Cooperation Drives Antimicrobial Program

BY JEFF EVANS
Elsevier Global Medical News

BETHESDA, MD. — The antimicrobial stewardship program at the Health Sciences Center of West Virginia University, Morgantown, has been successful in reducing resistance in some pathogens, while generating more questions about others, according to Dr. Arif R. Sarwari, the program’s director.

In its first 5 years, the program at the tertiary care teaching hospital principally used prospective auditing methods and protocols for antibiotic cycling, coupled with educational strategies, to reduce the use of specific antibiotics and, in some instances, see a drop in rates of resistance.

Such results may not have been possible without the support and involvement of administrators and clinicians from different specialties, many of whom are members of the university’s Antimicrobial Review Subcommittee and participated in the creation of the program. Cooperation is necessary because the interventions needed in various departments may differ and may cross a variety of disciplines, Dr. Sarwari said at an annual conference on antimicrobial resistance sponsored by the National Foundation for Infectious Diseases.

The antimicrobial stewardship program began in 2003 and follows many of the recommendations formulated in guidelines issued by the Infectious Diseases Society of America.

Anticholinergics Linked to CV Death, Stroke in COPD

BY PATRICIA WENDLING
Elsevier Global Medical News

The use of two widely prescribed inhaled anticholinergics significantly increased the risk of cardiovascular death, myocardial infarction, or stroke by about 58% among patients with chronic obstructive pulmonary disease, according to the findings of a meta-analysis involving 14,783 patients.

The findings were reported in the Sept. 24 issue of JAMA (2008;300:1439-90).

During follow-up ranging from 6 weeks to 5 years, cardiovascular death, MI, or stroke occurred in 135 of 7,472 patients (1.8%) receiving either inhaled tiotropium bromide or ipratropium bromide for more than 30 days, compared with 86 of 7,311 patients (1.2%) receiving control therapy (relative risk 1.38). The difference was statistically significant.

However, inhaled anticholinergics did not significantly increase the risk of all-cause mortality, a secondary outcome of the meta-analysis (2.0% vs. 1.0% for control; RR 1.26).

“Clinicians and patients should carefully consider these potential long-term cardiovascular risks of inhaled anticholinergics in the treatment of COPD, and decide whether these risks are an acceptable trade-off in return for their symptomatic benefits,” wrote Dr. Sonal Singh of Wake Forest University, Winston-Salem, N.C., and associates.

In the 17 studies included in the meta-analysis, patients had a diagnosis of COPD of any severity. They had received either inhaled tiotropium or ipratropium or control, which could be placebo or active.

Surgeon General Issues DVT Call to Action

BY DENISE NAPOLI
Elsevier Global Medical News

WASHINGTON — Despite progress that has been made in preventing deep vein thrombosis and pulmonary embolism, the persistently high incidence of these conditions has prompted a Call to Action statement by Acting Surgeon General Steven K. Galson.

Among hospitalized spinal cord injury patients who do not receive venous thromboembolism prevention, the risk of developing a deep vein thrombosis (DVT) is 60%-80%. The risk is 40%-60% among similar hip or knee surgery patients, 20%-40% among patients undergoing major general surgery or gynecologic procedures, and 10%-20% for patients with acute illnesses like pneumonia, according to the Venous Disease Coalition, a network of organizations working to increase public and health professional awareness of venous disease.

The Call to Action statement was issued at the second annual meeting of the Venous Disease Coalition.

“There is now a public acknowledgment that this is a very significant health care issue that deserves attention from multiple facets of the medical community,” Dr. Thomas Wakefield said in an interview. “Although we’ve known for a long time that this is a very significant problem, since it doesn’t belong to one group or another and it spans so many specialties, it has been difficult to mobilize and raise awareness,” said Dr. Wakefield, head of vascular surgery at the...
Meta-Analysis Raises Questions

**Anticholinergics • from page 1**

The analysis includes new data from the industry-sponsored UPLIFT (Understanding Potential Long-Term Impacts on Function With Tiotropium) trial, one of the two trials which combinations of modalities for reducing antimicrobial resistance work best, and “until I have 15 different institutions using 15 different combinations and putting their results out there, how do I know which one works and which one doesn’t?” This was our attempt to put out what we think is a sensible approach.” Dr. Sarwari said in an interview.

Although many hospitals have programs to monitor and reduce antimicrobial resistance, most simply restrict the use of certain agents by having one person who approves or denies the order. West Virginia University prospectively audits antimicrobial use and resistance every 6 months, and implements changes through external interventions. “Although it was relatively simple to decide to define antimicrobial use through the measurement of defined daily doses per 1,000 patient-days, it took about 6 months of effort to convert data that are captured for billing purposes into data that can be used longitudinally, he said.

Educational programs were established to encourage or discourage the use of selected antimicrobial agents, while strategies to promote the use of alcohol-based hand sanitizers were put in place. In addition, the committee made a pocket-card guide available on an educational Web site. The card featured choices of antimicrobials for various clinical scenarios, listed the susceptible proportion of microorganisms that had been identified for that particular year, and gave the top three choices of antimicrobial agents for a particular pathogen (as perceived by the physician). Interventions centered on the principle of cycling the selection of antimicrobial drugs based on local surveillance of resistance rates, and were tailored for different units of the hospital.

The committee members decided not to keep a very restricted formulary except for quinolines, because more than half of the Pseudomonas strains in the ICU were resistant to ciprofloxacin, Dr. Sarwari said.

During 2003-2007, the number of defined daily doses per 1,000 patient-days of quinolones declined by 81%; the same defined measure of cefazidine declined by 37%, he said. The committee saw a concomitant rise in the use of agents that were designated to replace quinolones and cefazidine (aminoglycosides and cephalosporins, respectively). At the same time, the antimicrobial drug proportion of the pharmacy procurement budget declined from 16% to 8%.

Changes in drug resistance during the period yielded “mixed results,” Dr. Sarwari said. During 2004-2006, rates of ciprofloxacin resistance for Pseudomonas declined from 18% to 22% and that for ciprofloxacin-resistant Enterobacteriaceae fell from 59% to 20%. Klebsiella resistance to cefazidine remained stable at about 5%.

The proportion of nosocomial bacteremia cases caused by methicillin-resistant Staphylococcus aureus declined from 20% to 10%, whereas rates for bacteremia caused by vancomycin-resistant enterococci held steady at about 7%.

The hospital’s antimicrobial stewardship program “appears to be reasonably successful in affecting institutional use and resistance, but I’m not sure it has [had much] influence on the problem of import resistance,” Dr. Sarwari said.

In the future, “the big thing we want to try to introduce is some form of molecular microbiology to better get a sense of how many resistant bugs are new strains versus the same strains being passed around due to poor infection control.” Dr. Sarwari disclosed no conflicts of interest.

**Hospital Sees Mixed Results**

**Antimicrobial • from page 1**

CHEST 2008 Late-Breaking Symposium Monday, October 27, 10:30 a.m.

Are Heart Attacks a Side Effect of Anticholinergic Inhaled?

► Results From the Lung Health Study (Ann. J. Respir. Crit. Care Med. 2002;166:333-9): Introduction, Dr. Paul Enright, FCCP, Moderator

► Results From the Manitoba Health Database...The Bronch. Obstruct. Pulmon. Dis. 2008; 3:163-9

► Results From the National VA Database (Ann. Intern. Med. 2008; 149:189-90): Dr. Todd Lee

► A Systematic Review and Meta-Analysis (JAMA 2008;300:1439-50): Dr. Curt Furberg

► Results From the UPLIFT Trial (www.upliftcopd.com): Dr. Donald Tashkin, FCCP

► Panel Discussion and Rebuttals, With Questions From the Audience

E-mail: chestphysiciansnews@chestnet.org

control, including inhaled β-agonists or inhaled steroid and β-agonist combinations. Inhaled tiotropium is comarkedeted in the United States by Boehringer Ingelheim GmbH & Co. KG under the trade name Spiriva. Ipratropium is available generically and also is marketed by Boehringer Ingelheim as Atrovent.

In a statement, Pfizer and Boehringer Ingelheim said they “strongly disagree with the conclusion reached by Singh et al.” The two companies released a new analysis of 30 controlled clinical trials involving 19,545 patients with COPD. That analysis showed no increased risk of all-cause mortality, cardiac mortality, stroke, or MI (http://us.boehringer-ingelheim.com/newsroom/2008/09-23-08_spiriva_safety.html).
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University of Michigan, Ann Arbor. He was one of the roughly 44 physicians and nonphysicians who met with former Surgeon General Richard H. Carmona in May 2006 to urge the medical establishment to help raise awareness of DVT and pulmonary embolism (PE), and to increase research funding. Dr. Galson’s Call to Action was a direct result of that meeting, and will ‘mean great things for the prophylaxis and treatment of this disease,’ according to Dr. Wakefield.

Along with the Call to Action, the National Heart, Lung, and Blood Institute has awarded 5 years’ worth of funding to eight research groups that will investigate venous thromboembolism treatments and prevention—among them, a group to be co-led by Dr. Wakefield.

Other ongoing studies include a multicenter, randomized clinical trial of genotype-guided dosing of warfarin therapy, which is currently the most commonly used treatment for prophylaxis of recurrent venous thromboembolism, according to Dr. Elizabeth Nabel, director of clinical research at the NHLBI (see sidebar).

However, more studies are needed, Dr. Wakefield pointed out, including more studies of newer drugs and pharmacologic therapies that have less adverse effects and interactions, and less need for monitoring than has warfarin.

Also worthy of consideration, he said, are studies of short- and long-term outcomes associated with more aggressive interventions for DVT and PE. One such study, which has been funded by the National Institutes of Health and is slated to start soon, will compare pharmacomechanical thrombolyis plus standard anticoagulation versus standard anticoagulation alone for the treatment of significant proximal venous thrombosis.

As of Oct. 1, 2008, any DVT or PE associated with total knee and hip replacement procedures acquired during an inpatient stay will have “payment implications,” according to the Centers for Medicare and Medicaid Services.

Just how many patients are affected annually by venous thromboembolism is debated among different groups. Without an autopsy, many cases—perhaps as many as 50%—are misclassified as heart attack, Dr. Wakefield said. According to Dr. Roy S. Silverstein, chair of the committee of government affairs for the American Society of Hematology, the disease affects almost 1 million Americans annually, and “the estimated number of deaths from PE is higher than the combined number of deaths from breast cancer, HIV disease, and motor vehicle crashes.” Dr. Galson put PE- or DVT-related deaths at 100,000 annually, with 350,000-600,000 Americans developing DVT or PE each year. The American Heart Association estimated the incidence of venous thromboembolism to be 250,000-2 million cases per year (Circulation 2002;106:1436). Meanwhile, upcoming studies put the number somewhere in between.

In any case, Dr. Galson said, “We know that as the U.S. population ages, these numbers are only going to increase.”

AHRQ Releases Clot Prevention Guides

Two new booklets aim to help educate patients and physicians on preventing blood clots.

“Your Guide to Preventing and Treating Blood Clots” is a 12-page consumer booklet summarizing the causes and symptoms of clots, ways to avoid them, and what to expect from treatment.

“Preventing Hospital-Acquired Venous Thromboembolism: A Guide for Effective Quality Improvement” is a 60-page “tool to help hospitals and clinicians implement processes to prevent dangerous blood clots,” including case studies, according to Dr. Carolyn Clancy, director of the U.S. Department of Health and Human Services’ Agency for Healthcare Research and Quality, which published the reports.

Free copies are available by calling 800-358-9295 or by e-mailing ahrqpubs@ahrq.hhs.gov.

Warfarin Genotype Study Set to Begin

The National Heart, Lung, and Blood Institute is about to launch its first-ever multicenter, double-blind, pharmacogenetic trial—one focused on warfarin therapy.

The COAG (Clarification of Optimal Anticoagulation Through Genetics) trial aims to determine whether targeting patients according to their genotype during the initiation of warfarin therapy would lead to better and safer anticoagulation control, especially in patients with deep vein thrombosis (DVT), according to an NHLBI representative. Results are anticipated in 2011.

Warfarin is the most commonly used blood-thinning treatment, and the 10th most prescribed medication in the United States, with more than 21 million prescriptions per year, according to the NHLBI.

Patients with certain genotypes metabolize warfarin better than do others, and some researchers believe there may be an optimal genotype for toleration of the drug.

“It is hoped that prospectively using the genetic information in addition to the clinical information will help clinicians determine better and safer initial dosing for specific patients,” an NHLBI spokesperson said.

The COAG trial will be coordinated by the center for clinical epidemiology and biostatistics at the University of Pennsylvania, Philadelphia. By the end of 2008, study coordinators hope to begin enrolling 1,965 patients. Details are still being finalized, but the NHLBI spokesperson said that she expects participants will have to be starting on warfarin therapy with an indication of at least 3 months of treatment. They will likely have to be warfarin naïve, and without any major contraindications to anticoagulant treatment.

For more information about patient enrollment, send an e-mail to dambrauskass@nhlbi.nih.gov.

Investigational Once-Daily Drug Disappoints in COPD Trial

Two studies evaluating the efficacy and safety of aclidinium bromide in the treatment of chronic obstructive pulmonary disease have met their primary end point but demonstrated less benefit than anticipated, according to a corporate statement.

The double-blind, placebo-controlled phase III studies “confirm the bronchodilatory effect of aclidinium at the dose tested, although the magnitude was lower than seen in previous studies,” according to a statement from Almirall, a Spanish pharmaceutical company.

The company is working to further evaluate the data and determine dosing alternatives for the novel long-acting inhaled anticholinergic bronchodilator. A dose of 200 mcg aclidinium administered once daily through a dry-powder inhaler was selected for the two phase III studies. ACCLAIM/COPD was designed to assess aclidinium bromide for the treatment of moderate to severe chronic obstructive pulmonary disease (COPD). The primary end point was trough forced expiratory volume in 1 second. Both ACCLAIM/COPD trials were conducted across 23 countries, with 1,647 COPD patients randomized worldwide. The first was conducted in Europe, the other primarily in North America.

This newspaper and “The Pink Sheet” are published by Elsevier.
Risk was a strong predictor of adult-onset asthma, according to findings from an 18-year population-based study in Europe.

In the European Community Respiratory Health Survey, data from 6,461 participants showed that allergic rhinitis was associated with an increased risk of adult-onset asthma (adjusted relative risk of 3.53), as was nonallergic rhinitis, although to a lesser degree (adjusted relative risk of 2.71), Dr. Réfaa Shaaban of Bichat Teaching Hospital, Paris, and colleagues reported in the Sept. 20 issue of the Lancet. Participants were aged 20-44 years with or without asthma at baseline. They were divided into four groups: a control group including 3,163 individuals with no atopy and no rhinitis, an atopy-only group including 704 individuals with atopy but no rhinitis, a nonallergic rhinitis group including 1,377 people with rhinitis but no atopy, and an allergic rhinitis group including 1,217 people with atopy and rhinitis.

A total of 140 individuals developed asthma during the 8.8-year study period, for a cumulative incidence of 2.2%. The incidence in the groups, respectively, was 1.1%, 1.9%, 3.1%, and 4.0%. The differences among the groups were statistically significant, but only allergic rhinitis in those identified by a skin-prick test as having dust mite sensitization was found to be associated with increased risk of asthma independently of other allergens (Lancet 2008;372:1049-57).

A possible explanation for the dust mite link, the investigators said, is that patients with allergic rhinitis in response to mites are likely to have nasal symptoms over a longer period of time, because mites are a perennial indoor allergen. That theory is consistent with the findings of at least one other study showing that early exposure to dust mite allergen is associated with an increased risk of childhood asthma.

Sensitization to allergens in addition to mites was associated with additional small increases in asthma risk. For example, in those sensitized to dust mites, sensitization to cats raised asthma risk from 4.6% to 6.4%, and sensitization to grass raised the risk to 7.0%. Sensitization to birch increased the risk to 9.1%, the investigators noted. Those increases did not reach statistical significance, but that may be because of the small number of patients with those sensitivities, the researchers suggested.

Although prior epidemiological and clinical studies have shown a close relationship between asthma and allergic rhinitis, the nature of the link between the two has remained unclear. The current study, however, provides new evidence that rhinitis is predictive of asthma development, the investigators said, along with support of hypotheses suggesting that rhinitis might be a cause of asthma.

The current findings also suggest bronchial hyperresponsiveness (BHR) is “an intermediate factor in the process leading from allergic rhinitis to asthma,” the investigators noted. Not only is allergic rhinitis shown in this and prior studies to be a risk factor for BHR in nonasthmatic adults, they added, but there is now substantial evidence that asymptomatic BHR frequently precedes—and can be considered a risk factor for—symptomatic asthma.

Because the association between asthma and allergic rhinitis in the current study decreased substantially after controlling for BHR, it is likely that part of the effect of allergic rhinitis on development of asthma is mediated through the development of BHR, the investigators said. “This observation is important, because BHR is thought to be a dynamic process, and can be decreased by anti-inflammatory therapy,” they wrote.

Interventional studies to assess the effects of rhinitis treatment on reducing the incidence of asthma—an effect that has been observed in clinical trials—are necessary to verify this effect, they concluded.

In an editorial that accompanied the study, Dr. Erika von Mutius of Children’s Hospital in Munich noted that “the idea that allergic rhinitis could cause asthma raises the possibility of preventing asthma by preventing atopic sensitization, which could in turn prevent allergic rhinitis.”

The long-term preventive effect that immunotherapy might have is unknown, she added, although it can improve nasal symptom scores, reduce airway responsiveness, and thus cut asthma burden in patients with allergic rhinitis (Lancet 2008;372:1012-14). However, “even if immunotreatments work, the fairly low population-attributable risk might diminish the overall effect of this therapeutic approach,” she cautioned.
Stereoids Decreased Resistance to Albuterol Therapy

By Pran Lowry
Elater Global Medical News

Stereoids may prevent or reverse the desensitization that occurs with prolonged or short-acting β-adrenergic agonist therapy in patients with asthma and chronic obstructive pulmonary disease. In this study, researchers found that asthmatic patients who received inhaled steroids had a significantly decreased β-adrenergic receptor agonist albuterol for periods of 3, 6, 12 and 18 hours at different concentrations.

The investigators included slices of normal lung tissues from humans containing small airways with the short-acting β-adrenergic receptor agonist albuterol for periods of 3, 6, 12 and 18 hours at different concentrations. After 12 hours of albuterol incubation, the researchers noted a 40% decrease in maximum relaxation and a 49% decrease in airway sensitivity, compared with control values. The differences were statistically significant. In contrast, preincubation of the slices of lung tissue with desmethylamino for 1 hour prevented the albuterol-induced desensitization. However, a shorter (30- minute) desmethylamino treatment did not change albuterol-induced desensitization, according to the investigators.

The authors noted that their study is the first to demonstrate a mechanism of β-adrenergic receptor tolerance in normal human small airways. That is important, they wrote, because previous research in this area has attempted to study the mechanistic mechanisms of inducing β-adrenergic tolerance in animal models and single-cell preparations, which has made translating the findings to humans extremely difficult.

“The great thing about this work is that we are actually using small airways, which is the part of the lung that has the airway obstruction that we see in COPD,” Dr. Cooper said in an interview. “So we were looking specifically at the correct part of the lung.”

The study provides a platform to determine the exact mechanisms of β-adrenergic desensitization in human small airways, as well as ways of preventing tolerance to those agonists in human airborne disease, the investigators wrote.

For now, they noted, the important take-home message is that steroids can potentially reverse this tolerance. “Our work promotes combination therapy—supplying patients with a steroid and a β-agonist together,” Dr. Cooper said. The authors declined they had no conflicts of interest.

Dr. Susan Harding, FCCP, comments: “In this vitro study gives us potential translational information that is useful. Although the bronchomodel was induced by carbactam, a cholinergic agonist, and combined simulation incubation with desmethylamino and albuterol was not reported, this study supports the concept that combined use of corticosteroids with short-acting β-agonists may ameliorate resistance to SABAs.”

FDA Site Lists Drugs With Safety Issues

The Food and Drug Administration has posted on its Web site its first quarterly report that lists certain drugs being evaluated for potential safety issues. The drugs in the report, “Potentially Important Safety Risks/New Safety Information,” have been identified by FDA reviewers based on reports from the FDA’s Adverse Event Reporting System (AERS). The FDA says it will continue to disseminate the report, visit www.fda.gov/cder/aers/potential_signals/potential_signals_2008Q1.htm.

Pulmonary Medicine: Chest Physician • October 2008

6
Stockholm — Screening for mutations in the epidermal growth factor receptor (EGFR) enabled investigators from the Spanish Lung Cancer Group to achieve significant survival gains by selecting patients most likely to benefit from the drug erlotinib.

“Any patient who harbored an EGFR mutation would benefit from the drug,” Dr. Rafael Rossell, the principal investigator of the study, said during a press briefing at the European Society for Medical Oncology Congress.

Dr. Rossell presented data on the first 191 of more than 300 patients in a prospective study of customized treatment for lung cancer.

Median survival reached 22 months for patients with metastatic non-small cell lung cancer (NSCLC) who had exon 19 or 21 mutations. The time to progression was 12 months for these patients, and 71% had a response to erlotinib (Tarceva), a tyrosine kinase inhibitor of the epidermal growth factor receptor (EGFR).

Even better results were achieved in subgroups of patients who had a performance status of 0, were adenocarcinoma, or did not have brain metastases. Those whose performance status was measured as 0 had yet to reach median survival, he said.

In contrast, only 30% of patients with metastatic NSCLC typically respond to chemotherapy in cancer studies, according to Dr. Rossell. Their time to progression is just 5 months, and their median survival only half as long at 11 months.

“There is no excuse not to test for these mutations,” said Dr. Rossell, chief of the medical oncology service and scientific director of the Spanish Lung Cancer Group to achieve the significant survival gains by selecting patients most likely to benefit from the drug erlotinib.

EGFR assessment was performed at a central laboratory and results were delivered in 8 days. Dr. Rossell said such testing is widely available, he added. Some patients have inadequate tumor specimen, but testing circulating DNA in serum is an option.

EGFR mutations were discovered in 2004, he noted, and have previously been shown to occur primarily in small subgroups of lung cancer patients: women, never smokers, and Asians.

In contrast, only 30% of patients with bronchioloalveolar carcinoma, 11.9% of large-cell anaplastic lung cancers, and 6.3% of those classified as others (P less than .0002). Despite the relatively small proportion of the lung cancer population that stands to benefit from erlotinib, Dr. Rossell emphasized that the improved survival is sufficiently great to make testing worthwhile. The benefits achieved in the trial are “a new landmark in lung cancer,” he said.

To further illuminate “the prognostic and predictive relevance of EGFR mutations,” the Spanish Lung Cancer Group has started a phase III study, the European Randomized Trial of Tarceva vs Chemotherapy (EURTAC) for stage IV NSCLC.
HONOLULU — When women are given influenza vaccine in their third trimester of pregnancy, their infants receive protection against flu infection, results of a randomized controlled trial of more than 300 pregnant women confirm.

“This is the first randomized controlled trial of maternal immunization with influenza vaccine,” Dr. Mark C. Steinhoff reported at the annual meeting of the Pediatric Academic Societies. “Although [maternal immunization] is a U.S. government policy, it’s one of the few not based on randomized controlled trials.”

Dr. Steinhoff is professor of pediatrics and associate professor of epidemiology at Johns Hopkins University, Baltimore. He called the study the first randomized controlled trial of maternal immunization and Prevention guideline states. “Vaccination with inactivated influenza vaccine is recommended for the following persons who are at increased risk for complications from influenza . . . Women who will be pregnant during the influenza season (MMWR 2006;55[No. RR-10]:11-2).”

The study was part of the Maternal Gift Study, which involved 140 pregnant women and 331 live births in a middle-class urban population in Bangladesh. Women in the study were randomized to receive either influenza vaccine or pneumococcal conjugate vaccine during their third trimester of pregnancy. For the purposes of this analysis, the investigators used the mother-infant pairs receiving the pneumococcal vaccine as the control group.

The mothers were an average 25 years old, and were vaccinated an average 55 days before giving birth. Ninety-two percent gave birth in a hospital or clinic, 46% by cesarean delivery. The infants averaged just above 3 kg at birth and were breast-fed exclusively an average of 14 weeks.

The investigators looked both at proven influenza illness and at all febrile respiratory illnesses as outcome measures. The trivalent influenza vaccine was associated with a 63% reduction in proven influenza in infants 0-6 months of age and a 30% reduction in all febrile respiratory illnesses in infants and their mothers. The vaccine’s protective effect appeared to last at least until the infants were 5 months old. This is particularly important because current U.S. guidelines do not recommend influenza vaccine for children younger than 6 months old.

Dr. Steinhoff disclosed that he has served on Sanofi’s speakers bureau and has received research support from Sanofi-Aventis, Wyeth, and Merck & Co. “None of these interactions had any bearing on this particular study,” he said.
Airway responsiveness is more severe in postpubertal females with asthma, compared with their male counterparts, according to results from a large novel study.

The reason for the association is not clear, but it may have to do with hormonal regulation of airway responsiveness, study investigators reported in the Aug. 15 issue of the American Journal of Respiratory and Critical Care Medicine.

“In females with asthma, studies have demonstrated an impaired ability to increase β2-adrenergic receptor numbers despite a significant increase in airway responsiveness accompanying the luteal phase of the menstrual cycle,” Dr. Kelan G. Tantisira and colleagues said.

“This increase in airway responsiveness may be related to relative reductions in serum estrogen or relative excesses in progesterone,” which begins as early as Tanner stage II, the investigators reported.

In addition, they continued, studies conducted in animal models have shown that testosterone “can relax previously contracted airway smooth muscle in what appears to be a nitric oxide mediated mechanism. “Therefore, it is possible that the postpubertal decreases in airway responsiveness that occur among males may be mediated through increases in testosterone levels.”

The researchers prospectively evaluated 1,041 children (aged 5-12 years) who had mild to moderate asthma and who were enrolled in CAMP (Childhood Asthma Management Continuation Program).

The mean follow-up was 8.6 years, and participants were administered yearly methacholine challenges to determine the provocative concentration necessary to produce a 20% decrease in forced expiratory volume in 1 second (Am. J. Respir. Crit. Care Med. 2008;178:325-31).

Over the course of the follow-up period, each study participant had undergone eight to nine methacholine challenges. The researchers found that the amount of methacholine that was required to provoke airway constriction did not change markedly in girls over that time period. However, boys became increasingly tolerant to increasing methacholine doses, which suggests a possible decrease in disease severity.

By age 16, more than twice as much methacholine was needed to provoke a 20% constriction in the airways of boys, compared with girls. By age 18, only 15% of girls did not demonstrate any significant degree of airway responsiveness, compared with 27% of boys.

“While our results were not expected, they do point to intriguing mechanisms,” Dr. Tantisira of Brigham and Women’s Hospital and Harvard Medical School, both in Boston, said in a prepared statement. “Especially intriguing is that the differences in gender begin at the time of transition into early puberty.”

The researchers acknowledged the study had limitations, including that the study involved a cohort that followed a clinical trial period, making treatment assignment during the trial a potential confounder.

In an accompanying editorial, Dr. Jorrit Gerritsen of Beatrix Children’s Hospital and the University of Groningen (the Netherlands), recommended that the study participants “be followed for as long as possible since these individuals offer a unique opportunity that may provide insight into the natural course of asthma both in male and female subjects” (Am. J. Respir. Crit. Care Med. 2008;178:321-4).

The National Heart, Lung, and Blood Institute, and the National Center for Research Resources supported the study. Two of the study researchers disclosed ties to pharmaceutical companies that manufacture asthma medications.
Sleep Apnea Linked to BP Nondipping

BY DAMIAN MCNAMARA
Elsevier Global Medical News

People with sleep-disordered breathing were less likely to experience a normal nighttime decrease in systolic blood pressure, and they were at increased risk of adverse cardiac and other outcomes, according to a new prospective study.

Most people experience a 10%-20% dip in their blood pressure at nighttime (Hypertension 1995;26:60-9). Previously, cross-sectional studies showed an association between sleep apnea syndrome and a failure to experience that nighttime decrease in blood pressure (Am. J. Hypertens. 2001;14:887-92; Chest 2002;122:1148-55).

The new study’s findings are important because “nocturnal nondipping” associated with sleep-disordered breathing (SDB) has been linked to target organ damage and a poor cardiovascular prognosis (Can. J. Cardiol. 2007;23:132-8; Chest 2002;122:1148-55).

SDB “is a growing problem, but few studies have examined whether conscious sedation during an endoscopy puts patients who are at risk for OSA at increased risk for hypoxia,” Dr. Vijay Khiani of Case Western Reserve University, Cleveland, and his colleagues identified 143 endoscopy patients who were at low risk for hypoxia and 90 patients as being at high risk for hypoxia, based on patients’ responses to the Berlin Questionnaire, a standard measure of OSA risk. The mean patient age was 57 years and the mean BMI was 28 kg/m².

The chances of developing systolic nondipping were significantly correlated with baseline severity of SDB in a dose-response fashion. Mean patient age was 49 years, 63% were men, and the mean body mass index was 29 kg/m². Dr. Hla and her associates controlled for possible confounders, including age, gender, body mass index, smoking, and alcohol use.

Use of continuous positive airway pressure (CPAP) by 11 patients, antihypertensive medication use by 42 patients, and inclusion of 8 patients with a history of cardiovascular disease did not significantly alter the findings.

Patients using CPAP were included because researchers were unable to determine whether treatment was optimal. That was a possible limitation of the study, the researchers noted, as was a failure to follow all participants who had a baseline 24-hour blood pressure study.

Grants from the National Institutes of Health helped to fund the study. The authors had no financial relationships to disclose.

Conscious Sedation Was Safe Despite Apnea Risk

SAN DIEGO — Increased risk for obstructive sleep apnea does not increase the risk for hypoxia in people who undergo standard conscious sedation during endoscopy, based on data from 233 adults presented in a poster at the annual Digestive Disease Week.

Obstructive sleep apnea (OSA) is a growing problem, but few studies have examined whether conscious sedation during an endoscopy puts patients who are at risk for OSA at increased risk for hypoxia.

Dr. Khiani of Case Western Reserve University, Cleveland, and his colleagues identified 143 endoscopy patients who were at low risk for hypoxia and 90 patients as being at high risk for hypoxia, based on patients’ responses to the Berlin Questionnaire, a standard measure of OSA risk. The mean patient age was 57 years and the mean BMI was 28 kg/m².

The low-risk group included 66 men and 77 women, and the high-risk group included 43 men and 47 women.

Overall, 9 patients (10%) at high risk for OSA and 10 patients (7%) at low risk for OSA became hypoxic during conscious sedation, a non-significant difference. There was no significant difference in the rates of transient hypoxia (defined as a pulse oximetry measure of 92% or less) between the high- and low-risk groups (90% vs. 93%).

Average amounts of sedatives used were 81.4 mg meperidine and 3.6 mg midazolam in the low-risk group and 79.8 mg meperidine and 3.8 mg midazolam in the high-risk group, plus an average of 127.5 mcg and 114.6 mcg fentanyl, respectively, as needed.

Dr. Khiani stated that he had no relevant financial relationships to disclose.

—Heidi Splete

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Minimally Invasive Access to Peripheral Lung Lesions

It’s incredible, but my tenure as the 70th President of the American College of Chest Physicians is coming to an end! It has been a wonderful year! In this report, I will look back over the year, and summarize the highlights for the College and me.

From my perspective, what have been the most prominent College programs, events, and activities this year (since November 2007)?

The CHEST journal is an increasingly robust medical journal. It is well organized; the original research articles are of high quality and quite pertinent to our clinical practices; and the special features, such as Topics in Practice Management, Postgraduate Education Corner, Pectoriloquy, and Second Opinion, are wonderful. I give my highest kudos to Editor in Chief Richard Irwin, Executive Editor Stephen J. Welch, and their editorial staff. I also thank the Associate, Section, and International Editors, as well as the Editorial Board, for their high quality contributions to the journal.

The College’s advocacy efforts, in cooperation with our sister societies (ATS, ACCN, and SCCM), have been quite successful this year. The Pulmonary Rehabilitation Bill was passed, as part of the Medicare legislative package that eliminated the negative 10.5% cut in physician Medicare reimbursement, after many years of frustrating failure.

We were (and are) able to have substantial impact on the dialogue and decisions in response to the ruling of the Office for Human Research Protection (OHRP) of the US Department of Health and Human Services (HHS) that contradicted the institutional review board (IRB) of Johns Hopkins on the issue of research and quality improvement initiatives and the need for IRBs to scrutinize such processes.

We, in cooperation with our sister societies, have provided comments and are involved in an ongoing manner in the deliberations by the Centers for Medicare and Medicaid Services (CMS) for proposed changes in the Inpatient Prospective Payment Systems for Hospital-Acquired Conditions (HACs).

The College has been increasingly active in the international arena. We actively support our international members’ numerous international educational efforts by sending speakers to symposia and endorsing their educational programs. The availability of the online CHEST journal to many has also supported that effort. The College is continually trying to improve and refine our efforts by an active international committee structure (eg, the International Strategy Committee) that has improved the transparency and objectivity of our efforts. A highlight of the year has been our continued and increasing cooperation with our sister societies (ATS, ACCN, and SCCM), as well as the Society of Hospital Medicine on issues of common interest, such as the OHRP and HAC issues mentioned. I have been particularly impressed and pleased with the level of goodwill and cooperation between the College and the ATS. We have been able to work seamlessly on many common issues. I want to give a special thanks to Dr. David Ingbar.

Continued on following page
the immediate past president of ATS, who has been fiercely committed to the concept and need for cooperation between our two societies, and to Dr. Jo Rae Wright, current ATS president, who has fostered our joint projects and relationships.

As many of you know, the issues of disparities in health and health care have been a central concern of my presidency. My goal was to have these issues become priority issues for the College, and that has largely happened. At CHEST 2008, the issues will be discussed at several venues and will be presented as part of several clinical symposia.

The issues are very much a part of our national discourse on health insurance during this presidential campaign year, and over the last few years, I have noted an increasing number of articles on disparities in our pulmonary, critical care, and sleep journals (including CHEST). Issues related to care of the underserved must be central issues if we are to substantially improve the quality of US health care.

It has been a great year! Being actively involved in so many essential issues of the College has been a tremendous learning experience. Working with the highly qualified enthusiastic, greatly motivated, and highly professional leadership and staff of the College has been wonderful. I look forward, with great anticipation, to Dr. James Mathers’ upcoming year as ACCP President and wish him the very best. I also want to wish Dr. Kay Guntupalli a wonderful presidential year, as she will succeed Dr. Mathers as President in 2009-2010. What a solid and successful future we have secured for the College with these two great leaders.

It has been an invigorating and humbling experience to be the ACCP President and a distinct privilege for my wife, Zorita (Chair of the Ambassadors Group), and me, to serve the College! We remain committed to the College and all of its programs and activities. Thank you!

Dr. Alvin V. Thomas, Jr., FCCP ACCP President 2007-2008

Continued from previous page

This Month in CHEST—Editor’s Picks

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

► Differences in the Response to Methacholine Between the Tidal Breathing and Dosimeter Methods: Influence of the Dose of Bronchoconstrictor Agent Delivered to the Mouth. By Dr. L. Prieto, et al.

► Effects of CPAP on Cardiovascular Risk Profile in Patients With Severe Obstructive Sleep Apnea and Metabolic Syndrome. By Dr. Z. Dorkova, et al.

► Topics in Practice Management: Practical Guidance for Evidence-Based ICU Family Conferences. By Dr. J. R. Curtis, FCCP, and Dr. D. B. White.

► Editorial: Sleeping at Home. By Dr. I. M. Rosen, FCCP, and Dr. S. M. Manaker, FCCP.


► Clinical Commentary: Alpha-1 Antitrypsin Augmentation Therapy for PI*MZ Heterozygotes: A Cautionary Note. By Dr. R. A. Sandhu, et al.

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USA Programs

October 25 - 30, 2008
CHEST 2008 Philadelphia, PA

January 22 - 25, 2009
Sleep Medicine 2009 Scottsdale, AZ

February 27 - 28, 2009
Eliminating Borders: STS/ACCP Multidisciplinary Evaluation of Pulmonary/Hypertic Issues Lake Tahoe, CA

April 3 - 5, 2009
Celebration of Pediatric Pulmonology 2009 Scottsdale, AZ

April 24 - 26, 2009
Fundamentals of Ultrasound Ft. Lauderdale, FL

August 21 - 24, 2009
Sleep Medicine Board Review 2009 Phoenix, AZ

ACCP Simulation Center for Advanced Clinical Education

Northbrook, Illinois

October 25 - 29, 2008
Critical Care Board Review 2009 Phoenix, AZ

August 25, 2009
Lung Pathology 2009 Phoenix, AZ

August 25, 2009
Mechanical Ventilation 2009 Phoenix, AZ

August 25, 2009
ABIM Critical Care SEP Module 2009 Phoenix, AZ

August 25, 2009
ABIM Pulmonary Disease SEP Module 2009 Phoenix, AZ

August 26 - 30, 2009
Pulmonary Board Review 2009 Phoenix, AZ

October 31 - November 5, 2009
CHEST 2009 San Diego, CA

Northbrook, Illinois

March 6 - 8, 2009
Difficult Airway Management Northbrook, IL

May 6 - 7, 2009
Human Patient Simulation (HPS): Basic and Advanced Course Northbrook, IL

November 9 - 12, 2009
Emergency Care Simulator (ECS): Basic and Advanced Course Northbrook, IL

February 20 - 22, 2009
Bronchoscopy Skills Northbrook, IL

March 7 - 9, 2009
Update on Asthma and COPD Piscataway, NJ

March 22 - 23, 2009
IX IACP Course: XXII Central American and the Caribbean Meeting of Pulmonology and Thoracic Surgery San José, Costa Rica

March 24 - 27, 2009
29th International Symposium on Intensive Care and Emergency Medicine Brussels, Belgium

May 9 - 10, 2009
University Hospital of Lung Diseases Tirana, Albania

2008 - 2009 Education Calendar
COPD and Asthma: Overlapping Histologic and Inflammatory Features—Part 2

There is a growing body of evidence suggesting that asthma and COPD are not separate entities.

Both COPD and asthma are chronic inflammatory conditions of the lung associated with alterations of structural components. Differences in these alterations have long been recognized in tissue specimens taken from patients with asthma and COPD selected from polar ends of the clinical spectrum of reversibility and in a stable phase of the disease.

However, there is a growing body of evidence suggesting that asthma and COPD are not separate entities. COPD and asthma may represent disease states along a continuum, with varying degrees of each disease often present in the same patient (see table). In a subset of patients diagnosed with COPD, eosinophilic inflammation in the airways has been documented. Management strategies that aim to minimize eosinophilic airway inflammation are associated with a reduction in severe exacerbations of COPD (Siva et al. Eur Respir J 2007; 29:906).

Similarly, a subset of patients clinically diagnosed with COPD that is irreversible in response to an inhaled β-agonist show a partial reversibility of airflow obstruction when treated with 2 weeks of oral corticosteroids.

Research suggests that the responders to corticosteroid therapy may be patients with features of asthma that include reticular basement membrane thickening and eosinophilic inflammation. Such findings support the notion of a significant overlap between these two chronic inflammatory disorders.

In severe asthma, there is epithelial fragility and thickening of the reticular basement membrane, increased airway smooth muscle mass, hypertrophy of mucus-secreting glands, increased vascularity, greater numbers of fibroblasts, and increased deposition of collagen. Biopsy specimens from patients with asthma have demonstrated changes of a similar nature to COPD, but at different degrees and at different anatomic sites.

As more evidence is collected, the histologic and immunohistologic distinctions between these two conditions become less clear (Jeffery. Proc Am Thorac Soc 2004; 1:176).

A neutrophilic pattern of airway inflammation emerges in both asthma and COPD when exacerbations result in hospitalization (Qu et al. Thorax 2007; 62:475). Neutrophil recruitment results from chemotraction by chemokines, including interleukin 8 (or CXCL8). Furthermore, in mild COPD, exacerbations of bronchitis are associated with eosinophilia seen in bronchial tissue, and spumon and bronchovascular lavage fluid, as well as up-regulation of the eosinophil chemottractant, RANTES. These two features normally are associated with asthma. In fatal asthma, increased numbers of CD8+ cells have been reported. This mirrors the inflammatory pattern found in mild to moderate COPD and contrast with the CD4+ predominance found in mild asthma.

Homogenous thickening and hyaline appearance of the reticular basement membrane are pathognomonic of asthma. Another example of asthma and COPD overlap may be seen in an intermediate thickening of this membrane in mild asthma and COPD, with both conditions demonstrating similar remodel ing features (Bourdin et al. J Allergy Clin Immunol 2007; 119:1367). A study of eosinophilic bronchitis (Brindigling et al. Thorax 2003; 58:328) also revealed a thickened reticular basement membrane and further challenges the concept of histopathologic distinctions between asthma and COPD.

Possible Mechanisms of Evolution From Asthma to COPD

Airway remodeling, or changes in airway structure, occurs in response to chronic injury and inflammation in both asthma and COPD. The presence of airway remodeling may be particularly associated with more severe airflow obstruction, longer duration of disease, and hyperresponsiveness.

COPD is characterized by a slowly progressive, irreversible airflow obstruction; loss of lung elasticity resulting from parenchymal destruction; and peripheral airway inflammation. Small airways dysfunction may play a major role in the progression of asthma to COPD.

Inflammation and fibrosis in the small airways are present in smokers, with and without COPD. The early pulmonary structural changes seen with cigarette smoking result in small airway remodeling by the induction of growth factors in the airway wall (Chung et al. Am J Respir Crit Care Med 2006; 174:1327). Remodeling and repair thicken the airways walls, reduce lumen calibre, and restrict the normal increase in caliber produced by lung inflation. Similar structural changes are thought to lead to fixed airway obstruction seen in severe asthma (Bai and Knight. Clin Sci [Lond] 2005; 108:463).

Theoretically, this peripheral airway inflammation can lead to airways-parenchyma uncoupling, reducing the elastic load pulling the airways open and resulting in widespread small airway obstruction. Therefore, small airways dysfunction could play a major role in the progression of asthma to COPD, just as smoking-induced lung disease originates in the lung periphery.

Just as Orte and colleagues (Bronchitis. Assen, Netherlands: Royal van Gorcum; 1961; 43) had predicted almost 50 years ago, the differentiation between asthma and COPD is modulated by environmental factors (exposure to allergens, respiratory infections, and smoking) and other host factors (airway hyperreactivity, atopy, and genetic predisposition). Future preventive therapy should target the distal lung, as well as the proximal lung, for effective treatment of asthma.

Only further longitudinal prospective studies will determine whether the availability of effective treatment for childhood asthma targeting the small airways will help prevent the rising rates of COPD in the adult community.

Read part 1 of this Pulmonary Perspectives article in the September issue of CHEST Physician online at www.chestnet.org/ about/publications/chestPhysician.php.

Dr. Tanya Gulliver
Pulmonary Attending
John Hunter Children’s Hospital
Newcastle, NSW, Australia

Dr. Ronald Morton, FCCP
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Louisville, KY

Dr. Nemr Eid, FCCP
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Editor’s Insight

Eid and colleagues point to new directions in long-term therapeutic trials of patients with asthma. They ask whether attention should be paid to more effective control of airway inflammation during childhood and adolescence in hopes of ensuring maximal lung growth and development during these critical years. Ensuring that lungs grow normally may be an important influence on minimizing the risk for developing irreversible obstructive airway disease in later adulthood.
The syndrome of acute lung injury (ALI) and the more severe subset, acute respiratory distress syndrome (ARDS), affect an estimated 200,000 Americans each year and many more worldwide. Despite evidence that clinicians are making progress in diagnosis and treatment that has led to reductions in mortality, management strategies continue to evolve and, in many cases, provoke controversy.

A cornerstone of current management is to provide mechanical ventilation support, which delivers satisfactory gas exchange while avoiding exacerbation of lung injury. Considerable evidence from in vitro research, animal models, and human studies provides a solid rationale for preventing alveolar overdistention, as well as repetitive recruitment-collapse of alveoli. These phenomena, sometimes called “volutrauma” and “atelectrauma,” are intimately tied to the elaboration of proinflammatory cytokines, as well as to recruitment and activation of inflammatory cells that produce “biotrauma.” This biotrauma is postulated to contribute to multiple organ failure and perpetuate lung injury.

Two of five randomized controlled trials (RCTs) conducted in the 1990s (Amato et al. Am J Respir Crit Care Med 1995; 152:1835; Brochard et al. Am J Respir Crit Care Med 1998; 158:1831; Brower et al. Crit Care Med 1999; 27:1492; Stewart et al. N Engl J Med 1998; 338:355; The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301) demonstrated that ventilation with small tidal volumes was associated with lower mortality and shorter duration of ventilation compared with conventional tidal volume ventilation. The first four RCTs were smaller studies (<120 subjects) and arrived at conflicting conclusions. However, the multicenter RCT (The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301), conducted by National Institutes of Health-funded ARDS Network investigators, demonstrated the following in 863 subjects with ALI: (1) a significant reduction in mortality and increase in ventilator-free days, and (2) organ failure-free days associated with tidal volumes of 6 mL/kg of predicted body weight (PBW) compared with 12 mL/kg PBW tidal volumes. A metaanalysis of these clinical trials (Petrucci et al. Cochrane Database Syst Rev 2004; CD003844) confirms the mortality benefit of ventilation with low tidal volumes, and this strategy has been widely endorsed as beneficial evidence-based practice.

The ventilator parameters used by the ARDS Network investigators included use of the volume-targeted assist control mode, 6 mL/kg PBW tidal volumes, plateau airway pressure (Pplat) levels <30 cm H2O, and the adjustment of respiratory rate to achieve acceptable acid-base status. A relatively conservative positive end-expiratory pressure (PEEP) approach was used, resulting in PEEP levels averaging 8 to 9 cm H2O. Interestingly, oxygenation (PaO2/FIO2) levels were similar in the 6 mL/kg group and the 12 mL/kg group. This set of parameters was used in the study that demonstrated mortality benefit, so widespread endorsement of these parameters has followed.

Certain aspects of the ARDS Network approach to lung-protective ventilation have been challenged. Specifically, within the context of low tidal volume ventilation (LTVV), what is the role of pressure-targeted ventilation, more liberal Pplat limits, or recruitment maneuvers? The question of how much PEEP to use for patients with ARDS had been widely debated before LTVV was tested and continues to provoke controversy in the era of lung-protective ventilation. In the other LTVV RCT from the 1990s that yielded positive results, Amato and coworkers (Amato et al. Am J Respir Crit Care Med 1995; 152:1835) used pressure-targeted ventilation, allowed Pplat levels as high as 40 cm H2O included recruitment maneuvers when needed, and applied PEEP levels 2 to 3 cm greater than the lower inflection point on a static pressure-volume curve, resulting in an average PEEP value in the 13 to 16 cm H2O range.

In other small RCTs that targeted low tidal volume and higher PEEP values (Ranieri et al. JAMA 1999; 282:54; Villar et al. Crit Care Med 2006; 34:1311), positive results have been demonstrated in direct comparisons with conventional ventilatory strategies, including reductions in alveolar and systemic inflammation, better oxygenation, shorter duration of mechanical ventilation support, and lower mortality.

In subsequent RCTs (Brower et al. N Engl J Med 2004; 351:327), the ARDS Network investigators compared higher PEEP and low-PEEP strategies in 349 subjects. PEEP and FIO2 levels were adjusted according to a table for each arm of the study, resulting in average PEEP values of 13.2 cm H2O and 8.3 cm H2O for the two groups, respectively. While oxygenation was significantly better with higher PEEP levels, there were no differences in frequency of barotraumas, duration of mechanical ventilation support, or organ failure between groups. A study of this RCT (Brower et al. Crit Care Med 2003; 31:292) examined the effects of recruitment maneuvers (40 cm H2O pressure for 30 s), which had no sustained impact on gas exchange.

Earlier this year, the results of two large multicenter RCTs that examined various features of lung protective ventilation for ALI were published. These studies examined PEEP strategies and other variables in the delivery of LTVV that should influence patient care. Meade and colleagues (JAMA 2008; 299:637) studied 983 patients with ALI and compared low tidal volume ventilation, using traditional ARDS Network parameters, with an open-lung strategy modeled on parameters from Amato’s approach, as previously described. The two approaches yielded very similar outcomes, including outcomes for all-cause hospital mortality, duration of ventilation, and barotrauma. The open-lung approach resulted in higher PaO2/FIO2 ratios, lower rates of refractory hypoxemia, and less use of rescue therapies, such as inhaled nitric oxide, prone positioning, high-frequency ventilation, or extracorporeal membrane oxygenation.

Mercat and colleagues (JAMA 2008; 299:646) compared an “increased recruitment strategy” that resulted in higher PEEP values (averaging 13.4 cm H2O on day three) with a “minimal distention strategy,” with PEEP values averaging 6.7 cm H2O on day three. Delivery of tidal volumes of 6 mL/kg PBW by volume-targeted assist control was used in both groups in this RCT of 767 patients with ALI. Using a novel approach, PEEP levels were increased progressively, as long as the Pplat level was <28 to 30 cm H2O and, subsequently, PEEP was reduced using a defined strategy. The increased recruitment strategy was associated with better oxygenation, lower utilization of rescue therapies, and more ventilator-free and organ.
Continued from previous page

failure-free days, with no difference in barotraumas or mortality. While this approach was needed to the staff longs of patients with severe ARDS; when applied to patients with milder forms of lung injury, alveolar overdisten-
tion can result in the reduction in duration of ventilation support and trend for lower mortality seen in patients with ARDS was lost in patients with PaO2/FiO2 levels of 200 to 300 mm Hg. One can conclude from the cumulative study results that the primary goal is delivery of lungprotective ventilation with tidal volumes of 6 ml/kg PBW using volume-
targeted or pressure-targeted ventilation. Use of a more aggressive early PEEP strat-
tification was combined with a PBW-deri-

Table 1: Adverse Reactions with ≥ 7% Incidence Reported in Patients ≥12 Years of Age with ALVESCO compared to US Placebo-Controlled Clinical Trials in Patients Previously on Bronchodilators and/or Oral Steroids

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo 40 mcg, n=158</th>
<th>Placebo 80 mcg, n=158</th>
<th>ALVESCO 40 mcg, n=158</th>
<th>ALVESCO 80 mcg, n=158</th>
<th>ALVESCO 160 mcg, n=158</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>7.3%</td>
<td>4.9%</td>
<td>11.0%</td>
<td>8.7%</td>
<td>10.7%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>5.0%</td>
<td>4.4%</td>
<td>8.7%</td>
<td>5.0%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>3.7%</td>
<td>4.4%</td>
<td>8.7%</td>
<td>4.4%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>3.7%</td>
<td>4.4%</td>
<td>8.7%</td>
<td>4.4%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Back pain</td>
<td>3.7%</td>
<td>4.4%</td>
<td>8.7%</td>
<td>4.4%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Other</td>
<td>2.5%</td>
<td>3.7%</td>
<td>6.8%</td>
<td>5.0%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Controlled clinical studies have shown that orally inhaled corticosteroids may cause a reduction in growth velocity in children and adolescents. Growth velocity should be measured at the beginning of corticosteroid treatment and at appropriate intervals during continued therapy. If growth velocity is more than 2 standard deviations below the mean for the normal population, growth should be monitored at adequate intervals to determine whether they respond differently than younger patients. Other reported clinical experience has

Non-cardiac Effects: Drug-Induced Acute Kidney Injury in the ICU

Injury in the ICU

By Dr. Ghousia Wajida; and Dr. Richard Fatica

In summary, the majority of recent RCTs built upon work that supports the use of low tidal volume ventilation for patients with ALI, as well as higher PEEP earlier in the course of ARDS. Broad application of lung-protective ventilation for all patients who might benefit will be improved through consistent use of explicit written protocols in the ICU.

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NEWS FROM THE COLLEGE

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October 31 - November 5
San Diego, California

NEWS FROM THE COLLEGE

NetWorks
Palliative Care, Women’s Health, Practice Administration

Palliative and End-of-Life Care
A significant challenge for all of modern medicine is the task of translating the growing evidence base from efficacy trials into clinical practice. The National Institutes of Health has been transforming the research enterprise with the hope of more rapid implementation and uptake of new discoveries. Studies have demonstrated the importance of enhancing family communication as a part of best practices in the ICU, and guidelines and statements cite the data showing that improved family communication benefits overall care, ICU utilization, and family outcomes.

However, changing routine practice requires locally adaptive strategies and novel tools to aid practitioners and delivery systems to incorporate expanding knowledge. To advance provider-family communication, V.A.L.U.E. has emerged as a brilliant new approach. The V.A.L.U.E. acronym combines five evidence-based practices in family communication, resulting in an easy clinical reminder for practitioners to take advantage of opportunities to listen and respond within a paradigm of shared decision-making and family-inclusive interdisciplinary care. V.A.L.U.E. stands for the following: Value and appreciate what family members say; Acknowledge family members’ emotions; Listen actively and empathetically; Understand the patient as a person; and Elicit questions from family.

Critical care requires technical and specialized skills, including palliative care, which has always emphasized effective patient- and family-centered communication. It is essential that such care be offered concomitantly with life-preserving therapy for all ICU patients. For patients in the ICU who experience the end of life, family members become both partners and recipients of care. As one important way to start realizing improved translation from scientific discovery into better societal health, V.A.L.U.E. is ready for ICU practice enhancement and quality innovation efforts.

Dr. Richard A. Mularski, FCCP
Palliative and End-of-Life Care Steering Committee Member

Women’s Health
Tobacco companies have a long-standing relationship with Hollywood, including compensating actors to smoke their brands of cigarettes and paying producers to place tobacco products in their films. The 1998 Master Settlement Agreement attempted to address this issue by prohibiting tobacco companies from paying to place their products in movies. However, this practice continues. Hollywood promotes tobacco use as glamorous, rebellious, and a desirable social norm. The negative depictions of tobacco use are rarely shown.

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Why is this important? Research shows that smoking in movies contributes to smoking initiation in youth. Kids exposed to smoking in films have a higher likelihood of using tobacco and are twice as likely to smoke when their favorite stars smoke on screen. Advocates have been calling on Hollywood to stop allowing this method of recruitment.

Hollywood is starting to respond. Last year, the Motion Picture Association of America (MPAA) announced that it would consider smoking as a factor in the rating of films. In July 2008, six Hollywood studios agreed to place anti-smoking public service announcements on all DVDs rated G, PG, and PG-13 that included tobacco use. The State of California will provide the antismoking spots. As welcomed as these steps are, they are not meeting Smoke Free Movies’ four policy recommendations endorsed by health advocates nationwide.

Smoke Free Movies, a project of
Continued on following page
Master Fellow Receives Prestigious Award

D r. Allen I. Goldberg, Master FCCP, a Past President of the ACCP, has been honored by his medical school alma mater: The Clark-Curran Award for outstanding leadership in medical administration was awarded to Dr. Goldberg in June, as he celebrated his 40th year following his graduation from the State University of New York, Downstate Medical Center. This is a very prestigious award and is one of the highest non-teaching awards offered by SUNY Downstate to its alumni. The Clark-Curran award is named in honor of Dr. Duncan Clark, a 1936 graduate from Downstate who served as Dean and President of SUNY Downstate; and Dr. Alonso Curran, a former President of the Long Island College Hospital, the forerunner of SUNY Downstate Hospital. The ACCP and The CHEST Foundation congratulate Dr. Goldberg on this distinguished honor.
PROFESSIONAL OPPORTUNITIES

Southwest Florida Seeking Pulmonary/Critical Care Physician

This location is on the Gulf of Mexico and next to the Caloosahachee River; this city offers ponds, lakes and canals. Some of Florida’s finest beaches are at Bonita Beach, Ft. Myers Beach, Captiva and Sanibel Islands. Boating enthusiasts can enjoy a direct channel west to the Gulf of Mexico and east to the Atlantic Ocean and north to mid-state Florida. Within the community, residents enjoy year-round freshwater fishing, golf at five championship courses, biking, tennis, walking and numerous recreational facilities, entertainment opportunities and schools abound! This established practice is looking to expand due to growth. Excellent compensation plus production bonus, benefits and partnership track. Income potential will exceed 90th percentile of MGMA. Average patient volume daily is outpatient (15-20%) and inpatient (10-15%); practice focus: pulmonary (40%), critical care (30%), sleep (30%). Eric Rubin, Phone: 888-647-5005, ext. 221, Fax: 800-793-8028, grubin@nghpartners.com

Pulmonary/ Critical Care Physician

Pulmonary/ Critical Care Physician sought for – IL/MO (St. Louis region). This excellent employed position is ideal for someone who seeks Directorship of an ICU. Physicians completing training are also encouraged to apply. Practice consists of 80% Critical Care 20% Pulmonary. ICU is seven beds with census of four – five patients. Must be BE/BC located within 20 minutes of St. Louis. Enjoy small community/suburban or city living. Competitive compensation, production bonus, full benefits and relocation offered. To expedite consideration reply with your CV to: Marie Mann: 314-409-8800ammann@mannlic.com or FAX: 636-536-1729. This opportunity does not qualify for J-1 visa waiver.

Suburban Pittsburgh

Pulmonary and Sleep Medicine Physician needed in suburban Pittsburgh, PA. Excellent salary and benefits package. Equal Opportunity Employer. J-1 Visa consideration. Please send CV to Chest #84, P.O. Box 996, Abington, MA 02109.

North Shore, Long Island

Excellent opportunity for an intensivist to join a successful, well-run hospital. Fixed schedule, 12 days per month in this full time position. Competitive salary and full benefits. Shift work available. Easy access to Manhattan, desirable real estate and gorgeous beaches. Submit CV today to Rhonda Beamer 443-512-8899 Ext 106

Northeast Pennsylvania

Rutgers Cancer Institute of New Jersey (RCINJ) is seeking full-time Pulmonary/Critical Care Physicians to join our team of providers at the new, state-of-the-art Rutgers Cancer Institute. RCINJ has one of the largest cancer centers in the country and is dedicated to developing the treatment of cancer patients. The goal is to offer the patient the best possible care in a pleasant environment. The position will primarily have a shared call with 1:4 responsibility for ICU coverage.

We want you to be aware of the many employment opportunities available nationally. We represent hospitals and groups who have current and future recruitment needs. IntensivistJobs will work with you to identify professional opportunities that utilize your individual training and capabilities.

• Providence Nationwide Opportunities • Critical Care Medicine • Intensivist • Pulmonary Medicine • Critical Care Medicine • Intensivist Program Medical Director • Nightscout

IntensivistJobs will be conducting interviews October 27, 28 & 29 at CHEST 2008, in Philadelphia. We will be available to meet with you by appointment or at our booth (P 619) in the exhibit hall. To schedule a specific interview time call 888-397-0044. We look forward to meeting with you.

A System of Distinction

Sutter Medical Group (SMG) is seeking a BE/BC Pulmonologist. This medical group is located in a beautiful city situated at the foot of the Sierra Nevada foothills. This city offers ponds, lakes and canals. Some of California’s finest beaches are in close proximity. Boating enthusiasts can enjoy a direct channel west to the Gulf of Mexico and east to the Atlantic Ocean and north to mid-state Florida. Within the community, residents enjoy year-round freshwater fishing, golf at five championship courses, biking, tennis, walking and numerous recreational facilities, entertainment opportunities and schools abound! This established practice is looking to expand due to growth. Excellent compensation plus production bonus, benefits and partnership track. Income potential will exceed 90th percentile of MGMA. Average patient volume daily is outpatient (15-20%) and inpatient (10-15%); practice focus: pulmonary (40%), critical care (30%), sleep (30%). Eric Rubin, Phone: 888-647-5005, ext. 221, Fax: 800-793-8028, grubin@nghpartners.com

Northern California

Sutter Medical Group is seeking a Hospitalist to join their successful expanding Hospitalist program in Auburn, CA. Candidate must have two years of recent experience doing procedures and be able to handle ICU coverage.

• 2-year shareholder track
• Generous compensation
• Competitive benefits package
• Excellent retirement package
• Wide variety of shifts available
• School system is one of the best in CA
• Great quality of life

Sutter Auburn Faith Hospital, has 95 beds, a 24/7 Hospitalist program, open ICU, high resolution CT scan, cardiac cath lab, full nuclear medicine department, bronchoscopy suites and a pulmonary function laboratory.

The community of Auburn is nestled in the Sierra Nevada foothills approximately 35 miles northeast of Sacramento. Auburn is known for its family-oriented atmosphere and for its excellent schools. Residents enjoy year-round outdoor recreations such as golfing, hiking, biking, and white water rafting.

Physician Recruitment: 800-650-0623
916-643-6677 Fax
develop@sutterhealth.org
www.sutterhealth.org

Pulmonary Critical Care Opportunity

Northern California

Sutter Auburn Faith Hospital is a medium sized hospital with a 24/7 hospitalist program, open ICU, high resolution CT scan, cardiac cath lab, full nuclear medicine department, bronchoscopy suites and a pulmonary function laboratory.

Auburn is centrally located in the Sierra Nevada foothills between Sacramento and Lake Tahoe. Auburn is close to shopping and restaurants, and offers a variety of outdoor activities.

Physician Recruitment: 800-650-0623
916-643-6677 Fax
develop@sutterhealth.org
www.sutterhealth.org

Mesothelioma

HELP YOUR PATIENTS COPE with this diagnosis.

We are a nationally recognized plaintiffs’ asbestos law firm and built our reputation representing those diagnosed with mesothelioma, and other asbestos diseases. We can help your patients understand the legal implications of their diagnosis. Our website has been recognized as “providing useful information for patients and their families.” [Robinson et al, Malignant Mesothelioma, The Lancet, 2005; Vol. 366:387-393] KAZANLAW.COM Helping Asbestos Victims Since 1974. Kazan, McClain, Abrams, Lyons, Greenlaw & Harley, A Professional Law Corporation - 171 Twelfth Street 3rd Fl, Oakland, CA 94607, 1-877-955-6372 - www.kazanlaw.com email: skazan@kazanlaw.com

Mesothelioma

BEAUTIFUL COAST OF MAINE

BC/BE Pulmonologist

Modern, multi-specialty community hospital seeks full-time physician for outpatient practice. Belfast offers beautiful views of Penobscot Bay. Ideal for outdoor enthusiasts. Family oriented with excellent schools. Immediate availability. Contact Mark Biscoe, Executive Director, Waldo County General Hospital, PO Box 287, Belfast, ME 04915, 207-338-9302, E-mail: ceo@wchi.com Website: www.wchi.com

PRIVATE PRACTICE

LUNG and SLEEP CENTER

Fifth Pulm/CCM for private practice. Partnership: 1/3 call. Comp with productivity; full practice. Single hospital - ArMed Health System; 507 beds. LUNG / SLEEP CENTER with all latest procedural capabilities; stents; thermoplasty, adjacent to office. HealthGrades PULMONARY CARE EXCELLENCE AWARDS - South Carolina’s number one pulmonary program. Also 2008 HealthGrades distinguished hospital awards: PATIENT SAFETY and CLINICAL EXCELLENCE - Northeastern SC; I-85 on Lake Hartwell near Greenville. Midway Charlotte - Atlanta... to Charleston by lunch. Sherry Chastain, ArMed Health Medical Center, sherry.chastain@armedhealth.org 800-226-3103.

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Airways Disorders
During the 20th century, enormous resources were devoted to medical discovery COPD received compara-
tively little attention, and yet, during the decades of the 1970s through the 1990s, mortality for COPD rose in this country by 163%.

In response to these alarming statistics, there has been an intense research effort to better under-
stand the pathogenesis of COPD and new approaches to treatment. While the pulmonary community has shown renewed interest in COPD as a “preventable and treatable” disease, there has been a lag in disseminating new advances re-
garding COPD to the primary care community.

In 2007, I was granted the Second GlassoSmithKline Disting-
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based and guideline-driven chronic disease management for COPD. The COPD chronic care model was developed through a part-
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In May, during phase 1 of the project, a meeting was held to summarize current COPD guide-
line recommendations and discuss how they can be incorporated into a delivery system that will be user-
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BRIEF SUMMARY OF PRESCRIBING INFORMATION

Zemaira®

Alpha-1-Proteinase Inhibitor (Human)

Zemaira® is indicated for chronic augmentation and maintenance therapy in individuals with alpha-
fibrinogen deficiency and Prolastin® did not include sufficient numbers of subjects aged 65 and over

32

Also

- Infusion rates and the patient’s clinical state should be monitored closely during infusion. The

is supplied in a single use vial containing the labeled amount of functionally active A

Individuals with selective IgA deficiencies who have known antibodies against IgA (anti-IgA antibodies)


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

• Pure — The only Alpha-1 augmentation therapy approved by the FDA as highly purified (lot release specification, ≥94% purity)* 1-3

• Effective — Three times fewer COPD exacerbations than with Prolastin®†

• Well tolerated — Six times fewer infusion-related adverse events than with Prolastin®‡

• Fast — Half or less the infusion time of other augmentation therapies§ 1-3

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

Zemaira® is indicated for chronic augmentation and maintenance therapy for adults with alpha-1-proteinase inhibitor (A-1-PI) deficiency and emphysema. Clinical data demonstrating the long-term effects of chronic augmentation therapy with Zemaira® are not available.

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

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

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

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

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

* Shelf life purity specification is ≥90%
† In a retrospective analysis in the pivotal clinical trial, Zemaira® patients were three times less likely to experience exacerbations of their COPD than Prolastin® patients
‡ No clinically significant differences were detected between the treatment groups
§ Based on recommended dosage as stated in the product package inserts of 60 mg/kg body weight at the infusion rate of 0.08 mL/kg/min

Prolastin® is a registered trademark of Talecris Biotherapeutics, Inc.