Artificial Lung Moves Closer to Reality

**BY DOUG BRUNK**
Elsevier Global Medical News

H
ternal clinical trials of an implantable artificial lung that can serve as a bridge to lung transplantation may be just 3-4 years away.

In August, the National Institutes of Health awarded a $5 million, 5-year grant to a team of researchers, led by Dr. Robert Bartlett, to refine the device for use in patients. The device, known as the Biolung, has thus far been tested in sheep.

"We are currently developing the Biolung for the purpose of temporary support until a lung transplant becomes available to patients," said Dr. Bartlett, professor emeritus of surgery at the University of Michigan, Ann Arbor, and a pioneer in the development of artificial organs. "But clearly that won’t be practical, at least in the foreseeable future. It will be just a bridge to transplantation. It will come along in the usual fashion of artificial organs: relatively slowly."

In the 1980s, Dr. Bartlett led the researchers who developed the extracorporeal circulation membrane oxygenation (ECMO) machine, which is used worldwide to circulate and oxygenate the blood of patients with acute lung failure. ECMO can be used safely for weeks while a patient is bedridden in the intensive care unit, but the typical wait for a lung transplant is many months.

The purpose of the Biolung device is to help lung transplant patients who can live active, full lives while minimizing their risk of asthma exacerbations and other problems," explained panel chairman Dr. William W. Busse, of the department of medicine at the University of Wisconsin, Madison.

Proper asthma control depends on both current impairment and future risk, Dr. Busse said during a teleconference on the guidelines.

Incorporating the latest in asthma research findings, the panel expanded four key components of asthma care outlined in the original guidelines, which were introduced in 1991 and updated in 1997. Those components include assessment and monitoring, patient education, control of environmental factors and other conditions that can affect asthma, and medications.

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Barcelona — Cases of drug-induced lupus have been reported in patients who were treated with anti–tumor necrosis factor agents, Dr. Manuel Ramos-Casals said at the annual European Congress of Rheumatology.

“As these drugs are being used in an expanding number of diseases, there has been a corresponding increase in the number of reports of the development of autoimmune processes, including lupus, vasculitis, and interstitial lung diseases,” said Dr. Ramos-Casals of the department of autoimmune diseases, Hospital Clinic, Barcelona.

As of December 2006, Medline searches identified 92 cases of patients being treated with biologic drugs who developed a lupus-like syndrome after a mean 41 weeks of therapy, he said.

Of these patients, 77 (84%) were female and 15 (16%) were male, with a mean age of 51 years at the development of lupus features.

A total of 77 were receiving the drugs for rheumatoid arthritis, eight for Crohn’s disease, and seven for other rheumatic diseases.

The anti–tumor necrosis factor (anti–TNF) agents involved were infliximab in 40 patients (44%), etanercept in 37 (40%), and adalimumab in 15 (16%).

Lupus features included the presence of antinuclear antibodies and anti–double-stranded DNA antibodies in 86 cases (94%), cutaneous manifestations in 82 (89%), musculoskeletal features in 36 (39%), and general manifestations such as fever, malaise, and asthenia in 27 (29%).

Only 32 patients (35%) fulfilled the full criteria for systemic lupus erythematosus, however.

Cutaneous features were more common among patients who were receiving etanercept than among those receiving infliximab (44% compared with 12%), while serositis was more common among patients receiving infliximab (24% compared with 3%). “There may be differences in the expression of lupus features according to the anti–TNF drug used,” he said.

The anti–TNF drug was withdrawn in 86 (94%) of cases, and treatment of the syndrome included corticosteroids in 37 (40%) and immunosuppressive agents in 11 (12%).

All but one of the patients improved, and there were no deaths.

Dr. David A. Isenberg of the Centre for Rheumatology, University College, London, noted that it was important to consider the frequency of these events.

“The British Society for Rheumatology biologics registry now includes 11,000 patients, 4,000 each on infliximab and etanercept and 3,000 on adalimumab. In 5 years we have seen only four to six cases of drug-induced lupus, for a frequency of 0.1%-0.5%. It happens, but it’s rare,” Dr. Isenberg said.

San Francisco — Patients with HIV do just as well as patients without the virus when faced with bacterial community-acquired pneumonia, according to a poster presentation by Dr. Maricar Malinis at the International Conference of the American Thoracic Society.

Dr. Malinis, of the University of Louisville (Ky.), and colleagues concluded that “the decision to hospitalize a patient [with community-acquired pneumonia] should not be based on the HIV status, but rather on the severity of illness.”

The investigators conducted a large, retrospective study based on a database maintained by the Community-Acquired Pneumonia Organization (CAPO). A total of 2,908 patients were included in the analysis, of whom 118 (4.1%) were HIV positive.

There were no significant differences between the groups in all-cause mortality or mortality related to community-acquired pneumonia, measured at hospital discharge.

Dr. Malinis and her co-investigators wrote that the results of the study suggest that, at least in the area of hospitalization, the current national guidelines for managing patients with community-acquired pneumonia can be applied to patients who have HIV.

Robert Finn

Lupus Induced by Biologics: ‘It Happens, but It’s Rare’
Exposure to substances in the workplace causes more than 10% of all cases of adult-onset asthma, according to an international prospective population-based survey published in the July 28 issue of the Lancet.

The occurrence of occupational asthma is about 250-300 cases/million people, much higher than the 20-30 cases/million people seen in previous studies in France, the United Kingdom, and the United States, investigators said. The highest increased risk of occupational asthma was seen in printing, woodworking, and nursing, wrote the researchers, led by Dr. Manolis Kogevinas of the Center for Research in Environmental Epidemiology of the Municipal Institute of Medical Research in Barcelona.

They studied 6,837 participants, aged 20-44, who had taken part in the European Community Respiratory Health Survey from 1990 to 1995. These participants did not report respiratory symptoms or a history of asthma. They were followed for a mean of 9 years and completed a follow-up survey between 1998 and 2003 (Lancet 2007;370:336-41). The researchers obtained occupational histories from the participants, asking if they had 1 of 13 types of high-risk jobs—including baking, painting, chemical industry positions, nursing, hairdressing, and cleaning; if they had jobs with a risk of exposure to irritants linked to occupational asthma; and if they had been exposed to inhalation accidents. All measurements were adjusted for age, sex, smoking status, and research site.

Participants were at higher risk of having had an asthma attack or had used asthma drugs in the 12 months before the follow-up survey if they worked in a high-risk occupation, compared with participants who worked in professional, clerical, or administrative jobs (relative risk 1.69). Those in high-risk occupations also were at increased risk (RR = 1.58) of occupational asthma if their job involved exposure to one of several high-risk substances, including latex, flour, industrial chemicals, and bioaerosols. The risk of occupational asthma was greatest in printing (RR = 2.37), woodworking (RR = 2.22), and nursing, RR = 2.22).

—Jonathan Gardner

**Printers, Nurses at Higher Risk of Occupational Asthma**

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candidates stay alive and mobile while they wait for a donor lung. The Biolung prototype Dr. Bartlett is studying uses tiny hollow fibers and the heart's own pumping power to oxygenate blood. The device is made of plastic, weighs about 2 pounds, and is about the size of a soda pop can. It is connected to the patient's artery and is strapped in a vest outside the chest wall. The device weighs 7-8 pounds when it's full of blood.

“The device will be outside [the chest wall] because we expect to have to change it from time to time. This makes it easy to change, rather than having to do a new operation every time we change it.” Dr. Bartlett said.

The Biolung prototypes are being made by MGI Inc., a bioengineering firm in Ann Arbor that Dr. Bartlett cofounded 15 years ago with two bioengineers. Investigators at the University of Maryland, Baltimore, the University of Kentucky, Lexington, and Osaka, Japan, are working on Biolung prototypes.

Dr. Bartlett said: “The device will be outside [the chest wall] because we expect to have to change it from time to time. This makes it easy to change, rather than having to do a new operation every time we change it.”

“I feel very strongly that the [Food and Drug Administration] is going to allow us to first use [an artificial lung] device that is paracorporeal—partly to improve safety, partly to allow ready access to this developing technology, and partly to allow immediate large-animal testing to continue device improvement,” he said.

At the University of Kentucky, Dr. Joseph Zwischenberger, FCCP, and his associates are studying a version of the Biolung that is intended to tolerate right heart failure. The modification contains a pump about the size of a 35-mm film cartridge.

“Learning from that experience, I feel very strongly that the [Food and Drug Administration] is going to allow us to first use [an artificial lung] device that is paracorporeal—partly to improve safety, partly to allow

The Biolung uses tiny hollow fibers and the heart's own pumping power.
Panel Revises Asthma Guidelines

**Update** from page 1

Inhaler instructions, for example, remain the best long-term control treatment for asthma patients of all ages, the panel said. However, new information and developments were substantial enough to warrant the update, he said.

Changes to the four components of asthma care include:

- **Assessment and monitoring.** Key additions to the assessment and monitoring component of the guidelines include the use of multiple measures to assess patient impairment, such as frequency and intensity of symptoms, heart rate function, and effects on daily activities. In particular, the guidelines stress that although patients may experience few day-to-day effects of asthma, they may still be at risk for exacerbations due to seasonal effects (such as a peak in viral infections in the fall).

- **Patient education.** The updated guidelines call for greater efforts to teach patients self-monitoring skills and asthma management—including the use of a written asthma action plan that includes instructions for daily treatment and methods for handling symptoms that may arise. Other recommendations include improved communication with patients and families, as well as the expansion of educational opportunities in settings such as schools and community centers.

- **Control of environmental factors.** The panel added new evidence supporting a variety of approaches to limit exposure to allergens and other substances that can worsen asthma. The revisions call for the use of multiple approaches rather than single steps, which are rarely sufficient.

- **Medications.** The guidelines now recommend a stepwise approach, in which medication doses or types are stepped up or down as needed, based on an individual’s level of asthma control.

Another important new feature in the updated guidelines is increased stratification by age group. Previously, patients were divided into two age groups: 0-5 years and older than 5 years. The updated version divides patients into 0-4 years, 5-11 years, and older than 11 years to account for differences in developmental stages and greater understanding about how medications work in each age group. The NAEPP appointed a new panel to develop an action plan for improving implementation of guidelines. A report on implementation is expected to be released in October.

**News From the College**

Sleep Strategies
Physicians must take a proactive approach to the identification, prevention, and reporting of drowsy driving.

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**CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Elsevier Inc., 655 Madison Avenue, New York, NY 10022. Copyright 2007, by the American College of Chest Physicians. Medicare’s high-cost outlier policy CMS will continue to use the hospital’s total charges for all inpatient services provided during a patient’s stay when determining whether the case qualifies for an outlier payment.

The policy was issued as part of the Medicare acute care hospital outpatient prospective payment system final rule, which was published in the Federal Register on Aug. 22.

The move was applauded by payers and quality advocates, but hospitals and physicians raised some red flags about the change.

In a June 12 letter to CMS, the American Medical Association voiced concerns that the policy could have “unintended consequences for patients.”

“The concept of not paying for complications that are often a biological inevitability rather than preventable, regardless of whether the patient is discriminatory and could be punitive to those patients at the greatest risk,” wrote Dr. Michael D. Maves, executive vice president and CFO of the AMA. “Certain patients, including those who are older, have medical comorbidities, or have otherwise compromised immune systems, are more susceptible to infection and other complications.

Although the CMS focuses on quality and patient safety is laudable, agency officials are overseeing with their list of conditions, said Dr. Junaid Khan, a cardiothoracic surgeon in Oakland, Calif.

For example, surgical site infections are a significant problem, but it’s unlikely that they can be eliminated even with proper adherence to guidelines, he said, adding that a more global approach would be more useful at identifying systems issues and improving patient safety.

The devil is likely to be in the details, said Dr. Jeffrey Miliken, FCP, a cardiothoracic surgeon at the University of California, Irvine. The nature of the underlying disease and whether clinical guidelines were followed must be considered in order for the policy to be fair and effective.

The American Hospital Association supports the inclusion of only three of the conditions outlined by CMS (an object left in during surgery, air embolism, and blood incompatibility). However, there are concerns about whether the other conditions are always or even usually preventable, even with excellent care, said David Allen, an AHA spokesman.

But the Medicare policy shift was welcomed by health plans and some quality advocates.

The announcement by CMS is consistent with the move to pay for quality, said Susan Pisanos, a spokesperson for America’s Health Insurance Plans. The new policy provides an incentive for hospitals to develop processes to avoid these conditions, she said.

Officials at the National Committee for Quality Assurance (NCQA) also favor the policy change. “If we can’t say no to the wrong kinds of care, it going to be virtually impossible to say yes to the right kinds,” said Jeff Van Ness, a spokesperson for NCQA.

The CMS policy sends a “loud and clear signal” to hospitals that they must pay attention to these preventable events, said Rachel Wensburg, a program associate at the Leapfrog Group, a coalition of employers focused on health care quality and transparency.

In fact, officials at the Leapfrog Group would like to see CMS expand the list of hospital-acquired conditions to include the 28 serious reportable events—rare medical errors that should never happen to a patient—that have been compiled by the National Quality Forum.

The Leapfrog Group launched a project last year to encourage hospitals to develop plans to avoid these serious reportable events.
Gene Mutations Predicted Response to Erlotinib, Gefitinib

Screening tests can help select NSCLC patients who are likely to benefit from tyrosine kinase inhibitors.

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

CHICAGO — Two prospective studies suggest that clinicians will be able to improve survival in non–small cell lung cancer by selecting patients with specific mutations that respond to erlotinib and gefitinib for treatment with those agents.

The approach is feasible, according to results of the first prospective, multicenter, phase II trial to attempt it in the United States. Based on the presence of epidermal growth factor receptor (EGF-R) mutations in tumor samples, Dr. Leica V. Sequist and her colleagues gave gefitinib (Iressa) to 31 patients as a first-line treatment for advanced non–small cell lung cancer (NSCLC). She reported overall survival as 73% at 1 year.

A second prospective study, conducted by the Spanish Lung Cancer Group, reported that the presence of EGF-R mutations on exons 19 or 21 in serum samples was associated with poorer performance status in advanced NSCLC patients and with variations in responses to erlotinib. Dr. Teresa Morán reported finding mutations in nearly 100% of performance status 2 patients with clinical characteristics suggestive of EGF-R mutations.

Dr. Sequist of Massachusetts General Hospital, Boston, and Dr. Morán of the Institute Catalá d’Oncologia, Hospital Ger- mans Trias i Pujol, Barcelona, presented the studies at the annual meeting of the American Society of Clinical Oncology.

The U.S. study received support from AstraZeneca Pharmaceuticals L.P., maker of gefitinib, which is indicated for advanced or metastatic NSCLC only in patients who respond to it. Gefitinib and erlotinib are tyrosine kinase inhibitors that target EGF-R. Since somatic EGF-R mutations were discovered in 2004, retrospective studies cited by the two investigators have found that most lung cancer patients with these mutations respond to the two therapies.

The mutations are more common, Dr. Sequist noted, in women and in people with East Asian genetic heritage, with little or no history of smoking, and with adenocarcinoma histology (possibly with features of bronchioloalveolar carcinoma). About 10% of lung cancer patients in North America and Western Europe harbor the mutations; they are 2.3 times more prevalent in Asia.

Dr. Sequist and her colleagues screened tumor samples from 98 advanced NSCLC patients over 23 months. They found 34 patients with mutations; the most common of which were an exon 19 deletion and a change on exon 21 known as L858R. Three patients declined gefitinib therapy, leaving 31 who were treated.

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Radio Surgery Shows Promise For Inoperable Stage I NSCLC

BY MITCHEL L. ZOLER
Elsevier Global Medical News

WASHINGTON — Stereotactic radio surgery was a safe and reasonably effective alternative treatment for inoperable, stage I non–small cell lung cancer in a series of 21 patients at one center.

Based on these results and reports on the same treatment for inoperable patients with stage I NSCLC, Dr. Arjun Pennathur said at the annual meeting of the American Association for Thoracic Surgery.

Dr. Pennathur, a thoracic surgeon at the University of Pittsburgh, and his associates use a CyberKnife system, and they usually treat a patient with more than 100 individually delivered radiation beams; treatment takes 60-90 minutes. A dynamic tracking system monitors breathing motion and synchronizes the beam’s location to the breathing. Treatment is guided by fiducial markers placed in and around the tumor with CT guidance.

The median dose was 20 Gy, which corresponds to an effective biologic dose of more than 70 Gy. The series included 14 patients with stage IA disease and 7 with stage IB disease. The average tumor size was 2.2 cm, and the patients were about 70 years old.

The most common treatment complication was pneumothorax (10 patients). No treatment-related deaths occurred. Initial responses included complete response (seven cases), partial response (five), stable disease (five), and disease progression (three); one patient could not be evaluated. Local progression recurred in nine patients (43%) at a median of 12 months after treatment. Eleven patients were alive after a median follow-up of 21 months. The 1-year survival rate was 81%, and the 2-year rate was about 60%.

Although stereotactic radio surgery is still being refined, these results suggest it is superior to no treatment of stage I inoperable NSCLC, which has been documented to have a median survival of 14 months.

Dr. Robert Cerfolio, FCCP, comments: Dr. Pennathur and associates have provided some early but important data from the United States that is similar to previous data reported recently from Japan. The authors’ study suggests that stereotactic radio surgery, or what is most commonly delivered by the Cyberknife system in the United States, may provide improved results over external beam radiation for patients with stage I NSCLC who are not surgical candidates. The key is to ensure that patients are “really not surgical candidates,” which means they have been denied surgery by at least two general thoracic surgeons who perform a large volume of lung surgery and that the patient’s lymph nodes are pathologically negative. The issue of pneumothorax from fiducials may be resolved in the near future.

Families Overriding Organ Donation Plans

ORLANDO — Patient wishes for organ donation were overridden by their families in about 20% of cases, according to research conducted at a level I trauma center in Charlotte, N.C.

Dr. A. Britton Christmas and colleagues at the F.H. Sammy Ross Jr. Center at the Carolinas Medical Center reviewed 3 months of organ donation referrals at their center. About 17 potential transplant recipients did not receive organs because a patient’s previous donation intentions were overridden by family members, they wrote in a poster at the annual congress of the Society of Critical Care Medicine.

The researchers compared information from medical charts with data from the state department of motor vehicles (DMV) related to organ donation designations.

They analyzed information on 84 individuals who had DMV information on file and whose families had been approached by hospital staff for organ donation over the 3-month period. In the DMV records, 25 individuals were listed as organ donors, and 39 had not designated organ donation. For the 25 individuals designated as organ donors, 20 consents for donation were obtained from family members. Of the other 59 individuals, 22 consents were obtained.

The researchers estimated that the five individuals whose consent was withdrawn by the families resulted in 17 potential organ recipients who would not receive organs.

—Mary Ellen Schneider
New IDSA/ATS Guidelines for Community-Acquired Pneumonia

Clinical Indications for Extensive Diagnostic Testing

1. Severe CAP (BC, ETA, Sp, PUA, LUA, possibly BAL)
2. Failure of outpatient therapy (Sp, LUA, PUA)
3. Cavitary infiltrates (BC, Sp, fungal and tuberculosis cultures)
4. Leukopenia (BC, PUA)
5. Active alcohol abuse (BC, Sp, LUA, PUA)
6. Chronic liver disease (BC, PUA)
7. Severe COPD/structural lung disease (Sp)
8. Aplasia (BC, PUA)
9. Recent (within 2 weeks) travel (LUA)
10. Pleural effusion (BC, Sp, LUA, PUA, pleural fluid culture (PUA and LUA can be done on pleural fluid))
11. Positive Legionella urinary antigen (Sp)
12. Positive Pneumococcal urinary antigen (BC, Sp)

BAL = bronchoalveolar lavage, either bronchoscopic or nonbronchoscopic; BC = blood culture; ETA = endotracheal aspirate culture; LUA = bronchoalveolar lavage, either bronchoscopic or nonbronchoscopic; PUA = pleural fluid culture

Minor Criteria for Severe CAP

ICU admission should be considered if patients with CAP have three or more of these criteria:

- Respiratory rate ≥ 30 breaths/min
- Fever (core temperature > 38°C)
- Hypotension requiring aggressive fluid resuscitation
- Confusion or disorientation
- Multilobar infiltrates
- Pao2/Fio2 < 250
- Uremia (BUN > 20 mg/dL)
- Leukopenia (WBC count < 4,000 cells/µL)
- Thrombocytopenia (platelet count < 100,000 cells/mm³)

The recommended antibiotic regimens have not changed significantly. One of the controversies areas is the need for cephalosporin-based combination therapy for patients with severe CAP. To my knowledge, only one study has addressed this issue. The study excluded patients with shock but did include patients with respiratory failure. There was a trend toward worse outcomes when fluoroquinolone monotherapy was used for patients with respiratory failure. This suggested that previous recommendations by both societies, that combination therapy should be given to all patients with severe CAP be maintained. Initial combination therapy was recommended for patients with severe CAP, based on several prospective observational studies and retrospective analyses. Several options for treatment are offered within each group of patients with CAP because one of the guidelines’ main emphasis is to avoid the use of an antibiotic that was previously prescribed for the patient.

An earlier decision to group health-care-associated pneumonia (HCAP) was developed (see list of criteria). If a patient is not intubated or receiving vasopressors in the ED. However, both PSI and CURB-65 must be supplemented with additional clinical information, including oral intake ability, reliability of taking medications, return for care if a condition worsens, and comorbid medical conditions.

There is a major change in the guidelines for the criteria for severe CAP, which requires initial admission to the ICU. The guidelines committee felt that none of the previously available criteria for ICU admission was helpful in making decisions, especially if the patient was not intubated or receiving vasopressors in the ED. Therefore, a new set of minor criteria was developed (see list of criteria). If a patient has three or more of the minor criteria, ICU admission should be considered, even if the patient is not intubated or receiving vasopressors—major criteria that would automatically deserve ICU admission. This new set of minor criteria needs prospective validation. The goal of the new criteria is to attempt to identify patients who are initially admitted to a general medical floor, but then require transfer to the ICU within 24 h of admission for hypotension or respiratory failure. Recommendations for the extent of diagnostic testing to define the microbiologic etiology were determined predominantly by the site-of-care decision. Outpatients should be treated empirically in the majority of circumstances. In contrast, patients with severe CAP who require ICU admission should have an extensive diagnostic workup. Not only are diagnostic test results more likely to be positive in patients with severe CAP, there is an increased likelihood that the cause of CAP is a microorganism not covered by the usual empiric therapy. For patients admitted to non-ICU settings, diagnostic testing was not routinely recommended but should be done selectively for a variety of predisposing conditions (see list of indications). One example is the attempt to obtain a sputum specimen in a patient with severe COPD and a productive cough, because of the increased risk of infection with Pseudomonas aeruginosa as the etiology of CAP. The guidelines also encourage the use of rapid urinary antigen tests for Legionella pneumophila and Strep-tococcus pneumoniae in patients with severe CAP. Also recommended for the urinary antigen-positive cases because of the epidemiologic implications for infection with Legionella (to establish whether part of cluster requires positive cultures) and the antibiotic resistance pattern for pneumococci.
O n June 1, 2007, Stephen S. Lefrak, MD, FCCP, Professor of Medi-
cine, Associate Dean, and Director of the Humanities Program in Medicine at Washington University School of Medicine, wrote to Richard S. Irwin, MD, FCCP, CHEST Editor in Chief, about setting the record straight on the American College of Chest Physicians having given a “Master Clinician Award” to Friedrich Wegener, MD, at the ACCP Convocation in 1989.

Dr. Wegener is renowned for his description and investigations of the necrotizing granulomatous vasculitides that we know as “Wegener’s granulomatosis.” What we did not know is that Wegener had ties with the Nazi party at its inception, and that he was an official in the army and a pathologist in Lodz, the site of a notorious Jewish ghetto from the time of the German invasion of Poland in 1939 until he fled with thousands of other Germans in 1945.

Dr. Lefrak asked that we set the record straight “for the historical record as well as the College’s integrity.” I will record straight “for the historical record of the time of the German invasion of Poland and the Nazis consolidated their power, starting a “Transition From Intravenous Epoprostenol to Subcutaneous Treprostinil in Pulmonary Arterial Hypertension: A Controlled Trial.”

BY DR. RICHARD S. IRWIN, FCCP

Editor in Chief, CHEST

This Month in CHEST: Editor’s Picks

Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines (2nd edition) – CHEST Supplement

• Venous Thromboembolism Prophylaxis in Acutely Ill Hospitalized Medical Patients: Findings From the International Medical Prevention Registry on Venous Thromboembolism. By Dr. V. F. Tapson, FCCP, et al

• Point/Counterpoint: The Ethics of Unilateral DNR Orders: The Role of “Informed Assent.” By Dr. J. R. Curtis, FCCP, and R. A. Burt, JD

• COUNTERPOINT: Is It Ethical To Order “DNR” Without Patient’s Consent? By Dr. C. A. Manthous, FCCP

• REBUTTALS: By Dr. J. R. Curtis, FCCP, and R. A. Burt, JD; and Dr. C. A. Manthous, FCCP

www.chestjournal.org

Continued on following page
There were passionate and persuasive arguments that Wegener should have not taken a commission in the army, and should have declined or resigned from his appointment in Lodz.

Others reflected the Committee’s consensus that revoking an award that reflects Wegener’s indisputable scientific achievements absent evidence of direct involvement in war crimes would not be appropriate.

The young and no doubt ambitious Wegener made very poor choices in embracing a monstrous movement and serving the German war effort for which his mentor and chairman was an enthusiastic participant. On the other hand, half of German doctors were members of the Nazi party during the war.

By analogy, George Washington and Thomas Jefferson were slave owners, but their images are still on Mount Rushmore and our currency.

In the end, the Executive Committee elected to inform the membership about the facts of Wegener’s past, about the facts of the award the College gave him, and about what we will do to prevent a similar episode.

My opinion. Speaking for myself, I can only conclude that Wegener was, at best, deeply flawed and collaborated with very bad people in a bad cause to maintain and advance his career.

How can any of us be sure we would not have done the same thing in that situation? I hope I would have had the courage and conscience to resign and end such a career, but how could I know?

That Wegener did autopsies and saw the consequences of Nazi philosophy makes him especially culpable.

Judging with 21st century sensibilities and perfect hindsight, I am reconciled to the decision that withdrawing an improvised award 17 years after the fact for a person’s actions 45 or 50 years before dignifies the award more than it deserves. It accomplishes little other than to affirm that the ACCP condemns the actions of Nazis and those who supported them, and that should be obvious enough and not need a symbolic action.

I personally regret deeply that the College unknowingly bestowed an award to a former Nazi who surely took part in support of the Holocaust and apologize to the families and memories of its victims.

How would current ACCP policies prevent another situation like this? First, I am certain that no ACCP awards committee would ever consider a candidate with ties to the Nazi party or any other hate group. The College also precludes granting awards to scientists who serve the tobacco industry and to any other enterprises that conflict with the College’s core values.

In addition, I believe we have learned not to devalue formal ACCP recognition by inventing an award for single use, especially when it is a “gold watch” in anticipation of a colleague’s retirement or imminent death.

These have been difficult issues for us to consider. They will probably provoke considerable controversy, and they should.

As this will be discussed by the ACCP Board of Regents in October, I invite you to submit comments to me directly at mrosen@chestnet.org.

Continued from previous page

2. Woywodt A, Matteson EL. Wegener’s granulomatosis: probing the untold past of the man behind the eponym. Rheumatology 2006; 45: 1303-1306
It was recently brought to the attention of the ACCP Industry Advisory Council that not all convention attendees understand the purpose of the medical information section of a promotional exhibit. In their commitment to the free exchange of scientific information between health-care professionals, pharmaceutical companies deploy medical information teams to leading medical conferences in order to respond to unsolicited inquiries from health-care professionals. The medical information staff consists of trained health-care professionals who uphold the highest professional standards of rigor and integrity in addressing the health-care community and in disseminating nonpromotional medical information upon request.

Through the medical information booths at conferences, the pharmaceutical companies invite, encourage, and sustain the free exchange of scientific information between health-care professionals—a cornerstone of medical research, innovation, and progress.
The Ambassadors Group—CHEST 2007 Events

Sunday, October 21—“Train the Trainer” Session, 2:30 PM – 4:00 PM
The CHEST Foundation provides tobacco prevention health education and encourages lung health among youth. In this interactive session, Susan Koale, with the help of Monir Almassi and Kathy Wilder, will demonstrate antismoking teaching methods for children in fifth grade, as part of the Lung Lessons® curriculum. Monir also will distribute a flyer to attendees about how to organize a 5K run for teenagers.

Monday, October 22—Global Outreach Tea, 3:30 PM – 5:00 PM
The Ambassadors Group's fourth annual Global Outreach Tea is a great opportunity to socialize and learn more about the Ambassadors Group.

Tuesday, October 23—Annual Open Meeting, 9:30 AM – 11:30 AM
Everyone is invited to the Ambassadors Group Annual Open Meeting to learn more about our programs and brainstorm plans for future activities. Come, and bring a friend! Meet the 2007 Ambassadors Group Humanitarian Recognition Award recipient, Mr. Al Keith, CEO and Founder of CTK Clinical Consultants, L.L.C.

Tuesday, October 23—Designology (Hospitality and Information Room), 4:00 PM – 5:00 PM
Meet the designers from Susan Fredman & Associates, one of Chicago's leading interior design firms, and discover how the experts reveal your design aesthetic. Learn how to make the best choices for your home and lifestyle by understanding how you live, more than knowing simply what you like.

Wednesday, October 24—Resculpt Your Lifestyle (Hospitality and Information Room), 2:30 PM – 4:00 PM
Perhaps, it is time to resculpt your lifestyle before your health and body take on the shape of that comfy old couch! Discover the secrets to staying in shape at any age at this exciting, innovative, and interactive program by Marla Richmond, MS, exercise physiologist and author.

Membership: Join the Ambassadors Group or renew your membership now, and you'll be a member through CHEST 2008. Sign up and pay online at www.chestfoundation.org.

Ambassadors Group Membership Directory: A membership directory will be distributed to Ambassadors Group members by mid-November, as an email attachment. You are encouraged to respond with your edited contact information to Kathy Wilder at wilderkw@ak.net, even if all information is correct. If you are a new or current member, and have not received your directory from Kathy through email, contact her directly.
WHAT’S HAPPENING AT CHEST 2007

BY ED DELLERT, RN, MBA
Vice President, Educational Resources
JENNIFER STAWARZ
Manager, Public Relations

If you have attended CHEST annual meetings in the past and have CHEST 2007 on your fall schedule this year (and we hope you do), you are likely to notice some changes.

The majority of these changes are related to the education curriculum, but more specifically, how we deliver and track continuing medical education (CME).

**Learning Categories**

We are introducing the new ACCP Learning Categories, labels that will help you identify the types of educational opportunities being offered at CHEST 2007.

These new Learning Categories clearly specify the type of instruction and methodology used for each session, which will allow you to choose sessions related to your clinical interests, educational goals, and learning style.

There are many theories and evidence in general higher educational literature that has led to the development of this ACCP learning taxonomy. The key to the ACCP Learning Categories is to provide a variety of educational opportunities.

The six learning categories are as follows:

- **Learning Category I: Lecture-Based**
- **Learning Category II: Self-Directed**
- **Learning Category III: Evidence-Based**
- **Learning Category IV: Case- and Problem-Based**
- **Learning Category V: Simulation**
- **Learning Category VI: Quality Improvement**

You will see these learning labels on the sessions you are attending at CHEST, and you will find them being identified in the Final Program (see the illustration above for an example).

The ACCP Learning Categories are being formally introduced at CHEST 2007, and they will be used to categorize all subsequent educational activities that the ACCP offers.

**Maintenance of Licensure**

You will also find that sessions have another category label, Maintenance of Licensure (MOL), identified by each session with areas related to state medical licensure, specifically relevant to the chest physician (see sample above).

Depending upon the state in which you practice, your requirements could include a set number of CME hours in general scopes of practice, but there is a growing trend to denote those CME hours into specific areas, such as ethics, end-of-life care, geriatrics, patient safety, and others.

When you obtain your CME certificate at CHEST 2007, you will notice that your total for CME hours is still listed, but the credit hours will be divided into the ACCP Learning Categories and the MOL hours from the sessions you attended.

Our hope is that this CME certificate will provide education documentation for your records or assist you in meeting institution requirements where you have privileges, state licensing documentation, certification requirements, or a combination of all of these areas.

Your CME certificate will resemble the sample to the right.

**CME Evaluation and Certification—No More Paper**

Another noticeable change at CHEST 2007 will be the process of how to evaluate sessions and, ultimately, obtain your CME certificate.

There will be no paper version of the evaluation form in your registration packets. There will be no paper form of a CME certificate to exchange at the registration desk.

What you will find, however, is that the evaluations document and the subsequent CME certificate will be available online through the ACCP Web site. Letters of attendance for our international attendees will also be available only on the Web site.

You can complete the online evaluation in several ways: special computers will be set up in the convention center for this use; you can use your own computer in any location you wish; or complete the task when you arrive home, at your convenience (just note that you will only have about 1.5 months following CHEST to complete this).

As you complete the form online, your CME certificate will be generated automatically. Just evaluate the sessions you attended, and we will automatically take care of the rest.

Once completed, the CME certificate is available for you to save electronically or print for your records. (Printers will not be available at CHEST.)

Log back into our system anytime, and all of your CME activities and certificates will be archived for you to print off again.

There will be other noticeable changes at CHEST 2007, but we don’t want to spoil the whole surprise for you. As the learning categories and MOL, evaluation, and CME certificate are different than the learning categories and MOL, evaluation, and CME certificate are different than what you might expect in other educational venues outside of ACCP, we wanted you to have a chance to understand these new additions.

So when you leave CHEST 2007, you will have hopefully acquired new skills, knowledge, and/or attitudes that affect your clinical practice and help you meet your goals of lifelong learning. I look forward to hearing from you. Let us know what you think. See you Chicago!

For more information, contact Ed Dellert at edellert@chestnet.org.

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November 18-21, 2007 200
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A cute kidney injury (AKI) is a common clinical problem defined as an injury or insult that causes an abrupt functional or structural change in the kidney. Recent studies have shown increased hospital mortality following AKI, and even minor short-term changes in serum creatinine (sCreat) are associated with increased mortality and/or accelerated progression of preexisting chronic kidney disease.

In order to foster the development of clinical practice recommendations, and to facilitate clinical and translational research in AKI, a group representing members from the Acute Dialysis Quality Initiative (ADQI), critical care, and nephrology societies recently established the Acute Kidney Injury Network (AKIN). The fundamental goal of this group is to ensure the best outcomes for patients with, or at risk for, AKI.

The first AKIN conference, held in Amsterdam in September 2005, focused on the development of uniform standards for definition and classification of AKI. Wide variation in definitions of acute renal failure has made it difficult to compare information across studies and populations. ADQI proposed the RIFLE criteria (risk [R], with injury [I], with failure [F], with sustained loss [L] and with end-stage [E] status) for classification of AKI, and these criteria have been validated in several studies.

However, recent evidence suggests that even small changes in sCreat values are associated with adverse outcomes in a variety of settings. The proposed new criteria and staging are shown in the accompanying table and callout. The proposed staging system retains the emphasis on changes in sCreat values and urine output and corresponds to the risk, injury, and failure categories of the RIFLE classification, with the stage 1 criteria representing the new diagnostic criteria for AKI. These proposed standards will need to be validated in future studies.

AKIN described the five key elements that should be addressed by the professional communities involved in the care of patients with AKI: evaluation of the global epidemiology of AKI, delineation of clinically meaningful outcomes, development and implementation of strategies to improve outcomes, promotion of research studies, and assessment of the effectiveness of these collaborative approaches. Watch for future updates on AKIN. A list of AKIN members can be found in Crit Care 2007;11:R31.
According to the National Highway Traffic Safety Administration, at least 100,000 police-reported motor vehicle accidents annually are the direct result of driver fatigue, resulting in more than 1,530 deaths, 71,000 injuries, and $12.5 billion in diminished productivity and property loss.

Many crashes resulting from drowsy driving are underreported due to limited police training in detecting sleep-related incidents and the absence of mechanisms to report drowsiness on accident report forms.

According to the National Sleep Foundation’s (NSF) 2005 “Sleep in America” survey, 60% of adult drivers reported driving while feeling sleepy within the past 12 months.

In the 2007 NSF survey, which focused on women and sleep, 37% of women between the ages of 18 and 24 reported driving drowsy at least once a month, while 31% reported driving drowsy during pregnancy. Thirty-eight percent of new mothers reported being fatigued, while behind the wheel, on a monthly basis.

In 2004, the AAA Foundation for Traffic Safety Internet survey reported that 90% of police officers in the United States and Canada pulled over drivers they suspected were drunk, but were, in fact, drowsy.

Sleep disorders that lead to driver fatigue include primary and comorbid insomnia, obstructive sleep apnea, and restless legs syndrome. Those at a particularly high risk include men aged 16 to 29, people who drive at night or alone; people with poor sleep hygiene; frequent travelers; shift workers; people who drive long, rural, dark, or “boring” roads; and individuals taking sedative medications.

The effects of driver fatigue include impaired vigilance, attention, and reaction time. Fatigued drivers are more likely to succumb to “road rage.” Fatalities to the driver, passengers, and people in other vehicles may occur when sleep onset results in a complete loss of control of the motor vehicle.

Unlike the driver who is pulled over for driving while intoxicated, there is no “breathalyzer,” blood test, or any other easy way to identify a person who is drowsy driving. Physicians must depend upon patient reports of drowsiness by obtaining a history or by using diagnostic surveys, such as the Ewspworth Sleepiness Scale. Patients at high risk for drowsy driving should be questioned, and physicians should also determine if they have any recent history of motor vehicle accidents. Unfortunately, because the problem of drowsy driving is widespread and so many people “get away with it,” as well as because many physicians also have poor sleep hygiene, there is an unfortunate tendency to minimize the problem.

Prevention and Reporting
Regrettably, a patient’s problem of drowsy driving may not come to a physician’s attention until after a serious accident has occurred. Therefore, a proactive approach is required. Some of the best approaches include the identification of people at risk, followed by careful questioning and patient education. Public awareness campaigns, such as those sponsored by the NSF and the National Highway Safety Traffic Administration, have also been effective. The NSF is declaring November 5-11, 2007 Drowsy Driving Prevention Week™, a national public awareness campaign about the tragic consequences of driving while drowsy.

A number of state and federal legislative initiatives have focused on the physician’s role in reporting impaired drivers. In 1999, the challenges of such reporting were noted by the American Medical Association’s Council on Ethical and Judicial Affairs:

Physicians are in a unique position to anticipate the impact of physical and mental conditions on driving impairment...Motivated by a respect for the individual and a desire to promote patient autonomy, physicians traditionally have not been allowed the patient to make the ultimate decision whether to continue driving. The decision not to interfere with the patient’s decision to drive also may derive from a physician’s commitment to a patient’s well-being. The privilege of driving is a source of freedom.

NSF has declared November 5-11, 2007, Drowsy Driving Prevention Week™. The campaign was launched to help save the lives of young drivers by raising awareness of the dangers of drowsy driving. In addition to teens, it will target other groups at high risk of drowsy driving, including commercial drivers, shift workers, and people with untreated sleep disorders. The campaign also aims to build a national grassroots network of advocates. According to NSF’s 2006 Sleep in America poll, only one in five adolescents (20%) gets an optimal amount of sleep during the week, and more than half (51%) report having driven drowsy in the past year.

Drowsy Driving Prevention Week

Where To Report Drowsy Drivers

Each state has its own regulations, laws, and mechanisms, whereby a physician may report an impaired driver, including drowsy drivers. States vary widely regarding (1) the duty of the physician to report impaired drivers, (2) the anonymity of the physician, (3) immunity, (4) legal protection, and (5) reporting procedures.

A very comprehensive guide was published by the American Medical Association with data as recent as May 2003. This 79-page document can be accessed at www.ama-assn.org/ama1/pub/upload/mm/483/chapter8.pdf. The Web site also contains contact information for obtaining updated local regulations.

Identifying, Preventing, and Reporting Drowsy Driving

Maggie’s Law and Oregon Law

In 1997, Maggie McDonnell, a 28-year-old college student, was killed by a driver who crossed three lanes of traffic and crashed into her car directly from the front. The driver had not slept in 30 hours and had been using drugs. In the absence of any laws pertaining to drowsy driving, the driver received a suspended jail sentence and a $200 fine. Maggie’s mother, Carole McDonnell, lobbied vigorously to make drowsy driving a criminal offense. In August 2003, New Jersey became the first state to consider a fatal accident by a drowsy driver as vehicular homicide: “For the purposes of this section, driving a vehicle or vessel while knowingly fatigued shall constitute recklessness. Fatigued, as used in this section, means having been without sleep for a period in excess of 24 consecutive hours” (excerpt from 210th Legislature, State of New Jersey).

Current Oregon regulations make it mandatory for physicians to report impaired driving to the Oregon Department of Motor Vehicles (Oregon Administrative Rules, Division 74). Types of impairments that require physician reporting and may be experienced by drowsy drivers, include the following: decreased awareness, reduction in the ability to efficiently switch attention between multiple objects, reduced processing speed, a deficit in decision making ability, delayed reaction time, a deficit in the ability to anticipate or react to changes in the environment, lack of emotion control, and loss of consciousness or control.

Pending Legislation

There are more than a dozen bills pending in various state legislatures that may affect the way physicians address drowsy driving. These bills can be reviewed by clicking on the “public policy link” at www.drowsydriving.org.
Transplant, Members in Industry, Respiratory Care

Transplant

For the potential lung transplant candidate, there is a bewildering amount of information to process in order to make an informed decision about whether to proceed with this emotionally and physically demanding procedure. Physicians caring for a transplant candidate must be equally familiar with the risks and benefits of the procedure in order to effectively counsel patients. Physicians must also be familiar with the seemingly vast array of potential complications and complexities of the immunosuppressive medications.

Members of the Transplant NetWork have been engaged in two important education projects to assist patients and caregivers with navigating the complex issues related to lung transplantation. The patient education guide, A Guide to Lung Transplantation, has been updated and posted on the Transplant NetWork webpage at www.chestnet.org/networks/transplant/index.php. This document provides a comprehensive description of the transplant process.

Another recently completed project is the ACCP NetWork Transplant Considerations for the Community Pulmonologist, which is also available online.

This guide provides community pulmonologists with recommendations on routine and preventive care for patients who receive transplants, as well as specific discussions of the clinical manifestations, diagnosis, and management of the potential complications that commonly arise.

Members in Industry

Physicians working in the pharmaceutical industry face increased scrutiny of their interactions with internal colleagues, industry face increased scrutiny of their interactions with other external colleagues, regulatory environment, and knowledge. In addition, members of the Committee on Accreditation for Respiratory Care will attend to help answer questions and provide suggestions regarding the credentialing process and the role of the medical director.

Respiratory Care

The NetWork invites all medical directors of respiratory care training programs to attend a special meeting at CHEST 2007. The meeting, scheduled for Monday, October 22, from 11:00 AM to 12:00 PM, will provide an opportunity to share concerns, problems, and knowledge. In addition, members of the Committee on Accreditation for Respiratory Care will attend to help answer questions and provide suggestions regarding the credentialing process and the role of the medical director.

Networks

Transplant, Members in Industry, Respiratory Care

This year’s NetWork open meeting presenter is Dr. David Landsberg, FCCP. He will present “Utilizing Levalbuterol and Breath-Actuated Nebulizers to Optimize Respiratory Therapy Department Performance” on Wednesday, October 24, at 8:30 AM. Recent Respiratory Care NetWork projects include:

- Supporting the development of a Spanish version and a large print English version of the ACCP Inhaled Aerosol Device Patient Handouts.
- Advocating policies to government officials to ensure that civilian and military respiratory therapists undergo equivalent accredited education and credentialing.
- Reviewing existing ACCP position statements, including: Medical Director of Respiratory Care Department and Pulmonary Function Laboratory and Role of Respiratory Care Practitioners in the Delivery of Respiratory Care Services.
- Reviewing the utilization of respiratory therapists on medical emergency teams.
- For more information about this NetWork, go to www.chestnet.org/networks/accp_industry or e-mail networks@chestnet.org.
Deep Sedation in Intensive Care Worsened Risk of PTSD

SAN FRANCISCO — A substantial proportion of patients experience posttraumatic stress disorder after their stay in an intensive care unit, and a new study has isolated three factors associated with an increased risk of developing the disorder: Christina Jones, Ph.D., reported at the International Conference of the American Thoracic Society.

In a prospective, observational study involving 238 patients from five ICUs in the United Kingdom, Sweden, Italy, and Norway, Dr. Jones of the University of Liverpool, England, and her colleagues found that 9.2% of the patients showed evidence of posttraumatic stress disorder (PTSD) 2 months following their discharge.

Among the factors independently associated with an increased risk of PTSD were deep sedation with physical restraint without sedation, and recall of delusional memories (Intensive Care Med. 2007;33:978-85).

In addition, a history of psychological problems indirectly predisposed patients to PTSD. Structural equation modeling showed patients with such a history were more likely to have delusional memories and to be sedated, and those two factors were in turn directly associated with PTSD.

The five ICUs were mixed, general, adult units. They were selected specifically because they had differing case mixes and different protocols reflecting the diversity of adult ICU practice across Europe. For example, different ICU units used different mixtures of sedative and opioid drugs at varying doses. And some ICU units used padded straps to restrain patients as an alternative to sedation.

Dr. Jones found it especially noteworthy that patients’ delusional memories—not factual traumatic memories—were related to PTSD. Many delusional memories are based on actual events that the patients misinterpret. For example, a patient may interpret a simple injection as an attempted homicide. Such perceived losses of safety in the ICU make these memories particularly traumatic.

During the study, the investigators prospectively recorded each patient’s sedative and opioid drug type, duration, and dosage; the patient’s level of sedation using the Motor Activity Assessment Scale; the presence and duration of delirium following sedation using the Confusion Assessment Method; the use and duration of physical restraint; and several other clinical and demographic parameters. All opioid and benzodiazepine doses were converted to morphine or lorazepam equivalents based on tables of relative potency.

Between 1 and 2 weeks after discharge from the ICU, investigators assessed the patients’ recall using the ICU Memory Tool. Patients were asked about previous psychological problems, including anxiety and depression. Investigators excluded from the study all patients with preexisting or comorbid psychotic illness or those who had attempted suicide.

At 2 months following discharge, investigators administered the Posttraumatic Stress Syndrome-14 Questionnaire Inventory (PTSS-14). One month later investigators repeated the PTSS-14 and added the Posttraumatic Diagnostic Scale.

Dr. Jones said that further research is needed to understand whether the risk of PTSD can be reduced through changes within the ICU or whether it would be better to emphasize helping patients after ICU discharge.
MINNEAPOLIS — Sleep apnea, stroke, and sleep disorders are interrelated, Dr. Claudio Bassetti said at the annual meeting of the Associated Professional Sleep Societies.

Dr. Bassetti reviewed three areas in which studies support an association between sleep and stroke. Data suggest that sleep apnea is an independent risk factor for stroke, that sleep apnea and stroke are interrelated in cases of acute stroke, and that stroke-induced focal brain damage can promote hypersomnia and other sleep disorders.

Recognizing the relationship between sleep and stroke can help clinicians manage patients with sleep complaints who have other risk factors for stroke, and perhaps reduce the risk of stroke by treating sleep problems, said Dr. Bassetti, a neurologist at the University Hospital Zurich who specializes in sleep medicine.

Sleep Apnea and Stroke Risk
Studies of stroke and sleep-disordered breathing (SDB) done in the 1990s revealed that SDB was prevalent in patients who had suffered strokes. Recent studies that controlled for multiple risk factors support a possible link between SDB and stroke. Dr. Bassetti cited an observational study of 1,022 adults, 698 of whom met the criteria for obstructive sleep apnea. In 6 years of follow-up, the individuals with obstructive sleep apnea were almost twice as likely to suffer strokes as were those who didn’t have sleep apnea, even after controlling for age, gender, race, body mass index, alcohol and tobacco use, diabetes, hypertension, hyperlipidemia, and atrial fibrillation (N. Engl. J. Med. 2005;353:2034-41).

A clinical implication of these findings is that using continuous positive airway pressure (CPAP) devices might reduce stroke risk in patients with obstructive sleep apnea. A 10-year follow-up study of more than 1,600 adult men showed that patients with untreated severe obstructive sleep apnea/hypopnea were significantly more likely to have a fatal or nonfatal cardiovascular event than the following groups of men: patients treated with CPAP, untreated severe obstructive sleep apnea/hypopnea who were significantly more likely to have a fatal or nonfatal cardiovascular event than the following groups of men: patients treated with CPAP, untreated severe obstructive sleep apnea/hypopnea, and healthy controls (Lancet 2005;365:1046-53).

Sleep Apnea’s Role in Acute Stroke
About 50% of acute stroke patients will have obstructive sleep apnea, Dr. Bassetti said. His prospective study of 152 patients with acute ischemic stroke showed that SDB improved after the acute phase of stroke (Stroke 2006;37:967-72). But the presence of SDB predicted a greater risk of long-term mortality following a stroke. Clinicians can treat stroke patients with CPAP to reduce this risk, but compliance is a problem in patients with acute stroke, Dr. Bassetti explained.

Unfortunately, there are no data suggesting which patients will tolerate CPAP, he said. But patients who can tolerate CPAP may reduce their risk of cardiovascular events following a stroke, he said.

Central sleep apnea, the rarer form of SDB in which the brain fails to signal the respiratory muscles to breathe during sleep, also may be associated with acute stroke. Studies of stroke patients with central sleep apnea are rare, but central sleep apnea was recorded during 18%-24% of sleep in three patients who underwent polysomnographies after having first-time ischemic strokes. Breathing improved in all patients as they recovered from the strokes (Stroke 2007;38:1082-4).

Stroke as a Cause of Sleep Disorders
Hypersomnia is very frequent in cases of stroke, Dr. Bassetti said. Hypersomnia can lead to attention and memory deficits in stroke patients. Be sure to ask about presleep behavior to help identify external causes of poststroke sleep problems, he said. Some patients recover or at least improve their symptoms with time, in part because hypersomnia is often caused by dysfunction of the arousal systems rather than by the stroke itself.

Insomnia rarely arises directly from a stroke, but focal brain damage has been associated with some cases of parasomnias, such as sleepwalking or night terrors, as well as with rare cases of neuropsychological dysfunction, Dr. Bassetti said.

He described one of his patients who developed Charcot-Wilbrand syndrome, which involves loss of the ability to dream as a result of focal brain damage. The patient, a 73-year-old woman, had a history of being able to dream and recall dreams, but she reported a total dream loss after an acute bilateral stroke. She showed no cognitive deficits and had normal REM sleep (Ann. Neurol. 2004;56:583-6). The case suggests that a stroke can affect sleep in different ways.

Stroke as a cause of sleep disorders is a potentially rich area of research, noted Dr. Bassetti. “I personally believe that sleep modulation may have an impact on stroke recovery,” he said.
Sleep Apnea Impairs Drivers’ Vigilance, Study Reveals

BY ANY ROTHMAN SCHOFNED
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Boston — People with obstructive sleep apnea syndrome showed poorer vigilance while driving than did normal controls, a result that could not be predicted by pretest measures of disease severity or subjective reports of sleepiness, according to a poster presented by Dr. Jon Tippin at the annual meeting of the American Academy of Neurology.

Obstructive sleep apnea syndrome can now be added to the list of diseases, including dementia and illnesses like Alzheimer’s disease and Parkinson’s disease, that cause vigilance problems” during driving, said Dr. Tippin, a clinical professor of neurology at the University of Iowa, Iowa City.

Vigilance was assessed using the Simulator for Interdisciplinary Research in Ergonomics and Neuroscience (SIREN), an interactive driving simulator adapted from the Iowa SEQ-2000 (Senn-Bernard, D. 1992). The simulator was used to assess the overall hit rate of drivers and reaction time to a car-fitting with projection screens in front of and behind the driver.

During simulations, drivers were asked to respond by clicking the high-beam to things in the peripheral field. As for all patients, dosing for geriatric patients should be adjusted to their renal and hepatic function. Safety and effectiveness in pediatric patients have not been established.

Internet access to the SIREN was restricted to a pregnant woman or can affect reproduction capacity. Zemaira® should be given to a pregnant woman or inactivate at this time. Parvovirus B19 may most seriously affect pregnant women and immune-compromised patients. 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, chills, and muscle pain followed by 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-1-Proteinase Inhibitor (Human).

It is not known whether Zemaira® can cause harm to human pregnancy or if it affects reproductive 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 years and over to determine whether they respond differently from younger subjects. As all patients, dosing for geriatric patients should be adjusted to their renal and hepatic function. Safety and effectiveness in pediatric patients have not been established.

CONTRAINDICATIONS

Zemaira® is contraindicated in individuals with a known hypersensitivity to any of its components. Zemaira® is contraindicated in individuals with a history of anaphylaxis or severe systemic response to A-PI products. Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some infectious agents can not be totally eliminated. Any infections thought by a physician possibly to have been transmitted with Zemaira® and Prolastin®. No clinically significant differences were detected between the two treatment groups.

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 with adverse events regardless of causality (%) 69 (78%) 20 (63%) 70
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Zemaira® is indicated for chronic augmentation and maintenance therapy for adults with alpha 1-proteinase inhibitor (A1-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 A1-PI products or their components and individuals with selective IgA deficiencies who have known antibodies against IgA.

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

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

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

References: 1. Prolastin® Alpha1-Proteinase Inhibitor (Human), Full Prescribing Information, January 2005. 2. Aralast™ Alpha-Proteinase Inhibitor (Human), Full Prescribing Information, August 2005. 3. Data on file, CSL Behring LLC.