With Duchenne Muscular Dystrophy Undergoing Anesthesia or Sedation.** *By Dr. D. J. Birnkrant, FCCP (Chair); Dr. H. B. Panitch, FCCP (Co-Chair); and Members of the Authoring Committee*
- **Responsibilities of Authorship.** *By Dr. W. M. Vollmer*

www.chestjournal.org

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

NETWORKS
Educational Sleep Slide Kit

BY RICHARD CASTRIOTTA, MD, FCCP
Chair, Sleep Medicine NetWork

The Sleep Medicine NetWork of the American College of Chest Physicians developed an educational slide kit to (1) educate members of the College about sleep medicine, and (2) help members of the Sleep Medicine NetWork use their expertise to teach others about the important aspects of sleep medicine. These slides may also serve to help those who are preparing for certification examinations in sleep medicine.

The slides have been authored by national experts in the field who are excellent, experienced teachers. Educating physicians who are not trained in sleep medicine about this subspecialty will allow more rapid diagnosis and therapy for patients and increase access to specialized care, as needed.

In the United States population, there is a prevalence of about 5% for sleep apnea, 10 to 20% for insomnia, and 3 to 15% for restless legs syndrome. Similar findings are found throughout the world. Some 40 million Americans suffer from excessive sleepiness or difficulty sleeping. Sleep disorders may lead to impaired work performance, lost productivity, increased motor vehicle and other types of accidents, and an increased risk of cardiovascular disease (with sleep apnea).

Members of the ACCP Sleep Medicine NetWork are among the leaders in becoming the primary subspecialists who identify and treat patients with sleep disorders. This newly posted Educational Sleep Slide Kit (www.chestnet.org/networks/presentations/Sleep) will allow physicians to better serve their patients, thus resulting in improved health and quality-of-life. ■

Introducing the New Ambassadors Group Chair

The CHEST Foundation's Ambassadors Group is pleased to introduce Zorita Thomas as the Ambassadors Group Chair for 2007-2008. Zorita was born in Cassopolis, MI, and has a large family. She attended Andrews University in Berrien Springs, MI, where she majored in vocal music. She has a special interest in Negro spiritual music and has recorded her first CD entitled *Forget Me Not, Negro Spirituals by Zorita*.


ZORITA THOMAS

She serves as a mentor and life coach in doing what she can to generate peace in families and communities. She is her family's historian and enjoys planning family reunions. Zorita also uses her time as a hospice-care volunteer.

When asked what goals and objectives she has set for the Ambassadors Group for the upcoming year, she responded that she would like to see Ambassadors Group members expand and strengthen their reach to more youth, particularly in the area of lung health education. She would like to see follow-up with students who have been taught the Lung Lessons℠ curriculum. Zorita feels that since smoking starts at a young age, more effort should be made to develop higher self-esteem in youth so that they never start smoking. In addition, Zorita would like more ACCP members to be part of the Ambassadors Group so that they can be involved in the lung health education efforts of the group. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

PRACTICE MANAGEMENT UPDATES

Share New Codes With Practice Staff

BY DIANE KRIER-MORROW, MBA, MPH, CCS-P

The College leadership was pleased with the significant work of its committees this past year. The Practice Management Committee (PMC), chaired by Richard M. Hamrick III, MD, MBA, FCCP, includes the ACCP CPT Advisor, Steve G. Peters, MD, FCCP, and the ACCP RUC Advisor, Scott Manaker, MD, PhD, FCCP. The ACCP partners with ATS representatives, including the ATS CPT Advisor, Stephen Hoffmann, MD, FCCP, and the ATS Practice Committee Chair and RUC Advisor, Alan L. Plummer, MD, FCCP.

New Codes

The Practice Management Committee met on October 22 and was pleased to hear of the significant number of preprint orders for the 12th edition of the ACCP coding and practice management book, renamed Coding for Chest Medicine 2008: A Practice Management Tool.

There are several coding changes this year related to pulmonary medicine.

Smoking Cessation Counseling

The Medicare smoking cessation codes are transitioning into CPT; it is important for members to ask their patients to request this benefit from other third-party payers.

Patients are more likely to stop tobacco use when they are encouraged by their physicians.

Most pulmonologists provide this service, yet the vast majority is not using these codes.

The codes listed in the sidebar below are reported in addition to an evaluation and management code, appended with modifier **25**. Smoking cessation counseling less than 3 minutes is included in the E/M code.

Medicare will cover a total of eight sessions in a 12-month period. Medicare requires the medical record to show medical necessity. Use appropriate ICD-9-CM diagnosis codes, such as **305.1** Tobacco dependence and **492.8** Emphysema.

Dr. Peters recommends that counseling time be documented and smoking cessation modalities discussed, along with the medical condition or therapeutic agent that is adversely affected by tobacco use.

Lungs and Pleural Codes Renumbered

In addition, CPT renumbered five codes in the Lungs and Pleural subsection of the Surgery/Respiratory section of CPT.

The practice will have significant payment denials if you do not use the new numbers listed after January 1 for thoracentesis, insertion of pleural catheter, tube thoracostomy, and chemical pleurodesis.

New Subcutaneous Infusion Codes

For physicians working in the allergy field, there are three new codes, **90769-90771**, for subcutaneous infusion of immune globulin.

Please note that there is a new allergy chapter in the 2008 book, *Coding for Chest Medicine 2008: A Practice Management Tool*.

To purchase your copy of the book, call (800) 343-2227 or order online at www.chestnet.org. ■

New 2008 CPT Codes

New 2008 CPT Code	2007 Code	Descriptor
99406	**G0375**	Smoking and tobacco use cessation counseling visit; intermediate, greater than 3 minutes, up to 10 minutes
99407	**G0376**	Smoking and tobacco use cessation counseling visit; intensive, greater than 10 minutes
32421	**32000**	Thoracentesis, puncture of pleural cavity for aspiration, initial or subsequent
32422	**32002**	Thoracentesis with insertion of tube, includes water seal (*eg,* for pneumothorax), when performed (separate procedure)
32560	**32005**	Chemical pleurodesis (*eg,* for recurrent or persistent pneumothorax)
32550	**32019**	Insertion of indwelling tunneled pleural catheter with cuff
32551	**32020**	Tube thoracostomy, includes water seal (*eg,* for abscess, hemothorax, empyema), when performed (separate procedure)
90769		Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to one hour, including pump set-up and establishment of subcutaneous infusion site(s) (For infusions of 15 minutes or less, use **90772**)
90770		Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure) (Use **90770** in conjunction with **90769**) (Use **90770** for infusion of intervals of greater than 30 minutes beyond one-hour increments)
90771		Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); additional pump set-up with establishment of new subcutaneous infusion site(s) (List separately in addition to code for primary procedure) (Use **90771** in conjunction with **90769**) (Use **90769** and **90771** only once per encounter)

Source: ACCP Practice Management Committee

Correction

In the November 2007 issue, the Web site listed in the "Now Showing" graphic should be **www.chestnet.org/networks/accp_industry/index.php**.

ELSEVIER GLOBAL MEDICAL NEWS

H. pylori May Protect Children Against Asthma

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Children aged 3-13 years who were seropositive for *Helicobacter pylori* were 53% less likely to develop asthma, compared with children who did not carry the bacteria in their stomachs, results from a large national study demonstrated.

This marks the first study to show an inverse association between *H. pylori* colonization and asthma in children.

"The inverse association between *H. pylori* and current asthma status in children independently confirms prior observations of a strong inverse association with early onset asthma in adults," Dr. Martin J. Blaser reported at the annual meeting of the Infectious Diseases Society of America.

Children and teens who were positive for *H. pylori* were 35% less likely to have ever had asthma.
DR. BLASER

He reported the finding on behalf of his associate, Yu Chen, Ph.D., of New York University, New York, who was unable to attend the meeting.

Dr. Blaser and Dr. Chen conducted a cross-sectional evaluation of data from 3,327 children aged 3-19 years who had participated in the Fourth National Health and Nutrition Examination Survey between 1999 and 2000.

Overall, children and teens who were seropositive for *H. pylori* were 35% less likely to have ever had asthma, compared with those who were seronegative for the bacteria, reported Dr. Blaser, chairman of the department of medicine and professor of medicine and microbiology at NYU. They were also 44% less likely to have asthma before the age of 5 years.

In addition, the researchers found that children aged 3-13 who were seropositive for *H. pylori* were 53% less likely to have ever had asthma, 60% less likely to have current asthma, and 71% less likely to have current allergic rhinitis, compared with children who did not carry the organism in their stomachs.

In responding to a question from an audience member about the interplay of *H. pylori* and asthma, Dr. Blaser said it is more likely that *H. pylori* protects children from asthma than the other way around.

He added that the protective relationship observed between asthma, allergic rhinitis, eczema, and skin sensitization among the seropositive study participants suggests an immunologic mechanism of action. "The speculation is that the relationship is immunologically based," said Dr. Blaser, who is a past president of the IDSA.

Dr. Blaser noted that 50 years ago more than half of children in the United States had *H. pylori* in their stomachs. Today, fewer than 1 in 10 children under the age of 13 carry the bacteria in their stomachs, due to the widespread use of antibiotics, improvements in childhood living conditions, and smaller family sizes. "*H. pylori* is rapidly disappearing," he said.

Meanwhile, the incidence of asthma in the United States has been rising rapidly over the past four decades. Today, 13% of children have been diagnosed with the disease, and it ranks as the third leading cause of hospitalization in children younger than 15 years of age, according to the Centers for Disease Control and Prevention. ■

19A Serotype Dominant Among Invasive Pneumococci

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Serotype 19A may be the most common serotype isolated from children's invasive pneumococcal infections in the United States, results from a multicenter study suggest.

The finding comes from the United States Pediatric Multicenter Pneumococcal Surveillance Study Group, a network of eight children's hospitals that has been identifying patients with systemic pneumococcal infections since 1993. The researchers send the isolates to a central laboratory for serotyping and complete a standardized case report form that includes demographic and clinical information, including the number of 7-valent pneumococcal conjugate vaccinations (PCV7) the child has received.

At the annual meeting of the Infectious Diseases Society of America, Dr. Sheldon L. Kaplan reported on 1,234 isolates collected between April 1, 2000 and December 31, 2006. Ages of patients ranged from 0 to 20 years of age, but most infections occurred in the first 5 years of life. Serotype 19A accounted for 19% of all nonvaccine serotype isolates in 2000, 22% in 2001, 18% in 2002, 23% in 2003, 39% in 2004, 34% in 2005, and 49% in 2006. Serotype 19A has been the most common nonvaccine serotype each year since 2003. In 2005 and 2006 combined, the next most common nonvaccine serotypes were 1 (21 cases), 3 (14 cases), 33, 15, and 7 (13 cases each), and 6A (11 cases).

No deaths were reported associated with pneumococcal infections in 2006. "The number of invasive infections reached its lowest point in 2004 and then increased 13% in 2005 and another 5% in 2006," Dr. Kaplan, chief of the infectious disease service at Texas Children's Hospital, Houston, noted in a later interview. "Nevertheless, the number of cases annually was still 60% less than seen each year before the pneumococcal conjugate vaccine was licensed for routine administration to infants."

The most common type of infection among children with serotype 19A was bacteremia, followed by pneumonia, bacterial meningitis, and other infections.

When the researchers applied the 2007 breakpoints for minimum inhibitory concentration (MIC) interpretations, they found that 28% of 19A isolates in 2006 were susceptible to penicillin, 34% were immediately susceptible to penicillin, and 37% were resistant to penicillin.

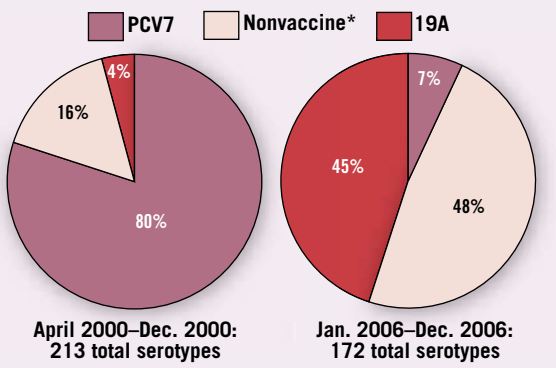
Dr. Kaplan, who is also a professor of pediatrics at Baylor College of Medicine, Houston, predicted that the percentage of isolates resistant to penicillin "will go down dramatically" when the Clinical and Laboratory Standards Institute publishes new *Streptococcus pneumoniae* penicillin breakpoints for nonmeningeal pneumococcal isolates in 2008.

He concluded that continued surveillance of invasive pneumococcal infections "will remain necessary following the inclusion of serotype 19A and other serotypes."

The United States Pediatric Multicenter Pneumococcal Surveillance Group includes clinicians from Texas Children's Hospital, Houston; Children's Hospital of Pittsburgh; Children's Hospital San Diego; Columbus (Ohio) Children's Hospital; Children's Memorial Hospital, Chicago; Arkansas Children's Hospital, Little Rock; Brenner Children's Hospital, Wake Forest, N.C.; and Children's Hospital Los Angeles.

Dr. Kaplan disclosed that he has received research grants from Roche and Wyeth Pharmaceuticals. ■

Prevalence of Serotypes Among Invasive Pneumococcal Infections in Children



*Excluding 19A.
Note: Based on data for 1,234 isolates.
Source: Dr. Kaplan

ELSEVIER GLOBAL MEDICAL NEWS

In Managing Diabetes, Track and Treat Sleep Apnea

Improved insulin sensitivity, lower postprandial glucose may be benefits of treating sleep apnea.

BY MIRIAM E. TUCKER
Elsevier Global Medical News

ST. LOUIS — Sleep apnea assessment and treatment should be considered an integral component of diabetes management, Susan M. LaRue, R.D., said at the annual meeting of the American Association of Diabetes Educators.

"Sleep apnea is highly prevalent in people with diabetes, people with hypertension and obesity, all of which we see in huge numbers in our patient population," said Ms. LaRue, a certified diabetes educator with Amylin Pharmaceuticals.

What's more, data suggest that the vast majority of obstructive sleep apnea (OSA) cases among people with and without diabetes are undiagnosed.

Because sleep apnea is so common among people with diabetes—concomitant with obesity and hypertension—the Scripps' Whittier Institute for Diabetes, La Jolla, Calif., has instituted a "best practice" in which every patient is screened for OSA, and those found to have the condition are referred for treatment and follow-up.

In a study published by the Whittier's Dr. Daniel Einhorn and his associates, 72.4% of 279 adults with type 2 diabetes were found to have some degree of sleep apnea, defined as an apnea-hypopnea index (AHI) of five events or more per hour. More than a third of the patients (35.8%) had an AHI of at least 15 events per hour, a more severe apnea level associated with a doubling of the risk for the development of hypertension after adjustment for comorbidities such as body mass index (BMI), alcohol use, and cigarette smoking (Endocrine Practice 2007;13:355-62).

The proportion of those with an AHI at or above 15 events per hour was much higher among men than women (49% vs. 21%). Other significant risk factors included age 62 years and older, a BMI of 30 kg/m^2 or greater, snoring, and reports of stopped breathing during sleep, said Dr. Einhorn, also with the University of California, San Diego, and his associates.

That study and the symposium in which Ms. LaRue spoke were both sponsored by the ResMed Corp., which manufactures continuous positive airway pressure (CPAP) devices for treatment of OSA.

Diabetes is among several cardiovascular-related conditions that are strongly associated with OSA. Data suggest that OSA is present in about 80% of individuals with drug-resistant hypertension (35% of all hypertension), in 50% of those with congestive heart failure, and in 50% of those with atrial fibrillation. It is also found in 77% of the morbidly obese population.

The mechanism for the association is not known, but theories focus on the increased sympathetic nervous activity resulting from repeated apneas. The resulting higher cortisol levels are related to insulin resistance, which predisposes to impaired glucose tolerance and other cardiovascular risk factors, said Ms. LaRue, formerly with the Whittier Institute.

A study in which the results of overnight polysomnography and oral glucose tolerance testing were compared in 30 obese (but not diabetic) patients with OSA and in 27 equally obese individuals without OSA demonstrated that those who had OSA were more insulin resistant, independent of the degree and distribution of adiposity. The authors hypothesized that the worsening in insulin sensitivity in the OSA patients could reflect the hypoxic state and would account for the increased vascular risk (Clin. Endocrinol. 2003;59:374-9).

Treatment of OSA with CPAP not only reduces apneic episodes and improves sleep quality, but also appears to improve the cardiovascular and metabolic abnormalities. In a German study of 60 patients with moderate to severe OSA, those who were given "therapeutic" levels of CPAP for an average of 9 weeks had a 95% reduction in apneas and hypopneas and a decrease in mean arterial blood pressure of 9.9 mm Hg.

That level of decline would be predicted to cut coronary heart disease event risk by 37% and stroke risk by 56%, the investigators said (Circulation 2003;107:68-73).

Insulin sensitivity was significantly improved at 2 days and at 3 months of CPAP therapy among 40 patients with an AHI greater than 20, more so among those with BMIs less than 30 kg/m^2 than among those with higher BMIs (Am. J. Respir. Crit. Care. Med. 2004;169:156-62).

Another study of 25 patients with type 2 diabetes and sleep-disordered breathing demonstrated that an average of 83 days' treatment with CPAP significantly reduced postprandial glucose values, by about 60 mg/dL after each meal (Arch. Intern. Med. 2005;165:447-52). ■

INDEX OF ADVERTISERS

Sleep Medicine Strives to Unite Multiple Disciplines

BY HEIDI SPLETE
Elsevier Global Medical News

MINNEAPOLIS — The need to unite sleep specialists from multiple academic departments challenges the field of sleep medicine, Dr. Ronald D. Chervin said at the annual meeting of the Associated Professional Sleep Societies.

"Because sleep is relevant to so many different departments, there is not always good integration across campus," said Dr. Chervin, a professor of sleep medicine, a professor of neurology, and director of the sleep disorders center at the University of Michigan, Ann Arbor.

For example, a sleep scientist may not rub elbows daily with a pulmonologist or ENT specialist, he said.

The structural challenges that persist at many research universities can make interdisciplinary integration difficult, even though such integration may be the way to provide the best patient care, Dr. Chervin noted.

But the tug-of-war persists between clinician desires to provide good multidisciplinary care versus departmental concerns for the bottom line.

Most sleep specialists agree that patients receive the best care when they see clinicians from a variety of medical fields, Dr. Chervin said.

But sharing human resources is not always a priority for any given academic department, and it is not always easy to give up billing opportunities to another department in order to serve a higher goal and allow faculty to pursue diverse interests, he explained.

The role of sleep medicine can be difficult to explain to administrators and faculty outside the field, in part because there often is inadequate investment in sleep medicine specifically.

For example, even at the University of Michigan, which has a large and successful sleep disorders center, there is no administrator dedicated to sleep medicine to help the director manage budgets and financial spreadsheets, "which we are not trained in medical school to do," Dr. Chervin said. Also, billing and hiring issues still create interdepartmental friction. "I'm proud of our faculty here at Michigan, but we have lost some opportunities to hire qualified personnel because of these departmental issues," he said.

One strategy that the university has used to overcome some of the interdepartmental barriers has been the creation of an "Alternatives to CPAP" clinic.

"We can see patients shoulder to shoulder with an ENT specialist, maxillofacial surgeon, and dentist. It serves the patients' interests and is wonderful for education," he said. "And we managed to satisfy all the departments in terms of billing." The university has developed two other clinics that follow the CPAP program model—a multidisciplinary pediatric sleep and behavior clinic and another behavioral sleep medicine clinic for adults.

What does the future hold for sleep medicine? Dr. Chervin said he believes that creating comprehensive sleep centers at universities would improve patient care and promote the basic scientific research that continues to drive advances in sleep medicine.

Ideally, a "center for sleep science" would unite sleep specialists on campus, at least for joint grand rounds, for training, and for promoting grant submissions that could cross department boundaries, he said. In his view, sleep centers should uphold a tripartite mission that includes research, education, and patient care and provide both clinical and preclinical programs.

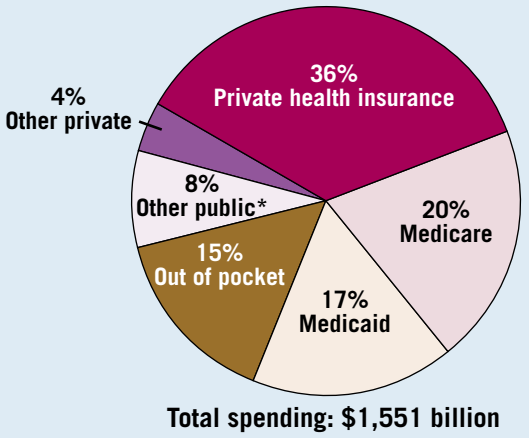
Sleep centers need their own physical space and dedicated funding, in part to allow them to bill for clinical and laboratory services and then reimburse other departments for faculty effort, Dr. Chervin said. And sleep centers should have a greater say in hiring decisions, he added.

As more data emerge to support the impact of sleep and sleep problems on a range of medical conditions, support for interdisciplinary work in sleep medicine and the establishment of sleep centers may gain traction.

"How does a new interdisciplinary field fit within a traditional, department-based academic medical center?" Dr. Chervin asked. "It's like trying to put a square peg in a round hole." ■

DATA WATCH

Who Pays for Personal Health Care?



Total spending: $1,551 billion

*Includes SCHIP spending. Note: Based on 2004 data.
Source: Health Affairs 2007 Nov. 6

ELSEVIER GLOBAL MEDICAL NEWS

Revised Modafinil Labeling Highlights Rash Risks

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Warnings about serious rashes—including Stevens-Johnson syndrome and hypersensitivity reactions—as well as psychiatric symptoms have been added to the label of modafinil, according to a MedWatch notice issued by the Food and Drug Administration on Oct. 24.

Modafinil, described as a "wakefulness-promoting agent," is marketed as Provigil by Cephalon Inc., and was first approved as a treatment for narcolepsy in 1998. It is approved for improving wakefulness in adults with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift-work sleep disorder. It is not approved for any pediatric indications, the advisory emphasizes, although some reports have been in children.

The MedWatch notice and a "Dear Healthcare Professional" letter issued by Cephalon describe worldwide postmarketing reports of life-threatening rash, including toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) in adults and children. There have also been postmarketing reports of angioedema and multiorgan hypersensitivity reactions.

The reporting rate—which is considered an underestimate, because postmarketing reports of adverse events tend to be underreported—of TEN and Stevens-Johnson syndrome (SJS) associated with modafinil use is higher than the background incidence rate, according to the letter. The background in the general population is estimated at 1-2 million cases per million person-years.

The potential for benign rashes—which have been associated with modafinil use—to develop into serious rashes cannot be reliably predicted, so "modafinil should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug-related," the letter says.

Because of postmarketing reports of angioedema, the letter says that patients should be advised to stop treatment and "immediately report to their physician any signs of symptoms suggesting angioedema or anaphylaxis."

The letter also recommends that discontinuation of the drug should be considered in patients who develop psychiatric symptoms during treatment, because mania, anxiety, hallucinations, and suicidal ideation are among the psychiatric adverse reactions reported in people treated with modafinil.

The "Dear Healthcare Professional" letter says that in studies, the incidence of rash resulting in discontinuation of the drug in pediatric patients (younger than age 17 years) was 0.8% (13 of 1,585). ■

CLASSIFIEDS

PROFESSIONAL OPPORTUNITIES

VA Palo Alto Health Care System (VAPAHCS)

VA Palo Alto Health Care System (VAPAHCS) – invites applications for a staff physician in the Pulmonary, Critical Care Medicine, Sleep Disorders Section of the Medical Service. Applicants should be BC/BE in Pulmonary and Critical Care Medicine. Training in interventional pulmonology and sleep disorders medicine is desirable. A commitment to academic achievement and teaching is expected.† Research interest and experience are desirable. Qualified applicants may be eligible for a faculty appointment in the Clinician – Educator track in the Department of Medicine in the Stanford University School of Medicine. VAPAHCS is committed to increasing representation of women and members of minority groups on its staff and particularly encourages applications from such candidates. Applicants should fax an updated CV and 3 references to the attention of Rajinder Chitkara, MD, Chief, Pulmonary, Critical Care Medicine, Sleep Disorders Section at fax #: 650-852-3276 or mail it to his attention at VAPAHCS (111), 3801 Miranda Avenue, Palo Alto, CA 94304. The Department of Veterans Affairs is an equal opportunity employer.

PULMONARY, CRITICAL CARE, SLEEP MEDICINE PHYSICIAN

Openings exist at the VA Medical Center Milwaukee, Wisconsin, for physicians with strong academic credentials to join the Pulmonary, Critical Care and Sleep Medicine Program. Extensive research opportunities exist through the Medical College of Wisconsin. Qualified candidates should be board certified or eligible in Pulmonary and Critical Care and in Sleep Medicine. A strong background in COPD, lung cancer and pulmonary infectious diseases, sleep medicine and critically ill patients is required. Clinical/research experience, a history of academic achievement, teaching in undergraduate and graduate medical education settings and a significant publication record is also required. Applicants must have appropriate credentials for a faculty appointment at the Medical College of Wisconsin at an Assistant Professor level or higher. Finally, applicant must have a commitment to teaching residents and students, and attend on a general medical service. Questions may be directed to Ralph Schapira, M.D., ralph.schapira@va.gov. Send cover letter and C.V. to Marilyn Denning, (HR-05), Clement J. Zablocki VA Medical Center, 5000 W. National Ave., Milwaukee, WI 53295

Pulmonary/Critical Care – Richmond, Virginia

Well-established group seeking BC/BE physician. 1:10 night call. 1:4 weekend daytime rounds. Considerable ICU nighttime coverage provided by EICU physician. Balanced call schedule spread amongst 20 FTE physicians. Practice includes Pulmonary, Critical Care, Sleep, Clinical Research, EICU. Sleep training great but not required. No grants to write. Teaching responsibilities not mandatory. Excellent base salary/benefits package with significant potential. No J-1 available. Position available immediately and for 2008. Contact Johnny Wong, MD. Send CV and cover letter to wongj@paraccess.com or FAX to 804-559-2357.

NORTH CAROLINA PULMONOLOGIST

Assume practice in, family community located less than two hours from Carolina beaches, Charlotte, Raleigh and just 35 minutes from golf resort of Pinehurst. Loan repayment assistance possible. To learn more contact Melisa Ciarrocca at 800-764-7497; Fax: 910-276-0470 or email: Melisa.Ciarrocca@scotlandhealth.org Website: www.scotlandhealth.org

BEAUTIFUL COAST OF MAINE

BC/BE Pulmonologist. Multispecialty community hospital in midcoast region seeks full-time physician. Safe, smog-free, and rapidly growing city with excellent schools and year-round recreation. Ideal family environment. Contact: Mark Biscone, Executive Director, Waldo County General Hospital, PO Box 287, Belfast, ME 04915. 207-338-9302; ceo@wchi.com www.wchi.com

FOR INFORMATION ON CLASSIFIEDS:
Contact: Rhonda Beamer, Walchli Tauber Group, Inc., 2225 Old Emmorton Road, Suite 201, Bel Air, MD 21015. (443) 512-8899 Ext 106. FAX: (443) 512-8909.
Email ad to: rhonda.beamer@wt-group.com

Large Study Backs Caffeine for Apnea of Prematurity

BY MARY ANN MOON
Elsevier Global Medical News

The benefits of caffeine therapy for apnea of prematurity clearly outweighed the risks in the first large, randomized, placebo-controlled study to examine the risks and benefits of this long-used therapeutic approach.

Caffeine therapy improves not just long-term survival, but also long-term survival without neurodevelopmental disability, according to the trial's principal investigator, Dr. Barbara Schmidt of McMaster University, Hamilton, Ont., and her associates.

The results of the international study were published in the New England Journal of Medicine.

"The number of infants who would need to be treated with caffeine to prevent one adverse outcome was 16," the investigators said. Caffeine therapy had no significant effect, however, on rates of death, severe hearing loss, or blindness.

While caffeine and other methylxanthines have been used as respiratory stimulants for apnea of prematurity for over 30 years, these findings show for the first time that the benefits of caffeine therapy "outweigh any potential risks up to 2 years after very preterm birth," the investigators said.

AMONG NEONATES RANDOMIZED TO CAFFEINE, THE RATE OF DEATH OR SURVIVAL WITH A DISABILITY WAS 40.2%, COMPARED WITH 46.2% FOR THE PLACEBO GROUP.

Without prospective study results, there were concerns that the drugs might adversely affect the development of the preterm brain and overall growth. Caffeine is known to reduce cerebral blood flow in adults; it can inhibit adenosine receptors, which might compromise brain-cell survival during hypoxia; and it can raise the metabolic rate and oxygen consumption, which might compromise long-term growth.

To address the concerns, Dr. Schmidt and her associates studied 1,869 infants who weighed 500-1,250 g at birth between 1999 and 2004 and were randomly assigned to receive intravenous caffeine therapy, which consisted of a loading dosage of 20 mg/kg and a daily dosage of 5 mg/kg until infants reached a median premenstrual age of 35 weeks.

Caffeine therapy significantly improved survival without neurodevelopmental disability to a corrected age of 18-21 months. Among neonates who had been randomly assigned to receive caffeine, the rate of death or survival with a disability was 40.2%, compared with 46.2% for those who had received placebo. The incidence of cerebral palsy was 4.4% in those given caffeine therapy, compared with 7.3% for placebo. Cognitive delay was seen in 33.8% of the caffeine-treated group, compared with 38.3% of the placebo group. Caffeine therapy also was associated with a reduced rate of severe retinopathy of prematurity (N. Engl. J. Med. 2007;357:1893-1902).

Caffeine therapy allowed neonates to discontinue positive airway pressure therapy an average of 1 week sooner than placebo did, and the investigators attributed most of the treatment's benefits to this difference.

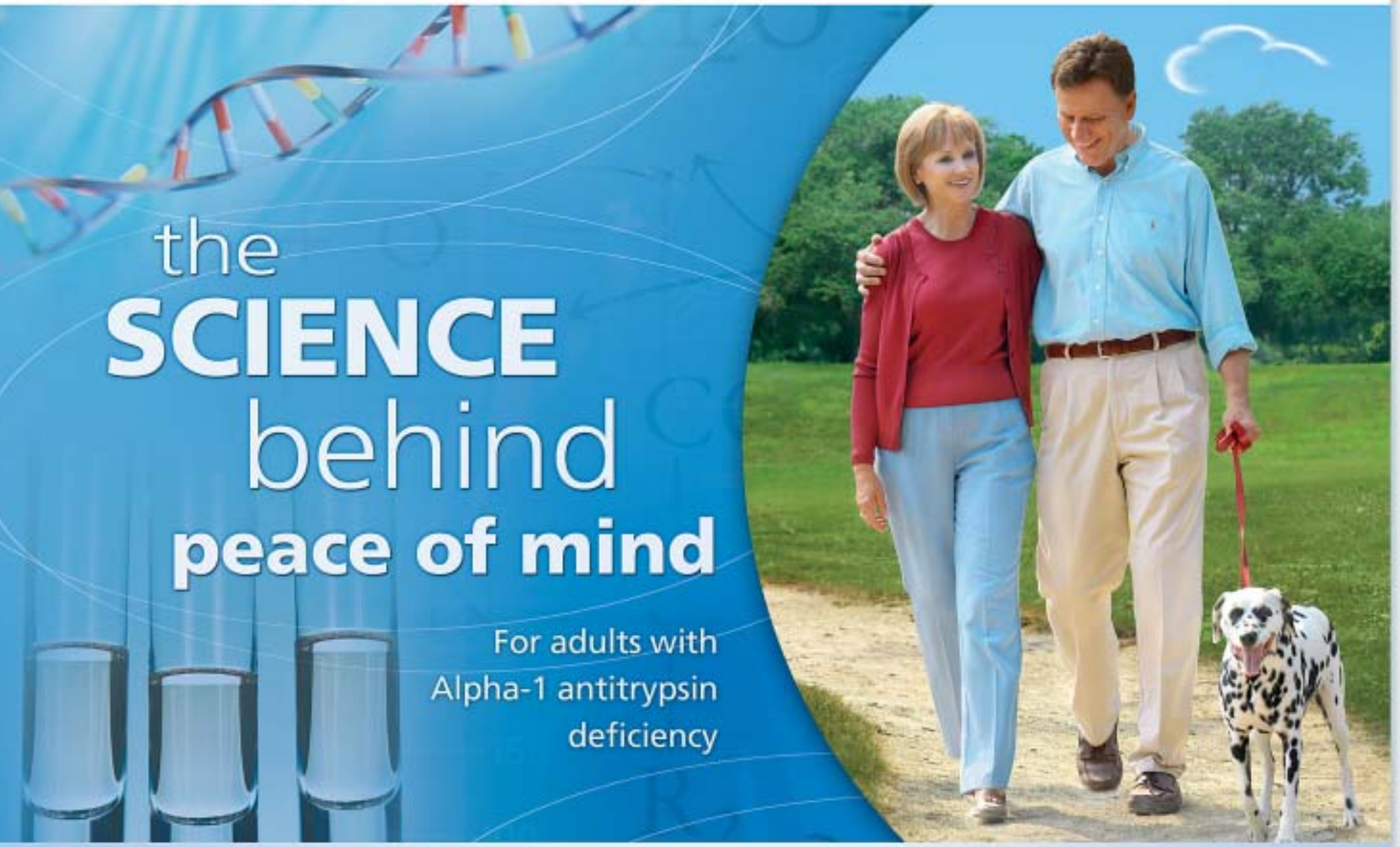
It is also possible that infants who received active treatment had better outcomes because they had fewer hypoxic-ischemic episodes due to apnea.

The researchers are continuing their follow-up of this cohort to a corrected age of 5 years so that they can assess possible longer-term effects on cognition, gross and fine motor function, vision, hearing, behavior, and general health.

In an editorial comment accompanying this report, Dr. David K. Stevenson of Stanford (Calif.) University said this investigation "provides needed support for a treatment approach that had already become routine clinical practice. In this case, physicians guessed correctly (or at least were lucky) that the benefits of caffeine outweighed the risks, long before they had conducted the necessary trials to confirm this," he said (N. Engl. J. Med. 2007;357:1967-8).

"For many proposed treatments, we are not so lucky, and our randomized controlled trials debunk our preconceived notions, as in the cases of prenatal phenobarbital treatment (which failed to prevent intraventricular hemorrhage) and postnatal steroids (which failed to prevent bronchopulmonary dysplasia)." ■

CSL Behring



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.**

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.

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