Gene Linked to Lung Protection in Asthma

BY MARY ANN MOON
Elsevier Global Medical News

A variation in the MMP12 gene appears to be associated with beneficial pulmonary effects in children who have asthma and in adults who smoke, particularly in smokers with COPD, according to a study published online in the New England Journal of Medicine.

“Our results suggest that variants of MMP12 are determinants of the level of lung function in subjects who are at risk for airflow obstruction,” said Dr. Gary M. Hunninghake and Dr. Michael H. Cho of Brigham and Women’s Hospital, Boston, and their research associates.

The investigators tested for an association between single-nucleotide polymorphisms in the MMP12 gene and lung function as assessed by FEV1 in cohorts participating in seven clinical trials.

The MMP12 gene encodes matrix metalloproteinase 12, which is produced by macrophages, “the predominant cell type that patrols the lower airspaces under normal conditions and the main inflammatory cell type that is recruited with smoking,” the investigators noted.

Matrix metalloproteinases degrade extracellular matrix molecules such as collagen and elastin and are also involved in epithelial repair and the regulation of cytokine and chemokine activity.

The researchers first found that the minor allele of SNP rs2276109 in the MMP12 gene was significantly associated with increased FEV1, in children with asthma (but not nonasthmatic children) who were subjects in the Genetics of Asthma in Costa Rica Study.

They then found the same link between the SNP and increased FEV1, among children taking budesonide—but not among those who were not taking budesonide—in the placebo arm of the ongoing phase 3 study of the anti-infective therapy peramivir.

Additional waves in subsequent influenza seasons in both hemispheres, Dr. Fukuda said. As a result, the WHO does not anticipate soon declaring that H1N1 is a seasonal virus subject to annual preparations by public health officials.

“Although the number of infections with the pandemic virus influenza A (H1N1) is plateauing or shrinking in many countries, the World Health Organization has not begun formal discussions about when to declare an end to the pandemic, an agency official said last month.”

At a media briefing, Dr. Keiji Fukuda, WHO special adviser on pandemic influenza, said the virus has been following an “up and down” pattern, with some countries already seeing caseloads diminish while others are experiencing increases.

In addition, because the virus could undergo genetic drift that will make it more or less virulent, it is hard to predict whether there will be additional waves in subsequent influenza seasons in both hemispheres, Dr. Fukuda said. As a result, the WHO does not anticipate soon declaring that H1N1 is a seasonal virus subject to annual preparations by public health officials.

“There’s no set date for when discussions on a transition would begin,” Dr. Fukuda said. “I anticipate that at least some time in 2010 we’ll be discussing this in a more formal way.”

British officials echoed Dr. Fukuda’s caution. In a press conference on the pandemic, Dr. David Salisbury, director of immunization at the English Department of Health, said, “Everybody is being very cautious about 2010 because we have no idea what will be the seasonal flu and what will happen with this pandemic.”

See page 2

Volume-Doubling Time May Reveal Risk

BY MARY ANN MOON
Elsevier Global Medical News

Among people at high risk for lung cancer, volume CT can be used to evaluate noncalcified pulmonary nodules to accurately identify lesions that have a low potential for malignancy, according to a report in the Dec. 3 issue of the New England Journal of Medicine.

Volume CT often detects suspicious nodules in patients who are screened because of their high risk for lung cancer, and clinicians often face the problem of deciding on the best course of action” in these cases, according to Dr. Rob J. van Klaveren of Erasmus Medical Center, Rotterdam, the Netherlands, and his associates.

“Targets of sensitization” can be identified in patients’ lung nodules, and the volume doubling time may be a more differential measure of risk for noncalcified nodules that are larger than 5 mm in diameter, but this often leads to expensive and invasive procedures for lesions that prove to be benign, the investigators noted.

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ACCP ONLINE REDESIGNED

Get the latest on all the new features unveiled this month.

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Pandemic Flu’s Future Unclear

Genetic Variant May Protect

Childhood Asthma Management Program. The same link between the SNP and the increased FEV1 noted among children with asthma (but not in asthmatic children) in the BAMSE (Children, Allergy, Milieu, Stockholm, Epidemiological Survey) study.

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

CHEST PHYSICIAN, the newspaper of the American College of Chest Physicians, provides cutting-edge reports from clinical meetings, FDA coverage, clinical trial results, expert commentary, and reporting on the business and politics of chest medicine. Each issue also provides material exclusive to the members of the American College of Chest Physicians. Content for CHEST Physician is provided by International Medical News Group and Elsevier Global Medical News. Content for NEWS FROM THE COLLEGE is provided by the American College of Chest Physicians.

Dr. Hunninghake and his colleagues then tested for the same association in adults who were subjects in the Boston Early-Onset COPD Study, the Lovelace Smokers Cohort, and the Normative Aging Study. The researchers found that the same SNP variation was associated with improved lung function in adults who were current or former smokers, but not in nonsmokers. Finally, the investigators found that the same MMP12 variant appeared to protect patients at risk for COPD against the disease in those three adult cohorts. The absence of the SNP rs2276185 was associated with a 54% increase in the risk of the onset of COPD and a population attributable risk of COPD of 28%.

The findings support the so-called ‘Dutch hypothesis,’ which states that asthma and COPD are different manifestations of a single disease entity and suggests that as-yet unknown genetic variants may underlie both asthma and COPD, the investigators said (N. Engl. J. Med. 2009;361:doi:10.1056/NEJMoa0904006).

Most previous studies of genetic associations in pulmonary function have relied on a single cohort, the study’s authors noted. ‘A strength of our study is that it included the analysis of multiple measurements of pulmonary function in a large number of subjects—more than 20,000 FEV₁ measurements in more than 8,300 subjects,’ they added.

‘Evidence is accumulating that asthma and COPD share common pathogenetic pathways,’ noted Dr. Guy G. Brussele of Ghent (Belgium) University Hospital, in an accompanying editorial. ‘This study … adds to the accumulating evidence that several mechanisms may lead to the development of COPD’ (N. Engl. J. Med. 2009;361:doi:10.1056/NEJMoa0904006).

The new study has several strengths, Dr. Brussele noted. Those strengths include the inclusion of seven cohorts with more than 8,300 subjects; the replication of an association between the SNP and FEV₁, both in adult smokers and children with asthma; and the researchers’ ability to repeat the analyses after stratification for asthma status and smoking status.

‘Hunninghake and colleagues have revitalized the Dutch hypothesis and set the scene for future genetic studies of chronic obstructive airway disease,’ Dr. Brussele concluded.

Dr. Hunninghake and Dr. Cho reported no conflicts of interest relevant to the study. Their associates reported receiving support from AstraZeneca Pharmaceuticals, Merck & Co., Johnson & Johnson, Golden Helix Inc., Novartis, GlaxoSmithKline, Sandvik, Sepracor Inc., Genentech Inc., and Phadia AB.
Autopsies Reveal That H1N1 Infection Damages Entire Airway

By Robert Finn

The 2009 pandemic influenza A(H1N1) virus differs from its predecessor, the seasonal strain, in many ways. In the United States, nearly 4.4 million people were infected with the pandemic strain, and about 284,000 cases of severe pneumonia were reported. The disease was seen most frequently in children and young adults, and it was more severe among those with underlying medical conditions, such as obesity and heart disease. Some of the cases were associated with respiratory failure requiring mechanical ventilation, and a few resulted in death. The following case study illustrates the findings of a study of H1N1 patients with severe pneumonia in the United States.

Case Study

The patient was a 15-year-old male with a history of asthma and chronic obstructive pulmonary disease. He was admitted to the hospital with a 1-week history of fever, cough, and shortness of breath. On examination, he was found to have bilateral rales and decreased breath sounds. Blood cultures grew Pseudomonas aeruginosa, and the patient was treated with intravenous antibiotics. Despite this treatment, his condition deteriorated, and he was intubated and placed on mechanical ventilation. Despite continued treatment, he died 3 days later. A postmortem examination revealed widespread pulmonary edema, widespread pneumonia, and widespread hemorrhage. The patient also had disseminated intravascular coagulation and multiorgan failure.

Pathologic Findings

The pathologic findings were consistent with severe pneumonia. The lungs were heavy and edematous, with widespread alveolar edema and hemorrhage. There was widespread consolidation of the lung tissue, with extensive areas of acute and organizing pneumonia. The bronchioles were filled with mucus and cellular debris, and there was extensive destruction of the alveolar walls. The interstitium was edematous, and there was widespread infiltration of inflammatory cells, including neutrophils and macrophages. The patient also had widespread thrombosis of the microvasculature, with widespread microthrombi in the lung vessels.

Discussion

The findings in this case are consistent with the findings of a study of H1N1 patients with severe pneumonia in the United States. The study found widespread pneumonia, widespread edema, and widespread hemorrhage. The findings are consistent with the findings of other studies of H1N1 patients with severe pneumonia, and they are consistent with the findings of other studies of influenza patients with severe pneumonia.

Conclusion

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Dr. Nicola A. Hanaian, FCCP

Comments: Initial reports suggested that clinical presentation of 2009 influenza (A/H1N1) may be similar to seasonal influenza. While this may indeed be the case in a majority of cases, many recent reports have documented that a subgroup of patients suffering from severe hypoxic respiratory failure requiring prolonged mechanical ventilation, occasionally leading to death. This report suggests that multiple sites in the lung are affected in these patients, including the small airways, in addition to the lung parenchyma. These findings support that the pulmonary complications in patients suffering from H1N1 influenza may be more extensive than those seen with seasonal influenza. Whether this is related to a higher incidence of the H1N1 virus, or to certain underlying host factors needs to be explored further.

Epitopes Similar to Those on A(H1N1) Influenza

By Denise Napoli

Many of the epitopes present in recently circulating seasonal influenza virus also can be found in the swine-origin pandemic H1N1 influenza virus, raising the possibility that “some level of immunity against [pandemic flu] might exist in the general population.” Indeed, the finding is borne out by reports detailing the incidence of clinically severe pandemic flu, which “so far appears to be similar to that experienced for seasonal flu,” according to a study released online Nov. 16 in the Proceedings of the National Academy of Sciences (doi: 10.1073/pnas.0911580106).

An epitope is the site on the surface of an antigen that elicits an immune response.

The authors of the current study, led by Dr. Jason A. Greenbaum of the La Jolla (Calif.) Institute for Allergy and Immunology, looked at epitope databases for seasonal flu, as well as the National Center for Biotechnology Information database and the Global Initiative on Sharing Avian Influenza Data database, which both contain information about swine-origin pandemic flu epitopes.

A total of 26 B-cell epitopes were found in recently circulating seasonal influenza strains, whereas 139 CD4 and 78 CD8 T-cell epitopes were found, wrote Dr. Greenbaum and colleagues. Of those, 8 B-cell epitopes were “conserved,” or shared by the swine-origin pandemic H1N1 strain (31%), as were 57 CD4+ T-cell epitopes (44%) and 54 CD8+ T-cell epitopes (69%). According to the authors, “a virus can carry substantial sequence differences in some regions but still be recognized by the immune system if the virus retains sequence identity in regions including the immune epitopes,” as the pandemic H1N1 virus does.

“Although T-cell responses do not prevent infection, they contribute to the clearance of infected target cells,” the investigators wrote, “and such pre-existing immunity may lead to a less severe course of disease” among infected patients.

The authors noted that, according to the Centers for Disease Control and Prevention, more than 1 million people in the United States were infected with pandemic flu between April 15 and July 24, 2009, which caused 5,011 hospitalizations and 302 deaths.

The National Institutes of Health provided funding for the study. The authors declared no individual conflicts of interest.
PULMONARY MEDICINE

H1N1-Associated Invasive Pneumonia Is Increasing

BY ROBERT FINN
Elsevier Global Medical News

Investigations at the Centers for Disease Control and Prevention are seeing a “worrisome spike” in serious bacterial pneumonia associated with pandemic influenza A(H1N1) virus, Dr. Anne Schuchat said at a press briefing.

In the Denver metropolitan area, for example, there were 58 reported cases of invasive pneumococcal infections during the month of October. Over the last 5 years, there has been an average of only 20 cases each October.

Invasive bacterial pneumonia is normally seen in individuals older than age 65. But about two-thirds of the patients in the Denver area are between the ages of 20 and 59 years, Dr. Schuchat said. The majority of these patients had underlying risk factors in addition to H1N1 influenza.

"People at risk for invasive pneumococcal [infection] include adults with chronic health conditions like diabetes or COPD, intravenous drug users, or other chronic lung diseases, chronic heart, kidney or liver disease, cancer and other immunosuppressive conditions like HIV," Dr. Schuchat said. "So a lot of adults are at higher risk for pneumococcal complications."

Studies show that only one-quarter of patients in these high-risk groups have received the highly effective and available pneumococcal vaccine. Adults typically require only one dose of the vaccine for lifetime protection.

In a person infected with influenza, an easing of symptoms followed by a sudden worsening is a key warning sign of a secondary bacterial infection. "We can see that in children or in adults," Dr. Schuchat said. "And it doesn’t necessarily always mean bacterial pneumonia, but it very much can mean that."

Other H1N1 influenza news discussed during the press briefing included confirmation that a physician in West Virginia appears to have come down with laboratory-verified H1N1 influenza even over a period of 3 to 4 months. This is uncommon but not impossible, Dr. Schuchat said, and this case does not bear on the efficacy of the H1N1 virus vaccine, which is highly—but not 100%—effective.

To date 61.2 million doses of the vaccine have been made available, with an additional 7 million doses since Nov. 20. "We are expecting vaccination efforts to really step up as we come into December in concert with these improved supplies," Dr. Schuchat said.

The CDC continues to investigate adverse events associated with the vaccine. So far 94% of such reports relate to mild reactions such as soreness, tenderness, or injection-site pain. Anaphylaxis is not occurring more frequently than expected.

There have been 10 reports of possible cases of Guillain-Barré syndrome (GBS) associated with the vaccine, but not all of those have been confirmed. GBS is of particular concern because of a large number of cases associated with the 1976 swine flu vaccine. Dr. Schuchat said that 10 cases is a small number, given the large number of vaccine doses that have been administered.

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CRITICAL CARE MEDICINE

Nasopharyngeal Swab Tests May Miss H1N1 Cases

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — Antigen testing for the pandemic influenza A(H1N1) virus using nasopharyngeal swabs is not sensitive enough to be reliable in ICU patients, the experience at one busy inner-city New York hospital suggests.

Just 3 of 15 critically ill adults admitted to the ICU at Lincoln Medical Center in the South Bronx with H1N1 flu during the May-July outbreak had a positive nasopharyngeal swab. The other 12 tested positive only on bronchial washings or tracheal aspirates. Dr. Raghu S. Loganathan, FCCP, reported at CHEST 2009, the annual meeting of the American College of Chest Physicians.

Lincoln Medical Center has one of busiest emergency departments in the country, serving a minority population hard hit by 2009 H1N1. The hospital’s experience during the first wave of H1N1 influenza in the United States was so different from what was happening in the United States, Dr. Loganathan noted, probably reflecting the demographics of the South Bronx, Dr. Loganathan observed.

Four ICU patients had normal chest X-rays. Eight had unilateral radiographic abnormalities, in contrast to the typical bilateral abnormalities seen in patients with seasonal flu. The radiographic findings consisted of alveolar consolidation in seven patients, interstitial infiltrates in two, and nodular infiltrates in two.

Lymphopenia was present in 10 of 15 patients, with a median value of 600 cells/µL. Elevated creatine phosphokinase, with a median value of 563 U/L. The median lactate dehydrogenase level in the 15 patients was 362 U/L, with 7 patients having a significantly elevated level indicative of hemolysis.

Twelve patients were placed on mechanical ventilation, including seven with acute respiratory distress syndrome. Ten patients had severe sepsis or septic shock. The mean ICU length of stay was 9.6 days. Four of the 15 patients died.

How do critically ill H1N1 flu patients compare with those requiring ICU care for seasonal influenza? Dr. Loganathan noted that a recent report (J. Clin. Virol. 2009 November;46:275-8) from the Mayo Clinic in Rochester, Minn., is illuminating on that score. The Mayo investigators reported on 103 ICU patients with seasonal influenza A and 8 with seasonal influenza B. The mean ICU length of stay for the critically ill patients with seasonal flu was just 3 days, compared with 9.6 days for the H1N1 flu patients, and the in-hospital mortality rate was 18.8% for the seasonal flu group, compared with 26% for the New York patients with severe H1N1 influenza.

HHS Funds Research for Hospital-Acquired Infections

BY JANE ANDERSON
Elsevier Global Medical News

The Department of Health and Human Services has awarded $17 million to fund research projects aimed at reducing central line–associated bloodstream infections and other hospital-acquired infections, including methicillin-resistant Staphylococcus aureus.

Nearly half of the funds will go toward financing a national expansion of the Keystone Project, which uses a checklist of evidence-based safety practices, staff training, careful measurement of infection rates, and teamwork-building tools for hospital staff to reduce the rate of central line–associated bloodstream infections (CLABSI), according to the HHS.

The program, which has been implemented in more than 100 Michigan intensive care units, has saved more than 1,800 lives, more than $271 million in health care costs, and more than 140,700 excess hospital stay days in that state between 2004 and 2009, according to the Michigan Health and Hospital Association in Lansing.

In addition, data indicate that the CLABSI rates of hospitals participating in the Keystone program were consistently lower than the national average, the hospital association said in an October report.

Last year, the Agency for Healthcare Research and Quality (AHRQ) funded an expansion of the Keystone Project to 10 states. Now, with additional funding from the AHRQ and a private foundation, it is operating in all 50 states, the HHS said. The additional $8 million from the HHS will allow the program to expand to more hospitals, to extend to other settings in addition to intensive care units, and to broaden the focus to address other types of infections, the HHS said.

Dr. Thomas W. Barrett, a hospitalist at the Portland (Or.) VA Medical Center, said in an interview that this type of implementation research is difficult to conduct because there are so many potentially confounding variables.

“This is a great step forward—it’s very important for patient safety and patient care,” Dr. Barrett said. “It’s encouraging to see AHRQ take a great step in the right direction. I hope that since AHRQ is funding this, the level of rigor in the research will continue to improve.”

To spend the remaining $9 million of the $17 million in new funding, the AHRQ said it collaborated with the Centers for Disease Control and Prevention to identify projects.

The projects chosen will focus on reducing Clostridium difficile infections through a regional hospital collaborative, reducing the overuse of antibiotics by primary care physicians treating patients in ambulatory and long-term care settings, evaluating two ways to eliminate MRSA in ICUs, and improving the measurement of the risk of infections after surgery.

Additional projects will attempt to identify rates of hospital-acquired infections, to reduce infections caused by Klebsiella pneumoniae carbapenemase-producing organisms by applying recently developed recommendations from the CDC’s Healthcare Infection Control Practices Advisory Committee, to standardize antibiotic use in long-term care settings, and to implement teamwork principles for frontline health care providers, the AHRQ said.
New Test Sped Bacterial Infection Detection in Sepsis

A testing method that uses positive and negative bacteria to detect in an automated DNA-based polymerase chain reaction and microarray system accurately identified bacteria in sepsis much faster than a standard culture-based process. The test identified bacterial species in patients with suspected sepsis with 95% sensitivity and 99% specificity, with a mean turnaround time of 23 hours—compared with 41.5-48 hours for the standard culture-based method, according to a report published online in the Lancet.

Although the sepsis assay is a “major advance” that encompasses the best of nucleic acid and standard culture-based methods, it is unknown yet whether determining the species of a pathogen 18 hours earlier than usual will “translate into demonstrable clinical benefit” compared to the cost of undertaking the additional test, the investigators reported.

In the study, Dr. Päivi Tissari of the Helsinki University Hospital Laboratory and colleagues tested the Prove-it sepsis assay, manufactured by Helsinki-based Mobidiag, against standard blood culture and pathogen identification. The analysis included 3,138 blood samples from patients with suspected sepsis at two large academic medical centers (Lancet 2009 Dec. 10 [doi:10.1016/S0140-6736(09)61569-5]).

The assay identifies more than 50 species of gram-positive and gram-negative bacteria that cause most cases of sepsis. A total of 2,107 blood culture samples tested positive, including 1,807 covered by the sepsis assay. The investigators compared pareid DNA sequences of toxigenic and 16S RNA genes and original microbiological laboratory data for samples when the results of the assay and standard blood culture method were not the same.

For organisms that could be detected with the sepsis assay, the results of the assay were between 93% and 100% concordant with the results of blood culturing for all species except one. The assay identified 133 of the 163 coagulase-negative staphylococci that were identified through blood culture. False-positive results were identified in 52 of the 3,138 samples put through the assay. Those 52 false positives included 34 that were excluded due to contamination or software failure, 11 with more bacterial species detected than with conventional blood culture, 3 with Staphylococcus epidermidis reported instead of coagulase-negative staphylococci, 3 attributed to cross-hybridization between species, and 1 sample in which the assay also detected Bacillus fragilis.

False-negative results occurred in 34 samples due to inadequate sensitivity for certain species, and in 6 samples because the sepsis assay did not detect all the bacteria it should have. The assay also had difficulty in resolving species in polymicrobial samples.

The median difference in turnaround time between the Prove-it assay and the reference method for 39 samples was 18 hours 19 minutes (range of 17 hours 29 minutes to 43 hours 8 minutes).

A baseline study of 316 patients showed 95% specificity and 100% sensitivity, with a false-negative rate of only 39%.

Although antibiotic resistance testing is not generally available, the assay can detect MRSA with 100% sensitivity and specificity. Given the frequency of empiric coverage for this pathogen, the ability to narrow or add coverage is important. As with many new technologies, this assay is expensive. Whether the cost will be supported by improved patient outcomes remains for future studies. Factors such as difficulty with variable DNA extraction efficiency and potential for contamination must also be considered, especially outside of the research setting.

Comprehensive Effort Can Boost VTE Prophylaxis Results

BY SUSAN BIRK
Elsevier Global Medical News

Rosemont, Ill. — A multifaceted intervention enabled a large health system to increase compliance with evidence-based guidelines for venous thromboembolism prophylaxis, according to Dr. Valerie Allusson, director of inpatient medical services at Atlantic Health, Morristown, N.J.

Although the health system has not yet reached all of its quality benchmarks, compliance has risen substantially as the result of measures such as the creation of a physician order set and daily monitoring of compliance, Dr. Allusson reported at the Joint Commission national conference on quality and patient safety.

Atlantic Health’s 504-bed Overlook Hospital was one of 41 hospitals to complete a 6-month Joint Commission-sponsored pilot study of VTE quality measures in 2006-2007. Following the pilot, Atlantic Health adopted VTE prevention and management as a systemwide quality goal and has spent the past 2 years focusing on VTE prophylaxis for medical and surgical patients at Overlook Hospital and the 629-bed Morristown Memorial Hospital.

VTE is 100 times more common in hospitalized patients than in the general population (Mayo Clin. Proc. 2001;76:1102), Dr. Allusson noted. She cited figures indicating that up to 2 million Americans experience VTE each year, and of these, 800,000 develop pulmonary thromboembolism (PTE), 600,000 develop pulmonary embolism (PE), and 300,000 die from PE (Lancet 1999;353:1386-9).

A baseline study of 100 randomly selected charts in one of Atlantic Health’s medical units showed that only 39% of patients received VTE prophylaxis.

The system implemented a quality improvement initiative based on recommendations from the American College of Chest Physicians (Chest 2004;126:338S-400S) and the National Consensus Standards for the Prevention and Care of Deep Vein Thrombosis developed by the National Quality Forum and The Joint Commission.

Areas of particular focus included risk assessment/prophylaxis within 24 hours of hospital admission and VTE written discharge instructions for patients on warfarin addressing follow-up monitoring, compliance issues, dietary restrictions, and potential drug reactions or interactions.

The system set a 6-month goal to conduct a VTE risk assessment and provide appropriate prophylaxis within 24 hours of hospital admission or surgery end time for 95% of all patients. A second 6-month goal was to reach 99% of patients who had “fallen through the cracks” and had been admitted without prophylaxis. “The goal was to get VTE assessment and prophylaxis ordered as often as possible at admission, but also on the floor, in transfer between units, or postoperatively,” Dr. Allusson said.

Toward these ends, a multidisciplinary steering committee developed a VTE prophylaxis order set with a standardized risk assessment, contraindications for prophylaxis, and a checklist of appropriate options. It also developed a prototype daily VTE prophylaxis outlier list to indicate, by room, patients who were and were not receiving acceptable medications (including arthrogastin, fondaparinux, heparin, and low-molecular-weight heparin, and warfarin). A sticker was placed at the front of outlier charts to alert physicians about patients who had not received prophylaxis.

As of June 2009, the system had surpassed its target of 95% for prophylaxis in ICU patients (90%) and overlap therapy (82%), and was continuing to work on the remaining goal of 95% for prophylaxis in medical/surgical patients (68%) and discharge instructions (79%). In an interview, Dr. Allusson noted that the 95% target for prophylaxis in medical/surgical patients was ambitious considering the baseline rate of only 39%.

The increase to 68% within 6 months represented significant progress, she said. The system also achieved a 3% decrease in in-hospital mortality related to VTE during this time, but whether the decline was due to the VTE quality improvement project is not known. Dr. Allusson attributed the progress to date in part to the frequent and routine sharing of data at every level of the organization, and to the multidisciplinary collaboration.

Efforts to systematize and streamline procedures related to VTE prophylaxis also helped. The new VTE prophylaxis order set, for example, allows physicians to document medications administered simply by checking the appropriate box. In addition, collaboration with information technology on such projects as the outlier report helped reduce the likelihood of human error.

In the future, the health system aims to develop a business plan for inpatient and outpatient anticoagulation management, include pharmacists in rounds to discuss anticoagulation issues and customized discharge instructions, create a unit performance tracking system, and establish mandatory prophylaxis order forms for all admissions.

Dr. Joseph Barney, FCCP comments: Applause for the motivation and efforts we read about from Dr. Allusson and all the staff involved in this project of process improvement. We live in a time of constant change in the delivery of health care in North America. Many health care dramatic changes have taken place to globally reorganizing their measures for mortality review and changing the paradigm of implementing core measures of health care, such as DVT/VTE prophylaxis in efforts to become part of the solution to our growing problems with health care costs and quality. Clearly, a model at Atlantic Health is an example of where we can go as institutions when there is collaboration and systematic oversight.
Announcing 2010: The Year of the Lung

BY DR. KALPALATHA K. GUNTAPALLI, FCPP

NEWS FROM THE COLLEGE

PRESIDENT’S REPORT

The announcement of life itself at birth by a loud cry has brought joy to millions from time immemorial. The tragedy of leaving this world with “last breath” has also dramatized the lungs more than any other organ in the body.

Then why has it taken so long for this organ to get its fair shake in modern times?

The heart has earned its place as the “heart of the...” “at the heart of it all,” “has no heart,” and “comes from the heart” in today’s popular usage.

What about the lungs that supply oxygen to the heart? When the New York Times published public education material on different organs in the body (May 13, 2008), lungs were conspicuously missing!

Is it then, as practitioners of lung health, that we have not done justice to bring the organ we care for so much to the public notice?

Grim Statistics

The readers are familiar with these numbers—lung disease is very common and accounts for 19% of total deaths and 15% of disability-adjusted life-years in the world.

Tobacco-related diseases kill 5 million people worldwide and 1.5 million from lung cancer.

Despite the staggering numbers of 9 million new cases in 2007 and 0.7 million deaths a year from TB, no new drugs have been developed for TB since the 1970s, and the only vaccine available is a century old.

Pneumonia kills 2 million children under 5 each year; more than 210,000 asthma deaths a year are attributable to lack of treatment; and COPD will become the third most common cause of death worldwide in the near future, and, yet, it is frequently underdiagnosed.

Each year, 250,000 to 500,000 people die of seasonal flu in the world; and when new strains strike, the morbidity and mortality can be very high.

While the attention of the entire world community is focused on lungs, such as during the current H1N1 pandemic, it fades as soon as the threat is over. Lung disease exacts a tremendous financial burden on the patient, caregiver, and society.

Nearly half of the world’s population breathes air that is polluted. Early lung disease detection methods, such as spirometry, are either not readily available or not utilized when available, making early detection a challenge.

Policies to regulate air quality are lagging. As of 2007, only 148 of the 193 World Health Organization member-states have ratified the Framework Convention on Tobacco Control.

2010: The Year of the Lung

That the year 2010 be designated as “The Year of the Lung” was proposed by the leading world respiratory associations to raise awareness of lung health and advocate for lung health globally.

The Forum of International Respiratory Societies (FIRS) has come together to declare “2010: The Year of the Lung” (YOL). FIRS comprises the American College of Chest Physicians (ACCP), American Thoracic Society (ATS), European Respiratory Society (ERS), Asociación Latinoamericana de Torax (ALAT), Asia Pacific Society of Respiratory (APSR), and International Union Against Tuberculosis and Lung Diseases (IUAATLD).

As a group of respiratory and public health experts from around the globe, we want to engage our partners to raise the awareness of the deep impact of lung diseases worldwide. We eventually want policymakers to increase funding for lung disease research, enact smoking cessation legislation, support preventive measures, and support air quality legislation.

Objectives of 2010: The Year of the Lung

1. Promote global awareness of lung health issues and diseases.
2. Increase funding for lung health research.
3. Develop and implement tools to prevent lung disease and disability.
4. Diagnose and treat lung disease early in the course of illness.
5. Research new diagnostic tools and medicines to treat and cure lung disease.
6. Encourage programs that promote personal lung health (smoking cessation, lung hygiene, protective masks, flu vaccine).

The ACCP and 2010: The Year of the Lung

For the past 75 years, the ACCP has been committed to the prevention and treatment of diseases of the chest. This commitment, combined with the persistent efforts of 17,500 members in more than 100 countries, has helped disseminate ACCP’s valuable lung health programs, initiatives, and education materials to reach countless patients and families in need.

The ACCP motto for 2010: YOL is “From Prevention to Intervention.” As part of 2010: YOL, the ACCP will encourage worldwide lung health from “prevention to intervention,” with core initiatives focusing on the areas of tobacco prevention, as well as the diagnosis and management of COPD and lung cancer.

The ACCP will coordinate with all national and international members to integrate YOL messages and promote YOL initiatives, including targeted Web pages that highlight ACCP clinical and patient tools and education material.

What Are We Doing Now?

Tobacco Prevention: For the last decade, members of the ACCP (www.chestnet.org) and The CHEST Foundation (www.chestfoundation.org), the ACCP’s philanthropic arm, have delivered the Foundation’s Lung Lessons program to schoolchildren across the United States and around the world. As part of the program, students learn how to keep their lungs healthy and about the dangers of tobacco use from ACCP members and patient advocates of the College.

Each year, the ACCP organizes a special education program for schoolchildren in the host city during the College’s annual meeting. The next Lung Lessons school outreach event will take place in November 2010 in Vancouver, BC, Canada, coincident with the ACCP CHEST 2010 annual meeting.

Beyond the Lung Lessons program, the ACCP and The CHEST Foundation will showcase and distribute the ACCP Evils of Tobacco, a culturally sensitive CD-ROM-based program that illustrates the severe hazards of tobacco use. The program, which includes talking points and material for presenters, has been developed in seven languages and has already been shared with thousands of children around the world.

The program “Ant E’ Tobacco,” which includes a cartoon video, cartoon book, and coloring book for elementary schoolchildren, has been presented to more than 20,000 children in Texas.

COPD: Through its regional COPD education program, COPD: What Really Works, A Best Practices Workshop for Primary Care, the ACCP will provide pertinent COPD screening, diagnosis, and treatment information to primary care health clinicians. In 2010, the programs will be hosted in 20 major markets around the country and will be a timely vehicle for spreading the YOL messages, especially as they relate to COPD.

Lung Cancer: The ACCP publishes Diagnosis and Management of Lung Cancer, one of the leading evidence-based guidelines in lung cancer diagnosis, staging, and management.

Throughout the 2010: YOL, the ACCP will build on the strong foundation of the guidelines to increase awareness regarding lung cancer prevention, diagnosis, and management. The ACCP also will provide education material for clinicians, patients, and patient families regarding critical care units and end-of-life and critical care family assistance.

I invite your active participation to take this campaign to your neighborhood and welcome any comments or suggestions.

ACCP President, Dr. Guntupalli, signs the declaration of “2010: The Year of the Lung,” which was signed by the FIRS members organizations.
On January 2, 2010, the American College of Chest Physicians unveiled its redesigned Web site. More than 2 years in the making, the redesign combines best practices in interface design and member feedback, with the goal of providing a powerful resource for the members and others.

This combination provides a singular focus for the Web site, creating a polished showcase of most everything the ACCP has to offer.

Among the changes are the following:
- A clear organization of content into three major groups: News, Events, and Resources.
- A homepage that is always updated with the newest offerings from the ACCP.
- A vastly improved search engine, which makes finding relevant content easier than ever.
- Cross-site linking that puts related content at your fingertips.
- Three weekly updates of full news articles and daily updates of relevant news feeds.
- Regular blog postings, starting with It Ain’t Rocket Surgery, written by CHEST Executive Editor Steve Welch.
- Monthly education content created by the ACCP NetWorks.
- New opportunities to earn CME through multimedia tools.
- A new events calendar that can be synced to your iCal®.

This is just a sample of the features the ACCP will be rolling out for its family of Web sites over the next year. As your needs grow and change, this new site will allow the ACCP to meet those needs. Please contact the ACCP with your questions and concerns at techsupport@chestnet.org.

**www.chestnet.org**

**BY KEITH SENKOWSKI**
Digital Media Solutions Manager

On January 2, 2010, the American College of Chest Physicians unveiled its redesigned Web site. More than 2 years in the making, the redesign combines best practices in interface design and member feedback, with the goal of providing a powerful resource for the members and others.

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**This Month in CHEST: Editor’s Picks**

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

**TOPICS IN PRACTICE MANAGEMENT**
- Specialists/Subspecialists and the Patient-Centered Medical Home. By Dr. N. Kirschner; and Dr. M. S. Barr.

**ORIGINAL RESEARCH**
- Cardiovascular Events Associated With Ipratropium Bromide in COPD. By Dr. S. S. Ogale et al.
- Cardiovascular Safety of Tiotropium in Patients With COPD. By Dr. B. Celli et al.

**G/W EDITORIAL**
- Anticholinergic Drugs for the Treatment of COPD Are Safe ... Are They? By Dr. K. F. Rabe.

- Use of Epidermal Growth Factor Receptor/Kirsten Rat Sarcoma 2 Viral Oncogene Homolog Mutation Testing To Define Clonal Relationships Among Multiple Lung Adenocarcinomas: Comparison With Clinical Guidelines. By Dr. N. Girard et al.

- Cost and Outcomes of Patients With Solitary Pulmonary Nodules Managed With PET Scans. By Dr. P. G. Barnett

**COMMENTARY**
- An Approach to Interventional Pulmonary Fellowship Training. By Dr. C. R. Lamb et al.

**Where Others See a Wall**

**We See a Way**

**INTERMUNE**
Working hard for IPF patients

For more than a decade, InterMune has been focusing its resources on an unmet medical need in pulmonology: Idiopathic Pulmonary Fibrosis (IPF), a progressive and fatal lung disease for which there is no approved therapy in the United States or Europe. By funding clinical research and supporting the development of innovative therapies, we are doing more than contributing to the understanding and treatment of IPF. We’re working hard to create a better future for IPF patients.

For more information, go to www.intermune.com
Healthy Sleep in Teens and Antibiotics Delivery in CF

Allied Health

Project SIESTA Promotes Healthy Sleep Habits in Teens

Lata Casturri, RPSTG, a senior sleep technologist at the Baylor College of Medicine (BCM) Sleep Center and an Allied Health NetWorks member, has been instrumental in guiding an extraordinary community service project that has brought a much needed awareness to the issue of healthy sleep habits for teenagers.

The impetus for the project originated when Anita Rao, a 7th grader, decided to do a science fair project about sleep. She approached Lata and, with input from Dr. Shyam Subramanian, FCCP, the Medical Director of the BCM Sleep Center, they formulated a comprehensive questionnaire that queried the bedtime and sleep habits of early teenagers, as well as their use of electronic media close to bedtime. Anita single-handedly coordinated the administration of this questionnaire to more than 100 middle-school students. The results showed a high prevalence of poor sleep hygiene, primarily due to a technology invasion of the bedroom environment in the early teenagers and a negative correlation with the daytime alertness of these students. Anita won first prize at the district science fair in recognition of her efforts.

Taking these results as a call to action, Lata suggested that Anita start a community education campaign to promote healthy sleep habits among teenagers. The results have been extraordinarily effective and rewarding.

Under the mentorship of Lata, a team of six girls and two boys designed themselves as the project SIESTA (Students Involved in the Education about Sleep hygiene for Teen Adolescents). In 4 months, the School Board endorsed Project SIESTA. The mayor of Houston, Bill White, declared October 30 as Healthy Sleep Day. The project team is promoting their message in many schools in the Houston area. The project has attracted national attention, and Anita Rao presented the findings of the group at the ACCP-Sleep Institute meeting at CHEST 2009.

Dr. Kalpalatha K. Guntupalli, FCCP, ACCP President and Chief of Pulmonary, Critical Care, and Sleep section at BCM, says, “It is very gratifying to note that the BCM Sleep Center has been a resource for the Houston community youngsters and schools in promoting healthy sleep habits early in life.” The project is featured on an informational Web site at www.projectsiesta.com.

Chest Infections

Is it Just “the Bug” or Is There a Missing Link?

The 2009 Pandemic Influenza A (H1N1) Virus Hospitalizations Investigation and Caring study published its first report on the clinical characteristics of patients who were hospitalized with 2009 H1N1 influenza in the United States from April 2009 to mid-June 2009 (Jun et al. N Eng J Med 2009; 361(20):1935. Epub 2009 Oct 8). It is the first comprehensive report and suggests the following two interesting points.

A high percentage of hospitalized patients with H1N1 (>73%), specifically children (60%), had at least one underlying medical condition predisposing them to severe illness. This is in comparison with 31% to 43% of children who were hospitalized with seasonal flu as mentioned in their report. This observation suggests that this novel virus is not any more virulent than the seasonal flu or may even be less virulent, so far, considering the fact that severe illness is more likely with seasonal flu infection than with H1N1 in the individual/child is otherwise healthy.

The other important point is that hospitalized patients with H1N1 have a much higher prevalence of obesity, particularly morbid obesity (defined by BMI equal to or greater than 40 in adults only), compared with the general population. It was reported that morbid obesity prevalence was five times greater in these hospitalized patients than in the general population. We will learn more about this H1N1 pandemic as more reports are published. In the meantime, early initiation of antiviral therapy should be prompt, along with supportive care, as initiation of the antiviral treatment within 2 days of the onset of influenza-like illness was the only treatment significantly associated with a positive outcome among hospitalized patients in this study. It is, nevertheless, time to acknowledge the significance of obesity not only as it relates to our health-care system but also to the current H1N1 epidemic and to question ourselves: Is it just “the bug,” or is there a missing link?

New Antibiotic Formulations

A pitfall in the treatment of chronic lung infection in cystic fibrosis and bronchiectasis is the inability of systemic antibiotics to penetrate into the affected areas. There is currently one US Food and Drug Administration-approved antibiotic formulation in cystic fibrosis, tobramycin solution for inhalation, which has also been used in the above diseases. Nebulization requires significant time, and intolerance, although uncommon, occurs in some patients.

However, recent research led to the development of antibiotic formulations for inhalation in both cystic fibrosis and bronchiectasis. These formulations are in different stages of clinical trials in both diseases and, if found effective, will be available for patient use. Most of these formulations consist of known antibiotics with improved efficient delivery or improved half-life, requiring fewer daily treatments.

Dry powder inhalation can lead to decreased time of administration. This method is used by tobramycin inhalation powder, which is currently in phase 3 trials (Geller et al. Pediatr Pulmonol 2007;42(4):307) and by inhaled ciprofloxacin, which is in phase 2 trials. An efficient nebulizer device has been used for aztreonam lysinate for inhalation and has successfully completed two phase 2 trials in cystic fibrosis and a phase 2 trial in bronchiectasis.

(Betesh Borgotar GZ et al. Chest 2009; 135(5):1223; and McCoy KS et al. Am J Respir Crit Care Med 2008;178(9):921). It is also used for nebulized levofloxacin in phase 2 trials. Another approach uses liposomes to deliver medication deep into the lungs, releasing it in a controlled fashion, leading to once-daily administration. It has been used by liposomal amikacin in a phase 2 trial. These medications could lead to a dramatically different form of care for patients with bronchiectasis and cystic fibrosis, resulting in better control of chronic infection, fewer exacerbations, less lung function decline, and improved compliance.

Denis Hadjislihidis, MD, MHS, FCCP
Steering Committee Member

Note: Dr. Hadjislihidis has participated, or is currently participating, as a local principal investigator in multicenter clinical trials involving aztreonam lysinate for inhalation (AZLI; Gilead Pharmaceuticals) and inhaled ciprofloxacin (Bayer Pharmaceuticals).

Clinical Pulmonary Medicine

Recognizing Obesity Hypoventilation Syndrome

Obesity hypoventilation syndrome (OHS) has been defined as obesity (BMI >30) associated with hypoventilation (awake arterial carbon dioxide tension (PaCO2)>45 mmHg not attributed to other obvious causes, such as hypo-thyroidism, kyphoscoliosis, or severe COPD. The syndrome has been recognized for more than 50 years, but the significant morbidity and mortality associated with this syndrome has only recently been appreciated.

It is important to note that OHS is not obstructive sleep apnea (OSA). Though the majority of patients with OHS has OSA, the diagnosis associated with the diagnosis of OHS appears to be significantly worse than that of OSA. Although comparative studies are lacking, reported mortality associated with OHS ranges between 5% at 18 months, in patients highly adherent to therapy, to 23% at 18 months, in patients not receiving appropriate therapy. This significant mortality associated with OHS far exceeds that associated with OSA.

Diagnosis of OHS requires a measurement of PaCO2. At this time, direct measurement with arterial blood gas (ABG) testing is the accepted standard. Dr. Littleton and Dr. Mokhlesi compiled available epidemiologic data and report that patients with OHS tend to be severely obese (BMI equal to or greater than 40), hypertensive, and, if diagnosed with OSA, have an apnea-hypopnea index > 30 (Clin Chest Med 2009;30(3):467). The diagnosis of OHS should be sought after in this patient population; however, less obese patients and patients without OSA may also develop OHS.

The disconnect associated with ABG testing often causes physicians to seek alternate diagnostic options. Elevated serum bicarbonate levels and awake hypoxemia are strongly suggestive of OHS in the appropriate clinical setting but are not specific for the hyperventilation necessary to diagnose the disorder. Transcutaneous capnometry is a promising tool but, as of yet, has not been utilized in the diagnosis of OHS. Thus, given the current reliable and readily available tests, ABG testing remains the gold standard for diagnosis and needs to be utilized.

Treatment of OHS is primarily aimed at treating the associated sleep-disordered breathing, usually present in the form of OSA.

Thus, continuous positive airway pressure (CPAP) is often part of the treatment plan. Since many patients with OHS require high CPAP pressures to address their OSA, CPAP intolerance becomes a significant concern. In that case, bilevel PAP therapy should be the next therapeutic consideration. Bilevel PAP may also be used to treat the hypoxemia that sometimes persists in these patients, despite adequate CPAP therapy for underlying OSA.

In patients with OHS without concomitant OSA, bilevel PAP may be used to address their sleep-related hypoventilation.

Philip Alapat, MD, FCCP
Steering Committee Member
Snapshots of CHEST 2009


A Resounding Success

The CHEST Foundation and the ACCP Industry Advisory Council 2009 Community Outreach Event

On Monday, November 2, 2009, more than 40 ACCP- and Ambassadors Group-member volunteers attended a training session to learn about the school and receive tips on working with children before boarding a bus to Sycamore Canyon Elementary School in Santee, California.

Located in a suburb east of San Diego, the school is uniquely designed wherein there are no interior hallways. Taking advantage of San Diego’s mild climate, the 370 students, in grades preschool to grade 6, assemble each morning in the open courtyard of the school for the “Pledge of Allegiance” and general school announcements and proceed to their classrooms.

The superintendent and school principal greeted the volunteers at the general school assembly and then volunteers and children in grades 3 to 6 filed into their various classrooms to learn the facts about their lungs, asthma, and the dangers of smoking. A variety of educational tools were used to illustrate the anatomy of the lung, a healthy and diseased lung that could be pumped up so children could see the difference, and the cumulative effect of smoking one pack of cigarettes a week for 1 year in the notable “jar of tar.” At the end of the lesson, the children were encouraged to sign the “I will never smoke” poster mounted on the wall of each classroom.

The ACCP Industry Advisory Council gave the Santee School District Foundation $10,000 to support educational programs for the children in the school district. This grant will be used to enhance after-school enrichment programs and purchase new laptop computers to replace the outdated computers in the elementary school classrooms.

PCCU Lessons for January 2010

- Respiratory Airway Medications: Select Toxicities and Drug Interactions
  By Raymond Y. Ho, PharmD

- Biostatistics and Epidemiology for the Clinician
  By Dr. Arnold M. Schwartz, FCCP
NEWS FROM THE COLLEGE

FCCP CONNECTIONS
A Father and Son Story Not To Be Missed

BY PAMELA L. GOORSKY
Assistant Vice President, Editorial Resources

Dr. Ari Ciment, FCCP sent a short e-mail to the ACCP just before CHEST 2009 asking if there would be any other father/son FCCP duos attending the CHEST meeting. After a little investigating, and speaking with the junior Dr. Ciment, I found that not only are he and his father an enthusiastic pair, but they have a unique story linking them to the ACCP in more ways than one.

As Ari took part in the Convocation Ceremony and became an FCCP at CHEST 2009, his father, Dr. Lawrence Ciment, FCCP, proudly watched from the audience. Years earlier, “Larry” Ciment trained in pulmonary/critical care with Dr. Marvin Sackner, FCCP, at Mt. Sinai Hospital in Miami Beach and was examined his father’s slide. Ari, too, was able to “weasel” his way into the waiting for the pathologist’s report. Ari, too, was able to “weasel” his way into the frozen section room as the pathologist examined his father’s slide.

He continues, “I reminded the pathologist of all the possible benign diagnoses. The pathologist squealed, ‘I’m sorry son, but this looks like metastatic adenocarcinoma of the lung.’ At this point, I still didn’t give up and said, ‘But the epithelium does look unusual for lung cancer.’ He replied that there did seem to be some elements that resembled the salivary tissues. A light-bulb went off in my head, and I joyfully exclaimed, ‘Perhaps this is a remnant of a somewhat benign jaw tumor my father had 29 years before!’ The pathologist looked at me and incredulously remarked, ‘I’ll keep that in my differential diagnosis.’” Delivering his first-ever diagnosis of lung cancer to a patient, Ari had to disclose the findings to his own father.

But wait . . . there is more to this story. As Ari tells it, at the postpathology review with the “gray-haired” chief pathologist who systematically reviewed all slides for a final diagnosis, an unbelievable thing happened. The pathologist noted cells typical of metastatic adenocarcinoma of the lung, but he then continued, “But upon closer review, I haven’t seen this tumor but one other time, 29 years ago when, as a chief resident here at Mount Sinai, I made the diagnosis of ameloblastoma in your father! If he lived with it for 29 years, there is no reason to believe he won’t live with it for another 29 years.”

The father and son together submitted the case report to CHEST, and it was published in April 2002 (CHEST 2002;121[4]: 1359-1361). Dr. Larry Ciment is alive and well today.

In ending my conversation with Ari, I asked him why he decided to become an FCCP just as his father did years ago. He replied, “I believe that in order to excel in his field, I have to be involved in the society that harbors the top clinicians and educators of our era.” Thank you, Drs. Ciment!
CHEST Physician Welcomes New Editorial Advisory Board Members

Dr. Joseph Barney, FCCP, is Assistant Professor, Pulmonary and Critical Care Medicine, at the University of Alabama at Birmingham (UAB), Birmingham, AL. He is the Director of the Department of Resuscitation at UAB and the Associate Director of the Medical Intensive Care Unit at the University of Alabama. Dr. Barney is also the Director of the Multidisciplinary Sarcoisosis Clinic at The Kirklin Clinic at UAB. He serves as core clinical faculty in the Department of Medicine at UAB, and he is intimately involved in resident and fellow training. Among his clinical and research interests are sarcoidosis, lung transplantation, interstitial lung diseases, and critical care medicine.

Dr. Jun R. Chiong, FCCP, is an Associate Professor of Medicine and the Medical Director of the Cardiomyopathy Program at Loma Linda University, Loma Linda, CA. Dr. Chiong completed his residency at the University of Illinois at Chicago Medical Center, Chicago, IL, and is currently doing his fellowship in cardiology at the University of Florida Health Science Center in Jacksonville, FL, serving as Chief Fellow during his final year. He was elected Chair of the ACCP Cardiovascular and Surgery Network for 2010.

He is a recipient of two Young Investigator Awards, one from the ACCP and the other from the Florida Chapter of the American College of Cardiology.

Dr. Stephen K. Field, FCCP, is a specialist in respiratory medicine and a Clinical Professor in the Department of Medicine, Division of Respiratory Medicine, at the University of Calgary, Calgary, AB, Canada. In addition to maintaining a large general respiratory consultative practice, he has also worked in the asthma/COPD and cystic fibrosis clinics at the university. He was a cofounder of the Calgary COPD & Asthma Program and the University of Calgary idiopathic pulmonary fibrosis/interstitial lung disease interest group. He has participated in numerous clinical trials in asthma, COPD, the role of gastroesophageal reflux in respiratory disease, lower respiratory tract infection, and mycobacterial disease, and he has published more than 60 papers on a variety of topics in respiratory medicine.

Dr. Carl A. Kaplan, FCCP, is a Professor of Internal Medicine at Saint Louis University School of Medicine and a member of the Respiratory Care and Sleep Medicine, St. Louis, MO, where he is the Associate Director of the Fellowship Program. He is the Medical Director of Respiratory Care and Bronchoscopy Services at Saint Louis University Hospital, in addition to being the Director of the Interventional Pulmonary and Procedural Services and Minimal Invasive Thoracic Oncology Program. Dr. Kaplan is the Chair of the ACCP Respiratory Care Network Steering Committee and member of the ACCP-Critical Care Institute, and he is past Chair of the Critical Care NetWork Steering Committee. His interests are in the areas of critical care medicine, mechanical ventilation, respiratory care, bedside ultrasound and echocardiology, and medical education.

New Editor and Deputy Editor Announced for Pulmonary Perspectives

Dr. Marilyn Foreman, FCCP, is the new Editor for Pulmonary Perspectives. She is an Associate Professor of Medicine at Morehouse School of Medicine in Atlanta, GA. Dr. Foreman is a Fellow of the ACCP and has participated in the ACCP as a member of the CHEST Program Committee, the Basic Science Subcommittee, the Scientific Presentations and Awards Committee, and the Cultural Diversity in Medicine Network Steering Committee. At Morehouse School of Medicine, Dr. Foreman has held a variety of administrative and supervisory roles in the Department of Medicine. Though she continues to participate in resident education, her primary focus is research on the genetics of COPD and tobacco-related health disparities, serving as a PI on several associated research trials and grants.

Dr. Loren Harris, FCCP, is the new Deputy Editor for Pulmonary Perspectives. He is Chairman of the Department of Surgery and the Director of the Division of Thoracic Surgery at Richmond University Medical Center in Staten Island, NY, and an Associate Professor of Surgery at New York Medical College. He has a multitude of national and international publications and presentations and is an investigator in several ongoing multicenter trials within the field of thoracic oncology. Dr. Harris is a Fellow of the ACCP and Vice-Chair of the ACCP Marketing Committee. He is a member of the advisory board of the American Cancer Society, Staten Island Region and continues to participate in several outreach programs on Staten Island for smoking cessation and lung cancer awareness education.

Special Note: The ACCP would like to acknowledge Dr. Gene Colice, FCCP, for 3 years of outstanding service as Editor of Pulmonary Perspectives. The articles that he secured for publication in this section of CHEST Physician have been of great interest to our readers, and it is no small task to get a 1,400-word paper from an expert in the field to reach and every month. Thank you for a job well done, Dr. Colice!
Awards and Honors Presented at the 2009 Convocation Ceremony

- College Medalist Award
  - Richard S. Irwin, MD, Master FCCP
- Presidential Citation Honor Lecture
  - Stephanie M. Levine, MD, FCCP
- Roger C. Bone Memorial Lecture
  - J. Randall Curtis, MD, MPH, FCCP
- Margaret Pfrommer Memorial Lecture in Long-term Mechanical Ventilation
  - Nicholas S. Hill, MD, FCCP
- Pasquale Ciaglia Memorial Lecture in Interventional Medicine
  - Ko-Pen Wang, MD, FCCP
- Edward C. Rosenow III, MD, Master FCCP/Master Teacher Honor Lecture
  - Mark J. Rosen, MD, FCCP
- MasterFellow Award
  - Richard S. Irwin, MD, Master FCCP
  - Dario Olivieri, MD, Master FCCP
- Alfred Soffer Award for Editorial Excellence
  - Loren J. Harris, MD, FCCP
- Glenn S. Tillotson, PhD, FCCP
- Alton Ochsner Award Relating Smoking and Health
  - Steven A. Belinsky, PhD
- Canadian Thoracic Society Christie Memorial Lecture
  - Arthur S. Slutsky, MD
- The CHEST Foundation Clinical Research Award in Women’s Health
  - Ghada R. Bourjeily, MD, FCCP
- CTS/Institute of Circulatory and Respiratory Health Distinguished Lecture in the Respiratory Sciences
  - James G. Martin, MD
- Roger C. Bone Advances in End-of-Life Care Award
  - Graeme Martin Rocker, MBChB, FCCP
- American College of Chest Physicians and The CHEST Foundation Grants in Venous Thromboembolism (VTE)
  - Elie A. Aki, MD, PhD, MPH
  - Timothy A. Morris, MD, FCCP
- Association of Specialty Professors and The CHEST Foundation of the ACCP Geriatric Development Research Award
  - Kathleen M. Akgun, MD
- The CHEST Foundation and the LUNGevity Foundation Clinical Research Award in Lung Cancer
  - Johann C. Brandes, MD, FCCP
- Alpha-1 Foundation and The CHEST Foundation Clinical Research Award in COPD and Alpha-1 Antitrypsin (AAT) Deficiency
  - Robert M. Reed, MD
- The CHEST Foundation California Chapter Clinical Research/Medical Education Award
  - Vivam S. Nair, MD
- Third Eli Lilly and Company Distinguished Scholar in Critical Care Medicine Award
  - Steven Q. Simpson, MD, FCCP

Sponsored Courses

- **January 28 - 31**
  - Sleep Medicine 2010
    - Scottsdale, AZ
- **April 30 - May 2**
  - Ultrasonography: Fundamentals in Critical Care
    - Austin, TX
- **August 25 - 28**
  - Guidelines International Network Conference 2010
    - Chicago, IL
- **August 27 - 30**
  - ACCP Pediatric Pulmonary Medicine Board Review 2010
    - Orlando, FL
- **August 27 - 30**
  - ACCP Sleep Medicine Board Review 2010
    - Orlando, FL
- **August 27 - 31**
  - ACCP Critical Care Medicine Board Review 2010
    - Orlando, FL
- **August 31**
  - Lung Pathology 2010
    - Orlando, FL
- **August 31**
  - Mechanical Ventilation 2010
    - Orlando, FL
- **September 1 - 5**
  - ACCP Pulmonary Medicine Board Review 2010
    - Orlando, FL
- **October 30 - November 4**
  - CHEST 2010
    - Vancouver, BC, Canada
- **February 12-14**
  - Basic and Advanced Bronchoscopy Skills With a Focus on Endobronchial Ultrasound
- **February 19-21**
  - Critical Care Bundle
- **February**
  - METI iStan Course
- **March 26-28**
  - Difficult Airway Management
- **May**
  - Human Patient Simulator
- **June 11-13**
  - Critical Care Bundle
- **July 23-25**
  - Difficult Airway Management
- **June 25-27**
  - Mechanical Ventilation
- **July 30 - August 1**
  - Basic and Advanced Bronchoscopy Skills With a Focus on Endobronchial Ultrasound

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D. Robert McCaffree, MD, Master FCCP Humanitarian Award Recipients

- $15,000 Project Development Grant Recipients
  - Nicola A. Hanania, MBBS, FCCP
  - Anmoor Sanatorium for Chest Diseases
    - Mafraq, Jordan
  - Stephen M. Winter, MD, FCCP
  - Sustainable Health Promotion for the Indigenous Populations of the Northern Amazon Basin
    - Iquitos, Loreto, Peru
- $5,000 Humanitarian Award Recipients
  - Henri G. Colt, MD, FCCP
  - Community Based Educational Program for Lung Cancer Awareness and Smoking Cessation
    - La Paz, Sucre, and Cochabamba, Bolivia
  - Don Hayes, Jr., MD, FCCP
  - University of Kentucky Salvation Army

Pulmonary Clinic
Lexington, Kentucky

Subhakar Kandi, MD, FCCP
Care and Support Foundation for Children
Hyderabad, Andra Pradesh, India

$5,000 Ambassadors Group Humanitarian Award

- Martin L. Bauer, MD, FCCP
  - Child Care and Conference for Parents Support Group of the Arkansas Center for Technology-Dependent Children
  - Little Rock, Arkansas
Attendees Were “Winners All” at CHEST 2009

Our CHEST 2009 attendees were all winners, as they were the first to “Experience ACCP” and first to encounter the newly structured and named “Clinical Resource Center.”

The attendees were rightfully awarded with innovations, education, and practice solutions, including robust presentations, experts on-hand for discussions, new products and initiatives, and, of course, CHEST t-shirts.

Convocation brought forth award winners in medicine and science, as did The CHEST Foundation Awards Program.

The Attendees Were Rightfully Awarded With Innovations, Education, and Practice Solutions, Including Robust Presentations.

And then, there were winners in several contests held during CHEST. The following companies won the best educational activity in their cluster in the Clinical Resource Center:

- Airways
  Merit Medical Endotek
- Cardiovascular (There was a tie.)
  Actelion Pharmaceuticals US, Inc.
  Gilead Sciences, Inc.
- Critical Care
  Edwards Lifesciences
- Professional Development
  The France Foundation
- Sleep
  Philips Respiration
- Telemedicine and E-health
  ACCP/HIMSS IT Showcase

The bingo winners at CHEST 2009 received a $75 ACCP educational product gift certificate:

- CHEST Bingo (Monday)
  Sara Ghendehari, MD - Los Angeles, CA
  Allen Goldberg, DDS - Frankfort, IL
  Robert Goodman, MD - Los Angeles, CA
  Fernanda Paulino, MD - Belo Horizonte, Brazil
  Christopher Spradley, MD, FCCP - Temple, TX
- COPD Bingo (Tuesday)
  Linda Tan, MD, FCCP - Loma Linda, CA
  Alison Kole, MD, MPH - Los Angeles, CA
  Abdul M. Memon, MD, FCCP - Louisville, KY
- PAH Bingo (Wednesday)
  John Baron, MD, FCCP - Geneva, OH
  Jeffrey Rymuza, MD, FCCP - Warner Robins, GA
  Goutham Dronavalli, MD, MBBS - Louisville, KY
  Patricia A. Smith, MSN - Gaines, MI
- William Schoenhöld, MD - San Diego, CA
  Bingo was supported by Actelion Pharmaceuticals US, Inc.; Astra-Zeneca LP; CSL Behring; Hill-Rom; KCI; Talecris Biotherapeutics; The CHEST Foundation; United Therapeutics and LungRx; and Wyeth Pharmaceuticals.

We had many abstract and case report winners, and you can view the names of these winners at www.chestnet.org/CHEST/program/about/winners.php.

Plus, our CHEST Challenge Championship awarded the grand prize to the National Capital Consortium team from Bethesda, MD.

Everyone who participated in the 2009 Walk/Run was a winner, and the best times in each of the many categories are far too numerous to list here.

We congratulate and thank everyone who participated.

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Rapid identification of bloodstream pathogens with PNA FISH can help physicians improve antimicrobial selection and has been shown to:

- Reduce mortality rates for S. aureus bacteremia
- Improve time to appropriate therapy for E. faecium bacteremia by 1.8 days
- Reduce mortality rates for E. faecium bacteremia
- Improve antifungal selection for candidemia
- Reduce unnecessary vancomycin use, LOS and costs due to blood culture contamination

Species Distribution in Positive Blood Cultures

<table>
<thead>
<tr>
<th>Gram Stain - Dilemma</th>
<th>Species</th>
<th>% of Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPCC (55%)</td>
<td>S. aureus</td>
<td>25%</td>
</tr>
<tr>
<td>Infection vs. Contamination</td>
<td>Coagulase-Negative Staph</td>
<td>75%</td>
</tr>
<tr>
<td>GPCC (15%)</td>
<td>E. faecalis</td>
<td>40%</td>
</tr>
<tr>
<td>Ampicillin and</td>
<td>E. faecium</td>
<td>25%</td>
</tr>
<tr>
<td>Vancomycin Resistance</td>
<td>Streptococcus sp.</td>
<td>35%</td>
</tr>
<tr>
<td>GNR (20%)</td>
<td>E. coli</td>
<td>35%</td>
</tr>
<tr>
<td>P. aeruginosa vs. non-P. aeruginosa</td>
<td>K. pneumoniae</td>
<td>20%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>Other GNRs</td>
<td>30%</td>
</tr>
<tr>
<td>Yeast (25%)</td>
<td>C. albicans</td>
<td>50%</td>
</tr>
<tr>
<td>Echinocandin vs. Fluconazole</td>
<td>C. glabrata</td>
<td>25%</td>
</tr>
<tr>
<td>C. parapsilosis</td>
<td>Other Candida sp.</td>
<td>15%</td>
</tr>
<tr>
<td>Other (15%)</td>
<td></td>
<td></td>
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SLEEP MEDICINE

Urine Test May Help Identify Kids With OSA

BY TERRY RUDD
Elsevier Global Medical News

Proteins detectable in urine may offer a relatively simple screening target to identify children with obstructive sleep apnea, a study of 120 children suggests.

Abnormal levels of at least three of four proteins identified by the researchers proved to be 95% sensitive and 100% specific for obstructive sleep apnea (OSA) in young children aged 2-9 years.

Up to 3% of children have obstructive sleep apnea, which is characterized by habitual snoring and partial or complete upper airway obstruction. Differentiating those children from the 10%-12% of children who have primary snoring, but not OSA, requires challenging and expensive overnight sleep studies.

"Development of noninvasive biomarkers capable of reliably distinguishing children with [primary snoring] from those with OSA would greatly facilitate timely screening and diagnosis of OSA in children," noted Dr. David Gozal, FCCP, of the pediatrics department at the University of Chicago and his associates (Am. J. Respir. Crit. Care Med. 2009;180:1253-61).

The researchers studied 90 children referred to a pediatric sleep medicine center in Louisville, Ky., for evaluation of habitual snoring and suspected sleep-disordered breathing. A total of 60 children met polysomnographic and clinical criteria for OSA, while 30 had primary snoring. The study authors also included as controls 30 children who didn’t snore and had no history of chronic or acute disorders.

The investigators used two-dimensional differential in-gel electrophoresis to assess protein expression in urine and identify proteins that were altered in the children with OSA.

In children with obstructive sleep apnea, levels of 12 urinary proteins differed from those in children with primary snoring or in controls. The investigators focused on three proteins whose levels increased in OSA—urokinase-type plasminogen activator, uromodulin, and urocortin-3—and one protein whose levels decreased, kallikrein-1.

Abnormal levels of two or more of these four proteins predicted OSA with 100% sensitivity and 96.5% specificity. Abnormal levels of at least three of the proteins produced 95% sensitivity and 100% specificity.

What may link the four proteins to OSA? “It is reasonable to assume that the intermittent hypoxia and globally increased oxidative stress and inflammatory processes activated by OSA may lead to mild renal dysfunction,” the researchers noted.

Dr. Gozal serves on a Merck & Co. speakers bureau. Some of the other study researchers have received corporate funding to develop biomarker assays and to study pediatric sleep apnea.

Sleep Duration Associated With Type 2 Diabetes Risk

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Sleeping more or less than 7-8 hours a night was associated with a significantly greater risk of developing type 2 diabetes or impaired glucose tolerance, in a 6-year study of 276 adults.

The results “concur with a growing body of epidemiological evidence showing a U-shaped relationship between sleep duration and body weight, type 2 diabetes, coronary heart disease, and all-cause mortality,” wrote Dr. Jean-Philippe Chaput of Laval University, Quebec City, and his associates. The study is in press at Sleep Medicine (doi:10.1016/j.sleep.2008.09.016).

Among the 276 men and women (aged 21-64) in the current cohort study, 21% who slept an average of 6 hours or less a night and 19% of those who slept an average of 9 hours or more a night developed type 2 diabetes or impaired glucose tolerance (IGT) over a mean of 6 years, compared with 7% of those who slept an average of 7-8 hours a night.

After adjusting for confounding factors associated with sleep duration and/or type 2 diabetes/IGT, such as age, smoking habits, shift work, and vigorous physical activity, those who slept 6 hours or less a night had a 2.78 times greater risk of developing diabetes and those who slept 9 or more hours a night had a 2.54 times greater risk, compared with those who slept 7-8 hours; the differences were significant.

Sleeping less than 7-8 hours a night was associated with a significantly greater risk of developing diabetes and those who slept 9 or more hours a night had a 2.54 times greater risk, compared with those who slept 7-8 hours; the differences were significant.

Continued on following page
Probable RBD Common in Patients With Parkinson’s Disease

BY BRUCE JANCIN
Elsevier Global Medical News

San Diego — Marked racial differences exist in the prevalence of restless legs syndrome among adults, findings from a new study indicate.

The racial differences also have a gender overlay. Among men attending a primary care clinic for a wide range of reasons, restless legs syndrome (RLS) was twice as prevalent in non-African Americans as in African Americans. Among women, however, the racial disparity was even more striking: RLS was four times as prevalent in non-African American as in African American women, after adjustment for potential confounders, Dr. Ammar Alkhazna reported at CHEST 2009, the annual meeting of the American College of Chest Physicians.

Another noteworthy finding in the 190-patient study was that the overall prevalence of RLS in the primary care patient population, 23%, was far higher than in previous studies by other investigators, where rates of 3%-10% have typically been reported, observed Dr. Alkhazna of the University of Missouri, Kansas City.

“RLS is underdiagnosed,” he said. “The literature tells us more and more that we as doctors don’t do a particularly good job of detecting patients with RLS and treating them.”

The 103 African American and 87 non-African American study participants were attending a hospital primary care clinic in a multicultural, low-income, medically underserved area of Kansas City. They were interviewed one on one by personnel trained to use the Johns Hopkins Telephone Diagnostic Interview, a validated tool with 91% sensitivity and 93% specificity for the diagnosis of RLS.

A definite diagnosis of RLS was made in 12% of African Americans, among both men and women. Among non-African Americans, the diagnosis of RLS was definite in 40% of women and 29% of men, with an overall rate of 36%.

The explanation for the gender difference in RLS among non-African Americans is unclear, the researcher said.

However, women have higher rates of rheumatoid arthritis and iron deficiency, both of which are known risk factors for RLS.

Why the African American women did not have a higher rate of RLS than African American men also is unknown.

Restless Legs Syndrome Less Common in African Americans

BY SUSAN LONDON
Elsevier Global Medical News

Seattle — Half of patients with Parkinson’s disease meet criteria for probable rapid eye movement sleep behavior disorder, according to findings using a new screening tool.

What’s more, patients with probable rapid eye movement (REMS) behavior disorder are more likely to have other sleep disorders as well.

Studies using polysomnography or history suggest that REM behavior disorder (RBD) is prevalent in the Parkinson’s disease population, supporting the need for a screening tool, according to Dr. Rositsa Poryazova, a neurologist at the University Hospital Zurich.

Such a tool—the REM Sleep Behavior Disorder Screening Questionnaire—recently was developed and validated in Germany, she noted. But its performance among patients with Parkinson’s disease is unclear.

Dr. Poryazova and her coinvestigators surveyed randomly selected patients who were members of the Swiss Parkinson Association, a national Parkinson’s disease patient organization. The patients were asked to complete the questionnaire and to rate the frequency of sleep problems on scales ranging from 1 (never) to 5 (almost always). Dr. Poryazova presented the results at the annual meeting of the Associated Professional Sleep Societies.

Analyses were based on 417 patients who had idiopathic Parkinson’s disease, she reported. Fully 50% had a score of 3 or higher on the questionnaire, meeting the criterion for probable RBD.

Compared with their counterparts without probable RBD, the patients with probable RBD had significantly higher Epworth Sleepiness Scale scores (10.7 vs. 9.5) and had Parkinson’s disease for a significantly longer duration (11.1 vs. 9.6 years). Age, sex, scores for activities of daily living, and a levodopa-equivalent dose of medication did not differ significantly between groups.

Overall, 57% of patients reported having at least one sleep problem often or almost always.

Patients with probable RBD had significantly higher mean frequencies than did patients without probable RBD of nearly a dozen sleep problems, including talking or crying (2.9 vs. 1.8), restless legs syndrome symptoms (2.5 vs. 1.9), cursing or violence (1.9 vs. 1.2), nightmares (2.4 vs. 1.6), and hallucinations (2.0 vs. 1.4).

Discussing the findings, Dr. Poryazova acknowledged that a limitation of the questionnaire is its self-reported nature. “[Input] from the bed partner was allowed but not required,” she noted, as many patients simply did not have bed partners. Overall, about half of the patients used such input.

“Probable RBD in Parkinson’s disease patients is associated with various sleep disorders leading to higher arousability and sleep fragmentation,” she concluded.

“These disorders may play a role as a precipitating factor in the occurrence of RBD,” she said. In addition, “the higher frequency of concomitant sleep disorders leading to sleep fragmentation may result in increased daytime sleepiness in patients with probable RBD.”

Dr. Poryazova reported that she had no conflicts of interest in association with the study.

The overall prevalence of RLS in the primary care population was far higher than in previous studies.

Dr. ALKHAZNA
Prophylactic Brain Irradiation Results Mixed in NSCLC

BY PATRICIA WENDLING
Elsevier Global Medical News

CHICAGO — Prophylactic brain irradiation significantly reduces the likelihood of brain metastases in patients with non-small cell lung cancer, but offers no survival advantage and produces temporary declines in memory.

The lack of survival benefit runs contrary to a 5% improvement observed with PCI in small cell lung cancer.

DR. MOVSAS

They conducted a population-based randomized clinical trial of 7,357 high-risk patients undergoing spiral CT in the Netherlands and Belgium to determine whether assessing the volume and the volume-doubling time of such nodules could be used as the main criteria for deciding on further action.

NCIMF researchers considered a nodule significant if the volume was less than 50 mm³, if the volume was 50-500 mm³ but did not increase by 25% or more during the interval between scans; or if the nodules grew but the volume-doubling time was calculated to be 400 days or more, signaling slow growth.

Results of the first CT screen were negative for lung cancer in 5,987 subjects (79%) and positive in 119 (2%). The remaining 1,451 subjects with indeterminate results underwent repeat scanning 3 months later.

A total of 116 nodules in these subjects were found to have a volume-doubling time of more than 400 days. This was considered to be a negative result, and the subjects could avoid further work-up. In contrast, lesions that showed a faster doubling time were considered to be positive, and subjects with these lesions underwent further, usually invasive, assessment.

All the subjects were followed for another 2 years to track the development of cancer in any lesions. “We found that the chances of finding lung cancer on a CT scan at 3 months, 1 year, and 2 years after a negative first-round test were 0.1, 1 in 1,000, and 3 in 1,000, respectively,” Dr. van Klaveren and his colleagues wrote (N. Engl. J. Med. 2009;361:2221-9).

The study was supported in part by a grant from Roche Diagnostics and with computer software and work stations from Siemens Germany. Dr. van Klaveren reported receiving research support and travel grants from Eli Lilly & Co., Roche Pharmaceuticals, and Roche Diagnostics. Dr. Mulshine reported receiving consulting fees from Servier Pharmaceuticals, participating in being an inventor on patents involving molecular methods of lung cancer diagnosis.

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Voolumedoubling • from page 1

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**FURTHER MEASURES TO AVOID OR DISCONTINUE ADVERSE EVENTS**

- **Cardiovascular and cerebrovascular effects:**
  - Avoid use of PDE5 inhibitors, including tadalafil, in patients with severe hepatic cirrhosis (Child-Pugh Class C) or acute or chronic liver disease.
  - Avoid use of PDE5 inhibitors in patients with restrictive or congestive cardiomyopathy.
  - Patients with clinically significant aortic and mitral valve disease.
  - Patients with symptomatic coronary artery disease.

- **Otologic effects:**
  - Cases of sudden decrease or loss of hearing have been reported postmarketing in temporal association with the use of PDE5 inhibitors, including tadalafil. Therefore, physicians should also discuss with patients the potential for Other Drugs to Affect ADCIRCA.
  - Hearing loss (including bilateral loss and/or deafness), tinnitus, and/or vertigo were reported as adverse events with tadalafil use.

- **Non-arteritic anterior ischemic optic neuropathy (NAION):**
  - Since there are no clinical data on the safety and efficacy of tadalafil in patients with NAION, or in patients who have had an episode of NAION, use of tadalafil is contraindicated in these patients.
  - Physicians should also advise patients to discontinue tadalafil if they experience any visual symptoms suggestive of NAION, including transient monocular visual impairment, visual obscurations, blind spots, or夜间视野 defect.

**ADVERSE REACTIONS**

- **Postmarketing Experience:**
  - This review of adverse events has been identified during post approval use of tadalafil. These events have been chosen for inclusion because they represent serious adverse events for which there is a possibility that the events may be a direct result of the use of tadalafil or may be expected to occur if tadalafil were used for conditions for which it is not indicated. These should be considered to be an estimate of the adverse event frequency and may not reflect the frequency of adverse events during clinical practice.

**Use in Specific Populations**

- **Geriatric Use:**
  - No overall differences in safety were observed between subjects over 65 years of age compared to younger individuals over 65 years of age.

- **Contraception:**
  - No effects on male fertility or female reproductive function have been observed in animal studies with tadalafil.

- **Pregnancy:**
  - Tadalafil is Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. If tadalafil is used in pregnancy, or if tadalafil use is inadvertently discontinued during pregnancy, advise the patient to discontinue tadalafil use and to seek medical attention if any fetal abnormalities are noted.

- **Lactation:**
  - Tadalafil levels in breast milk have been identified as being greater than 0.1% of the maternal dose. Maternal milk is not an important source of tadalafil for an infant. Infants and children should be monitored for tadalafil-related adverse events.

- **Nursing Mothers:**
  - Tadalafil is excreted in breast milk. If tadalafil is used in woman who is breastfeeding, advise the patient to discontinue tadalafil use and to seek medical attention if any tadalafil-related adverse events are observed in the nursing infant.

**ADVERSE REACTIONS**

**Postmarketing Experience**

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Powerful first-line PAH therapy in a simple, once-daily PDE-5 inhibitor.1,2

• Once-daily dosing due to 35-hour half-life in patients with PAH1
• 33-meter mean improvement of 6MWD**
• 68% reduction in relative risk of clinical worsening at 16 weeks compared with placebo1,2
• The most common adverse event with Adcirca was headache (42% Adcirca; 15% placebo). Others included myalgia, nasopharyngitis, flushing, respiratory tract infection, extremity pain, nausea, back pain, dyspepsia, and nasal congestion1

Adcirca, a phosphodiesterase type 5 (PDE-5) inhibitor, is indicated for the treatment of pulmonary arterial hypertension (WHO Group 1) to improve exercise ability

Important Safety Information

Adcirca should not be used in patients taking medicines that contain nitrates, as the combination could cause a sudden, unsafe drop in blood pressure. If a patient experiences anginal chest pain after taking Adcirca they should seek immediate medical attention. Adcirca contains the same ingredient (tadalafil) as Cialis, which is used to treat erectile dysfunction (ED). The safety and efficacy of combinations of Adcirca with Cialis or other PDE-5 inhibitors have not been studied. Therefore, the use of such combinations is not recommended. Patients with a known serious hypersensitivity to tadalafil should not take Adcirca. PDE-5 inhibitors, including tadalafil, have mild systemic vasodilatory properties that may result in transient decreases in blood pressure. Before prescribing Adcirca, physicians should carefully consider whether their patients with underlying cardiovascular disease could be adversely affected by such actions. Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD) and administration of Adcirca to these patients is not recommended. The use of Adcirca with alpha blockers, blood pressure medications, and alcohol may lower blood pressure significantly and may lead to symptomatic hypotension (fainting). Tadalafil is metabolized predominantly by CYP3A in the liver. Use of Adcirca with potent CYP3A inhibitors, such as ketoconazole and itraconazole, should be avoided. For patients on Adcirca therapy that require treatment with ritonavir, Adcirca should be discontinued at least 24 hours prior to starting ritonavir. For patients on ritonavir therapy that require treatment with Adcirca, start Adcirca at 20 mg once a day. Use of Adcirca with potent inducers of CYP3A, such as rifampin, should be avoided. The use of Adcirca is not recommended for patients with severe renal or hepatic impairment. Please see full prescribing information for dosing recommendations for patients with mild to moderate renal or hepatic impairment. In rare instances, men taking PDE-5 inhibitors (including tadalafil) for ED reported a sudden decrease or loss of vision or hearing, or an erection lasting more than four hours. A patient who experiences any of these symptoms should seek immediate medical attention. The most common side effects with Adcirca seen in the PHIRST-1 clinical trial were headache, myalgia, nasopharyngitis, flushing, respiratory tract infection, extremity pain, nausea, back pain, dyspepsia and nasal congestion. For full prescribing information and/or patient information, visit http://www.ADCIRCA.com or call 1-800-545-5979.


*In patients with PAH treated with Adcirca 40 mg at 16 weeks compared with placebo.

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Adcirca

tadalafil tablets

Version 29 September 2009