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CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

BOB BEVERLY/WVU BIOMEDICAL COMMUNICATIONS

West Virginia University's antimicrobial stewardship program has reduced the use of some antibiotics, explained Dr. Arif R. Sarwari.

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

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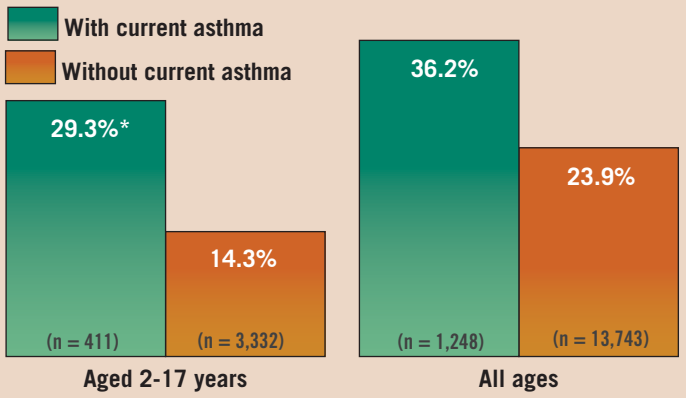
VITAL SIGNS

Influenza Vaccination Utilization Is Higher for People With Asthma



*Statistically significant compared with children who do not currently have asthma.
Source: 2005-2006 data, Centers for Disease Control and Prevention

ELSEVIER GLOBAL MEDICAL NEWS

Anticholinergics Linked to CV Death, Stroke in COPD

Meta-analysis findings stir controversy.

BY PATRICE 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;300:1439-50).

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 1.58). 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. 1.6% 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.

A new symposium at CHEST 2008 will address anticholinergic inhaler safety. See page 2 for details.

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

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INSIDE

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

See **Surgeon General** • *page 4*

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Meta-Analysis Raises Questions

Anticholinergics • *from page 1*

control, including inhaled β-agonists or inhaled steroid and β-agonist combinations.

Inhaled tiotropium is comarketed in the United States by Boehringer Ingelheim GmbH and Pfizer Inc. 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.boehringeringelheim.com/newsroom/2008/09-23-08_spiriva_safety.html).

The analysis includes new data from the industry-sponsored UPLIFT (Understanding Potential Long-Term Impacts on Function With Tiotropium) trial, which appeared online Oct. 5 in the New England Journal of Medicine (see story, p. 7).

Earlier this year, Boehringer Ingelheim informed the Food and Drug Administration that ongoing safety monitoring had identified a "possible increased risk of stroke" in a safety analysis of 29 trials involving approximately 13,500 patients.

The investigators of the current meta-analysis acknowledged that the analysis was limited by the quality of reported data. Many of the trials analyzed were small and short term, resulting in few events. "As a result of small numbers, the 95% [confidence intervals] are wide, resulting in some uncertainty as to the precise magnitude of the observed risk," Dr. Singh and associates wrote. "None of these trials was specifically designed to monitor the risk of cardiovascular events, which were not adjudicated."

A sensitivity analysis restricted to the five long-term studies (48 weeks to 5 years) involving 7,267 patients confirmed the significantly increased risk of cardiovascular death, MI, and stroke (2.9% vs. 1.8% for controls; RR 1.73). However, there was no statistically significant increase in these events in a sensitivity analysis of the 12 short-term trials (ranging from 6 weeks to 26 weeks) involving 7,516 patients (0.6% vs. 0.6%; RR 1.16).

The authors reported no financial disclosures. ■

Information about this topic is provided at www.chestnet.org/networks/airway_disorders/copd.php. The ACCP and its Airways NetWork are not offering any opinion now, but are making information available to keep our members informed.

CHEST 2008
Late-Breaking Symposium

Monday, October 27, 10:30 a.m.

Are Heart Attacks a Side Effect of Anticholinergic Inhalers?

- ▶ **Results From the Lung Health Study** (Am. J. Respir. Crit. Care Med. 2002;166:333-9): ***Introduction, Dr. Paul Enright, FCCP, Moderator***
- ▶ **Results From the Manitoba Health Database** (Int. J. Chron. Obstruct. Pulmon. Dis. 2008; 3:163-9)
- ▶ **Results From the National VA Database** (Ann. Intern. Med. 2008; 149:380-90): ***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**

Hospital Sees Mixed Results

Antimicrobial • *from page 1*

Society of America and the Society for Healthcare Epidemiology of America (Clin. Infect. Dis. 2007;44:159-77), said Dr. Sarwari, who is a member of the committee.

It is unclear 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 their use. But West Virginia University prospectively audits antimicrobial use and resistance every 6 months, and implements changes through educational 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 select 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 institution).

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 quinolones, 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 ceftazidime declined by 37%, he said. The committee saw a concomitant rise in the use of agents that were designated to replace quinolones and ceftazidime (aminoglycosides and cefepime, 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 38% to 22% and for *Acinetobacter* from 25% to 0%. In 2007, rates rose again to 34% and 16%, respectively. In the same period, resistance to ciprofloxacin gradually increased in *Escherichia coli* from 7% to 20%. *Klebsiella* resistance to ceftazidime 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 imported 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. ■

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Note: Calculations are adapted from Brain JD. Control of breathing. The Merck Manual Online Medical Library Web site. http://www.merck.com/mmhe/sec04/ch038/ch038e.html#sec04-ch038-ch038e-17. Accessed August 13, 2008; and Heron MP, Hoyert DL, Xu J, Scott C, Tejada-Vera B; for the Division of Vital Statistics. Deaths: preliminary data for 2006. *Natl Vital Stat Rep*. 2008;56(16):1-52.

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Initiatives Target DVT, PE

Surgeon General • *from page 1*

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 thrombolysis 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 naive, 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

BY JESSICA MERRILL
"The Pink Sheet"

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.

Large Study Links Allergic Rhinitis to Adult-Onset Asthma

BY SHARON WORCESTER
Elsevier Global Medical News

Rhinitis was a strong predictor of adult-onset asthma, according to findings from an 8-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. Rafea Shaaban of Bichat Teaching Hospital, Paris, and colleagues reported in the Sept. 20 issue of the Lancet.

Participants were aged 20-44 years 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 7.6%. 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 University 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. ■

Steroids Decreased Resistance to Albuterol Therapy

BY FRAN LOWRY
Elsevier Global Medical News

Steroids may prevent or reverse the desensitization that occurs with prolonged exposure to short-acting β_2-adrenergic receptor agonists in the treatment of asthma and chronic obstructive pulmonary disease, according to a University of Pennsylvania study.

The findings suggest that combination therapy using a steroid and a short-acting β_2-agonist might offer therapeutic benefit greater than either therapy alone for the treatment of asthma and chronic obstructive pulmonary disease (COPD), wrote Phillip R. Cooper, Ph.D., and Dr. Reynold A. Panettieri Jr., the study authors.

Their study was released online Sept. 9, 2008, as an article in press by the Journal of Allergy and Clinical Immunology (J. Allergy Clin. Immunol. [doi: 10.1016/j.jaci.2008.07.040]).

The investigators incubated slices of normal lung tissue from humans containing small airways with the short-acting β_2-adrenergic receptor agonist albuterol for periods of 3, 6, or 12 hours at different concentrations. After incubation of the lung tissue slices with carbachol to induce smooth muscle contraction, they found that the albuterol incubation weakened subsequent isoproterenol-induced relaxation in a dose- and time-dependent manner.

After 12 hours of albuterol incubation, the researchers noted a 40% decrease in maximum relaxation and a 45% decrease in airway sensitivity, compared with control values. The differences were statistically significant. In contrast, preincubating the slices of lung tissue with dexamethasone for 1 hour prevented the albuterol-induced desensitization. However, a shorter (30-minute) dexamethasone incubation didn't change albuterol-induced desensitization, according to the investigators.

The authors noted that their study is the first to demonstrate a model of β_2-adrenergic receptor tolerance in normal human small airways. That is important, they wrote, because previous research in this area has attempted to study the mechanisms of inducing β-agonist tolerance in animal models and single-cell preparations, which has made translating the findings to human lung tissue very difficult.

The important take-home message is that steroids potentially can reverse that tolerance.
DR. COOPER

"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 in asthma and 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-agonist desensitization in human small airways, as well as ways of preventing tolerance to those agonists in human airway disease, the investigators wrote.

For now, they noted, the important take-home message is that steroids potentially can reverse that tolerance. "Our work promotes combination therapy—supplying patients with a steroid and a β-agonist together," Dr. Cooper said.

The authors declared they had no conflicts of interest. ■

Dr. Susan Harding, FCCP, comments: *This in vitro study gives us potential translational information that is useful. Although the bronchoconstriction was induced by carbachol, a cholinergic agonist, and combined simultaneous incubation with dexamethasone and albuterol was not reported, this study supports the concept that combined use of corticosteroids with short-acting β_2-agonists may avert 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, "Potential Signals of Serious Risks/New Safety Information," have been identified by FDA reviewers based on reports from the FDA's Adverse Event Reporting System (AERS) database. To view the report, visit www.fda.gov/cder/aers/potential_signals/potential_signals_2008Q1.htm.

Pages 6a—6b

Genetic Screening Boosted Survival in Metastatic NSCLC

Patients selected by genotype for erlotinib treatment achieved 22-month median survival.

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

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

"For the first time in lung cancer we have a useful predictive marker," 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 women, 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 oncology research at the Catalan Institute of Oncology, Hospital German Trias I Pujol in Barcelona.

"Testing is the first step toward a dramatic improvement in subgroups of patients," he said.

For the study, investigators screened tumor samples of 2,294 patients from 130 hospitals in Spain, Argentina, Colombia, Mexico, the United States, the United Kingdom, and Italy from April 2005 to July 2008.

Only patients whose tumor specimens showed a deletion in exon 19 of EGFR's tyrosine kinase domain or mutation in exon 21 were selected for treatment with 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 the new study, he reported that 30.3% of women but only 8.3% of men harbored a mutation (P less than .0001). Women with exon 19 deletions also appeared to benefit more, with a median survival of 28 months when erlotinib was given, compared with 23 months for men. This difference was not statistically significant, however ($P = .08$).

Mutations were found in 38.4% of never smokers, but only 9.2% of former smokers, and just 6.1% of current smokers, differences that were also highly statistically significant (P less than .0001).

Stratification by histology showed that mutations occurred in 17.3% of patients with adenocarcinoma, 23.7% of those 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. ■

Tiotropium Didn't Change Rate of FEV_1 Decline in COPD

BY PATRICE WENDLING
Elsevier Global Medical News

Regular use of the inhaled anticholinergic tiotropium did not significantly reduce the rate of decline in mean forced expiratory volume in 1 second in patients with chronic obstructive pulmonary disease, a large randomized, double-blind trial has shown.

However, tiotropium was associated with improvements in the secondary end points, including lung function, quality of life, and exacerbation rate, according to the study published online Oct. 5 in the New England Journal of Medicine (N. Engl. J. Med. 2008;359:1543-54).

The trial, known as UPLIFT (Understanding Potential Long-Term Impacts on Function with Tiotropium), randomized 5,993 patients at 490 centers in 37 countries to 4 years of therapy with either tiotropium 18 mcg inhaled once daily or placebo. They were allowed to use other respiratory medications, except inhaled anticholinergics. Patients (mean age 66 years) had moderate to very severe COPD and a mean baseline forced expiratory volume in 1 second (FEV_1) of 1.32 L after bronchodilation (48% of predicted value).

There were no significant differences between the treatment and placebo groups in the rate of decline in the mean values for FEV_1 and forced vital capacity (FVC) either before or after bronchodilation from day 30 to the end of study, lead study author Dr. Donald P. Tashkin of the University of California, Los Angeles, and his associates reported. The annual rate of decline was 30 mL/yr in both groups before bronchodilation, and 40 mL in the tiotropium group and 42 mL in the placebo group after bronchodilation.

Mean absolute improvements in FEV_1 in the tiotropium group, compared with the placebo group, were maintained at all time points after randomization, and ranged from 87 mL to 103 mL before bronchodilation and from 47 mL to 65 mL after bronchodilation. The differences were statistically significant.

The incidence of most serious adverse events was lower in the tiotropium group than in the placebo group, including a reduced risk of congestive heart failure, COPD exacerbation, dyspnea, and respiratory failure, the authors wrote. In addition, the incidence rate for myocardial infarction was 0.69/100 patient-years for tiotropium, compared with 0.97/100 patient-years for placebo (relative risk, 0.71).

The incidence rate of cardiac failure, however, was 0.61/100 patient-years for tiotropium, compared with 0.48/100 patient-years for placebo (RR, 1.25).

Those findings are noteworthy, as a recently published meta-analysis showed that the use of either inhaled tiotropium or ipratropium significantly increased the risk of cardiovascular death, MI, or stroke by about 58% among patients with COPD (JAMA 2008;300:1439-50) (see story, p. 1). Pfizer Inc. and Boehringer Ingelheim GmbH, which comarket inhaled tiotropium under the trade name Spiriva and funded the UPLIFT trial, strongly rejected those findings.

The yearly rate of decline in FEV_1 observed in UPLIFT was lower than rates reported in other prospective interventional trials, Dr. Tashkin and associates noted, including EUROSCOP (European Respiratory Society Study on Chronic Obstructive Pulmonary Disease) and ISOLDE (Inhaled Steroids in Obstructive Lung Disease in Europe).

Potential explanations for the discrepancies are that UPLIFT allowed for prescription of all respiratory therapies at the discretion of the physicians. In addition, only 30% of patients were current smokers at baseline, compared with 38%-90% in other studies. The UPLIFT investigators also cited differences in study design, patient selection, and regional factors.

The trial's failure to find a difference in the rates of decline in FEV_1 might have been predictable, given previous trials' results and the fact that smoking cessation is the only intervention that meets the criteria of disease-modifying therapy, said Dr. John J. Reilly of the University of Pittsburgh in an accompanying editorial (N. Engl. J. Med. 2008;359:1616-8).

However, Dr. Reilly argued that the issue with UPLIFT and other recent large trials may be a signal-to-noise problem.

"In our efforts to simplify and clarify our definition of COPD, we have promulgated an inclusive definition that relies primarily on spirometric measures to establish the diagnosis," Dr. Reilly wrote. "There is increasing recognition that FEV_1 alone, while important, does not capture and communicate the heterogeneity of COPD."

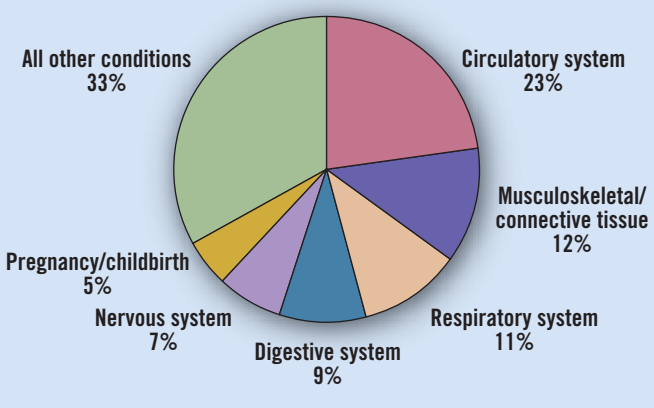
He supported ongoing attempts to define subgroups of patients with COPD to ensure that therapies that are effective in one subgroup will not be discarded because of results of studies that included patients with various types of COPD. "Although the characteristics that will define these subgroups remain to be determined …it is clear that the use of FEV_1 alone is not sufficient," Dr. Reilly wrote.

Dr. Tashkin disclosed receiving consulting fees from AstraZeneca, Boehringer Ingelheim, Dey Laboratories, and Schering; lecture fees from AstraZeneca, Boehringer Ingelheim, and Dey Laboratories; and grant support from Almirall, AstraZeneca, Boehringer Ingelheim, Dey Laboratories, GlaxoSmithKline, Ivax, MediciNova, Nabi Biopharmaceuticals, Novartis, Pfizer, and Sepracor.

Dr. Reilly reported receiving consulting fees from Indevus Pharmaceuticals and research support from Aeris Therapeutics. ■

DATA WATCH

Respiratory Conditions Accounted for 11% of Hospital Costs in 2006



Note: Based on data from the Healthcare Cost and Utilization Project.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

Third-Trimester Flu Vaccine Protected Infants

BY ROBERT FINN
Elsevier Global Medical News

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."

The Centers for Disease Control and Prevention guideline states. "Vaccination with inactivated influenza vaccine is recommended for the following persons who are at increased risk for severe 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 340 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 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 fact that the influenza vaccine was compared with the pneumococcal vaccine and not with placebo probably resulted in an underestimate of the influenza vaccine's effectiveness, said Dr. Steinhoff of Johns Hopkins University, Baltimore. "It's possible that pneumococcal vaccine could reduce some of the viral illnesses."

Furthermore, 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 More Severe in Asthmatic Girls

BY DOUG BRUNK
Elsevier Global Medical News

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 β_2-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.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The effect may have to do with hormonal regulation of airway responsiveness.

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; JAMA 1999;282:539-46).

Dr. Khin Mae Hla and her associates assessed 328 adults in the ongoing Wisconsin Sleep Cohort Study. All participants had a baseline polysomnography study and at least two 24-hour ambulatory blood pressure monitoring assessments during an average 7.2 years of follow-up. Dr. Hla and her colleagues of the departments of medicine and population health sciences at the University of Wisconsin, Madison, reported their findings in Sleep (2008;31:795-800).

A total of 18% of participants developed systolic nondipping, and 11% developed diastolic nondipping. Although the researchers did not find an association between SDB and diastolic nondipping, the longitudinal association with systolic BP alterations was significant.

"This failure to experience normal dipping adds to the amassing evidence that sleep-disordered breathing has a causal role in cardiovascular disease, possibly via multiple pathways [JAMA 2003;290:1906-14; J. Clin. Sleep Med. 2007;3:409-15]," the researchers wrote.

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/m^2. 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. Vijay Khiani of Case Western Reserve University, Cleveland, and his colleagues identified 143 endoscopy patients as being 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/m^2. 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 nonsignificant 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**

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS®

PRESIDENT'S REPORT

Looking Back With Thanks, Moving Forward With Hope

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

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

Continued from previous 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

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. Manaker, FCCP.*

▶ **SPECIAL FEATURE: Statins and Interstitial Lung Disease: A Systematic Review of the Literature and of FDA Adverse Event Reports.** *By Dr. A. B. Fernández, et al.*

▶ **CLINICAL COMMENTARY: Alpha-1 Antitrypsin Augmentation Therapy for PI*MZ Heterozygotes: A Cautionary Note.** *By Dr. R. A. Sandhaus, 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/Thoracic 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

August 21 - 25, 2009
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

ACCP Simulation Center for Advanced Clinical Education

Northbrook, Illinois

November 17 - 20, 2008
Emergency Care Simulator (ECS): Basic and Advanced Course
Northbrook, IL

February 2 - 5, 2009
iStan Basic and Advanced Course
Northbrook, IL

February 13 - 15, 2009
Critical Care Fundamentals
Northbrook, IL

February 20 - 22, 2009
Bronchoscopy Skills
Northbrook, IL

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

May 4 - 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

■ ACCP-Sponsored Courses
■ ACCP-Endorsed Courses

Endorsed International Program

October 30 - November 2, 2008
Second National Congress of the Bulgarian Respiratory Society
Plovdiv, Bulgaria

November 7, 2008
Symposium on Community-Acquired Pneumonia
Lleida, Spain

November 19 - 22, 2008
13th Congress of the Asian Pacific Society of Respirology
Bangkok, Thailand

November 21 - 25, 2008
Brazilian Pneumology Congress, ALAT, Brazil-Portugal Congress, Brazilian Bronchology Meeting
Brasilia, Brazil

December 5 - 7, 2008
3rd Asia Pacific Lung Cancer Conference
Hyderabad, India

December 6, 2008
Second Postgraduate Course from the American College of Chest Physicians: Hot Topics and Controversies
Oporto, Portugal

March 7 - 9, 2009
Update on Asthma and COPD
Lucknow, India

January 22 - 24, 2009
ACCP Italian Chapter Biannual Meeting
Paestrum, Italy

March 22 - 23, 2009
IX ACCP Course/ XXIII 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

April 13 - 17, 2009
XVIII Congress of the Mexican Society of Pulmonology and Thoracic Surgery
Veracruz, Mexico

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

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AMERICAN COLLEGE OF CHEST PHYSICIANS

Pulmonary Perspectives

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 (Qiu et al. *Thorax* 2007; 62:475). Neutrophil recruitment results from chemoattraction by chemokines, including interleukin-8 (or CXCL8). Furthermore, in mild COPD, exacerbations of bronchitis are associated with eosinophilia seen in bronchial tissue, and sputum and bronchoalveolar lavage fluid, as well as upregulation of the eosinophil chemattractant, RANTES. These two features normally are associated with asthma.

A NEUTROPHILIC PATTERN OF AIRWAY INFLAMMATION EMERGES IN BOTH ASTHMA AND COPD WHEN EXACERBATIONS RESULT IN HOSPITALIZATION.

In fatal asthma, increased numbers of $CD8^+$ cells have been reported. This mirrors the inflammatory pattern found in mild to moderate COPD and contrasts with the $CD4^+$ predominance found in mild asthma.

Homogenous thickening and hyaline appearance of the reticular basement membrane are pathognamonic 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 remodeling features (Bourdin et al. *J Allergy Clin Immunol* 2007; 119:1367). A study of eosinophilic bronchitis (Brightling et al. *Thorax* 2003; 58:528) 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 (Churg et al. *Am J Respir Crit Care Med* 2006; 174:1327). Remodeling and repair thicken the airway 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 Orie 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.*

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Overlapping Histopathologic Features Of COPD and Asthma

Feature	Asthma	COPD
Eosinophilic airway mild inflammation	Yes	Yes—during exacerbations of COPD and in severe COPD
Response to corticosteroid therapy	Yes	Yes—emergence of partial reversibility in subset of patients
Neutrophilic airway inflammation	Yes—during exacerbations	Yes—during exacerbations
Increased CD8 cells	Yes—fatal asthma	Yes
Reticular basement membrane thickening	Yes—pathognomonic	Yes—intermediate thickening

Editor's Insight

Dr. 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.

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Improving Lung-Protective Ventilation for ARDS

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 H_2O, 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 H_2O. Interestingly, oxygenation (PaO_2/FIO_2) 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 H_2O, 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 H_2O 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 ventilation, 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 high-PEEP and low-PEEP strategies in 549 subjects. PEEP and FIO_2 levels were adjusted according to a table for each arm of the study, resulting in average PEEP values of 13.2 cm H_20 and 8.3 cm H_20 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 mortality between groups. A substudy of this RCT (Brower et al. *Crit Care Med* 2003; 31:2592) examined the effects of recruitment maneuvers (40 cm H_2O pressure for 30 s), which had no sustained impact on gas exchange.

Critical Care Institute
American College of Chest Physicians

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 coinvestigators (*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 PaO_2/FIO_2, 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 H_2O on day three) with a "minimal distention strategy," with PEEP values averaging 6.7 cm H_2O 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 H_2O, 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

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NEWS FROM THE COLLEGE

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failure-free days, with no difference in barotraumas or mortality. While this approach may be well-suited to the stiff lungs of patients with severe ARDS, when applied to patients with milder forms of lung injury, alveolar overdistention may result. In fact, the reduction in duration of ventilation support and trend for lower mortality seen in patients with ARDS was lost in patients with PaO_2/FIO_2 levels of 200 to 300 mm Hg.

One can conclude from the cumulative study results that the primary goal is delivery of lung-protective ventilation with tidal volumes of 6 mL/kg PBW using volume-targeted or pressure-targeted ventilation. Use of a more aggressive early PEEP strategy combined with a PEEP de-escalation plan for patients with ARDS, but perhaps not for patients with ALI without ARDS, is supported by recent research.

The use of low tidal volume ventilation for patients with ARDS is widely regarded as one of the few high-level evidence-based strategies in critical care medicine, yet it is often not used by clinicians. Several studies (Weinert et al. *Am J Respir Crit Care Med* 2003; 167:1304; Young et al. *Crit Care Med* 2004; 32:1260) showed that low tidal volumes were rarely used, even in ARDS Network centers. Surveys by Rubenfeld and colleagues (*Crit Care Med* 2004; 32:1289) shed some light on under lying factors for physicians not initiating low tidal volume ventilation, such as lack of recognition of ALI, unwillingness to relinquish control of the ventilator, concern about contraindications, and concern about not continuing ventilation support (*ie*, concerns about gas exchange and patient comfort). Interestingly, the need for sedative and paralytic drugs was not different between low and conventional tidal volume study groups (Cheng et al. *Crit Care Med* 2005; 33:63).

Recent reports (Checkley et al. *Am J Respir Crit Care Med* 2008; 177:1215; Umoh et al. *Crit Care Med* 2008; 36:1463) offer encouragement that low tidal volume ventilation is being used more frequently. Of particular interest is the finding that the strongest independent risk factor for use of low tidal volume ventilation is the use of a written protocol (Umoh et al. *Crit Care Med* 2008; 36:1463). Such protocols should streamline calculation of tidal volume and predicted body weight, calculated based upon height from the following equations:

- Men: PBW = 50 kg for 60 inches in height + 2.3 kg/inch above 60 inches
- Women: PBW = 45.5 kg for 60 inches in height + 2.3 kg/inch above 60 inches

Calculations for 6 mL/kg PBW tidal volumes reveal that most men (those shorter than 6 feet 2 inches) require tidal volumes <500 mL, and most women (shorter than 5 feet 8 inches) require tidal volumes <400 mL.

In summary, the results of recent RCTs build 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. ■

Dr. Curtis N. Sessler, FCCP
Orhan Muren Professor of Medicine
Virginia Commonwealth University Health System
Medical Director of Critical Care
Medical College of Virginia Hospitals
Richmond, VA

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- **Weaning From Mechanical Ventilation**
By Dr. Timothy D. Girard; and Dr. E. Wesley Ely, Jr., FCCP
- **Drug-Induced Acute Kidney Injury in the ICU**
By Dr. Ghousia Wajida; and Dr. Richard Fatica

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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: **V**alue and appreciate what family members say; **A**cknowledge family members' emotions; **L**isten actively and empathetically; **U**nderstand the patient as a person; and **E**licit 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.

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 antismoking 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

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NEWS FROM THE COLLEGE

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Stanton Glantz, PhD, has outlined the following four steps Hollywood can take to substantially reduce the impact of adolescent exposure to smoking on screen: (1) Rate new movies that include tobacco use as "R"; (2) Certify that no payoffs are received; (3) Require strong antismoking ads to run before any film that contains tobacco use; and (4) Stop showing tobacco brands or imagery in the background of movie scenes. To learn more about this campaign, visit www.smokefreemovies.ucsf.edu.

The AMA Alliance launched the "Screen Out!" campaign to garner support for the Smoke Free Movies project. The campaign uses members nationwide to pressure media companies and the MPAA to remove tobacco use from youth-rated Hollywood films. To join this campaign, visit www.amaalliance.org.

Virginia Reichert, NP
Women's Health
Steering Committee Member;
Patricia Folan, RN;
and Susan Kennedy, LMSW, CASAC

Practice Administration

One of the many benefits of ACCP membership is participation in one or more of the 25 NetWorks. ACCP NetWorks provide education, information, direct consultation, and leadership opportunities relative to specific clinical areas, practice operations, or community health issues.

There is an incredible value in belonging to a NetWork. I have been a member of the Practice Administration, Private Practice, and Sleep Medicine NetWorks for the past 5 years, and I have gained valuable information and contacts that I have used as a practice administrator for a six-physician pulmonary medicine group.

Do you have concerns about maintaining physician compensation in an environment of declining reimbursement, controlling your practice's operating costs, selecting an electronic medical record system, forming alliances or contracts with hospitals, recruiting new physicians to your practice, and/or maintaining your current clinical knowledge?

If you answered yes to any of the above, what is your plan to address these issues for your practice(s)? Do you have a practice administrator or manager who has knowledge to address these issues? One of the values of a NetWork is gaining useful and practical information.

The Practice Administration NetWork comprises physicians, practice administrators, and managers who are addressing these issues. The NetWork provides members with various forms of education on issues through publications, sessions at the annual CHEST meetings, and NetWork conference calls.

Surprisingly, not many practice administrators are aware that they can become members of the ACCP. If you are already a member of the ACCP, I strongly encourage you to join and participate in the Practice Administration NetWork. If you are a physician and have a practice administrator or manager, I encourage you to have him or her join the ACCP as an allied health member, as well as join the Practice Administration NetWork. The cost for allied health membership is only $60 per year. My experience has been professionally rewarding, and I am certain that yours will be, too.

Michael K. McCormick, RRT, MBA
Practice Administration
Vice-Chair

Transplant

The Transplant NetWork is committed to enhancing the care of lung transplant candidates and recipients through projects that disseminate information to both the professional and patient communities. Important projects completed in the past include a survey of clinical practices among North American lung transplant centers (*Chest* 2004; 125:1224) and Web-based guides to lung transplantation for patients and community pulmonologists. The Transplant NetWork is now involved in two new projects that address areas of major importance in the field.

The first project is a proposed consensus statement on management of the organ donor in the ICU. This project would be a collaborative effort between the Transplant, Critical Care, and Palliative and End-of-Life Care NetWorks. The Society of Critical Care Medicine, American Association of Critical-Care Nurses, American Thoracic Society, American Academy of Pediatrics, and the United Network for Organ Sharing are potential collaborating organizations. Through rigorous literature review and expert opinion, the project seeks to define and standardize optimal practices in the management of organ donors. The working group hopes to publish the document in one of the collaborating organization's journals. We view this project as vital to ongoing national efforts to expand the organ donor pool at a time when demand continues to outpace the supply.

The second project involves a rigorous and systematic examination of barriers to optimal palliative care of lung transplant candidates. It is a collaborative project with the Transplant, Interstitial and Diffuse Lung Disease, and the Palliative and End-of-Life Care NetWorks. This project recognizes the potential conflict created in placing patients with advanced lung disease on the aggressive path of transplant listing, while concurrently trying to ensure that end-of-life and palliative care issues are addressed. A survey has been created that, once validated, will be sent to all members of the Transplant NetWork for completion. A scholarly publication is the anticipated outcome of this project.

We encourage ACCP members with an interest in the field of transplantation to join in all of the activities of our NetWork. These activities promote collaboration and scholarship and, ultimately, advance the field of transplantation for the benefit of our patients. Visit the Transplant NetWork Web pages at www.chestnet.org/networks/transplant/index.php for additional information.

Dr. Robert Kotloff, FCCP
Transplant
Chair

Affiliate

In order to better serve the junior members of the College, the Affiliate NetWork Steering Committee developed a survey for Affiliate members. A 15-question survey was sent via e-mail to 947 Affiliate members, and 140 members responded. We discovered that 51% of respondents had not attended the annual CHEST meeting. Of those who had attended CHEST, a majority (>60%) attended the case report sessions and the CHEST Challenge. Thirty percent attended the NetWork luncheon. A minority attended sessions on how to do a presentation, how to succeed in academic medicine, and education program development (3.2 to 12.9%). When asked how likely they would be to attend a session on various topics, the greatest number of responses was focused on pulmonary education and board review.

Many of the Affiliate member survey respondents would like a Web-based message board and reading list on clinical subjects, and 44% thought that membership in the ACCP was very valuable. They also would like to have the Affiliate NetWork focus on preparation for board exams and offer opportunities to interact with leaders in the field.

In summary, the survey of Affiliate members has been helpful in better defining our role as a NetWork. We have done extremely well in growing participation in the CHEST Challenge and Affiliate case report sessions. However, our constituents would appreciate clinical-pathologic conference discussion, board review preparatory sessions, and opportunities to interact with leading experts in the future. The Affiliate NetWork will adjust its focus accordingly to satisfy our members' needs.

Dr. Kevin Chan, FCCP
Affiliate NetWork Chair

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Master Fellow Receives Prestigious Award

Dr. 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 nonteaching 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. Alonzo Curran, a former President of the Long Island College Hospital, the forerunner of SUNY Downstate Hospital.

DR. ALLEN I. GOLDBERG

The ACCP and The CHEST Foundation congratulate Dr. Goldberg on this distinguished honor.■

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Airways Disorders

During the 20th century, enormous resources were devoted to medical discovery. COPD received comparatively 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 understand 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 regarding COPD to the primary care community.

In 2007, I was granted the Second GlaxoSmithKline Distinguished Scholar in Respiratory Health award. The objective of my project is to develop an integrated COPD chronic care model for primary care physicians and other health-care providers, encouraging high-quality, evidence-based and guideline-driven chronic disease management for COPD. The COPD chronic care model is being developed through a partnership with members of the Airways Disorders NetWork, members of the Institute for Healthcare Improvement (IHI), and community-based primary care physicians.

In May, during phase I of the project, a meeting was held to summarize current COPD guideline recommendations and discuss how they can be incorporated into a delivery system that will be user-friendly for providers, patients, and their families. Participants included Dr. Paula Anderson, FCCP, Dr. Jay Peters, FCCP, Dr. Nicola Hanania, MBBS, FCCP, and Dr. Sandra Adams, FCCP, from the Airways Disorders NetWork Steering Committee; Dr. Lawrence Mohr, Jr., FCCP, of The CHEST Foundation Board of Trustees; John Walsh, CEO of the Alpha-1 Foundation; and Marie Schall, IHI Director, Dr. Sean Townsend, FCCP, IHI faculty, and Susan Went, IHI Fellow. Additional participants were Dr. Sydney Parker and Dr. David Eubanks from the ACCP.

I have been encouraged and assisted by the Department of Family Medicine of Brown University in creating the COPD chronic care model.

Dr. Joshua Gutman, a family practice physician and member of the department, attended the May meeting and is working with me on the next phase of the project. He is a member of a group in Rhode Island called Quality Partners, sponsored by the Rhode Island Department of Health.

The Rhode Island Department of Health is a network of primary care physicians who have used a chronic care model for diabetes mellitus and, over the next year, will be the first site to test the ACCP COPD Chronic Care Model. ■

Dr. Sidney S. Braman, FCCP
Second GlaxoSmithKline Distinguished Scholar in Respiratory Health

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Zemaira®
alpha$_1$-proteinase inhibitor (Human)
Unmatched purity. Uncompromised care.

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

* Shelf life purity specification is ≥90%

† In a retrospective analysis in the pivotal clinical trial, Zemaira® patients were three times less likely to experience exacerbations of their COPD than Prolastin® patients

‡ No clinically significant differences were detected between the treatment groups

§ Based on recommended dosage as stated in the product package inserts of 60 mg/kg body weight at the infusion rate of 0.08 mL/kg/min