



# CHEST *Physician*

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Only 44% of hospitals take comprehensive steps to prevent central venous catheter-associated infections, Dr. Sanjay Saint said.

## Catheter-Associated Infection: Miles to Go

BY BRUCE JANCIN  
*Elsevier Global Medical News*

DALLAS — Fewer than half of U.S. hospitals—with the notable exception of those in the Veterans Affairs system—utilize all three widely recommended practices for preventing central venous catheter-associated bloodstream infections, according to a national survey.

The Veterans Affairs (VA) system stands head and shoulders above the pack with regard to implementation of these preventive measures. The survey showed 62% of VA hospitals take a comprehensive approach to prevention of central venous catheter-associated bloodstream infections, utilizing all three preventive

practices. That's true of only 44% of the nation's non-VA hospitals, Dr. Sanjay Saint reported at the annual meeting of the Society of Hospital Medicine.

He and his colleagues conducted a survey of catheter-associated infection prevention practices at all 119 VA medical centers and a random national sample of more than 400 non-federal hospitals with more than 50 beds and an ICU.

Central venous catheter-associated bloodstream infections constitute a significant cause of morbidity, mortality, and hospitalization costs. Guidelines strongly recommend three proven preventive strategies. Yet until now there have been no

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## Short Course of Steroids Tamed Asthma Relapses

*Cochrane review covered six studies.*

BY DIANA MAHONEY  
*Elsevier Global Medical News*

A short course of corticosteroid therapy following outpatient treatment for acute asthma exacerbation reduces the chances of a relapse within 2 weeks and lessens the need for using rescue inhalers without major adverse effects, a meta-analysis of current evidence has shown.

In a Cochrane literature review, Dr. Brian Rowe, FCCP, of the University of Alberta, Edmonton, and colleagues analyzed data from six randomized controlled trials comparing corticosteroids with placebo for acute care treatment of asthma attacks in adults or children. A total of 374 people were included in the analysis (Cochrane Database Syst. Rev. 2007;[3]:CD000195).

Studies considered for inclusion were those that randomized patients to receive either oral, intramuscular, or inhaled corticosteroids or placebo

following discharge from the acute care setting; those that compared two types of corticosteroids; and those in which patients were randomized to receive an intramuscular corticosteroid injection prior to discharge or intramuscular injection plus oral steroids, the authors stated.

The primary outcome measure was relapse to additional care at 7-10 days and 21 days. In addition, relapse requiring hospitalization, adverse outcomes, data from pulmonary function testing, symptom scores, and  $\beta_2$ -agonist use were also recorded. Patients generally required less than 80% predicted peak expiratory flow rates or forced expiratory volume in 1 second to be included in the studies.

In the meta-analysis, the investigators observed a 0.38 relative risk for relapse to additional care and a 0.35 relative risk for relapse to hospitalization in the first week post

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## Postop A-Fib May Double Mortality Risk

BY BRUCE JANCIN  
*Elsevier Global Medical News*

DENVER — Postoperative atrial fibrillation is often dismissed as a nuisance arrhythmia whose chief impact is a prolonged stay in the hospital.

But this common postsurgical complication may have previously unappreciated long-term adverse consequences, according to the results of a Swedish study.

Indeed, postop atrial fibrillation occurring within the first several days after coronary artery bypass graft surgery in patients without any history of atrial fibrillation was associated with nearly a twofold increased late all-cause mortality, mainly due to more deaths attributable to stroke, arrhythmias, and heart failure, Dr. Anders

Ahlsson said at the annual scientific sessions of the Heart Rhythm Society.

He reported on 1,443 patients who were in sinus rhythm with no history of atrial fibrillation or pacemaker therapy when they underwent a first CABG procedure in 1997-2000.

On postop days 1-5, 29% developed atrial fibrillation. They were on average more than 4 years older than those who did

not; however, left ventricular ejection fractions in the two groups were similar.

At a median of 8 years of follow-up, all-cause mortality was 33.3% in the postop atrial fibrillation group and 19.2% in the comparator arm.

In a multivariate regression analysis, postop atrial fibrillation proved to be a risk factor

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### VITAL SIGNS

#### States With the Highest and Lowest Cigarette Tax per Pack



Note: Taxes reported as of March 14, 2007.  
Source: American Cancer Society

## Steroids Cut Exacerbations

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discharge in the corticosteroid group, compared with placebo. Although only one of the studies reported 21-day relapse data, the favorable effect appeared to be maintained at 3 weeks, with a 0.47 relative risk of relapse, they wrote.

Number-needed-to-treat analyses of the pooled data showed that “only 10 patients would require treatment with corticosteroids to prevent one relapse to additional care in the first 7-10 days after outpatient care for an exacerbation, and only 11 patients would require such treatment to prevent one relapse to hospitalization,” the authors wrote.

With respect to steroid choice or mode

of administration, “no significant difference between [intramuscular] and oral agents was found when assessment was made within the first 7-10 days,” the authors reported. The reviewed articles contained insufficient follow-up data about inhaled corticosteroids for the authors to compare them with intramuscular and oral agents.

Regarding the need for  $\beta_2$ -agonists at 7-10 days, patients who received any form of corticosteroids required a mean 3.3 fewer activations than those receiving placebo. That finding is limited, however, in that it was provided in only two studies, the authors wrote.

Caution should also be used to interpret

the data on adverse effects and pulmonary function changes, the authors warned.

While total side effects were reported as being rare in most studies, “only two trials gave sufficient information to be included in this analysis,” they wrote.

A pooled estimate based on data from the two trials revealed similar rates of side effects in both groups, but the insufficient number of studies precludes “meaningful sensitivity or sub-group comparisons, or firm conclusions.”

Similarly, pulmonary function changes were reported sufficiently in only two studies, which showed no significant differences

between the treatment groups at 2-3 days or 7-10 days of follow-up, the authors wrote.

Although the limited number of studies included in the review suggests the conclusions should be interpreted carefully, “the results indicate that all patients requiring assessment for an exacerbation appear to warrant consideration for [corticosteroid] therapy,” according to the authors.

Since the choice of corticosteroid therapy does not seem to affect the outcome, “patient preference, compliance considerations, and cost should all be weighed in the treatment decision,” the review’s authors concluded. ■

**ONLY 10 PATIENTS WOULD REQUIRE TREATMENT WITH CORTICOSTEROIDS TO PREVENT ONE RELAPSE IN THE FIRST 7-10 DAYS AFTER CARE.**

## Strategies Can Prevent Infection

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national data characterizing the extent to which hospitals are using them, which was the impetus for the survey, explained Dr. Saint of the University of Michigan, Ann Arbor.

The three key evidence-based preventive practices are use of maximal sterile barrier

precautions, routinely employed in 84% of VA and 71% of nonfederal hospitals; chlorhexidine gluconate as an injection-site antiseptic, utilized in 91% of VA and 69% of non-VA hospitals; and avoidance of routine central line changes.

The survey also included semistructured telephone interviews with hospital infection control officers and on-site visits. The purpose was to identify facilitating factors and barriers to implementation of the preventive practices. Among the most commonly cited barriers were “organizational constipators,” Dr. Saint’s term for mid- to high-level managers resistant to change.

Factors identified as conducive to use of the three preventive strategies included a hospital culture that places a premium on patient safety, encouragement of multidisciplinary infection prevention collaboratives, and having an influential institutional champion of evidence-based change, which in most cases was an intensivist. That’s a role hospitalists could fill as well, Dr. Saint observed. ■

## Does A-Fib Boost Death Risk?

Postop A-Fib • from page 1

for mortality independent of patient age, diabetes, and other potential confounders. It conferred an adjusted 1.6-fold increased mortality risk, according to Dr. Ahlsson, a cardiothoracic surgeon at Orebro (Sweden) University.

Audience members wondered whether postop atrial fibrillation is truly the cause of the increased late mortality, in which case preventing the arrhythmia should produce an important mortality benefit, or if postop atrial fibrillation may just be an epiphenomenon reflecting some underlying abnormality that’s the cause of the increased risk.

That’s the key unanswered question, Dr. Ahlsson agreed.

Research in this area is complicated by a lack of predictors of which CABG patients will develop postop atrial fibrillation.

“There have been a number of suggestions, but they are too vague to find these patients before it

happens,” Dr. Ahlsson explained.

The practice at Orebro University Hospital is to perform radiofrequency ablation at the time of CABG in patients who have preoperative atrial fibrillation.

Nearly all patients undergoing CABG are on a  $\beta$ -blocker unless they have chronic lung disease or another contraindication. ■

**Dr. Peter McKeown, FCCP, comments:** *This paper reflects the significant and ongoing risks of postoperative atrial fibrillation after cardiac surgery.*

*The ACCP published clinical practice guidelines on the subject as a supplement to CHEST in August 2005. The guidelines focused not only on the management of postoperative atrial fibrillation, but also emphasized prevention by the use of  $\beta$ -blockers, as discussed by Dr. Ahlsson in this article.*

*Further clinical research is needed in this area to improve outcomes.*

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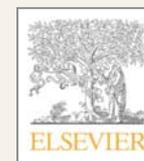
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# Anaphylaxis Reports Prompt Black Box for Xolair

*The biologic should only be administered in a health care setting under direct medical supervision.*

BY ELIZABETH MECHCATIE  
Elsevier Global Medical News

Patients treated with Xolair for asthma must now receive injections under direct medical supervision in a health care setting so they can be monitored for signs of anaphylaxis.

Last month, the Food and Drug Administration announced this and other new requirements—and a black box warning that has been added to the drug's label—for Xolair (omalizumab), a monoclonal antibody that selectively binds to human immunoglobulin E and is administered subcutaneously every 2-4 weeks.

Approved in June 2003, Xolair is indicated for treating adults and adolescents aged 12 years and older with moderate to severe persistent asthma, who have a positive skin test or in vitro reactivity to perennial aeroallergens and whose symptoms are inadequately controlled with inhaled corticosteroids.

"Anaphylaxis has occurred as early as after the first dose of Xolair, but also has occurred beyond 1 year after beginning regular treatment with Xolair," according to the FDA alert, posted on the agency's MedWatch Web site on July 2.

The alert says that the cases of anaphylaxis have presented as bronchospasm,

hypotension, syncope, urticaria, and/or angioedema of the throat or tongue.

Because of this risk, Xolair "should only be administered" to patients in a health care setting, under direct medical supervision by providers who meet the following qualifications: They should be prepared to identify and treat an anaphylactic reaction and to observe patients for an "appropriate period of time" after each injection. Providers also need to have trained personnel on staff and medications and equipment for treating anaphylaxis.

They also need to be aware that anaphylaxis can occur after any Xolair dose—even in patients who have tolerated previous doses without a problem—and that the onset of anaphylaxis after the injection can be delayed by 24 hours or more.

In the cases reported since Xolair was approved, the time to onset of anaphylaxis after Xolair was administered has ranged from 30 minutes or less in 35% of the reports to more than 12-24 hours in 8%, and more than 24 hours in 5% of patients.

In addition, treatment with Xolair should be discontinued once a patient has a severe hypersensitivity reaction.

Patients also need to be aware of the signs and symptoms of anaphylaxis and should carry contact information with

them and be prepared to start treatment for anaphylaxis.

Of the 3,507 patients who received Xolair in clinical trials, three cases of anaphylaxis were identified.

In two cases, anaphylaxis occurred 90 minutes after administration; in the third case, the reaction occurred 2 hours after administration.

There were two additional cases in these trials that were not reported as anaphylaxis, but meet the diagnostic criteria used to define postmarketing cases, according to the FDA.

**THE FREQUENCY OF XOLAIR-RELATED ANAPHYLAXIS IS ESTIMATED TO BE AT LEAST 0.2% OF TREATED PATIENTS, ACCORDING TO THE FDA.**

This information was included in the label, but in February, the FDA requested that Xolair manufacturer Genentech Inc. add these warnings to the drug's label because of postmarketing reports of anaphylaxis.

Between June 2003 and December 2006, there were 125 spontaneous case reports of anaphylaxis.

Based on an estimated 57,300 patients who received the drug during this

time, the frequency of Xolair-related anaphylaxis is estimated to be at least 0.2% of treated patients, according to the FDA.

However, because the adverse reaction reports are voluntary, the true frequency may be different.

In these cases, nearly 40% of anaphylactic reactions occurred after the first dose of Xolair, 19% after the second dose, 10% after the third dose, with the remainder occurring after later doses.

Nearly 90% of cases involved the lungs, with symptoms that included bronchospasm, dyspnea, cough or chest tightness, and in 14% of cases, hypotension or syncope was reported.

In 15% of the cases, the patient needed to be hospitalized. In 24% of the cases, the patient had a prior history of anaphylaxis.

The new warnings and guidelines are included in a boxed warning, warnings and precautions, and adverse reaction sections of the label.

Patients will also now receive a Medication Guide explaining these risks from the pharmacy when they fill and refill their prescriptions. ■

For more information, go to [www.fda.gov/medwatch/safety/2007/safety07.htm](http://www.fda.gov/medwatch/safety/2007/safety07.htm) #Xolair.

Reactions to Xolair should be reported to the FDA's MedWatch program at 800-332-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

## Anti-TNF Drugs May Increase Mortality in Some RA Patients

BY JEFF EVANS  
Elsevier Global Medical News

BARCELONA — Rheumatoid arthritis patients with interstitial lung disease have a high all-cause mortality that may be worsened by treatment with anti-tumor necrosis factor- $\alpha$  drugs, Will G. Dixon, Ph.D., reported at the annual European Congress of Rheumatology.

Multiple case reports have found that ILD is accelerated in rheumatoid arthritis patients following anti-TNF- $\alpha$  therapy. A causal relationship between the treatment and increased mortality from rheumatoid arthritis-associated interstitial lung disease (RA-ILD) has been suggested based on the observation that ILD gets worse soon after starting anti-TNF- $\alpha$  therapy in patients with previously stable disease, said Dr. Dixon, a clinical research fellow in the Arthritis Research Campaign epidemiology unit at the University of Manchester (England).

But on the other hand, TNF- $\alpha$  has been implicated in the pathophysiology of lung fibrosis, and case reports have shown improvement or stabilization of ILD following the start of anti-

TNF- $\alpha$  therapy, Dr. Dixon added.

To examine how RA-ILD and anti-TNF- $\alpha$  therapy affect mortality, he and his colleagues compared patients in the prospective British Society of Rheumatology Biologics Register who took anti-TNF- $\alpha$  drugs (etanercept, infliximab, and adalimumab) and a parallel cohort of patients with active rheumatoid arthritis who

**'IT'S IMPORTANT TO STRESS AT THIS STAGE THAT THIS ANALYSIS IS BASED ON A SMALL NUMBER OF DEATHS IN THE COMPARISON COHORT.'**

received traditional disease-modifying antirheumatic drugs (DMARDs) but did not take any biologics.

At baseline, RA-ILD occurred in 44 (1.8%) of 2,454 patients in the traditional DMARDs cohort and in 269 (2.9%) of 9,294 patients who took anti-TNF- $\alpha$  drugs.

Patients with RA-ILD at baseline had significantly greater odds of having other extra-articular manifestations of rheumatoid arthritis (3.1 times greater), test-

ing positive for rheumatoid factor (1.9 times greater), and having ever smoked (1.7 times greater) than those without RA-ILD at baseline.

The investigators found that all-cause mortality was more than two times higher among patients with RA-ILD at baseline than in those without it, even after adjusting for those associations and age, gender, disease severity, and anti-TNF- $\alpha$  therapy.

This means that RA-ILD at baseline is a strong, independent risk factor for mortality in RA patients, said Dr. Dixon.

Patients with baseline RA-ILD who received treatment with anti-TNF- $\alpha$  drugs had a nonsignificant, nearly twofold increase in the risk of all-cause death, compared with those who had RA-ILD at baseline in the traditional DMARD cohort, according to Dr. Dixon.

"It's important to stress at this stage that this analysis is based on a small number of deaths in the comparison cohort, and the confidence intervals are wide," he cautioned.

Overall, only four all-cause deaths occurred in patients in the traditional DMARD cohort who

had RA-ILD at baseline, and RA-ILD was not listed as the cause of death on the death certificate or mentioned anywhere on the death certificate in any of these cases.

On the other hand, 40 all-cause deaths occurred in patients with RA-ILD at baseline who received anti-TNF- $\alpha$  therapy.

Eleven of the patients had RA-ILD listed as the cause of death on the death certificate. RA-ILD was mentioned anywhere on the

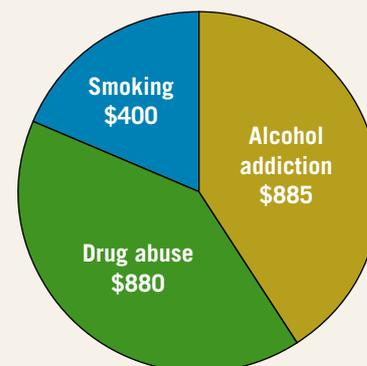
certificate in another 14 patients who died.

"Because of the low numbers [of deaths] in the comparison cohort, we can't make a direct comparison" between the cohorts, he said.

"And we don't know whether these rates [of rheumatoid arthritis-associated interstitial lung disease-specific mortality] are higher than we would otherwise expect if the patients weren't to receive anti-TNF- $\alpha$  drugs," Dr. Dixon cautioned. ■

### DATA WATCH

#### Worldwide Cost of Nicotine, Alcohol, and Drug Abuse (in billions of dollars)



Note: Based on 2005 world market data.  
Source: Kalorama Information

## ILD Linked to Poor Survival In Antisynthetase Syndrome

BY NANCY WALSH  
*Elsevier Global Medical News*

BARCELONA — A review of 30 patients with antisynthetase syndrome found that only half survived 10 years after diagnosis, Dr. Oyvind Palm reported at the annual European Congress of Rheumatology.

This idiopathic inflammatory myopathy is characterized by the presence of antibodies directed against RNA synthetase.

Clinical manifestations include interstitial lung disease, arthritis, Raynaud's phenomenon, and the hyperkeratotic rash known as mechanic's hands, said Dr. Palm of the department of rheumatology, Rikshospitalet-Radiumhospitalet Medical Center, Oslo.

Researchers reviewed all hospital records of patients diagnosed with an inflammatory myopathy and analyzed the charts of those who had antisynthetase antibodies and pulmonary disease. The mean age of these 30 patients was 45.5 years, and in one-third the disease onset was before age 40. Two-thirds were women.

Most patients had histologic evidence of inflammatory myopathy and elevated serum creatine kinase, but only four had creatine

kinase levels exceeding 3,000 IU/mL. Muscular manifestations rarely caused significant disability and were present at the onset of disease in only six cases.

Anti-Jo-1 antibodies were detected in 90%. Anti-SSA autoantibodies, commonly found in patients with Sjögren's syndrome, were detected in 50%, Dr. Palm wrote in a poster session.

Pulmonary involvement was classified as follows:

▶ Type I (acute): Found in 24%; rapid onset of dyspnea or cough with development of hypoxemia within 1 month of onset.

▶ Type II (subacute): Found in 64%; gradual onset of pulmonary symptoms.

▶ Type III (asymptomatic): Found in 12%; coincidentally detected pulmonary abnormalities on x-ray or CT scan with subsequent gradual onset of pulmonary symptoms.

All but one patient received treatment with immunosuppressive drugs including corticosteroids, cyclophosphamide, and rituximab. "While approximately 90% survive the first 3 years of disease, thereafter the mortality increases sharply, and new treatment strategies are clearly warranted," he concluded. ■

## Brain Irradiation Prolonged Survival in SCLS Patients

BY SARAH PRESSMAN  
LOVINGER  
*Elsevier Global Medical News*

CHICAGO — Radiation therapy to the brain given prophylactically to patients with advanced stage small-cell lung cancer prolongs survival, according to a study presented at the annual meeting of the American Society of Clinical Oncology.

"It is surprising that in a disease that has spread throughout the body, local treatment of the brain results in prolonged survival," said Dr. Ben Slotman of the VU University Medical Center in Amsterdam, the Netherlands, and the lead author of the study.

Small-cell lung cancer patients with extensive disease have a high risk of brain metastases, said Dr. Slotman.

This study evaluated 286 patients with small-cell lung cancer who had at least a minimal response to four to six cycles of chemotherapy. Of them, 143 were randomized to receive prophylactic cranial irradiation (PCI) following chemotherapy; the other 143 patients

received no additional treatment and served as the control group. The PCI doses ranged from 20 to 30 gray; patients received treatment daily for 1-2 weeks. Patients noted to have certain symptoms at baseline or during follow-up underwent a CT or MRI of the brain to look for brain metastases. The key symptoms included headache, nausea, vomiting, and seizures.

The primary end point was the cumulative risk of symptomatic brain metastases.

The results showed that PCI significantly cut the risk of symptomatic brain metastases. In 1 year, 14.6% of the treatment group developed symptomatic brain metastases compared with 40.4% of controls. PCI treatment did not affect extracranial progression rates. This treatment significantly prolonged progression-free survival time and overall survival. One-year survival rates were 27% for the treatment group and 13% for the control group.

Participants tolerated PCI and did not report poorer quality of life as a result of the additional treatment. ■

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Nashua, New Hampshire

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# Dexmedetomidine Topped Lorazepam for Sedation

ARTICLES BY ROBERT FINN  
Elsevier Global Medical News

SAN FRANCISCO — The results of a randomized controlled trial of medical and surgical intensive care unit patients suggest that dexmedetomidine helps keep patients at their target sedation level and decreases delirium, compared with lorazepam, Dr. E. Wesley Ely, FCCP, reported at the International Conference of the American Thoracic Society.

"It's a very interesting form of sedation [with dexmedetomidine]," said Dr. Ely of Vanderbilt University, Nashville, Tenn. "There's no respiratory suppression. Patients are more easily arousable while they're sedated. If they're on benzos, you can't wake them up. If they're on dex, they're chilled and calm. You can say, 'Mrs. Smith, open your eyes and look at me,' and she will simply open her eyes, [and] follow your hand."

An  $\alpha_2$ -agonist, dexmedetomidine acts at the locus ceruleus, not at the ventrolateral preoptic nucleus as do the GABAergic benzodiazepines. Dexmedetomidine does not suppress respiration, and it leaves patients more easily assessable. Preliminary evidence suggested that dexmedetomidine resulted in less delirium than did benzodiazepines.

To confirm this, Dr. Ely and his colleagues designed the MENDS (Maximizing Efficacy of Targeted Sedation and Reducing Neurological Dysfunction) trial. A total of 103 ventilated ICU patients were randomly assigned

to receive either lorazepam plus fentanyl as needed or dexmedetomidine plus fentanyl.

The patients were 60 years old on average and had APACHE (Acute Physiology and Chronic Health Evaluation) II scores of about 28, indicating very severe disease. Sepsis with acute respiratory distress syndrome was the most common admitting diagnosis.



**'If they're on benzos, you can't wake them up. If they're on dex, they're chilled and calm.'**

DR. ELY

The patients who were taking dexmedetomidine were at the sedation level targeted by their physicians during 67% of their ICU days, compared with 55% of ICU days for the patients taking lorazepam.

In addition, the dexmedetomidine patients required only 26% of the fentanyl needed by the lorazepam patients.

Patients taking dexmedetomidine spent 7 days free of delirium or coma, compared with just 3 days for patients taking lorazepam. The prevalence of coma was 68% in the dexmedetomidine patients, versus 92% in the lorazepam patients. All these differences were statistically significant.

There were no significant differences between the groups in the need for antipsychotic medications or in the prevalence of delirium.

With one exception, dexmedetomidine and lorazepam were equivalent in their safety profiles. Significantly more patients taking dexmedetomidine (17% vs. 4%) exhibited sinus bradycardia (a heart rate of 60 or below).

The study was funded by Hospira, the manufacturer of dexmedetomidine. ■

# Late ICU Admission Associated With Increased Mortality in CAP

SAN FRANCISCO — Patients with community-acquired pneumonia who were admitted to the intensive care unit 2 or more days after diagnosis were more than twice as likely to die within 30 days as were those who were admitted in 24 hours or less, according to a poster presentation at the International Conference of the American Thoracic Society.

The retrospective, observational study involved 161 patients seen over a 3-year period at two tertiary care hospitals in San Antonio.

All patients were 18 years old or older, all had received a chest x-ray within 24 hours of admission, and all had a diagnosis consistent with community-acquired pneumonia, wrote Dr. Marcos I. Restrepo and his colleagues at the University of Texas at San Antonio.

There were no significant differences in demographic or clinical characteristics between the 142 patients admitted to the intensive care unit early and the 19 patients admitted to the intensive care unit late.

There were also no significant differences

between the two groups in whether they received antibiotics within 4 hours, whether their blood was cultured appropriately, or whether they received guideline-concordant antibiotic therapy.

At the end of 30 days, 47% of the patients who had been admitted late to the intensive care unit had died, compared with 23% of the patients who had been admitted early to the intensive care unit, a significant difference.

The investigators wrote that further research would be necessary to isolate the factors underlying the association between late admission to the intensive care unit and increased mortality. ■

**Dr. Stephen M. Pastores, FCCP, comments:** *This study suggests that the prognosis of patients with severe community-acquired pneumonia may be influenced by the timing of their admission to the intensive care unit.*

*Earlier intensive care unit admission, in contrast to late admission, may result in more timely recognition and management of these patients who are at risk for developing multi-organ dysfunction.*

# Newspaper Reporting Often Inaccurate on 'Brain Death'

SAN FRANCISCO — An analysis of major U.S. newspapers revealed that articles describing brain death usually were inaccurate, according to a poster presentation by Dr. Ann L. Friedman at the American Transplant Congress.

Dr. Friedman and her colleagues from Yale University, New Haven, Conn., suggested that inaccurate reporting may promote confusion among the general public over the meaning of "brain death," creating a barrier to consent for organ donation.

The investigators identified 180 articles that used the phrase "brain death" or "brain dead" among 354,601 articles that appeared in 2005 in the New York Times, the Los Angeles Times, the Hartford Courant, the Christian Science Monitor, the Washington Post, and the Wall Street Journal.

Of the 180 articles, 56 used the terms in a nonmedical context and were excluded from the analysis.

An additional 36 articles were excluded because they contained insufficient information to determine their accuracy.

Four raters independently assessed each article using four criteria. The study questions were: Does the article identify a subject as brain dead and subsequently refer to him/her as being alive? Does the article identify a subject as brain dead and then describe his/her condition as something other than deceased (for example, "critical" or "guarded")? Does the article identify a subject as brain dead and subsequently

describe him/her "dying"? Does the article identify a subject as brain dead and subsequently describe the person as being "on life support"?

Of the 88 articles analyzed, 52 (59%) contained one or more inaccuracies. The most frequent error was a description of the patient being on "life support"; the raters found this error in 32 (36%) of the articles.

One example of a single sentence containing multiple inaccuracies was, "Brain-dead patients may be kept alive on life support, but if that support is stopped, they die within minutes."

Of the articles that had no inaccuracies, almost a quarter were written

by physicians who were seeking to correct previously published errors, the investigators wrote.

They suggested that authors of material addressing brain death,

coma, or artificial support should ask five questions as a self-test of accuracy:

► Is the article clear in stating whether the unresponsive person is in a coma or brain dead?

► When describing the brain-dead subject, is the article clear about when the declaration of brain death was made?

► Do all references temporally following declaration of brain death exclude the terms life, alive, or living?

► Are supportive measures being used for the brain-dead person, referred to as mechanical/respiratory or artificial support and not as life support?

► Is the cessation of cardiac function in a brain-dead person described as the heart stopping, not "death" or the "end of life"?

**INACCURATE REPORTING MAY CONFUSE THE PUBLIC OVER THE MEANING OF BRAIN DEATH, CREATING A BARRIER TO CONSENT FOR ORGAN DONATION.**

# Fresh Blood May Be Best for ICU Patients

SAN FRANCISCO — Critically ill patients who received red blood cell transfusions stored for less than 7 days had significantly lower in-hospital mortality than did patients who received red blood cell transfusions stored longer, according to a poster presentation by Dr. Hussam Jenad at the International Conference of the American Thoracic Society.

In a retrospective cohort study of 12,264 patients receiving a median of four RBC units, adjusted in-hospital mortality was 5% if the patient's oldest unit had been stored for less than 7 days, 8% if the oldest unit had been stored for 7-14 days, and 13% if the oldest unit had been stored for more than 14 days.

This corresponds to a reduction in the risk of in-hospital mortality of 62% for patients receiving RBC units less than 7 days old, compared with

patients receiving RBC units more than 14 days old.

The results were adjusted for the patient's age, severity of illness, surgical status, number of RBC units transfused, year of transfusion, and proportion of leukoreduced RBC units.

The patients had been seen over a 10-year period ending in December 2005 in four medical and surgical ICUs at the Mayo Clinic, Rochester, Minn. Dr. Jenad and his coauthors are all from the Mayo Clinic.

The mean age of the patients was 64 years, and 41% had undergone elective surgery. Only 1% of the patients received blood stored less than 7 days, 11% received blood stored for 7-14 days, and the remaining 88% received at least one unit of blood stored for more than 14 days. Overall, 24% of the patients received leukoreduced RBC transfusions. ■

# Wheezing Rhinovirus Illnesses Predict Later Asthma

BY DOUG BRUNK  
Elsevier Global Medical News

SAN DIEGO — More than 75% of children who have a wheezing illness at age 3 years will go on to develop asthma by age 6 years.

In addition, children who develop a wheezing illness caused by rhinovirus during the first year of life are three times more likely to develop asthma by age 6, compared with those who develop a wheezing illness caused by respiratory syncytial virus (RSV) or parainfluenza virus.

Those are new findings from the ongoing Childhood Origins of Asthma (COAST) study that were presented during a press briefing at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

"The big finding here is the association of the common cold virus with wheezing very early in life," said principal investigator Dr. Robert F. Lemanske Jr., professor of pediatrics and medicine at the University of Wisconsin, Madison.

Launched in 1998 by Dr. Lemanske and his associates at the University of Wisconsin School of Medicine and Public Health and funded by the National Institutes of Health, the COAST study is a birth cohort

study of 287 children. Participants were required to have at least one parent with confirmed aeroallergen sensitization and/or asthma. The researchers collected cord and annual blood samples to evaluate cytokine response profiles. They also collected nasal lavage samples at the time of scheduled study visits and during significant respiratory illness to ascertain viral illness.

Previous findings from the COAST study have reported the relationship between wheezing viral illness during the first year of life and continued wheezing at age 3, but this marks the first report of findings at age 6.

"Although findings from other research groups have demonstrated a relationship between persistent wheezing patterns and

children previously hospitalized with respiratory syncytial virus, there was no association between wheezing with RSV or

parainfluenza virus during the first year of life and a diagnosis of asthma at 6 years of age in the COAST study," Kathleen A. Roberg, R.N., a study manager in the department of medicine at the university, said at the briefing. "However, there was a threefold increase of an asthma diagnosis for those children who wheezed with rhinovirus during the first year of life."

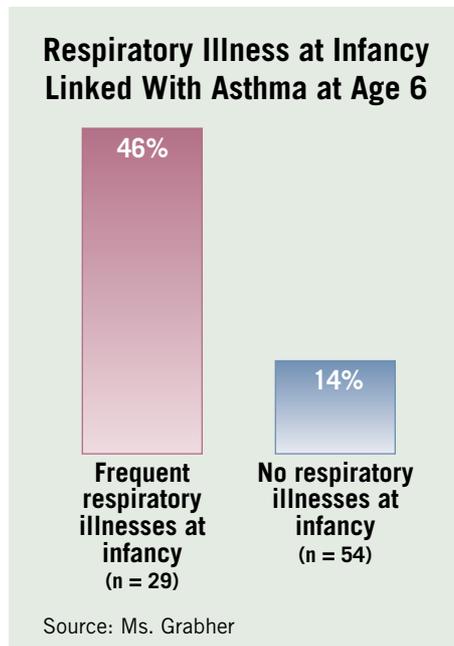
She noted that as the children reached 3 years of age, more than 75% of children who had a wheezing illness—regardless of the viral etiology—went on to develop asthma by age 6.

"Rhinovirus continues to be the most striking in this relationship," she said. "However, at age 3, RSV and parainfluenza viral wheezing illnesses are similarly related to the diagnosis of asthma."

In an interview, Dr. Lemanske pointed out that more study is needed to determine what drives the apparent association between wheezing rhinovirus illness early in the life and the subsequent development of asthma. "We're not saying that rhinovirus has caused this to happen," he said. "We're trying to determine if this is a host defect . . . versus whether or not there are certain strains of the common cold virus that are more likely to get kids to wheeze. In the next phase of this project, we'll look at that."

In another presentation at the briefing, Rochelle A. Grabher reported that children in the COAST trial who had frequent respiratory illnesses during the first year of life had a higher incidence of asthma at age 6, compared with those who had no respiratory illnesses during the first year of life, yet other markers of atopy were unremarkable.

During the first year of life, 54 children had no respiratory illnesses, 204 had between one and four, and 29 had five or more, which was defined as frequent, said Ms. Grabher, a research coordinator with the department of medicine at the university. Overall, 46% of children who had frequent respiratory illnesses during infancy had asthma at age 6 years, compared with just 14% of children who had no respiratory illnesses during infancy, a significant difference, she said. ■



ELSEVIER GLOBAL MEDICAL NEWS

## Call for Nominations

Chair, Executive Editorial Panel for  
*Antithrombotic and Thrombolytic Therapy:*  
*American College of Chest Physicians*  
*Evidence-Based Clinical Practice Guidelines, 9th Edition*

The ACCP is seeking nominations for Chair to the Executive Editorial Panel for *Antithrombotic and Thrombolytic Therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 9th Edition*. This is an excellent opportunity for someone with superb leadership, organizational, and innovative skills, and expertise in antithrombotic therapy. Lead the editorial panel for the prestigious guideline that has greatly impacted clinical decision-making, leading to the improvement of patient care worldwide.

A chair appointment will be announced in December 2007, and the term will begin January 2008. Open positions include:

• Chair

Help the ACCP maintain the high standard of the antithrombotic and thrombolytic guideline by nominating yourself or a colleague for the chair position.

### Eligibility Criteria

Candidates for the chair position should:

- Be a Fellow of the ACCP.
- Be experienced with evidence-based guideline development; specifically, the ACCP's guideline process.
- Possess strong knowledge of research, methodological skills, and potential impact upon economic and medicolegal areas.
- Have proven leadership experience, especially in clinical medicine and guideline development.
- Exhibit proficient editorial skills.
- Be an established expert with academic and clinical experience in antithrombotics.

- Have no significant or unmanaged conflicts of interest.
- Be willing to devote a set amount of time per week to the guideline, specifically at peak times in the development process.
- Possess the ability to efficiently supervise a large group of chapter editors to develop writing schedules, organize meetings, and meet writing deadlines. This should be accomplished through regular conference calls and occasional face-to-face meetings.

Nominated individuals will be required to secure two letters of recommendation, submitted directly to ACCP, to verify their current academic and clinical standing and their leadership skills.

### Submission Requirements

To nominate a candidate, you must submit:

- A typed document outlining the reasons for considering the candidate (no more than two pages, single-spaced).
- A list of the candidate's contributions to antithrombotic therapy.
- The candidate's CV.

Submit materials via e-mail to Sandra Zelman Lewis, PhD, at [slewis@chestnet.org](mailto:slewis@chestnet.org).  
Nomination deadline: September 15, 2007.

## Sleep Apnea Associated With Problem Behavior in Children

BY HEIDI SPLETE  
Elsevier Global Medical News

MINNEAPOLIS — Poor sleep caused by obstructive sleep apnea has a subtle but measurable impact on problem behavior in 5- to 7-year-olds, according to data from a community-based study of 747 children.

Obstructive sleep apnea was significantly associated with hyperactivity, oppositional behavior, and impulsivity among the 72 children who met the criteria for obstructive sleep apnea (OSA) compared with controls, based on the hyperactivity, oppositional behavior, and impulsivity subscale scores from an 80-item validated questionnaire, the Conners' Parenting Rating Scales-Revised (CPRS-R). By contrast, no significant differences in behavior were found between the children with sleep-disordered breathing and controls using the Child Behavior Checklist (CBCL).

"The CPRS-R appears to be more sensitive to the effects of sleep-disordered breathing on daytime behavior in children when compared to the CBCL," reported Dr. Oscar Sans Capdevila and his colleagues at the University of Louisville (Kentucky).

The message for clinicians: Consider sleep-disordered breathing problems such as OSA when evaluating a young child who has moderate to severe behavioral problems, especially oppositional, social, or cognitive problems, they suggested in a poster presentation at the annual

meeting of the Associated Professional Sleep Societies.

OSA is defined as an apnea/hypopnea index (AHI) of at least 5, which means five episodes of apnea per hour of sleep. An episode of apnea is a short period of a few seconds when someone stops breathing during sleep. The children underwent neurologic evaluations prior to the study to identify those who had sleep apnea.

Although all the children's average CPRS scores fell below the level of clinical impairment (65), the scores for children with OSA on the hyperactivity, oppositional behavior, and ADHD subscales were near or above the average range of 45-55.

In addition, the children with an AHI of at least 5 scored significantly higher on the CPRS-R subscale for total DSM-IV behavioral problems, compared with controls (56 vs. 51).

The relatively modest association between sleep apnea and children's behavior problems may reflect the stricter selection criteria. The study is the first of its size to focus on 5- to 7-year-olds in particular based on parental responses to validated questionnaires, the researchers noted.

The results support data from previous studies that suggested an increased risk for behavior problems in children who snore or have OSA, but most of the studies were limited by their small number of patients and a wide range of ages.

The study was supported by a grant from the National Institutes of Health. ■

# Genetic Variant Linked to Limb Movements in Sleep

BY MARY ANN MOON  
Elsevier Global Medical News

**A** newly discovered gene sequence variant is strongly associated with periodic limb movements in sleep, reported Dr. Hreinn Stefansson of deCODE Genetics, Reykjavik, Iceland, and associates.

Periodic limb movements of sleep (PLMS) occur in approximately 85% of patients with restless legs syndrome (RLS), but not all patients with RLS have PLMS.

Even though the authenticity of RLS has been called into question, "our study provides evidence that periodic limb movements in sleep is a genuine syndrome with an ascertainable phenotype and a genetic basis," the researchers said in the July 18 online version of the *New England Journal of Medicine*.

RLS is characterized by uncomfortable and distressing sensory urges to move the legs during rest or inactivity. Periodic limb movements are involuntary, highly stereotypical, regularly occurring foot and leg movements in sleep. The pathogenesis of RLS disorder is unclear, but it has been linked to low iron levels and has "a substantial" genetic component, according to the researchers.

Dr. Stefansson and associates genotyped 306 case subjects with periodic limb movements in sleep, most of whom also had RLS, as well as 15,633 control subjects from the general Icelandic population

They assessed more than 300,000 single nucleotide polymorphism (SNP) markers distributed across the human genome.

The researchers found a strong link between RLS with PLMS and allele A of rs3923809 on chromosome 6p.

To validate these results, they then conducted replication studies in an additional Icelandic cohort that included 123 case subjects

and 1,233 control subjects, and in a U.S. cohort of 188 case subjects recruited from a sleep disorders center and 662 control subjects.

The association was evident in each study population, and it was highly significant when all three samples were combined, the investigators said (*N. Engl. J. Med.* July 18 [Epub doi:10.1056/NEJMoa072743]).

Subjects who carried the gene sequence variant also had higher ferritin indexes, a measure inversely related to bodily iron stores, as well as decreased serum ferritin levels. This correlation "is consistent with the suspected involvement of iron

depletion in the pathogenesis" of RLS, Dr. Stefansson and his associates added.

In an editorial accompanying the study, Dr. John W. Winkelman of Brigham and Women's Hospital and Harvard Medical School, Boston, said that the "exciting and important" findings may improve RLS diagnosis.

The results also offer "hope to patients with periodic limb movements in sleep and RLS that the syndrome's pathophysiology will be understood, and that such knowledge will lead to additional effective and durable treatments," Dr. Winkelman said (*N. Engl. J. Med.* July 18 [Epub doi:10.1056/NEJMeO78129]).

**THE 'EXCITING AND IMPORTANT' FINDINGS MAY IMPROVE RLS DIAGNOSIS AND OFFER 'HOPE TO PATIENTS WITH PERIODIC LIMB MOVEMENTS IN SLEEP.'**

## Cognitive-Behavioral Treatment Can Ease Secondary Insomnia

BY JANE SALODOF MACNEIL  
Elsevier Global Medical News

SCOTTSDALE, ARIZ. — Cognitive-behavioral treatments can help people overcome chronic insomnia, even when a medical or psychiatric disorder appears to be the primary cause of sleeplessness, Edward J. Stepanski, Ph.D., said at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

Traditionally, behavioral treatments have been reserved for primary insomnia and not recommended for people whose lack of sleep is secondary to other conditions, according to Dr. Stepanski, vice president for scientific affairs of the Accelerated Community Oncology Research Network (ACORN) in Memphis.

The underlying assumptions—both of which he challenged—are that insomnia will remit if the primary condition is resolved and that cognitive-behavioral treatment (CBT) approaches will not be effective against an etiology such as pain or depression. People continue to sleep poorly after successful treatment of post-traumatic stress disorder, he said, and randomized controlled trials have shown that people with a primary condition such as arthritis can sleep better after CBT.

"Use [CBT] in any chronic insomnia," Dr. Stepanski said, suggesting comorbid insomnia would be a better name than secondary insomnia when diagnosed in patients with other conditions. "CBT has its place," he said. "There are always behavioral and cognitive features to a chronic patient with insomnia."

For most patients, he recommended that behavioral treatments precede cognitive therapy. Many worry that they will have a mental breakdown or lose their jobs if they don't get more sleep. Once they are sleeping better, he suggested they may be more open to cognitive restructuring—in particular, to considering how their lives would be different without insomnia. Not everyone will embrace the possibility.

"Some personality disorder patients don't really want help," Dr. Stepanski warned.

For insomniacs who do want better sleep, he recommended trying a variety of behavioral treatments, as there is no way to predict which would be the most beneficial to a particular patient. These include:

- ▶ **Sleep hygiene education.** For example, tell patients that they can't drink coffee before bedtime or nap 3 hours in the afternoon and then expect to sleep through the night.

- ▶ **Stimulus control therapy.** The patient should only go to bed when sleepy and not use the bedroom for activities, such as TV viewing or aerobic exercises, that are incompatible with sleep. If the patient can't sleep, he should get up and leave the bedroom. "If you force yourself to lie in bed awake, you are doing damage to yourself. [There's] nothing else to do but ruminate and catastrophize," said Dr. Stepanski.

- ▶ **Sleep restriction therapy.** The goal is to use partial sleep deprivation to increase homeostatic sleep drive. Use a sleep log to reduce time in bed to the amount of time the patient actually sleeps. Five hours of good sleep is better than 8 hours of intermittent sleep, said Dr. Stepanski: "Excess time in bed is death to normal sleep."

- ▶ **Relaxation training.** Examples include progressive muscle relaxation, guided imagery, biofeedback, and self-hypnosis.

As none of these techniques work quickly, Dr. Stepanski said practitioners should devote time early on to educating, reassuring, and encouraging patients—and preparing them for relapse. "Sleep is a biological rhythm. It doesn't change right away," he said.

Medication works faster than CBT, but is not as effective, said Dr. Stepanski.

The bottom line on combining therapies: "Some patients will do well with the approach, and some won't," Dr. Stepanski concluded. "CBT is probably most effective when not used with medication, but they may be combined."

## Medicare Hotline

**T**he Medicare Rights Center's Professional Hotline now includes guidance and advice on Medicare benefits, rights, and options to professionals working with older adults and people with disabilities who are on Medicare. Until now, the hotline has focused on benefits available through private drug plans. The service is available free, Monday through Friday, from 10:00 a.m. to 6:00 p.m. EST, at 877-794-3570.



## Thomas L. Petty, MD, Master FCCP Endowment in Lung Research

### A Legacy in Pulmonary Medicine

Considered a "Father of Pulmonary Medicine," Thomas L. Petty, MD, Master FCCP, is a recognized leader in chest medicine and outstanding contributor to the ACCP.

To honor Dr. Petty's accomplishments, The CHEST Foundation, in partnership with Boehringer Ingelheim, Inc., has established the Thomas L. Petty, MD, Master FCCP Endowment in Lung Research to support lung research and advances in patient care.

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Plan to attend The CHEST Foundation's Making a Difference Awards Dinner, where Dr. Petty will be honored.

**Making a Difference Awards Dinner**  
Saturday, October 20, 2007  
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# Pulmonary Perspectives

## Preventing Ventilator-Associated Pneumonia: Focusing on the Upper Airway and the Endotracheal Tube

**N**osocomial infection represents a major focus for quality improvement efforts because of its impact on mortality and morbidity. For the intensivist, ventilator-associated pneumonia (VAP) is of particular concern. VAP is the most common nosocomial infection in the ICU with an incidence of approximately 15%. Crude mortality rates for VAP range from 30 to 70%, although controversy exists regarding the attributable mortality of this condition. With respect to morbidity, VAP prolongs the duration of mechanical ventilation (MV) and results in an excess cost of more than \$10,000 per case.

Risk factors for VAP are well-known, and include factors associated with the underlying reason for MV, patient characteristics, and process of care. In the past, efforts to prevent VAP have included attempts to ensure head-of-bed elevation, less frequent ventilator circuit changes, and the avoidance of nasotracheal intubation. Two areas receiving renewed attention are the endotracheal tube (ETT) and oral care.

### The ETT

Duration of MV can represent the strongest risk factor for VAP. The risk for VAP is highest during the initial days of MV, but is never eliminated as MV continues. Multiple studies have documented that earlier extubation, and preventing the need for ETT placement, lower the rate of VAP (MacIntyre. *Chest* 2005; 128[suppl]:561S). One of the many benefits of protocols to enhance liberation from MV is that they reduce the incidence of VAP. Recently, Girard and colleagues (The awakening and breathing controlled [ABC] trial: a randomized controlled trial of the efficacy and safety of protocolized spontaneous breathing trials [SBTs] with or without daily spontaneous awakening trials [SATs]. Presented at: ATS 2007; San Francisco, CA) attempted to improve outcomes by combining protocol efforts and adjusting sedation with spontaneous breathing trials (SBT). In a multicenter study, they found that a global protocol, with sedation and SBT aspects, led to faster discontinuation of MV as compared with an SBT protocol lacking formal guidelines for sedation management. Therefore, by decreasing the duration of MV, systematic, multifaceted protocols can aid in VAP prevention.

With respect to the ETT, the emerging importance of biofilm in the pathogenesis of VAP represents a key target for VAP prevention. Biofilm coats the ETT, grows

as the duration of MV progresses, shrinks the lumen of the ETT, and also may serve as a reservoir for pathogenic bacteria. Prevention of biofilm accumulation has proven effective at limiting catheter-related bloodstream infections, and similar research is now underway for VAP prevention. Olson and colleagues (*Chest* 2002; 121:863) found that, in an animal model of VAP, coating the ETT with silver limited the evolution of biofilm, and was beneficial for the prevention of VAP. In a subsequent pilot study and randomized trial, Rello and colleagues (*Crit Care Med* 2006; 34:2766) observed that use of a silver-coated ETT, as compared with a standard ETT, resulted in delayed ETT colonization and a lower organism burden in tracheal aspirates. Results from a large, multicenter randomized trial of this device should be available shortly.

Leakage of secretions around the ETT cuff is another means by which upper airway pathogens reach the lower airway. Unfortunately, efforts to prevent aspiration of these secretions have been frustrating. Two strategies have been studied by which aspiration of secretions pooling around the ETT cuff can be prevented.

Low cuff pressures have typically been associated with VAP. Theoretically, better control of cuff pressure could prevent leakage of these secretions and, therefore, VAP. In patients supported by MV, cuff pressure also varies over the course of the day, so it is difficult to always respond to the variability. Valencia and colleagues (*Crit Care Med* 2007; 35:1543) developed an automatic device that constantly measures and maintains adequate cuff pressure. In a trial of the mechanism, they found that their device nearly eliminated inadvertent deflations. Despite studying over 140 subjects; however, the approach did not alter rates of VAP.

Continuous aspiration of subglottic secretions (CASS) has also been evaluated. ETTs exist that are designed to facilitate CASS, and have an additional port above the cuff that can be attached to a suction device. With wall suction in the ICU, these ETTs prevent secretion accumulation above the ETT cuff. Early trials indicated that this strategy could prove beneficial. Subsequent analyses failed to show a major benefit, in that only early onset VAP with low virulence pathogens (eg, *Haemophilus influenzae*) appeared to be prevented with these devices. CASS had no impact on duration of MV, ICU length of stay, or mortality. As a practical matter, the suction port for subglottic drainage often clogs in clinical practice.

### Oral Care

Colonization of the upper airway is a necessary, but often not sufficient, condition for the development of VAP. Therefore,

prevention of oral colonization with topical antiseptics appears attractive for VAP prevention because many of these antiseptics are safe and not associated with resistance.

Isegran, a novel, topical antimicrobial peptide, and example of a protegrin, is active in vitro against many VAP pathogens and also reduces airway colonization. However, in a large (n=709), multicenter randomized trial, iseganan application did not prevent VAP or alter mortality rates. VAP occurred in 16% of people randomized to iseganan and was diagnosed in 20% of placebo-treated subjects (Kollef et al. *Am J Respir Crit Care Med* 2006; 173:91). The failure of iseganan has raised many questions, given its theoretical appeal for VAP prevention.

Fortunately, the data supporting more traditional antiseptics are more positive. Recent randomized trials have indicated that regular administration of chlorhexidine can reduce rates of infection (Segers et al. *JAMA* 2006; 296:2460; Koeman et al. *Am J Respir Crit Care Med* 2006; 173:1348). In a prospective randomized analysis of patients who have had cardiothoracic surgery, the use of nasal and oral chlorhexidine reduced the pooled frequency of nosocomial infections, generally, and the incidence of nosocomial pneumonia, specifically (Segers et al. *JAMA* 2006; 296:2460). Koeman and colleagues studied a more mixed cohort of critically ill patients (*Am J Respir Crit Care Med* 2006; 173:1348). They randomized patients, believed to need greater than 48 h of MV, to one of three treatment arms: placebo, chlorhexidine, or chlorhexidine/colistin, applied in the mouth four times a day. Both interventions (eg, chlorhexidine and chlorhexidine/colistin) reduced the incidence of VAP by more than half, relative to the placebo. The researchers did not observe an effect on mortality or duration of MV.

Two metaanalyses confirm the utility of chlorhexidine (Chlebicki and Safdar. *Crit Care Med* 2007; 35:595; Chan et al. *BMJ* 2007; 334:889). Chlebicki and colleagues (*Crit Care Med* 2007; 35:595) reviewed seven clinical trials of antiseptics and determined they were effective for VAP prevention. The pooled risk for VAP was reduced by 25% with chlorhexidine. In a

more rigorous analysis exploring oral decontamination with either antiseptics or antibiotics, Chan and colleagues (*BMJ* 2007; 334:889) concluded that regular, prophylactic chlorhexidine application significantly lowered the incidence of VAP. Neither metaanalysis found that antiseptic use reduced mortality or duration of MV. In light of these findings, the benefit of chlorhexidine may be limited. Alternatively, studies of antiseptics may have been underpowered to detect a difference in mortality or duration of MV. What remains uncertain are how the effect of chlorhexidine varies based on the population studied (eg, mixed ICU patients vs homogenous cohorts of postcardiac surgery subjects) and if chlorhexidine decreases the use of antibiotics. Even if the benefit of oral antiseptics was limited to reducing the vast amount of antibiotics used annually for VAP, it would still be meaningful. Antibiotic overuse is associated not only with direct costs, but also the emergence of resistant pathogens.

In summary, recent attempts at VAP prevention address both the upper airway and the ETT. Previously promising interventions, such as iseganan, have failed when studied in clinical trials. Other tools, such as topical or oral antiseptics, require further study. However, reengineering the endotracheal tube to prevent biofilm accumulation continues to show promise. Clinicians will need to remain attentive to developments in VAP prevention if they hope to improve outcomes for patients needing MV. ■

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**Disclosures:** Dr. Shorr has served as a consultant to, received grant support from, or been a speaker for the following companies/organizations: Astellas Pharma Inc.; C. R. Bard, Inc.; Boehringer Ingelheim, Inc.; GlaxoSmithKline; Johnson & Johnson; Merck & Co., Inc; Pfizer Inc.; and sanofi-aventis.

## Editor's Insight

**V**AP is a vexing problem. We do not yet understand its effect on mortality, but it certainly complicates the care of patients who already have complex illnesses. VAP is difficult to diagnose and problematic to treat. The ideal solution

is to prevent it from occurring. Dr. Shorr reminds us of the predisposing factors for the disease and brings interesting insights into an active field of inquiry on approaches to reducing the risk of VAP.

—Editor

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

# NEWS FROM THE COLLEGE



## PRESIDENT'S REPORT Remembering Jeff Siegel

I went to a funeral this morning that shouldn't have happened. Jeffrey L. Siegel, MD, FCCP, was run down on a local street last Friday night while picking up pizza to take home to his family. The driver sped away, and Jeff was pronounced dead in the field after an hour-long attempt at resuscitation.

This column is not about his devotion to his wonderful family, his friends, his synagogue, and his community, which are exemplary and make his death tragic enough. This is about Jeff—the consummate doctor.

Jeff was 48 years old, and among the best physicians I have ever known. I met him in the 1980s when he started his fellowship in Pulmonary Medicine at Mount Sinai Hospital, New York, after completing his residency and serving as Chief Resident at NYU Medical Center. I was on the Sinai faculty then, and I believe that around once every 7 to 10 years, you have the privilege and the pleasure of matching and working with a truly extraordinary fellow, a gem with knowledge, common sense, commitment, curiosity, and the confidence to make a



BY DR. MARK J. ROSEN, FCCP

decision and act on it, even if some disagree. Jeff had it all, and it was all for his patients. Long hours, extra time in the library, and other behaviors, now deemed anachronistic, were how Jeff worked. Until last week, he still worked the hours, kept up with the journals, and continuously accrued

more CME hours than he needed.

I was recruited to become Division Chief at Beth Israel in early 1989, and offered Jeff a position when he graduated in June. A Division Chief with three Jeff Siegels in the division does not need to come to work. I was disappointed that he declined, preferring a job in private practice on Long Island with David Breidbart, an outstanding pulmonologist himself. Their patients were admitted to North Shore University Hospital, 5 minutes from my home. I challenged Jeff on the decision to forgo what would surely be a brilliant academic career, but he was resolute. He was also correct, and their practice is now enormously successful for all the right reasons.

My karma put me on my bicycle on

a Sunday morning in July 1989, and I was hit by another driver who also fled the scene. Unlike Jeff, I made it to the hospital, but seizing with fractures of my skull, clavicle, and around six ribs. I don't remember any of it. When I woke up, I learned that destiny smiled, because Jeff was rounding in the SICU that morning, a brand-new July attending. He saw me on a ventilator and deeply sedated, talked to the ICU folks, and promptly took charge. I will always be grateful for that, because Jeff was a terrific doctor who was not reluctant to make a decision and act on it. He extubated me, despite the surgeon's plan to proceed with a tracheostomy, anticipating that I would have a long haul on the ventilator with a flail chest. Needless to say, Jeff was right—no flail chest, and I breathed just fine on my own.

As important as Jeff and David's clinical expertise were, their kindness and attention to my wife are unforgettable. She has no medical background and

was bewildered by all that was happening around her, but they were always there to offer a plan, an explanation, sympathy, and a hug.

Jeff was my referral of choice for anyone who asked for a "pulmonary guy" on Long Island. That includes referring my father, mother-in-law, brother-in-law, friends and strangers. They all praise his expertise and his incredible caring—Jeff called everyone back the next day to see how they were feeling.

No wonder his patients loved him. We all did.

He was a first-rate doctor who embodied patient-focused care in all of its dimensions. His death is senseless and random, and each of us who knew him, along with the hospital and the community have suffered a great loss. We are angry, and we are very sad.

We doctors should also try to remember who Jeff was and what he was like, and try to be more like him. ■

**JEFF CALLED EVERYONE BACK THE NEXT DAY TO SEE HOW THEY WERE FEELING. NO WONDER HIS PATIENTS LOVED HIM. WE ALL DID.**

## Chicago 'Site'ings

With so much to see and do in Chicago, it may be difficult to know where to begin. However, if you happen upon some free time, here's a sneak peek of a few of the hundreds of landmarks that you shouldn't miss.

Right in the center of it all is Cloud Gate—or what is more affectionately known as "The Bean." One of the newest on the list, the 66-foot long, stainless steel Bean can be found in Millennium Park. A little farther north is The Chicago Theater (North State Street), famous host to stage plays, speeches, and concerts. Its marquee commonly appears in film and on TV (and even in our CHEST programs!).

Built in 1869, the Chicago Water Tower is located on north Michigan Avenue and is the only surviving structure of the Great Chicago Fire still standing today. Also on the Magnificent Mile is the gothic Tribune Tower. Its walls are embedded with stones, bricks, and debris, brought home by journalists. Included are pieces from the Taj Mahal, the Great

Pyramid, the Berlin Wall, and the World Trade Center.

Moving south, Hull House (South Halsted Street) was cofounded in 1889 by Jane Addams, as one of the first settlement houses in the United States.

The south side of town is also home to the University of Chicago and the site of the world's first nuclear chain reaction at Chicago Pile-1 (CP-1), built in

1942 on a racquet court under the west stands at the original Alonzo Stagg Stadium.

Finally, for the 'architect-at-heart,' the works of Frank Lloyd Wright are peppered about town. Aside from his many large and collaborative works, 17 of his private home projects can be found—many in the

most unexpected of places.

Need we say more? This city's permanent treasures, be them great or small, make Chicago our kind of town, and the perfect place for CHEST 2007!

For more information about Chicago, visit [www.choosechicago.com](http://www.choosechicago.com).

Visit [www.chestnet.org/CHEST](http://www.chestnet.org/CHEST) for details about CHEST 2007. ■



## This Month in CHEST: Editor's Picks

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

► **Paradoxical Worsening of Shock After the Use of Percutaneous Mechanical Thrombectomy Device in a Postpartum Patient With a**

**Massive Pulmonary Embolism.** By Dr. N. Kumar, et al

► **Catheter Embolectomy for Acute Pulmonary Embolism.** By Dr. N. Kucher

► **Registry and Survival Study in Chinese Patients With Idiopathic and Familial Pulmonary Arterial Hypertension.** By Dr. Zhi-Cheng Jing, et al

► **Instrument Accuracy and Reproducibility in Measurements of Pulmonary Function.** By Dr. R. L. Jensen, et al

► **Sources of Long-term Variability in Measurements of Lung Function: Implications for Interpretation and Clinical**

**Trial Design.** By Dr. R. L. Jensen, et al  
► **Spirometry Utilization for COPD: How Do We Measure Up?** By Dr. M. Han, et al

► **Conflict of Interest in Clinical Practice.** By Dr. M. R. Tonelli, FCCP

► **Comparison of the SpO<sub>2</sub>/Fio<sub>2</sub> Ratio and the Pao<sub>2</sub>/Fio<sub>2</sub> Ratio**

**in Patients With Acute Lung Injury or ARDS.** By Dr. T. W. Rice, et al

► **Prospective External Validation of the Clinical Effectiveness of an Emergency Department-Based Early Goal-Directed Therapy Protocol for Severe Sepsis and Septic Shock.** By Dr.

A. E. Jones, et al

► **Recent Advances in Idiopathic Pulmonary Fibrosis.** By Dr. I. Noth, FCCP, and Dr. F. J. Martinez, FCCP

► **The Importance of Diagnosing and Managing ICU Delirium.** By Ms. B. T. Pun and Dr. E. W. Ely, FCCP



**NETWORKS**

# Groups Highlight End-of-Life Programs, Leadership

## Palliative and End-of-Life Care

With an increasing aging population and the decentralization of the family unit, more individuals are outliving family members or have no family nearby. This trend has resulted in people dying without family or friends to witness the end of their life.

As a result, hospitals across the country are establishing "No One Dies Alone" (NODA) programs. The inspiration for NODA originated at Sacred Heart Medical Center in Eugene, OR. NODA is a volunteer companion program for patients who are in their final hours of life and have neither family nor friends regularly available.

In January 2006, Lehigh Valley Hospital and Health Network, Allentown, PA, implemented the program as part of the Robert Wood Johnson Foundation grant for integrating palliative care in the ICU. Using the basic administrative and training structure outlined by the original NODA

project, the pastoral care department added methodology from clinical pastoral education. Volunteers undergo 6 hours of intensive training focusing on the physical, emotional, and spiritual aspects of dying. This training is distinctly different than the training for hospice volunteers.

Although the pastoral care department provides a 0.2 FTE for overall coordination, the program is primarily administered by volunteers, including the phone dispatchers who fill requests. To date, 124 volunteers have been trained and have provided their presence for 87 patients across the Lehigh Valley Hospital and Health Network. Recently, NODA was expanded to include respite care for family members of dying patients.

NetWork steering committee member, Daniel E. Ray, MD, FCCP, is the Director of the ICU and Co-Director of the Neuroscience ICU at Lehigh Valley Hospital. He also is the recipient of The CHEST

Foundation 2006 Roger C. Bone Advances in End-of-Life Care Award.

For more details, contact Betsy Powers at [betsypowers@lvh.com](mailto:betsypowers@lvh.com), or visit [www.lvh.org/lvh/Your\\_LVH/Hospital\\_Services/Pastoral\\_Care](http://www.lvh.org/lvh/Your_LVH/Hospital_Services/Pastoral_Care) | 304.

## Private Practice

The Private Practice NetWork will again be hosting a Leadership Development Program at CHEST 2007 in conjunction with the academic members of the College. This exciting program provides ACCP members with tools to make them more effective ACCP members and help them become more involved in College leadership activities. The program will be held on Saturday, October 20, with more than 20 participants who will receive complimentary registration to both CHEST 2007 and a postgraduate course on Sunday, October 21.

Members of the Private Practice NetWork are also working with the Practice Management Committee and the Affiliate NetWork to develop a program for fellows-in training. The program will provide these physicians with the skills to effectively choose a practice upon the completion of their training. This program also will be available to practicing physicians to assist them with managing the "business aspects" of their practices. As an outgrowth of this conference, the NetWork hopes to develop a primer on choosing a practice for affiliates who are unable to attend the course.

## Sleep

The specialty of sleep medicine has evolved from its early beginnings in the research labs of psychiatry, psychology, physiology, and neurology departments. These pioneers laid the foundation for the development of the sleep medicine specialty, encompassing elements from all four areas. However, sleep medicine now has such an infusion of clinical expertise, and great interest from the pulmonary world, that it will be irrevocably changed. Just as critical care medicine evolved in a way that changed the training and practice of pulmonologists, sleep medicine has exerted a strong influence on the training and practice of chest physicians.

The American College of Chest Physicians has responded nicely to these changes and the varied needs of its membership.

The establishment of the Sleep Medicine NetWork and the Critical Care and Sleep Institutes is a good example. We are now in the process of a historical transition in the field of sleep medicine, with a new board certification recognized by the American Board of Medical Specialties and administered (for us, at least) by the American Board of Internal Medicine for the first time this November. The ACCP has become active in the process of representing its members and educating them, and others, about this new specialty and its close relationship to pulmonary medicine.

The most common sleep disorders causing excessive daytime sleepiness are sleep-related breathing disorders. Excessive sleepiness is a public health problem which is the leading cause of highway fatalities and a major cause of work-related accidents. Pulmonologists are diagnosing and treating not only sleep apnea but also narcolepsy, insomnia, sleep-related movement disorders, and circadian rhythm disorders. They have learned to read EEGs and administer cognitive-behavioral therapy, as well as apply CPAP and oxygen.

Over 2,000 ACCP members belong to the Sleep NetWork, and over 70 members attended the Sleep NetWork Open Meeting at CHEST 2007 in Salt Lake City. The College now offers a Sleep Medicine Board Review Course and a consensus statement, entitled, "Roles and Responsibilities of Medical Directors of Sleep-Disorders Centers/Sleep-Disordered Breathing Laboratories," and will soon have a slide set available on most of the important sleep medicine topics. The ACCP also has sponsored a very successful education program on sleep disorders for primary care physicians. There are major challenges ahead, as technology changes the shape of sleep medicine, but we expect that interest in and knowledge about sleep medicine will continue to grow. ■

## ACCP Board Review. The Proven Leader in Comprehensive Review Programs

Rely on the ACCP, the leader in board review curriculum for over 30 years, to bring you comprehensive review programs of proven success. World-renowned clinicians present exam-focused content to offer relevant board preparation courses that make best use of your study time.



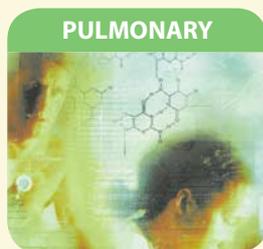
### ACCP Sleep Medicine Board Review Course 2007

August 24 – 27  
JW Marriott Desert Ridge  
Phoenix, AZ



### ACCP Critical Care Board Review Course 2007

August 24 – 28  
JW Marriott Desert Ridge  
Phoenix, AZ



### ACCP Pulmonary Board Review Course 2007

August 29 – September 2  
JW Marriott Desert Ridge  
Phoenix, AZ



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2. **Save 15%.** Register online for two board review courses, and save 15% off the combined registration fee. **Online offer only.**

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### NOW SHOWING ON CHESTNET.ORG

View presentation slides from the CHEST 2006 Members in Industry NetWork postgraduate course: Participating in Industry-Sponsored Pulmonary and Critical Care Trials.

[www.chestnet.org/networks/accp\\_industry/slides.php](http://www.chestnet.org/networks/accp_industry/slides.php)

# NEWS FROM THE COLLEGE



## Making a Difference Awards Dinner To Honor Dr. Petty

Join your ACCP colleagues and friends on Saturday, October 20, for an outstanding celebration at the Chicago Cultural Center. This year's Making a Difference Awards Dinner will feature:

- ▶ A special tribute to Thomas L. Petty, MD, Master FCCP, in celebration of his outstanding career and the establishment of the Thomas L. Petty, MD, Master FCCP Endowment in Lung Research
- ▶ A presentation of the Humanitarian

Award recipients and their pro bono projects from communities all over the world

▶ The ACCP Industry Advisory Council's presentation of support to this year's Community Outreach Event partner

As part of the special tribute to Dr. Petty, there will be a VIP Reception preceding the dinner, which is sponsored by Platinum Exclusive Sponsor, Boehringer Ingelheim Pharmaceuticals,

Inc. (See article below.)

The CHEST Foundation's 9th Annual Making a Difference Awards Dinner is sponsored by Platinum Exclusive Sponsor:

Boehringer Ingelheim Pharmaceuticals, Inc.

Participating Sponsors: Alpha-1

Foundation; AstraZeneca LP;

ALTANA Pharma US, Inc. – a

NYCOMED Company; Genentech

and Novartis; Holland & Knight, LLP;

National Lung Health Education Program;

The National Emphysema

Foundation; and Sepracor Inc.

Bus transportation to and from the Chicago Marriott

Downtown and InterContinental hotel will be provided

beginning at 5:40 PM for those

attending the VIP Reception, and will

continue to run until 7:40 PM. Buses

will return guests to these two hotels

at the end of the evening.

Making a Difference Society mem-

bers at the \$1,000+ level are entitled to

two complimentary tickets. Annual

donors at the \$500 level are entitled to one complimentary ticket. Register

online at [www.chestfoundation.org](http://www.chestfoundation.org).

To obtain more information, contact

Teri Ruiz at (847) 498-8308 or [truiz@](mailto:truiz@chestnet.org)

[truiz@chestnet.org](mailto:truiz@chestnet.org).



DR. THOMAS L. PETTY,  
MASTER FCCP

**Saturday, October 20**

Chicago Cultural Center  
Sidney R. Yates Gallery and  
Exhibit Hall

77 East Randolph Street  
Chicago, Illinois

**6:00 PM – 7:00 PM**

Boehringer Ingelheim Phar-

maceuticals, Inc. Thomas L.

Petty, MD, Master FCCP VIP

Reception (invitation only)

G.A.R. Hall and Rotunda

**7:00 PM – 8:00 PM**

Cocktail Reception

G.A.R. Hall and Rotunda

**8:00 PM – 10:30 PM**

Dinner and Ceremonies

Yates Gallery

## Petty Endowment in Lung Research

The CHEST Foundation, in partnership with Boehringer Ingelheim Pharmaceuticals, Inc., has established the Thomas L. Petty, MD, Master FCCP Endowment in Lung Research as an expression of admiration and appreciation of Dr. Petty's outstanding work.

A special tribute will be held in Dr. Petty's honor at the 9th annual Making a Difference Awards Dinner where Platinum Exclusive Sponsor, Boehringer Ingelheim Pharmaceuticals, Inc., will host the Thomas L. Petty, MD, Master FCCP VIP Reception preceding the dinner. This VIP Reception

is by invitation only for contributors to the endowment at the \$1,000+ level, and the Making a Difference Awards Dinner sponsors at the Bronze Sponsorship level and above. For more information, visit [www.chestfoundation.org](http://www.chestfoundation.org). You also can contact Teri Ruiz at (847) 498-8308 or [truiz@chestnet.org](mailto:truiz@chestnet.org).

Bus transportation to and from the Chicago Marriott Downtown and InterContinental will be provided beginning at 5:40 PM for those attending the VIP Reception, and will continue to run until 7:40 PM. Buses will return guests to these two hotels at the end of the evening.

## The Ambassadors Group: Our Invitation to You

CHEST 2007 attendees are invited to participate in a variety of activities and events sponsored by The CHEST Foundation's Ambassadors Group during CHEST 2007. Group members volunteer, educate, and network, on behalf of the ACCP and The CHEST Foundation, to improve lung health at the local level.

At CHEST 2007, members of the group will host a Hospitality and Information Room, where attendees can relax, make new connections, and renew old friendships. This year, the Ambassadors

Group has planned two special presentations in the Hospitality and Information Room. On Tuesday, October 23, there will be a presentation entitled, "Designology" from 4:00 PM – 5:00 PM. A presentation entitled, "Resculpt Your Lifestyle" will be featured on Wednesday, October 24, from 2:30 PM – 4:00 PM. New this year is a "Train-the-Trainer" session, on Sunday, October 21 from 2:30 PM – 4:00 PM, in which attendees are invited to learn how to pre-

sent the Lung Lessons™ program to elementary school children.

In addition to these new events, the Ambassadors Group has invited all attendees to join them at the Fourth Annual Global Outreach Tea on Monday, October 22, from 3:30 PM – 5:00 PM, and at the Annual Open Meeting

on Tuesday, October

23, from 9:30 AM –

11:30 AM. Ambassadors Group mem-

bers also participate

as volunteers at The

CHEST Foundation's

Community Outreach Event on

Monday, October 22.

Membership is

open to all ACCP members' families

and friends. Annual membership

dues are: \$10 for youth members,

\$35 for international members, and

\$50 for US and Canadian members.

Contact Sue Ciezadlo, Ambassadors

Group Liaison, at (847) 498-8363 or

[sciezadlo@chestnet.org](mailto:sciezadlo@chestnet.org), to join today.

Reminder: If you are an Ambas-

sador, it is time to send in your dues

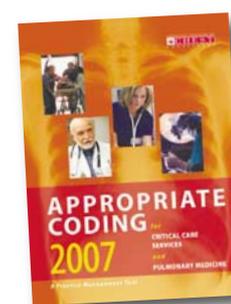
to renew your membership for another year.



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for sleep medicine, along with useful tools and templates you can use in your practice. New chapters on electronic medical records, pay for performance, and revenue cycle management provide must-have information to make your practice a success.

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## CRITICAL CARE COMMENTARY

# Celebration of Life

Being ill is an undesirable experience; however, being admitted to a hospital is even more frightening. Furthermore, a catastrophic illness requiring intensive care is unnerving—not only for patients, but also for their families. It is well known that patient recovery and health depends on the security and welfare of family members who are in the waiting room.

The medical intensive care unit (MICU) cares for the sickest medical patients in the hospital. The severity of illness in these patients is inherent by the nature of the disease and comorbid conditions that brought them to the MICU. Mortality is also higher in the MICU compared with other ICUs. The average length of stay for patients is fewer than 5 days; however, most get well and leave the unit. The few patients who are extremely ill have a more extended stay, and many hours are invested in these precious patients. Unfortunately, when they leave the unit, the staff does not usually get to see how well they are thriving. It is good for the morale of health-care teams to be able to see the fruits of their hard work. It is now time to let former MICU patients know that we were honored to have the opportunity to care for them when they were critically ill.

Ben Taub General Hospital (BTGH) is one of three hospitals in the Harris County Hospital District (HCHD), which covers an area of more than 4 million people. The 572-bed hospital cares for many of the uninsured and underinsured residents of Harris County, TX. These people typically are considered the “working poor” and cannot afford simple amenities taken for granted by more affluent members of society. In addition, more than two-thirds of the patients seen at BTGH belong to minority communities. Despite these limitations, BTGH has ranked among the top 100 hospitals in the country and continues to deliver high quality care. It is one of only two level I trauma centers in Houston.

BTGH MICU was the recipient of The CHEST Foundation’s Critical Care Family Assistance Program (CCFAP) grant in 2003. After receiving the grant, we identified the needs of our patients’ families, and a program was put into place very quickly. We determined the following information about our patients:

1. At least 30% of patients had family members out of town who needed to be contacted on a regular basis.
2. Sixteen percent of patients had family members out of the country who needed to be contacted on a regular basis.
3. Seven percent of patients needed to have family members located but were unable to provide the information.
4. Eleven percent of patients had medical care decisions delayed because family

members were out of town, or out of the country, and not immediately available for consent.

5. At least 10% of patients’ families needed intervention with US embassies in foreign countries.

6. Some patients died alone with no family member at their bedside, due to financial constraints.

7. Many patients’ families had no transportation to or from the hospital and could not afford parking fees.

To address many of these issues, the program provided social worker support during evenings and on weekends, in ad-



**Dr. Guntupalli (center) with Sharon (left), a patient in the MICU many times, who was very supportive to Sandy (right), a new mother who had been in the MICU.**

dition to regular staff. Compared to ICUs that had no such support, the CCFAP provided timely assessment and intervention to address the needs of patients’ families. In addition, the program provided food coupons, bus and parking tokens, family information booklets, lodging arrangements, and care packs. Knowing that informed patients, and their families, participate more actively in their care and get better faster, we also developed patient education materials.

Although I had worked at BTGH for over a decade prior to receiving this grant, the CCFAP has opened my eyes, along with many doors. Traditionally, providing superb patient care has been considered the utmost responsibility of caring physicians. As our program progressed, we also began to learn a great deal from our patients’ families. A variety of hospital services collaborated in the program’s development, including building services, food services, chaplains, volunteers, and the HCHD Foundation. It was amazing to see everyone working together and enthusiastically contributing to the program. After seeing its success, BTGH continued to support additional patient benefits (eg, an off-hours social worker) after the grant period was completed. The CCFAP

certainly resulted in the increased satisfaction of MICU patients, families, and health-care teams. The lessons learned, and tools developed, will be shared with and replicated by MICUs nationwide.

### Celebration of Life

The MICU is not about the structure. It is about the patients and team who cares for them, including nurses, doctors, respiratory therapists, pharmacists, dietitians, and physical therapists.

In the spring of 2006, members of the CCFAP and BTGH, along with several MICU patients, and their families, came

acquired pneumonia was supported by mechanical ventilation for 3 months, then left the hospital and came home to join his wife and 4-year-old daughter. He came back to our event with a new addition to the family—a 4-month-old daughter.

► A pregnant woman with sepsis delivered her baby while in the ICU and spent months supported by mechanical ventilation. She was very depressed about not being able to spend time with her new child, and initially refused tracheostomy. However, she was convinced to go through with the procedure by another volunteer patient who had chosen the same treatment route. She returned proudly to our event, showing off her most prized possession—her 2-year-old son.

► A pregnant woman, with severe asthma, was intubated for respiratory failure and delivered her baby. She was subsequently admitted to the MICU multiple times for different illnesses. She now walks proudly, 10 years later, with the child she delivered in the MICU.

Also in attendance were many grateful families whose loved ones did not survive. They felt proud and happy, reminiscing about the beautiful lives of their loved ones and final journeys carried with dignity. Some of these former patients were in their 20s, while others had lived a full life. All of them can teach us important lessons.

At the end of the event, I looked at the patients with awe, and once again remembered how life is so precious and beautiful. How fortunate we are, in the medical profession, to play such an important role for these people at the most critical time in their lives, when they need much more than the best medical care. They need someone to hold them, share memories with them, and cry with them at their most vulnerable moments.

Below is an excerpt from the speech of a former patient. Sharon was admitted to the MICU 20 times, with severe asthma, and even received ventilatory support. She eventually recovered to the point of being able to volunteer in the MICU and inspire others to have a positive attitude when battling a serious illness.

*“Everything that was done, and given to me, by the staff here, made me realize that my life does matter. So I now stand here, eternally blessed, with this wonderful opportunity to be able to celebrate my life everyday with every breath I take. God bless you all.”—Sharon*

DR. KALPALATHA GUNTUPALLI, FCCP  
 Professor of Medicine and Pulmonology  
 Baylor College of Medicine  
 Chief, Pulmonary Disease and Critical  
 Care Medicine  
 Director, MICU  
 Ben Taub Hospital  
 Houston, TX

► A young man with severe community-

## NEWS FROM THE COLLEGE



## EDUCATION INSIGHTS

## CHEST 2007: Promoting Evidence-Based Medicine

BY CARLA HERRERIAS, MPH  
ACCP Clinical Research Analyst

**E**vidence-based guidelines and evidence-based medicine will be showcased at CHEST 2007 through several different venues. Educational sessions will be offered on recent ACCP clinical practice guidelines.

The Diagnosis and Management of Lung Cancer: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 2nd Edition, which will be published in September 2007, is the foundation for a course and two educational sessions during the annual meeting:

▶ Best of the Guidelines: ACCP

Second Edition Lung Cancer Guidelines Postgraduate course, Sunday, October 21, 8:00 AM – 5:00 PM

▶ Lung Cancer II: Part 1—Diagnosis, Screening, Staging, and Surgical Treatment Tuesday, October 23, 1:00 PM

▶ Lung Cancer II: Part 2—Therapeutic Treatment Options and Palliative Care Wednesday, October 24, 4:30 PM

The updated Diagnosis and Management of Pulmonary Arterial Hypertension: ACCP Evidence-Based Clinical Practice Guidelines was published in June 2007. A session will be held during CHEST 2007 to review these changes to the treatment algorithm and recommendations:

▶ Pulmonary Arterial Hypertension

Medical Treatment Update; Monday, October 22, 2:30 PM

The recently published Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines will be reviewed:

▶ Understanding and Implementing the Guidelines: Pulmonary Rehabilitation; Tuesday, October 23, 4:00 PM

There will also be an important interactive session on knowledge uptake and creating better ways of transferring knowledge in order to incorporate evidence-based medicine in practice:

▶ Transferring Knowledge of Key Guideline Recommendations to Clinical Practice; Monday, October 22, 10:45 AM

This session, moderated by members of the Health and Science Policy (HSP) Committee, will focus on four guidelines: lung cancer, antithrombotics, cough, and pulmonary arterial hypertension. There will be a pretest of the participants' knowledge of these guidelines, followed by educational presentations on each of the guidelines. Finally, at the end of the session, there will be a posttest covering ways of implementing these guidelines into clinical practice. The moderator and speakers will request that the participants use interactive keypads to indicate how they use guidelines and what they know about the guidelines so that the

*Continued on following page*

## CLASSIFIEDS

## PROFESSIONAL OPPORTUNITIES

### Pulmonary/Critical Care Richmond, Virginia

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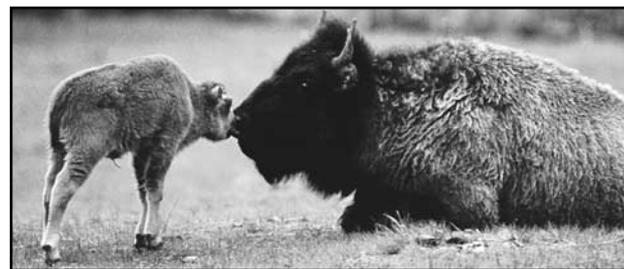
### Intensivists: Austin Texas

Austin Critical Care Specialists is a new Central Texas practice with ground-floor opportunities! We are a stable group offering a competitive salary, benefits and paid malpractice/tail. New hospital opening February 2008 with plans for 29 critical care beds, full range of services and state of the art equipment. Austin is known as the "Live Music Capital of the World", with concerts every night of the week. Nature trails, wilderness preserves and natural springs create an oasis in the heart of the city. Call Lynn Sprinkle at 512-610-0321 for more information. Fax your CV to 512-452-9306, attention Lynn or email lynn@accdocs.com

### Marietta Pulmonary Medicine Suburban Atlanta

Well-established, busy 12-physician single-specialty Pulmonary practice in suburban Atlanta, Georgia, looking for one or more BC/BE Pulmonary/Critical Care physicians. Sleep certification is a plus. Practice includes all aspects of pulmonary medicine, including critical care, sleep medicine, out-patient clinic, pulmonary rehab and clinical research. Practice located at one large acute-care hospital, with the busiest ER in Georgia, and also rounds at a near-by long term acute care hospital. Installation of an electronic ICU monitoring system planned for the near future. Competitive salary with bonus potential and generous benefits package. Fax CV to: 770-792-1738.

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



### Pulmonology/Critical Care Physician

From the thrill seeker to the nature lover, Cheyenne, Wyoming, has something to please everyone.

#### Location

- National Forest within 30 minutes
- Denver, Colorado within 90 minutes

#### Outdoor/Cultural/Lifestyle Appeal

- Herd cattle, bike, rock climb, ski, snowmobile or stargaze in the wide open spaces with crystal clear skies.
- Attend the symphony, theatre, museums and Cheyenne Frontier Days, the world's largest outdoor rodeo
- Low cost of living, no state income tax and minimal managed care makes practicing in Cheyenne ideal.

#### Cheyenne Regional Medical Center

- 218-bed premier regional healthcare system that prides itself on delivering the highest standard of quality care to meet the region's growing healthcare needs.
- Highly trained physicians and employees, state-of-the-art facilities and advanced technologies ensure our patients receive exceptional care close to home.

Contact: Selina Irby (307) 432-2648  
selina.irby@crmcwy.org



### BC/BE Intensivists

Prestigious pulmonary/critical care group practice seeking BC/BE intensivists for 24 hour/seven day a week in-house intensivist service for Chicago-area community hospital. This is a state-of-the-art facility in an attractive northwest suburb. We offer excellent compensation and benefits, including health and generous retirement programs, malpractice coverage and tail. Sorry, no J1 visas. For further information, please email CV and cover letter to sweissman@chest-md.com or fax to 773-935-2724.

### Pulmonary/ CCM

New Jersey: Busy two MD practice in central NJ seeks third MD to continue to expand this rapidly growing group. Privileges at two teaching hospitals with primarily critical care medicine. Office practice limited to pulmonary disease including on site PFT lab and pulmonary rehab. Area midway between NYC and Philadelphia with excellent area schools and housing opportunities. Call 1:3. BC/BE pulmonary and CCM required. Willing to consider flexible / part-time schedule. Reply with CV to pulmjob@patmedia.net

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### Pulmonary and Critical Care Physician

Well-established, dynamic and growing multi-specialty group in Terre Haute, Indiana is currently recruiting a qualified BC/BE Pulmonary/Critical Care physician with a specialty in sleep medicine to join our practice. Competitive salary and benefits. Please fax CV to attention Administrator: 812-235-2754 or email sbuis@provmed.net

Continued from previous page

HSP Committee can gather immediate data on issues related to implementation. Attendees should come away with innovative ways to incorporate evidence-based medicine into daily practice.

In addition, members of the HSP Committee will be educating CHEST 2007 attendees on the new HSP Web site, which focuses on guideline development and use of guidelines in practice. The new Web site (located at [www.chestnet.org](http://www.chestnet.org) under "education") will link to an orientation program focusing on key issues in evidence-based medicine, the functions of the HSP Committee, current guidelines, those in development, and others in review. The Web site will also provide numerous resources to assist clinicians. The site will be updated and reviewed on a consistent basis to ensure that ACCP members and other users receive the most current information.

The HSP Committee is committed to furthering the efforts of evidence-based guidelines and educating members on how to incorporate these into daily practice. As a leader in developing evidence-based guidance for chest medicine, HSP provides the most up to date information on relevant clinical issues.

For further information on activities in Health and Science Policy, please contact HSP staff at (847) 498-8388. ■

## Don't Miss Train-the-Trainer Session

Did you know?

- ▶ Ninety percent of new smokers begin as teenagers.
- ▶ Three thousand youth 18 years or younger start smoking every day—more than 1 million each year.
- ▶ Over 70% of American high school students have tried smoking cigarettes.
- ▶ Kids who smoke are three times more likely to use alcohol, eight times more likely to use marijuana, and 22 times more likely to use cocaine than kids who do not smoke.

These statistics are startling. Members of The CHEST Foundation's Ambassadors Group have been hard at work trying to make a difference in the lives of our youth. Since 2005, they have presented antitobacco education programs to more than 5,000 school-aged children in the United States and abroad.

Recently, Kathy Wilder talked with more than 1,700 youth in Anchorage, AK, and Lori Sinclair began an antitobacco education effort in Panama that already reached 500 children. These are just a few examples of exciting Ambassador Group programs already in progress.

Despite these efforts, there are many more youth who need to hear the antitobacco message. It is our responsibility, as trained health-care workers, teachers, parents, and concerned adults, to make a difference in the future lung health of our children.

At CHEST 2007 in Chicago, you will have a unique opportunity to attend a "Train-the-Trainer" session.

You will learn how to give antitobacco presentations in your community, using materials developed by The CHEST Foundation and the Women's Health

NetWork.

The program will be held in the Ambassadors Group Hospitality and Information Room at the Chicago Marriott on Sunday, October 21, from 2:30 PM - 4:00 PM. You will witness a presentation given to Chicago area youth by Monir Almassi, Susan Kvale, and Kathy Wilder. You also will learn how to approach schools and youth organizations about adopting the program, receive the many readily available materials, become a presenter, and train others to be presenters.

Take advantage of this opportunity, offered by our Ambassadors, to make a difference in the lives of our youth. Becoming involved in this antitobacco program is not only fun, exciting, and rewarding, but also absolutely essential to the health and future well-being of our children. ■

# Opportunity...

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2007 

October 20 - 25, 2007  
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### For Clinical Education

- The world's largest-of-its-kind ACCP Simulation Center will feature 25,000 square feet of hands-on clinical experiences.
- Leading sessions will address new and breakthrough topics.
- Highly rated sessions will be back by demand.
- Exclusive look at original research will offer the first-ever review of new science.
- Special sessions will focus on emerging developments in chest medicine and practice management. NEW!

### For Professional Growth

- The Pulmonary Office: A Blueprint for Innovation will showcase managing and building a practice. NEW!
- Renowned international faculty will be readily accessible for easy interaction.
- Original investigation presentations will offer opportunity to present your research.
- A large exhibit hall will showcase the latest technology advances.

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# Opioids Unmatched for Dyspnea Near End of Life

BY BRUCE JANCIN  
Elsevier Global Medical News

DALLAS — Of all the symptoms that occur in patients approaching the end of life, dyspnea is the one they find most distressing.

"It's very frightening. People feel like they're dying in that moment," according to Dr. Steven Pantilat, director of the palliative care program at the University of California, San Francisco.

It's also extremely common. Dyspnea—a subjective sensation of difficulty breathing—is experienced by 70% of patients in the last 6 weeks of life, he said at the annual meeting of the Society of Hospital Medicine.

A reversible cause may be present—for example, worsening heart failure, chronic obstructive pulmonary disease, infection, anemia, or bronchial obstruction—but the extent to which this is pursued depends on the goals of care.



**Opioids often are effective for dyspnea in lower doses than needed for pain management.**

DR. PANTILAT

When death is close, the goal may be simply to relieve the symptom of shortness of breath. And for that purpose, nothing matches opioids. These drugs have multiple mechanisms of benefit, including acting on the midbrain to reduce the sensation of shortness of breath, decreasing oxygen consumption by reducing muscle activity, suppressing cough, reducing chemoreceptor sensitivity to carbon dioxide, and decreasing cardiac preload and sympathetic tone.

Dyspnea is frequently associated with anxiety. "Some of the most anxious people I've ever seen are short of breath," Dr. Pantilat observed. His strategy in the palliative care setting is to always address the dyspnea first. Treating anxiety with a drug such as lorazepam causes sedation, which may limit the ability to give opioids in the doses needed to relieve the dyspnea that's often the underlying cause. Only if the patient's anxiety doesn't improve after the dyspnea is treated does he consider the possibility that it's pure anxiety.

Opioids often are effective for dyspnea in lower doses than needed for pain management. A good starting oral dose is 5 mg of hydrocodone every 4 hours or 5-10 mg of morphine elixir every 4 hours.

Alternatively, intravenous morphine can

be started at 1-2 mg every 4 hours; the rule of thumb is 1-2 mg IV is equal to 3-6 mg by mouth.

In general, the opioid dose can be increased by 50% every 4 hours until the dyspnea is relieved. But there are times when a much more aggressive approach is required, especially when the patient is already taking opioids for pain management.

"You need to have a plan because when people get short of breath, they need relief now. Sometimes you have to be there at the bedside with the opioid and the

nurse and keep pushing it. You give 2 mg, and 5 minutes later you give 4 mg, and 5 minutes later you give 8 mg, just to try to get them under control. If you give a dose of 2 mg and you come back a half-hour later, you're going to have a patient in great distress and a family that's freaking out completely," Dr. Pantilat explained.

Supplemental oxygen is widely overused in dyspneic patients in palliative care, he continued. Oxygen is appropriate if the patient is hypoxic, but it's important to realize most patients with dyspnea are not

hypoxic, so oxygen doesn't make them feel any better. And patients who are short of breath often really dislike having a mask on their face. It feels suffocating, interferes with speech, and makes it more difficult for family members to stroke the face and otherwise express affection.

"I would say more often than not we take away the oxygen, even the 2 L per minute by nasal cannula that seems to be standard for just about anybody in the hospital who's near the end of life. Most commonly, we get zero reaction from the patient," he said. ■

## BRIEF SUMMARY OF PRESCRIBING INFORMATION

### CSL Behring Zemaira® Alpha<sub>1</sub>-Proteinase Inhibitor (Human)

Manufactured by:  
CSL Behring LLC  
Kankakee, IL 60901 USA  
US License No. 1767

Rx only

Before prescribing, please consult full prescribing information, a brief summary of which follows:

#### INDICATIONS AND USAGE

Zemaira® is indicated for chronic augmentation and maintenance therapy in individuals with alpha<sub>1</sub>-proteinase inhibitor (A<sub>1</sub>-PI) deficiency and clinical evidence of emphysema.

Zemaira® increases antigenic and functional (ANEC) serum levels and lung epithelial lining fluid levels of A<sub>1</sub>-PI. Clinical data demonstrating the long-term effects of chronic augmentation therapy of individuals with Zemaira® are not available.

Safety and effectiveness in pediatric patients have not been established.

Zemaira® is not indicated as therapy for lung disease patients in whom severe congenital A<sub>1</sub>-PI deficiency has not been established.

#### CONTRAINDICATIONS

Zemaira® is contraindicated in individuals with a known hypersensitivity to any of its components. Zemaira® is also contraindicated in individuals with a history of anaphylaxis or severe systemic response to A<sub>1</sub>-PI products.

Individuals with selective IgA deficiencies who have known antibodies against IgA (anti-IgA antibodies) should not receive Zemaira®, since these patients may experience severe reactions, including anaphylaxis, to IgA that may be present in Zemaira®.

#### WARNINGS

Zemaira® is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. Because Zemaira® is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses during manufacture. (See **DESCRIPTION** section for viral reduction measures.) The manufacturing procedure for Zemaira® includes processing steps designed to reduce further the risk of viral transmission. Stringent procedures utilized at plasma collection centers, plasma testing laboratories, and fractionation facilities are designed to reduce the risk of viral transmission. The primary viral reduction steps of the Zemaira® manufacturing process are pasteurization (60°C for 10 hours) and two sequential ultrafiltration steps. Additional purification procedures used in the manufacture of Zemaira® also potentially provide viral reduction. Despite these measures, such products may still potentially contain human pathogenic agents, including those not yet known or identified. Thus, the risk of transmission of infectious agents can not be totally eliminated. Any infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to CSL Behring at 800-504-5434. The physician should discuss the risks and benefits of this product with the patient. Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections (see **Information For Patients**).

During clinical studies, no cases of hepatitis A, B, C, or HIV viral infections were reported with the use of Zemaira®.

#### PRECAUTIONS

**General** - Infusion rates and the patient's clinical state should be monitored closely during infusion. The patient should be observed for signs of infusion-related reactions.

As with any colloid solution, there may be an increase in plasma volume following intravenous administration of Zemaira®. Caution should therefore be used in patients at risk for circulatory overload.

**Information For Patients** - Patients should be informed of the early signs of hypersensitivity reactions

including hives, generalized urticaria, tightness of the chest, dyspnea, wheezing, faintness, hypotension, and anaphylaxis. Patients should be advised to discontinue use of the product and contact their physician and/or seek immediate emergency care, depending on the severity of the reaction, if these symptoms occur.

As with all plasma-derived products, some viruses, such as parvovirus B19, are particularly difficult to remove or inactivate at this time. Parvovirus B19 may most seriously affect pregnant women and immune-compromised individuals. Symptoms of parvovirus B19 include fever, drowsiness, chills, and runny nose followed two weeks later by a rash and joint pain. Patients should be encouraged to consult their physician if such symptoms occur.

**Pregnancy Category C** - Animal reproduction studies have not been conducted with Zemaira®, Alpha<sub>1</sub>-Proteinase Inhibitor (Human). It is also not known whether Zemaira® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Zemaira® should be given to a pregnant woman only if clearly needed.

**Nursing Mothers** - It is not known whether Zemaira® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zemaira® is administered to a nursing woman.

**Pediatric Use** - Safety and effectiveness in the pediatric population have not been established.

**Geriatric Use** - Clinical studies of Zemaira® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. As for all patients, dosing for geriatric patients should be appropriate to their overall situation.

#### ADVERSE REACTIONS

Intravenous administration of Zemaira®, 60 mg/kg weekly, has been shown to be generally well tolerated. In clinical studies, the following treatment-related adverse reactions were reported: asthenia, injection site pain, dizziness, headache, paresthesia, and pruritus. Each of these related adverse events was observed in 1 of 89 subjects (1%). The adverse reactions were mild.

Should evidence of an acute hypersensitivity reaction be observed, the infusion should be stopped promptly and appropriate countermeasures and supportive therapy should be administered.

Table 3 summarizes the adverse event data obtained with single and multiple doses during clinical trials with Zemaira® and Prolastin®. No clinically significant differences were detected between the two treatment groups.

Table 3: Summary of Adverse Events

	Zemaira®	Prolastin®
No. of subjects treated	89	32
No. of subjects with adverse events regardless of causality (%)	69 (78%)	20 (63%)
No. of subjects with related adverse events (%)	5 (6%)	4 (13%)
No. of subjects with related serious adverse events	0	0
No. of infusions	1296	160
No. of adverse events regardless of causality (rates per infusion)	298 (0.230)	83 (0.519)
No. of related adverse events (rates per infusion)	6 (0.005)	5 (0.031)

The frequencies of adverse events per infusion that were ≥0.4% in Zemaira®-treated subjects, regardless of causality, were: headache (33 events per 1296 infusions, 2.5%), upper respiratory infection (1.6%), sinusitis (1.5%), injection site hemorrhage (0.9%), sore throat (0.9%), bronchitis (0.8%), asthenia (0.6%), fever (0.6%), pain (0.5%), rhinitis (0.5%), bronchospasm (0.5%), chest pain (0.5%), increased cough (0.4%), rash (0.4%), and infection (0.4%).

The following adverse events, regardless of causality, occurred at a rate of 0.2% to <0.4% per infusion: abdominal pain, diarrhea, dizziness, ecchymosis, myalgia, pruritus, vasodilation, accidental injury, back pain, dyspepsia, dyspnea, hemorrhage, injection site reaction, lung disorder, migraine, nausea, and paresthesia. Diffuse interstitial lung disease was noted on a routine chest x-ray of one subject at Week 24. Causality could not be determined.

In a retrospective analysis, during the 10-week blinded portion of the 24-week clinical study, 6 subjects (20%) of the 30 treated with Zemaira® had a total of 7 exacerbations of their chronic obstructive pulmonary disease (COPD). Nine subjects (64%) of the 14 treated with Prolastin® had a total of 11 exacerbations of their COPD. The observed difference between groups was 44% (95% confidence interval from 8% to 70%). Over the entire 24-week treatment period, of the 30 subjects in the Zemaira® treatment group, 7 subjects (23%) had a total of 11 exacerbations of their COPD.

#### HOW SUPPLIED

Zemaira® is supplied in a single use vial containing the labeled amount of functionally active A<sub>1</sub>-PI, as stated on the label. Each product package (NDC 0053-7201-02) contains one single use vial of Zemaira®, one 20 mL vial of Sterile Water for Injection, USP (diluent), and one vented transfer device.

#### STORAGE

When stored up to 25°C (77°F), Zemaira® is stable for the period indicated by the expiration date on its label. Avoid freezing which may damage container for the diluent.

Prolastin® is a registered trademark of Bayer Corporation.

Revised: January, 2007

Adapted from 19131-05

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IO#8Z008

8/2007

## Antismoking Pamphlets Available

Four new antismoking pamphlets are available at a starting price of \$18 for 50 pamphlets. The titles are "How Tobacco Hurts Our World," "A Student's Guide to Secondhand Smoke," "Your Family and Secondhand Smoke," and "Quit Smoking for You and Your Family." For more information, visit [www.journeyworks.com](http://www.journeyworks.com). ■

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For adults with  
Alpha-1 antitrypsin  
deficiency



**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,  $\geq 94\%$  purity)<sup>\*,1-3</sup>
- **Effective** — **Three times fewer** COPD exacerbations than with Prolastin<sup>®†</sup>
- **Well tolerated** — **Six times fewer** infusion-related adverse events than with Prolastin<sup>®‡</sup>
- **Fast** — **Half or less** the infusion time of other augmentation therapies<sup>§,1-3</sup>

Zemaira® is indicated for chronic augmentation and maintenance therapy for adults with alpha<sub>1</sub>-proteinase inhibitor (A<sub>1</sub>-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<sub>1</sub>-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](http://www.Zemaira.com).

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

**Zemaira®**  
alpha<sub>1</sub>-proteinase inhibitor (Human)

**Unmatched purity. Uncompromised care.**

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

\* Shelf life purity specification is  $\geq 90\%$

† 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

Prolastin is a registered trademark of Talecris Biotherapeutics, Inc.