Experts Outline Therapy for H1N1, Seasonal Flu

First-line antivirals vary by flu strain.

BY BRUCE JANCIN

Vail, Colo. — The recommended antiviral therapy during the coming influenza season will depend on whether a patient has laboratory-confirmed novel influenza A(H1N1).

In patients with confirmed novel influenza A(H1N1), or in patients with laboratory-confirmed influenza A(H1N2) or B, the first-line antiviral is oseltamivir (Tamiflu). However, in patients with a positive laboratory test for influenza A or seasonal A(H1N1), the preferred agent is zanamivir (Relenza), according to Centers for Disease Control and Prevention recommendations based on antiviral resistance patterns.

Zanamivir is also the first-line agent in patients who are suspected of having influenza on clinical grounds but who did not have laboratory tests or had negative results. Dr. Adriana Weinberg explained at a conference on pediatric infectious diseases sponsored by the Children’s Hospital in Denver. Novel H1N1, A(H1N2), and B viruses share the same antiviral susceptibility pattern—all are susceptible to both zanamivir and oseltamivir. However, oseltamivir is preferred because as an oral agent it is easier to administer than the inhalation powder zanamivir, has fewer side effects, and is approved for use across a wider age range, added Dr. Weinberg, professor of pediatrics and medicine and medical director of the clinical virology laboratory at University of Colorado Hospital, Anschutz.

The recommended alternative to zanamivir in patients with laboratory evidence of influenza A, a negative test result, is rimantadine (Flumadine) or amantadine (Symmetrel). However, among children, amantadine is not recommended because of its narrow therapeutic index and potential for toxicity. The recommended antiviral therapy for influenza B is either zanamivir or oseltamivir.

See Flu • page 2

Compliance Cuts ICU Infection Rates

BY SUSAN BIRK

Chicago — Bundles of interventions aimed at reducing ventilator-assisted pneumonia and central line bloodstream infections in intensive care units significantly lowered infection rates only when all of the components were implemented correctly, according to a survey of hospitals participating in the National Healthcare Safety Network of the Centers for Disease Control and Prevention.

The findings have implications for the development of recommendations and mandatory reporting requirements for hospitals, said Patricia Stone, Ph.D., of the Columbia University School of Nursing, New York, in a poster at the annual research meeting of AcademyHealth. “Policy makers must consider that different settings may have different problems,” she said.

Reporting requirements are time consuming and could potentially hinder hospitals’ efforts to zero in on the

See Compliance • page 10
PULMONARY MEDICINE

Oseltamivir Resistance Feared

Flu • from page 1

To date, three cases of oseltamivir-resistant novel H1N1 have been reported to the World Health Organization. But in addition to the emergence of resistance, there is also a phenomenon known as regression of resistance, which works in favor of public health. For example, influenza A(H1N1) virus in Japan went from 100% oseltamivir resistant during the 2005-2006 season to 78% resistant the next season.

Numerous investigational antiviral agents are well along in clinical trials. One that could prove particularly valuable is an intravenous formulation of zanamivir, a drug still active against all strains of influenza. Another promising drug is peramivir, a neuraminidase inhibitor that appears to be effective and well tolerated. Peramivir has the same resistance pattern as oseltamivir. Its big advantage is it can be administered parenterally. That’s going to be really important in patients with severe influenza, in whom oral drugs aren’t going to be reliable,” Dr. Weinberg noted.

Ribavirin and several interferons that are already commercially available for other indications are known to have some activity against influenza. The use of these drugs is being better defined in ongoing clinical trials.

In severe influenza that’s not responding to recommended treatment, combined light therapy with neuraminidase inhibitors, adamantanes, interferon, and ribavirin will be appropriate. “It’s going to be trial and error, basically,” Dr. Weinberg said.

Dr. Mark Metzersky, FCCP, comments: It remains unclear how much that is true now about the novel H1N1 pandemic will remain true when (or if) the pandemic reoccurs itself in the United States this fall. Underscoring the dynamic nature of the pandemic is a recent report of two cases of oseltamivir-resistant H1N1 in the United States.

Device May Detect Lung Cancer Cells in Sputum

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Device May Detect Lung Cancer Cells in Sputum

BY ROBERT FINN

Elsevier Global Medical News

S AN FRANCISCO — An investigational device could make sputum screening a routine part of health exam inations in patients at risk for lung cancer, developers suggested at the World Conference on Lung Cancer.

The Lung Cell Evaluation Device (LuCED) can discriminate normal cells from cancerous cells in sputum with 90% sensitivity and near 100% specificity according to its manufacturer, VisionGate Inc.

LuCED is currently available as a research instrument. Dr. Robert Honig, VisionGate’s commercial chief medical officer, said that the company hopes to receive Food and Drug Administration approval for a noncancer indication—the detection of macrophages in a gastroesophageal reflux disease—by 2010, with approval of a lung cancer indication targeted for 2011.

Company officials discussed the device at a press briefing on innovative diagnostics organized by the International Association for the Study of Lung Cancer, which sponsored the conference. LuCED is based on a patented technology, Cell-CT, which uses light and fluorescence microscopy to assemble highly detailed three-dimensional images of individual cells as they rotate in a capillary tube.

The software then quantifies critical morphological features to discriminate normal cells from cancerous ones. The results are entered into a proprietary formula to produce a “LuCED Score.” The differentiates cancerous cells from normal cells, and also classifies different types of cancerous cells. Higher scores would signal the presence of cancer cells.

“We can get very close to 100% accuracy for normal sputum, and about 90% accuracy on sputum with cancer cells,” said Michael Meyer, VisionGate’s vice president for image engineering, who presented the company’s study. “The score gives us a basis upon which we can proceed with trage.”

In one scenario, he suggested, patients in a high-risk category might be screened at annual intervals. Those with precancerous cells would be subject to increased surveillance, whereas those with cancerous cells would receive additional diagnostic tests such as bronchoscopy and diagnostic CT.

About 75% of sputum samples from people with cancer contain abnormal cells, according to Mr. Meyer. These cells constitute only a small minority of the cells in sputum, however, which makes automated analysis challenging. In addition, the cells are trapped in a matrix of mucus, where they are often massed in large clusters of varied kinds of cells.

The first step in the analysis involves processing the specimen to dissolve some of the mucus. An immunomagnetic separation process removes a large number of the normal cells, and the specimen is further processed to break up some of the clusters. Individual cells are then introduced into a capillary tube one by one. As the tube rotates, the light microscope obtains images from many angles. When the device is fully developed, the examination of about 1,000 cells is expected to take about 20 minutes.

Dr. W. Michael Alberts, FCCP, comments: This is a promising screening technique. The report of very high sensitivity and specificity, however, will need to be confirmed, especially in real-world settings.
Protective Options Aboard Against H1N1 Influenza

Hospitals must decide which measures to use to contain the spread of pandemic flu.

BY HEIDI SPLETE
Elsevier Global Medical News

As hospitals prepare for a potential surge in cases of the pandemic influenza A(H1N1) virus this fall, planning efforts madeusions about protective measures based on limited evidence about the virus’s transmission and severity.

Planning for H1N1 influenza includes everything from ordering extra surgical masks to providing family support for hospital staff so they can come to work, said Leonard Mermel, D.O., professor of medicine at Brown University and medical director of the department of epidemiology and infection control at Rhode Island Hospital, both in Providence, R.I.

Dr. Mermel said that during the first wave of H1N1 influenza last spring, he had ‘rather draconian measures’ in place, based on data from Mexico suggesting a high mortality rate. ‘I had a triage desk in our [emergency department], and N95 respirators,’ he said in an interview.

But conversations with colleagues, resistance from his staff to routine N95 use, and emerging signs that the virus was behaving like the seasonal flu virus led to a transition to standard droplet precautions, said Dr. Mermel, who was part of a panel discussion on infection control measures at an Institute of Medicine-sponsored workshop on the use of personal protective equipment for health care workers.

Dr. Mermel meets regularly with a working group at Rhode Island Hospital to discuss infection control procedures. Their plans for responding to H1N1 influenza include ‘cough etiquette stations’ with surgical masks, hand hygiene products and instructions for their use at hospital points of entry, and a triage desk where a staff person will remind people to follow the instructions.

Other potential strategies to prevent H1N1 virus transmission include limiting unnecessary visitors to the hospital, limiting procedures that might increase the risk of virus transmission, and asking immunized personnel to perform such procedures, Dr. Mermel said.

As for personal protective equipment, ‘how far can you go?’ he said. The Centers for Disease Control and Prevention recommends the use of N95 respirators by health care workers who are treating patients with novel H1N1, but the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and other organizations have concluded that standard droplet precautions are probably sufficient.

‘At this moment, we are using droplet precautions for standard care and [N95] respirators for aerosol-generating procedures,’ Dr. Mermel said.

‘It’s of great importance to mitigate transmission from health care worker to health care worker,’ he added. A worker could do everything right in terms of personal protective equipment, and then become infected during a lunch break with a colleague who is coughing.

Dr. Mermel’s working group has been coordinating with the human resources department to reinforce the message that staff should stay home when ill. But the working group also has considered how to help boost the health care workers get to work if they need child care or elder care at home.

An especially tricky question is whether to reassign health care workers who may be at high risk for H1N1 infection, such as pregnant women, Dr. Mermel said.

The CDC recommends reassigning high-risk health care workers, but recent statements from the SHEA and the IDSA cite problems with that approach.

The CDC may change its guidance on protective measures after reviewing the IOM panel’s report. If the CDC maintains its recommendations, hospitals will have to decide how far to follow them. Dr. Mermel said.

Diagnostic Challenges Anticipated In Pandemic H1N1 Influenza

BY BRUCE JANCIN
Elsevier Global Medical News

VAIL, COLO. — Recent anecdotal reports suggest that the diagnosis of pandemic influenza A(H1N1) virus should not be ruled out by a negative upper respiratory tract specimen in a patient with pneumonia.

There have been two patients at Albany (N.Y.) Medical Center and one in Denver who were hospitalized with severe lower respiratory tract infections whose nasopharyngeal swabs were negative for influenza A by rapid tests—but who had endotracheal aspirates positive for the H1N1 virus by culture and polymerase chain reaction.

‘That’s something to watch for. It would be consistent with findings in animal models showing the virus replicates very well in the lower respiratory tract,’ said Dr. Adriana Weinberg, who reported on the cases at a conference on pediatric infectious diseases sponsored by the Children’s Hospital, Denver.

‘As the pandemic evolves, perhaps we may see more cases with florid infection in the lower respiratory tract,’ he said.

More than 90% of those patients presented with fever and cough, and two-thirds had a sore throat—all typical of seasonal influenza—but in addition, 25% presented with diarrhea and 25% had vomiting.

WHO Panel: Make Health Workers Top Priority for Pandemic Vaccine

BY JONATHAN GARDNER
Elsevier Global Medical News

Health care workers should be the top priority to receive immunization with the pandemic influenza vaccine, and individual countries should take their nations’ domestic needs into account when deciding how to prioritize inoculating subgroups vulnerable to the virus, a top international health panel has decided.

The World Health Organization’s Strategic Advisory Group of Experts on Immunization has said that vaccinating health care workers is necessary to maintain a functioning health care system and prevent infection with the pandemic influenza A(H1N1) virus in people who have pre-existing illnesses, Dr. Marie-Paule Kieny, director of WHO’s initiative for vaccine procurement, said in a press teleconference.

Countries are advised to prioritize the vaccination of such vulnerable groups as the chronically ill and children depending on each country’s domestic needs, Dr. Kieny said.

Thus, countries whose first priority is reducing sickness and death may choose to focus on inoculating the elderly and chronically ill first, whereas those countries whose priority is reducing the spread of infection may decide to inoculate schoolchildren first, she said.

The expert panel made its recommendations after a meeting the week of July 6. WHO Director-General Dr. Margaret Chan endorsed the recommendations July 11.

The panel also concluded that at this time there is no concern regarding the safety of the tested pandemic influenza vaccine, but there is still an ‘urgent need’ to collect more safety data on subgroups, Dr. Kieny said.

New adjuvants are being used in some pandemic vaccines that have not been fully tested, so postmarketing surveillance must also be effective, according to the panel.

In addition, the panel said data on immunogenicity and postmarketing safety and surveillance studies need to be shared among the countries to allow for adjustments in immunization policy, she said.

The panel added that Northern Hemisphere countries should proceed with plans for seasonal influenza vaccination as if there were no pandemic, because production of the seasonal vaccine is almost complete, she added.
EGFR Inhibitors Useful in Subset of NSCLC Patients

Women, nonsmokers, and former light smokers were among those more likely to carry EGFR mutations.

BY MARY ANN MOON
Elsevier Global Medical News

Two inhibitors of the epidermal growth factor receptor tyrosine kinase—gefitinib and erlotinib—were effective for patients with a non–small cell lung cancer who carried mutations of the EGFR gene, according to separate phase III clinical trials published online in the New England Journal of Medicine.

The populations most likely to carry the EGFR mutations are women, patients who have never smoked or who formerly were light smokers, patients with pulmonary adenocarcinomas rather than other lesions, and patients of Asian ethnic background.

In one of the studies, patients with EGFR mutations who were treated with gefitinib had “a remarkably high objective response rate (71%)” when treated with gefitinib. Patients with EGFR mutations had a remarkably high objective response rate (71%) when treated with gefitinib.

"Several questions remain to be answered before we can extrapolate the results of this study of Asian patients to other populations, Dr. Gazdar said, but the findings do suggest that first-line tyrosine kinase therapy should be considered for carefully selected subgroups of patients (N. Engl. J. Med. 2009 [doi:10.1056/NEJMc0905763])."

The overall study population, the objective response rate was significantly higher with gefitinib (43%) than with carboplatin-paclitaxel (32%). But the difference was much more striking in the subgroup of 261 patients who carried EGFR mutations: Their objective response rates were 71.2% with gefitinib and 47.3% with carboplatin-paclitaxel.

In dramatic contrast, among patients who did not carry EGFR mutations, “the objective response rate with gefitinib was 6.5% and 36.8% with carboplatin-paclitaxel. The rate of grade 3 or 4 adverse effects was lower with gefitinib (28%) than with standard chemotherapy (61%), as was the rate of adverse effects leading to discontinuation of therapy (7% and 14%, respectively) and the rate of dose modification because of toxicity (16% and 35%, respectively). The rate of serious events including death was approximately 16% in both groups.

"The incidences of rash or acne, diarrhea, and elevated liver aminotransferase levels were significantly higher with gefitinib than with carboplatin-paclitaxel, whereas the incidences of neurotoxic effects, nausea and vomiting, and hemorrhagic toxic effects were significantly higher with carboplatin-paclitaxel,” Dr. Mok and his colleagues said.

"Our findings suggest that, whenever possible, EGFR-mutation status should be determined before the initial treatment of pulmonary adenocarcinoma,” they added.

The second NSCLC study demonstrated that large-scale progression-free survival favored chemotherapy, Dr. Mok and his colleagues noted (N. Engl. J. Med. 2009 [doi:10.1056/NEJMoa0810699]).

However, overall survival did not differ appreciably between the two arms. Median survival times with gefitinib and 17.3 months with carboplatin-paclitaxel. Overall survival, perhaps the most important end point of cancer treatment, was not improved by gefitinib, for reasons not discussed by the authors,” Dr. Adi F. Gazdar of the University of South Texas Medical Center, Dallas, noted in an editorial comment accompanying the report.

Dr. Michael Alberts, FCP, comments: These studies suggest that EGFR-mutation status may provide guidance for the initial treatment of patients with advanced stage adenocarcinoma of the lung.

Difficult to Control Asthma May Be Vocal Cord Dysfunction

San Diego — About one-third of patients referred to an asthma specialty clinic who were believed to have difficulty to control asthma actually had vocal cord dysfunction, results from a single-center study showed.

"If patients have been on many different medicines—they’ve been on oral or inhaled steroids and they’re not responding—it’s worth checking to see if they actually have asthma or not,” study coauthor Catherine Vitari, R.N., said in an interview during a poster session at an international conference of the American Thoracic Society.

"If patients have been on many different medicines... it’s worth checking to see if they actually have asthma or not.”

In a study led by her associate, Dr. Sally E. Wenzel, FCP, a pulmonologist and the director of the Asthma Institute at the University of Pittsburgh Medical Center, the researchers reviewed the charts of 152 new patients who were evaluated at the institute between December 2006 and September 2008 in an effort to verify if the diagnosis of severe asthma was substantiated.

Of the 152 patients, 119 (78%) had a presenting diagnosis of asthma while 33 had another diagnosis such as dyspnea, cough, and emphyma. All patients underwent a full evaluation.

"We didn’t expect to see this,” Ms. Vitari commented. "That’s a pretty high percentage of people referred for asthma who didn’t actually have asthma.”

She also noted that four of seven patients who presented with a diagnosis of cough, which may indicate asthma, had methacholine challenges with laryngoscopy that showed vocal cord dysfunction; the three other patients were diagnosed with vocal cord dysfunction based on their exam and testing.

Ms. Vitari noted that it’s Dr. Wenzel’s practice to perform a laryngoscopy at the time of the methacholine challenge “to see if the vocal cords are closing or spasming, indicating vocal cord dysfunction, or if it’s truly asthma,” she explained. “If you think it’s vocal cord dysfunction and you send the patient to ENT instead to do a laryngoscopy and they don’t see anything, it could be that the vocal cord dysfunction isn’t acting up at that time since the spasms can be episodic and/or related to triggering events/stimuli.”

She acknowledged certain limitations of the study include its single center design and the fact that only one physician did the assessments.

The researchers had no conflicts to disclose.
Easy Quitting by Heavy Smokers May Be Red Flag

BY BETSY BATES
Elsevier Global Medical News

SAN FRANCISCO — An unusual pattern of sudden, effortless smoking cessation in long-term smokers may herald the onset of lung cancer in a small sub-group of patients, researchers reported at the World Conference on Lung Cancer.

It has been well documented that lung cancer patients often stop smoking shortly before their diagnosis, with the assumption that symptoms such as shortness of breath, coughing, or pain create a strong motivation for behavior change.

Now a pilot study suggests that in certain lung cancer patients—even some with long-term smoking histories and significant levels of nicotine addiction—smoking cessation occurs in the absence of symptoms or even a focused effort to quit.

“This has led us to speculate that in some cases, spontaneous smoking cessation may be a presenting feature of lung cancer, possibly caused by tumor secretion of a factor interfering with nicotine addiction,” said Dr. Barbara Campling, a medical oncologist with the University of Pennsylvania in Philadelphia.

In a study conducted at the Philadelphia VA Medical Center, 115 smokers and former smokers diagnosed with lung cancer were compared to 101 smokers and former smokers with prostate cancer or to 99 with myocardial infarction. Former smokers with prostate cancer had quit smoking an average of 23 years before their diagnosis; for myocardial infarction, the average interval was 10 years.

But smoking cessation was a more recent event for lung cancer patients, occurring, on average, just 2.7 years before diagnosis. Further comparisons among former smokers revealed striking differences among the three groups.

In the general population, you would expect that someone who quit smoking would be those who smoked less and were less severely addicted, she said at the meeting sponsored by the International Association for the Study of Lung Cancer. “That’s exactly what we found in patients with prostate cancer and myocardial infarction.”

In contrast, current and former smokers with lung cancer had similar levels of cumulative tobacco exposure and identical median scores on a scale measuring severity of addiction—scoring 7 on a scale of 0 (“Didn’t even think about it”) to 10 (“The hardest thing I’ve ever done.”)

Surprisingly, many of these lung cancer patients reported they had quit smoking with ease and with no symptoms of ‘alarm bell’ that compelled them to stop.

Among the 55 patients who quit smoking before being diagnosed with lung cancer, 49 (88%) were reportedly asymptomatic at the time. Nearly a third (17 of 55) reported quitting “with no difficulty,” even though they were moderately to severely addicted to nicotine based on the Fagertrom Test for Nicotine Dependence scale.

Many lung cancer patients reported that they had quit smoking with ease and with no ‘alarm bell.’

DR. CAMPLING

“Alarm bells do not imply that tobacco dependence is too severe to quit,” said Dr. Campling. “I think it’s a warning sign that something is wrong.”

For Dr. Campling and her associates hope their findings will be followed up with a long-term, prospective study of smokers to identify unusual patterns of smoking cessation that may precede a diagnosis of lung cancer.

In the meantime, she suggested that clinicians pay attention to this highly unusual pattern of smoking cessation in a long-term, heavy smoker, just as they would a sudden loss of appetite.

Dr. Carolyn Dresler, moderator of the session and an official discussant of the paper, questioned whether memory distortions and attribution errors may have influenced patients’ recall of their smoking histories and difficulty quitting.

In addition, little is known about the ease of quitting experienced by the majority of smokers who stop smoking cold turkey, said Dr. Dresler, a cardiac and thoracic surgeon who heads the Arkansas Department of Health.

Dr. Campling and her associates reported no financial disclosures with respect to their study.

DR. PHILIP MARCUS, MPH, FCCP: comments Smoking cessation remains a goal of all physicians for their patients.

What this study reports, if confirmed, could lead to the discovery of another tool that promotes or retards smoking. Some patients report that they can stop “cold turkey,” and the ease of their stopping may cause one to wonder why it is so easy.

Perhaps we should think further about current smokers who can stop easily, and repeat a chest x-ray just to be sure.

Table 1: Adverse events occurring in ≥ 3% of patients treated with bosentan (125/250 mg) in clinical trials and common or serious on bosentan in placebo-controlled studies in pulmonary arterial hypertension.

<table>
<thead>
<tr>
<th>Event</th>
<th>Bosentan (N = 163)</th>
<th>Placebo (N = 188)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>25 (15%)</td>
<td>19 (10%)</td>
</tr>
<tr>
<td>Nausea/emesis</td>
<td>16 (10%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Flushing</td>
<td>15 (9%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (8%)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>11 (7%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>6 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (3%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Feces</td>
<td>7 (4%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Infra</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (2%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Note: only AEs with onset start from treatment to 1 calendar day after end of treatment are included. All reported events (at least 3%) are included except those too general to be meaningful, and those related to the condition being treated or are very common in the treated population.*

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PULMONARY MEDICINE

Eosinophilic Granulomatosis with Wegener, Systemic Lupus Erythematosus, and Polyarteritis Nodosa

By K. D. Patel

Eosinophilic granulomatosis with Wegener (EGW) is a multisystemic disease characterized by necrotizing, granulomatous inflammation of the upper and lower respiratory tract. In the lung, the most frequent lesion of EGW is necrotizing arteritis and venulitis.

The clinical presentation of EGW may include cough, hemoptysis, dyspnea, and chest pain. Pulmonary function tests may show decreased diffusing capacity and low forced expiratory volume in one second. Periarteritis nodosa is a multisystemic disease that affects the pulmonary vasculature and can cause pulmonary hypertension. It is characterized by focal necrotizing granulomatous inflammation of the small and medium-sized arteries and veins in the lung.

Management of EGW is complex and depends on the extent of involvement in the lung. Corticosteroids are the mainstay of treatment for EGW, and their use is supported by numerous studies. Other treatments include cyclophosphamide, tocilizumab, and rituximab.

Gebhardt et al. (2014) conducted a retrospective study of 115 patients with EGW and found that cyclophosphamide was the most commonly used immunosuppressive agent, followed by rituximab and tocilizumab. The study also showed that corticosteroids were used in all patients, regardless of the predominant lesion in the lung.

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Iloprost Cuts Endobronchial Dysplasia in Ex-Smokers

BY BETSY BATES
Elsevier Global Medical News

SAN FRANCISCO — Endobronchial dysplasia was significantly improved in former smokers who received oral iloprost, a synthetic form of prostacyclin, during a phase II, placebo-controlled chemoprevention trial presented at the World Conference on Lung Cancer.

“We saw improvement at all different stages of dysplasia. This holds for [grade] 2s and 3s” as well as higher-grade lesions, says Keith, a pulmonologist at the University of Colorado, Denver.

Most study participants were male and white, and had smoked, on average, a pack of cigarettes a day for 50 years. Those classified as former smokers had smoked, on average, a pack of cigarettes a day for 50 years.

Biopsies obtained during baseline bronchoscopies revealed at least mild dysplasia in approximately 65% of 152 patients and any other site biopsied at baseline, Dr. Keith noted. Biopsies were taken from each of six standardized sites and any other site biopsied at baseline.

Histologic improvement was seen in every former smoker who received iloprost. In biopsies of former smokers, the composite histologic grade per patient declined from 2.12 to 1.73 according to World Health Organization classifications ranging from grade 1 (normal) to grade 8 (cancer). When the analysis included only subjects who had abnormal biopsies at baseline, the grade decreased from 3.27 to 2.06, and in their worst lesions, from 4.57 to 3.10.

Investigators also calculated a dysplasia index for each study participant, calculated as the number of biopsies with dysplasia (at least grade 4 on the WHO scale), divided by the total number of biopsies multiplied by 100. The mean dysplasia index for former smokers went from 20.81 to 10.90 in all patients, and from 43.18 to 19.58 in the subgroup of former smokers who had abnormal biopsies at baseline. No significant changes were seen in histologic grades or dysplasia index scores in current smokers enrolled in the trial.

Side effects associated with vasodilator use were seen more frequently in patients receiving iloprost than in those taking placebo. Most prominent was headache, reported in 40 patients receiving iloprost and in 17 receiving placebo. Other less common side effects included flushing, nausea, pain, and myalgias. Serious adverse events were more common in the placebo group than in the iloprost arm.

The majority of lung cancer in the United States is diagnosed in former smokers, but not in current smokers. This study may serve as the basis to investigate many other compounds in a similar fashion. This is an area that has not been investigated before, and the results are promising.

“The majority of lung cancer in the United States is diagnosed in former smokers, but not in current smokers. This study may serve as the basis to investigate many other compounds in a similar fashion. This is an area that has not been investigated before, and the results are promising.”

In the United States, iloprost (marketed under the name Ventavis) is available only as an inhalation solution approved for the treatment of pulmonary arterial hypertension. At the time of the study, Schering AG manufactured iloprost and provided an oral form of the drug for the trial. Actelion Pharmaceuticals US Inc. now markets Ventavis in the United States.

The trial was funded through the National Cancer Institute, and neither Dr. Keith nor his associates reported any other relevant financial disclosures.

View a video interview of Dr. Keith at www.youtube.com/watch?v=0J_F-jwWmAg

Dr. Philip Marcus, MPH, FCCP comments: For once, we have some possible good news about lung cancer. The investigators utilized an agent commonly used for the treatment of pulmonary hypertension and looked at lung cancer prevention in current and former smokers. Benefits were seen in former smokers, but not in current smokers. This study may serve as the basis to investigate many other compounds in a similar fashion. This is an area that has not been investigated before, and the results are promising.
Shortage of Cardiothoracic Surgeons Predicted

**Even under the most optimistic assumptions, the supply of cardiothoracic surgeons will fall.**

**BY ROBERT FINN**

*Elsevier Global Medical News*

Within the next 10 years the demand for cardiothoracic surgeons will greatly exceed the supply, according to a study appearing in the journal *Circulation*.

If current trends continue, the demand for cardiothoracic surgeons could increase by 46% between 2005 and 2025. Over the same time period, the supply of such surgeons will decrease 21% as a result of retirement coupled with insufficient numbers of physicians entering the specialty (*Circulation* 2009 Aug. 11 doi: 10.1161/CIRCULATIONAHA.108.776278).

Patients are likely to suffer if non-board-certified physicians fill the gap left by cardiothoracic surgeons or if patients delay care because of the shortage, wrote Dr. Atul Grover of the Association of American Medical Colleges (AAMC, Washington) and co-investigators. “Multiple strategies for ensuring adequate access to care must be explored if this crisis is to be averted.”

The investigators projected the supply of cardiothoracic surgeons using a variety of assumptions. From the American Medical Association Masterfile for 2005, they identified 4,734 currently practicing cardiothoracic surgeons. Recent survey data from an AAMC study suggested that the average age of retirement for cardiothoracic surgeons is 61 years and that 60% of physicians fully retire from clinical practice by age 65. At the same time the investigators assumed that 130 new trainees will enter the workforce each year. This is an optimistic assumption given that only 84 of 126 positions offered through the national match were filled in July 2007. The investigators also calculated supply based on two alternative assumptions: a gradual increase in newly trained cardiothoracic surgeons to 150 per year or a continued decline to 75 per year.

Even under the most optimistic assumptions, the supply of cardiothoracic surgeons will fall. If 150 physicians complete training annually, starting immediately, there would still be a 9% decline in the total number of active cardiothoracic surgeons in 2020 compared with 2005. If only 75 complete training annually there would be a 34% decrease in the number of cardiothoracic surgeons by 2020.

The investigators projected the demand under several alternative scenarios based on the increasing numbers of people over the age of 65 years, current patterns of health care use, and likely trends in technology. By 2020, the population of people over the age of 65 years will grow by 50%, and by 2030, there will be almost twice as many people in this age group as there were in 2005.

The most optimistic scenario assumes that coronary artery bypass grafting (CABG) will be completely eliminated over the next decade, decreasing the demand for cardiothoracic surgeons by about 40%. While the numbers of open revascularizations have been declining in recent years, few suggest that they will disappear completely.

Offsetting this decline in demand is an expected 20% increase in per capita rates of non-CABG cardiac and a general thoracic operations, including valve procedures, other open heart procedures, and lobectomies or pneumonectomies. Taking all assumptions into account, the investigators calculated that there would be a shortage of 1,500 surgeons, equivalent to 25% of the projected need, by 2025.

The study was supported by the American Association for Thoracic Surgery and the Society of Thoracic Surgeons. The investigators disclosed no other conflicts of interest.
dissatisfaction among oncologists around the world.”

The 7th edition of the guidelines is available as a handbook, a manual, a CD-ROM, and posters for the clinic, and is aimed at medical oncologists, surgeons, radiation oncologists, and pathologists. Highlights of the new staging system for non-small cell lung cancer (NSCLC) include the following:

1. New subcategories of stage I (early-stage) disease are based on size: Tumors measuring 2 cm or smaller will now be classified as T1a, whereas tumors larger than 2 cm and up to 3 cm will be classified as T1b. T2 disease will also be subdivided into T2a (tumors larger than 5 cm and up to 7 cm) and T2b (tumors larger than 5 cm and up to 7 cm).

2. A new category (T3) will be used to designate tumors larger than 7 cm.

3. Patients previously considered T4 because of additional tumor nodules in the same lung as the primary tumor will now be classified as T3. If these patients are node negative, they will be staged as T3N0M0.

4. Patients with additional tumor nodules in the bilateral lung (previously M1) will now receive a designation of T4, and they will be down-staged from stage IV to stage IIIA.

5. The presence of malignant pleural fissions, long referred to by oncologists as “wet lungs” and treated as if the patient had metastatic disease, will now be officially staged that way, as stage IV disease.

6. Temporizing of clinical practices: “Do NOT FORCE TREATMENT WITH REMEDIES IN WATER RAYS OR BY INJECTIVE REACTION”

7. Efficiency for this organ in this organ was studied in fewer than 10 cancers. Aztreonam is a trademark of EPI and licensed exclusively in the U.S. to EPI.
difficult to define and categorize, he explained; as a result, a uniform definition has now been agreed upon for the first time.

Medical oncologists will find a host of prognostic variables in the new guidelines, including performance status, age, sex, laboratory values, initial maximum standard uptake variable on initial PET scan, and a review of meta-analyses of the current stage of knowledge about the prognostic significance of biological markers.

In addition to changes in the staging of NSCLC, analysis of more than 13,000 cases of small cell lung cancer—the largest such database in the world—reaffirmed the usefulness of the TNM system in that disease.

Previously, staging guidelines for SCLC were primarily used by surgeons, whereas medical oncologists have tended to simply dichotomize patients as having extensive or limited disease, explained Dr. Goldstraw during the press conference.

Upcoming steps in efforts to modernize lung cancer staging will include the correction of geographical and treatment biases within retrospective data, the inclusion of prospective data based on the new staging system, implementation of a Web-based system for world data collection, and the extension of staging updates to include neuroendocrine tumors and mesothelioma.

Dr. Elisabeth Brambilla, chair of the IASLC pathology committee and chair of pathology at University Medical Center Grenoble (France), discussed the idea of dividing early-stage tumors according to a more finely defined measurement of solid invasive components, as opposed to the ground-glass opacity that can sometimes be visualized on CT scans. When multiple nodules are present, future staging parameters may be able to incorporate molecular features, so that primary vs. metastatic tumors can be determined, she said.

Dr. Edward F. Patz Jr., professor of radiology, pharmacology, and cancer biology at Duke University in Durham, N.C., said the new size criteria within the guidelines will require precise specificity by radiologists.

“We need to be enormously careful about this,” he said, cautioning that an overenthusiastic reading of tiny, likely benign nodules could serve to up-stage a patient, with significant treatment implications. “You can’t write the patient off, because we do see small nodules,” he said.

Dr. Patz recalled a mentor once telling him, “A radiologist with a ruler is a radiologist in trouble.” He urged colleagues to be circumspect in writing their reports, and simply characterize what they see rather than make inferences about the malignant potential of the small lesions on a scan.

He also warned that current imaging modalities are not uniformly accurate when it comes to lymph nodes and nodal groups.

CT scans are about 60% sensitive and specific in identifying involved nodes, whereas PET scans increase the accuracy to about 80%.

To view a video interview of Dr. Goldstraw, go to www.youtube.com/watch?v=2AjpGaUwKw.

Dr. W. Michael Alberts, FCCP, comments: I am sure that we will all be carrying around another pocket card (or find a new PDA application) until the new system becomes more familiar. It is impressive, however, that the new lung cancer staging system was derived from data compiled from more than 100,000 lung cancer cases from 46 centers in 19 countries.

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specific infection control problems that are most pressing in their institutions, she said.

As part of a larger study, the survey was sent to infection control specialists responsible for process and outcomes surveillance. Participants were asked about their ICU policies with regard to central line bloodstream infections (CLBSIs) and ventilator-associated pneumonia (VAP), CLBSI and VAP infection rates, and bundle compliance rates. The CLBSI bundle consisted of barrier precautions, use of chlorhexidine, optimal site selection, and daily site checks for signs of infection. The VAP bundle consisted of periodically reviewing the ventilator head and periodically interrupting sedation to facilitate deeper breathing. In all, 250 hospitals (57%) responded.

Respondents provided data on 41 ICUs, including 223 (54%) medical/surgical units. A total of 284 ICUs (68%) had adopted the full VAP bundle, and 204 (49%) had adopted the full CLBSI bundle. The mean infection rates per 1,000 device-days were 2.6 for VAP and 2.1 for CLBSI.

Rates of device-associated infections were significantly lower only in the ICUs that correctly implemented all bundle components at least 99% of the time (73 ICUs). Some believe that the ability to keep infection rates low stems from the overall quality of care in an ICU, but this study attributes low infection rates to highly targeted efforts aimed at specific infections in which the unit focuses on all components of a bundle at least 95% of the time, said Dr. Stone, who is also an RN, in an interview. No single component of either bundle significantly reduced infection rates.

“Moreover, always implementing the ventilator bundle correctly was not significantly associated with decreased CLBSI incidence,” she said.

“If you’re just focusing on one problem, you don’t get to be a better ICU,” Dr. Stone received support for this study from the National Institute of Nursing Research.

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**PERFOROMIST® (formoterol fumarate) Inhalation Solution**

20 mcg/ml vial

**BRIEF SUMMARY**

The following is a brief summary; please see full prescribing information for complete product information.

**WARNING: INCREASED RISK OF ASTHMA-RELATED DEATH**

Long-acting beta₂-agonists may increase the risk of asthma-related death. Data from a large placebo-controlled trial that compared the safety of another long-acting beta₂-agonist to placebo indicated that in some patients, increased risk was associated with asthma-related deaths in patients receiving salmeterol. This finding with salmeterol may be representative of long-acting beta₂-agonists, including the active ingredient in PERFOROMIST Inhalation Solution. See WARNINGS AND PRECAUTIONS, Asthma-Related Deaths and Exacerbations.

**INDICATIONS AND USAGE**

Maintenance Treatment of COPD

PERFOROMIST Inhalation Solution is indicated for the long-term, twice-daily (morning and evening) administration in the maintenance treatment of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

**Important Limitations of Use**

PERFOROMIST Inhalation Solution is not indicated to treat acute determinants of chronic obstructive pulmonary disease (see WARNINGS AND PRECAUTIONS, Determination of Disease and Acute Episodes).

PERFOROMIST Inhalation Solution is not indicated to treat asthma. The safety and effectiveness of PERFOROMIST Inhalation Solution in asthma have not been established.

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

**Asthma-Related Deaths and Exacerbations** (see BOXED WARNINGS)

Data from a large placebo-controlled study in asthma patients showed that long-acting beta₂-agonists may increase the risk of asthma-related death. Data are not available to determine whether the rate of death in patients with COPD is increased by long-acting beta₂-agonists.

A 28-week, placebo-controlled US study comparing the safety of salmeterol with placebo, each added to usual asthma therapy, showed an increase in asthma-related deaths in patients receiving salmeterol (15/37, 4.1%) in patients treated with salmeterol vs. 3/32, 9.4% in patients treated with placebo (p = .047, 95% CI, .016 - .054). The increased risk of asthma-related death may represent a class effect of the long-acting beta₂-agonist, including PERFOROMIST Inhalation Solution. It is not adequate to determine whether the rate of asthma-related death is increased in patients treated with PERFOROMIST Inhalation Solution has been conducted.

Clinical studies with formoterol fumarate administered as a dry powder inhaler suggested a higher incidence of serious asthma exacerbations in patients who received formoterol than in those who received placebo. The size of these studies was not adequate to precisely quantify the differences in serious asthma exacerbations between treatment groups.

**Determination of Disease and Acute Episodes**

PERFOROMIST Inhalation Solution should not be used in patients with acutely deteriorating COPD, which may be a life-threatening condition. PERFOROMIST Inhalation Solution has not been studied in patients with acutely deteriorating COPD. The use of PERFOROMIST Inhalation Solution in this setting is inappropriate.

PERFOROMIST Inhalation Solution should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. PERFOROMIST Inhalation Solution has not been studied in the relief of acute symptoms and extra doses should not be used for that purpose. Acute symptoms should be treated with an inhaled short-acting beta₂-agonist. When beginning PERFOROMIST Inhalation Solution, patients who have been taking inhaled, short-acting beta₂-agonists on a regular basis (e.g., four times a day) should be instructed to discontinue the regular use of these drugs and use them only for symptomatic relief of acute respiratory symptoms. When prescribing PERFOROMIST Inhalation Solution, the healthcare provider should also prescribe an inhaled, short-acting beta₂-agonist and instruct the patient how to use it. Increasing inhaled beta₂-agonist use is a signal of deteriorating disease for which prompt medical attention is indicated. COPD may deteriorate acutely over a period of hours or chronically over several days. If PERFOROMIST Inhalation Solution no longer controls the symptoms of bronchospasticity, or the patient’s inhaled, short-acting beta₂-agonist becomes less effective or the patient needs more inhaled short-acting beta₂-agonist, as usual, these may be markers of deterioration of disease. In this setting, a re-evaluation of the patient and COPD treatment regimen should be undertaken at once. Increasing the daily dosage of PERFOROMIST Inhalation Solution beyond the recommended 20 mcg twice daily is not appropriate in this situation.

**Excessive Use of PERFOROMIST Inhalation Solution and Use with Other Long-Acting Beta₂-Agonists**

As with other inhaled beta₂-agonists, drugs of this type should be used no more often, at higher dosages than recommended, or in conjunction with other medications containing long-acting beta₂-agonists, as an asthma exacerbation. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

**Paroxysmal Bronchospasm**

As with other beta₂-agonists, PERFOROMIST Inhalation Solution may produce paroxysmal bronchospasm that may be life-threatening. Administration of bronchodilator rescue therapy may be necessary in these instances. PERFOROMIST Inhalation Solution should be discontinued immediately and alternative therapy initiated.

**Cardiovascular Effects**

PERFOROMIST Inhalation Solution, like other beta₂-agonists, can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, systolic and diastolic blood pressure, and/or symptoms. If such effects occur with PERFOROMIST Inhalation Solution, therapy should be discontinued. In addition, beta₂-agonists have been reported to produce ECG changes, such as flattening of the T wave, prolongation of the QT interval, and ST segment depression. The clinical significance of these findings is unknown. Therefore, PERFOROMIST Inhalation Solution, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially primary myocardial ischemia, cerebrovascular insufficiency, and hypertension.

**Coexisting Conditions**

PERFOROMIST Inhalation Solution, like other sympathomimetic amines, should be used with caution in patients with concomitant disorders of the sympathovascular, and in patients who have responders to sympathomimetic amines. Dozes of the related beta₂-agonist, albuterol, if administered intravenously have been reported to aggravate preexisting diabetes mellitus and worsen 4% for PERFOROMIST Inhalation Solution and 4.4% for placebo. There were no frequently occurring specific cardiac adverse reactions. Results for PERFOROMIST Inhalation Solution (frequency > or equal to 1% and greater than placebo). The rate of COPD exacerbations was 4.1% for PERFOROMIST Inhalation Solution and 7.9% for placebo.

**Drug Interactions**

**Adrenergic Drugs**

If additional adrenergic drugs are to be administered by any route, they should be used with caution because of the potential for additive effects of beta₂-agonists. (see WARNINGS AND PRECAUTIONS, Asthma-Related Deaths and Exacerbations).

Beta₂, Adrenergic Antagonist Profile

If additional adrenergic drugs are to be administered by any route, they should be used with caution because of the potential for additive effects of beta₂-agonists. (see WARNINGS AND PRECAUTIONS, Asthma-Related Deaths and Exacerbations).
For additional information about overdose treatment, call a poison control center (1-800-222-1222).

The median lethal oral doses in Chinese hamsters, rats, and mice provide even higher multiples of times the maximum recommended daily inhalation dose in humans on a mg/m² basis) and above

PERFOROMIST® is a registered trademark of Dey, L.P.

USE IN SPECIFIC POPULATIONS

Beta-blockers
Beta-adrenergic receptor antagonists (beta-blockers) and formoterol may inhibit the effect of each other. In order to use this drug properly, patients must not only be aware of the effects of beta-adrenergic

agonists, but may produce severe bronchospasm in COPD patients. Therefore, patients with COPD should not normally be treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-blockers in patients with COPD. In this setting, cardioselective beta-blockers could be considered, although they should be administered with caution.

BETA-AGONISTS AND OTHER ADRENERGIC AGENTS

Common Adverse Reactions with Beta2-agonists

PERFOROMIST Inhalation Solution is not indicated for use in children. The safety and effectiveness of PERFOROMIST Inhalation Solution in pediatric patients have not been established.

The pharmacokinetics of formoterol has not been studied in preterm or full-term neonates. No data are available on the use of PERFOROMIST Inhalation Solution in nursing mothers. Women should be advised to contact their physician if they are nursing while taking PERFOROMIST Inhalation Solution.

Labor and Delivery

There is no adequate and well-controlled human studies that have investigated the effects of PERFOROMIST Inhalation Solution during labor and delivery.

Because beta-agonists may potentially interfere with uterine contractility, PERFOROMIST Inhalation Solution should be used cautiously only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

In reproductive studies in rats, formoterol was excreted in the milk. It is not known whether formoterol is excreted in human milk, but because many drugs are excreted in human milk, caution should be exercised if PERFOROMIST Inhalation Solution is administered to nursing women. There are no well-controlled human studies of the use of PERFOROMIST Inhalation Solution in nursing mothers.

Women should be advised to contact their physician if they are nursing while taking PERFOROMIST Inhalation Solution.

PEDIATRICS

PERFOROMIST Inhalation Solution is not indicated for use in children. The safety and effectiveness of PERFOROMIST Inhalation Solution in pediatric patients have not been established. The pharmacokinetics of formoterol has not been studied in preterm or full-term neonates.

The pharmacokinetics of PERFOROMIST Inhalation Solution has not been studied in elderly patients.

OVERDOSAGE

The expected signs and symptoms with overdosage of PERFOROMIST Inhalation Solution are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the signs and symptoms listed under ADVERSE REACTIONS. Signs and symptoms may include angina, hypertension or hypotension, tachycardia with rates up to 200 beats/min, arrhythmias, chest pain, dyspnea, sweating, numbness, paresthesiae, restlessness, fatigue, malaise, insomnia, hyperglycemia, hypoglycemia, anaphylaxis, circulatory collapse, cardiac arrest and even death may be associated with an overdose of PERFOROMIST Inhalation Solution.

Treatment of overdose consists of discontinuation of PERFOROMIST Inhalation Solution together with institution of appropriate symptomatic and supportive therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchodilatation. This is inesseceous to evidence in order to determine if its treatment of an overdose of PERFOROMIST Inhalation Solution, Cardiac monitoring is recommended in cases of overdose.

The minimal lethal inhalation dose of formoterol fumarate in rats is 156 mg/kg (approximately 32,000 times the maximum recommended daily inhalation dose in humans on a mg/m² basis).

The minimal lethal dose was determined in hamsters, rats, and mice and provide even higher multiples of the maximum recommended daily inhalation dose in humans.

For additional information about overdose treatment, call a poison control center (1-800-222-1222).
CHEST 2009 Will Usher in a New ACCP President

During Convocation ceremonies at CHEST 2009 next month, Dr. Kalpalatha K. Guntupalli, FCCP will be inaugurated as the new ACCP President. She is a Professor and Chief, Pulmonary/Critical Care and Sleep Section, at the Baylor College of Medicine in Houston, TX. Dr. Guntupalli has served ACCP in many capacities, including Resident at Large; Chair of the Critical Care Institute; Chair of Women’s Health Network; member of the CHEST Program Committee; and trustee of The CHEST Foundation. She currently serves as The CHEST Foundation’s Second Distinguished Scholar in Critical Care Medicine.

Her academic interests include ARDS and critical care education tools. She has developed antitobacco education material in seven languages and antitobacco cartoons for children in three languages, inspiring more than 200,000 children. Dr. Guntupalli is the recipient of numerous awards, including the “Parker J. Palmer Courage To Teach” award from the ACGME, and “Master of American College of Physicians” (MACP) award from the ACP. Dr. Guntupalli believes in fostering a culture of a “global family” of health caregivers to deliver the best of care to all patients and make meaningful contributions to society.

We asked Dr. Guntupalli to share some thoughts on her upcoming presidential term.

Q. What would you like to accomplish as President of the ACCP? As the President of the ACCP I will strive to retain and further strengthen the role of ACCP as the premier organization representing professionals who promote cardiopulmonary health throughout the world.

I want to actualize/realize the concept of the “global family” by increasing our reach to the international community.

DR. GUNTUPALLI

Q. What do you consider to be the greatest strengths of the ACCP and how will you build upon them? ACCP has always been a “member-friendly” and “member-responsive” organization that promotes continuing education and develops tools for improved practice management and patient care. With large US and international membership, ACCP is a champion for the voice of health-care professionals and patients with cardiopulmonary illnesses.

Q. What is the greatest challenge facing the College and how will you address it? The current financial atmosphere and health-care debate are potential causes for concern to our members, sponsors, and partners that support the organization. We need to leverage our current strengths to explore new opportunities to continue to serve our members. I am very confident we will not only survive but thrive by forging new programs and partnerships.

Q. What is your charge to the members and new Fellows of the ACCP? Members and new Fellows should remain actively engaged in the ACCP. Together, we can contribute and shape the change we want to accomplish in this era of health-care reform.

‘I want to realize the concept of the “global family” by increasing our reach to the international community.’

DR. GUNTUPALLI

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 Adcirca should not take Adcirca. PDE-5 inhibitors, including Adcirca, 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).

Adcirca 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...
The CHEST Foundation Honors Al and Norine Lever

The CHEST Foundation is proud to recognize Alvin Lever, MA, FCCP(Hon) and his wife, Norine Lever, for their outstanding leadership of the ACCP and The CHEST Foundation. The Al and Norine Lever Honorary Endowment Fund was established to continue the Lever’s practice of mentoring others by developing leaders in the field and strategic leadership initiatives that will transform pulmonary, critical care, and sleep medicine. By funding new generations of ACCP leaders who have demonstrated abilities in leadership, research, and innovation, the ACCCP will continue to be a leading resource for clinical research and education and an avid proponent of patient-focused care.

During Al Lever’s 18-year tenure, the ACCP has experienced unprecedented growth in all areas, including increases in membership, annual meeting attendance, and gross revenues that have nearly tripled since 1991. Norine Lever’s accomplishments have been more family-oriented as she championed for the ACCP staff, members, patients, and their families. In 2001, Mrs. Lever proposed the creation of the Ambassadors Group, an auxiliary group for The CHEST Foundation. Ambassadors Group members have made it their charge to foster initiatives that augment The CHEST Foundation’s programming in many areas.

To make your tax-deductible contribution to the Al and Norine Lever Honorary Endowment Fund, visit The CHEST Foundation’s Web site at www.chestfoundation.org and make a secure online donation, or download an endowment brochure to use when mailing in your donation. For more information about donating to the fund, contact Teri Ruiz at truiz@chestnet.org or at (847) 498-8308.

INTRODUCING A POWERFUL NEW THERAPY FOR PULMONARY ARTERIAL HYPERTENSION (PAH)

SIMPLE TO START  POWER TO MOVE

• Elimination half-life allows once-daily dosing
• No routine lab testing required
• Can be taken with or without food
• Available at retail and specialty pharmacies
• Reimbursement Hotline 1-877-948-9136

Adcirca 40 mg at 16 weeks compared with placebo
– 33-meter mean improvement of 6MWD in patients with PAH
– 44-meter improvement in treatment-naïve patients
– 23-meter improvement in background bosentan subgroup, p=NS
• 68% reduction in relative risk of clinical worsening with Adcirca 40 mg at 16 weeks compared with placebo

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

ONCE-DAILY
adcirca
(tadalafil)
tablets

Adcirca is 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.

Please see brief summary of Prescribing Information on next page.

ADCCIRCA™ (tadalafil) Tablets

BRIEF SUMMARY

The following is a brief summary of the full prescribing information on ADCCIRCA (tadalafil). Please review the full prescribing information prior to prescribing ADCCIRCA.

INDICATIONS AND USAGE

Pulmonary Arterial Hypertension

ADCCIRCA is indicated in patients with pulmonary arterial hypertension (PAH) to improve exercise ability and prolong survival.

CONTRAINDICATIONS

Do not use ADCCIRCA in patients who are using any form of organic nitrates, either regularly or intermittently, unless at least 24 hours have passed since the last dose of an organic nitrate, because of the risk of hypotension.

WARNINGS AND PRECAUTIONS

Cardiovascular Effects

Discuss with patients the appropriate action to take in the event that they experience anginal chest pain requiring nitroglycerin’s following initiation of therapy. Patients should be instructed to take their daily medication 1 hour prior to planned physical activity, if possible. A patient cohabiting with ADCCIRCA within 48 hours, administer intravenous therapy with appropriate hemodynamic monitoring. Patients who experience anginal chest pain after taking ADCCIRCA should receive immediate medical attention.

PFS Events, including tadalafil, have been reported in clinical trials that may result in transient decreases in blood pressure. Prior to prescribing ADCCIRCA, carefully consider whether patients with underlying cardiovascular disease could be affected adversely by such a change in blood pressure. Patients with severely impaired autonomic control of arterial pressure or with left ventricular systolic abnormalities (e.g., cardiomyopathy and hypotensive:subdiastolic cardiac) may be particularly sensitive to the antihypertensive effects of ADCCIRCA.

Use with Alcohol

An increased frequency of flushing, headache, and dizziness may occur when ADCCIRCA is used with alcohol. When mild vasodilators are taken in combination, blood pressure-lowering effects are additive.

Use in Renal Impairment

In patients with mild to moderate hepatic cirrhosis (Child-Pugh Class A and B), use of ADCCIRCA is not recommended.

Use in Renal Impairment

Co-administration of tadalafil with ritonavir for the treatment of HIV has not been shown to increase bleeding times in healthy subjects, use in patients with bleeding disorders or significant active peptic ulcers is not recommended.

Use in Hepatic Impairment

ADCCIRCA has not been studied in patients with moderate to severe hepatic impairment.

Use in Hepatic Impairment

PEARLS FOR THE PATIENT

Prolonged Erection

ADCCIRCA should be used with caution in patients who have conditions that might predispose them to priapism (such as sickle cell anemia, multiple myeloma, or leukemia), or in patients with abnormal development of the penis (such as angulation, cavernous fibrosis, or Peyronie’s disease).

Effects on Blood Pressure

ADCCIRCA is contraindicated in patients with a history of hepatic disease who are using organic nitrates, either regularly or intermittently, unless at least 24 hours have passed since the last dose of an organic nitrate because of the risk of hypotension.

ADCCIRCA is contraindicated in patients with uncontrolled severe hypertension.

ADCCIRCA should not be used in patients with a history of or who are using any form of organic nitrates, either regularly or intermittently, unless at least 24 hours have passed since the last dose of an organic nitrate, because of the risk of hypotension. ADCCIRCA is contraindicated in patients with uncontrolled severe hypertension.

ADCCIRCA should not be used in patients with a history of or who are using any form of organic nitrates, either regularly or intermittently, unless at least 24 hours have passed since the last dose of an organic nitrate, because of the risk of hypotension.
Biomarkers may eventually help us identify individuals at risk of developing lung cancer, help to screen for lung cancer, diagnose the nature of a lung nodule, prognosticate the outcome of the cancer, or predict the tumors’ response to therapy. A variety of avenues are being pursued in the search for biomarkers of lung cancer. Most of these involve the study of the molecular makeup of lung cancer tissue or blood. An alternative, readily available source of biomarkers is a person’s breath.

Exhaled breath contains nitrogen, oxygen, carbon dioxide, water, and inert gases. In addition, volatile organic compounds (VOCs), generated in the body or absorbed from the environment, can be detected in the breath in very low concentration (parts per billion volume to parts per trillion volume). The exogenous molecules are inhaled into and absorbed through the lungs or absorbed through the skin. The endogenous molecules are generated by the biochemical processes of the body. Measuring VOCs in the breath of people with lung cancer can provide a window into the biochemical processes of the body. There is evidence that many biochemical processes are different in lung cancer cells than they are in normal cells. These differences are likely to lead to the production of different patterns of VOCs in the breath of people with lung cancer. If these differences are unique, consistent, and detectable, they could serve as useful biomarkers for lung cancer (Table 1).

Lab-based studies support this concept. Reports include comparisons of the headspace of exhaled lung cancer cell lines, lung cancer cell culture media, naive media, and non-cancer cell lines. These studies have identified different patterns of VOCs between the samples that were included.

Others have reported comparisons of breath VOCs from patients with lung cancer to those of subjects without cancer. Until recently, most studies have used gas chromatography and mass spectrometry (GC-MS) to identify a discriminatory set of VOCs in the breath of patients with lung cancer. With GC-MS analysis, the breath sample is usually preconcentrated onto a medium that is transported to the device where the VOCs are described from the medium in order to be analyzed. GC-MS techniques allow specific VOCs to be identified and quantified. They can be sensitive into the low parts per billion or upper parts per trillion range with preconcentration. The disadvantages of GC-MS analysis are that some VOCs may be missed or lost in the concentration and desorption steps. GC-MS takes a considerable amount of time to process and analyze a sample; the equipment is large and expensive; and it takes an experienced person to run it. GC-MS analysis of exhaled breath to help identify lung cancer has been reported (Mazzone. J Thorac Oncol 2008;3:774; Mazzone. J Breth Res 2008;3:10.1088/1752). A discriminatory group of volatiles has been identified. The accuracy of the models of discriminatory volatiles produced has ranged from 70% to 85%. These studies have differed in the number of subjects included, the stages of lung cancer, the manner in which the breath was collected, the type of control subjects included (ie, healthy vs disease), the pattern recognition statistical techniques used, and the methods of validating the models that were developed.

More recently, advances in detecting technologies have been used to look at breath specimens. The devices being used have one major advantage over GC-MS. They are more sensitive, thus they do not require preconcentration of the breath sample. This leads to faster sample analysis (in some cases, near real time). They are also somewhat easier to use. The major disadvantage of many of these devices is that they are not able to fully identify the VOCs they are detecting (they identify a mass-charge ratio only) and may not be able to specify the concentration of the volatiles that are detected. Devices that have been reported include single ion flow tube mass spectrometry, ion mobility spectrometry, and proton transfer reaction mass spectrometry. There have been relatively small studies, showing promise for future development.

An alternative approach to the discovery of breath biomarkers has been analysis by non-specific chemical sensor matrices. Many types of sensors exist, including conductive polymers, nonconductive polymer/carbon black composites, metal oxide semiconductors, fluorescent dye/polymer systems, quartz microbalance sensors coated with metalloporphyrins, polymer-coated surface acoustic wave devices, and chemo-responsive dyes. The principle of these sensor systems is that their output is altered when VOCs bind to them. The output might be a change in conductance, vibration, or color, depending on the type of sensor that is used. Some sensors are reusable, and others are disposable. They can be inexpensive, portable, and easy to use, making them ideal as a point-of-care test. Typically, their output is related to the mixture of VOCs they are exposed to, and, thus, they do not identify the specific compounds, and their limit of detection may not be quite low enough to sense all of the discriminatory volatiles. A few of these sensor matrices have been used in studies in patients with lung cancer. They have reported accuracies similar to those from GC-MS (Mazzone. J Thorac Oncol 2008;3:10.1088/1752; Machado et al. Am J Respir Crit Care Med 2005;171:1286; Mazzone et al. Thorax 2007;62:565). As with GC-MS, the studies have differed in the number of subjects, stage of cancers included, type of control subjects, breath collection methods, statistical techniques used, and method of validation of their results.

There is, as yet, little agreement on how to make breath VOC biomarkers the chance to be clinically useful. Despite reports of reasonably accurate discrimination between cancers and controls, the models of VOC biomarkers have not been consistent between studies. Many studies have not included the spectrum of lung cancer patients that have been clinically or looked for differences in breath VOCs related to these differences (eg, histologic findings, stage, outcome). Many studies have not included a group of control subjects similar to those in whom the biomarker would be used as a clinical test. The ideal method of breath collection (an alveolar breath sample or a mixed sample), and the need to control for ambient volatiles to maximize the accuracy of the breath biomarker, have not been determined. Insight into the origin of the discriminatory VOCs is largely lacking. This may be necessary for widespread acceptance and clinical application. Advances in sensing technologies will need to be translated into reliable, easy to use, inexpensive, point-of-care tests. As progress is made in each of these areas, other applications of breath VOC biomarker development can be explored. It is possible that breath biomarkers will be able to provide information about the prognosis of the cancer or help predict the response of the cancer to different therapies.

Today, many groups around the world are working hard to discover clinically useful biomarkers, certain to benefit our patients with lung cancer. Groups invested in discovering breath VOC biomarkers have an unusual source of inspiration. A study that assessed the ability of dogs to distinguish the breath of subjects with lung cancer from healthy control subjects reported that the dogs were 99% accurate (McCulloch et al. Int J Cancer Ther 2006; 5:30). As our understanding and technology improve, we may approach this level, with the potential to impact many levels of lung cancer management.

Dr. Peter Mazzone, FCCP Cleveland Clinic Respiratory Institute
Cleveland, OH

Editor’s Insight

Dr. Mazzone describes the earliest steps in an extremely fascinating area, the analysis of exhaled breath as a reflection of metabolic activity in the lungs. We have already seen how exhaled nitric oxide levels may help in the management of asthma, and now we learn more about the possible use of exhaled breath volatile organic compounds for identifying lung cancer.

This observation comes at an extremely important time. Lung cancer is already a huge public health problem, but, as the number of smokers both in the United States and around the world increases, lung cancer will become even more of a concern in the near future. Pulmonary physicians recognize the difficulty in identifying lung cancer early enough to enable curative surgical resection.

Huge trials are ongoing in the United States and Europe, evaluating CT scans as a possible screening tool for detecting lung cancer. Whether these studies successfully demonstrate the value of chest CT scans as an early detection tool for lung cancer or not, it seems entirely reasonable to wonder whether combining analysis of exhaled breath volatile organic compounds with chest CT scans might improve our ability to identify early lung cancer.

Table 1. VOCs Present in Greater Concentration in Breath of Patients With Lung Cancer

- Acetone
- Acetophenone
- 1,2,4-Trimethylbenzene
- Benzene
- Decane
- 2,4,6,6-Pentamethylethane
- 2,4-Dimethylthepane
- Heptane
- Hexene (1-)
- Isoprene
- Octane
- 2-Methylpentane
- Pentane
- Styrene

Dr. Gene L. Colice, FCCP
Editor, Pulmonary Perspectives
There are few topics in the field of sleep medicine as controversial as complex sleep apnea syndrome (CompSAS). Recent debates as to its existence have been featured at national meetings and in the literature (Gay 2008; 4:403; Malhotra et al.). Recent debates as to its existence have been featured at national meetings and in the literature (Gay 2008; 4:403; Malhotra et al.). Recent debates as to its existence have been featured at national meetings and in the literature (Gay 2008; 4:403; Malhotra et al.).

The explanation proposed was that patients would arouse frequently due to discomfort from the device; the frequent central apneas noted were simply the normal decrease in respiratory drive during the transition from wakefulness back to sleep (Marrone et al. Eur Respir J 1991; 4:660). Labeling the events as side effects of therapy makes sense because the majority of patients do not demonstrate significant central sleep apnea during diagnostic polysomnography. Other explanations of disease development have arisen, also relating the central events to the administration of CPAP. One such explanation propo...
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CHEST 2009 online registration is open through October 29, and on-site registration begins October 30. Learn more and register at www.chestnet.org.

Watch for special celebrations and events at CHEST 2009, as the ACCP celebrates 75 years of inspiring leadership, education, communication, and clinical practice.

TO NEBULIZE OR NOT?

Recent survey reveals patient attitudes regarding nebulization in the treatment of COPD

KRC Research, in conjunction with the COPD Foundation, recently conducted the Nebulization for Easier Breathing (NEB) Survey to gain an understanding of the general attitudes toward nebulization in the treatment of COPD. There were 800 participants: 400 patients with COPD and 400 caregivers. The NEB Survey was completed March 2009.

The reality is 89% of patients with COPD are very satisfied with their current nebulizer treatment. In fact, patients claim that using a nebulizer is better than using only an inhaler.

It’s not just those with COPD who favor nebulized therapy—it’s caregivers, too.

As a matter of fact, nebulization helps patients feel confident that they are getting the right dose of their medicine. Again, caregivers concur.

Ultimately, patients who are using nebulized therapy as part of their treatment feel that it allows them to be more active—which reverses a stereotype.

Many COPD patients who utilize nebulization can still lead a fulfilling, active life.

When asked whether they agreed with the statement “The overall quality of my life has improved since beginning nebulization,” three-quarters of patients and caregivers agreed. What’s more, patients and caregivers agreed that the benefits of nebulization far outweigh any challenges.

All in all, more than half of the patients surveyed wished that they could have been prescribed nebulized therapy sooner!

You might ask yourself if patients consider their nebulizer device too bulky or cumbersome—and the conclusion is “no!” The majority of patients surveyed—75%—have no complaints.

With the recent NEB Survey results, maybe it’s time to reconsider starting your patients on the road to more active living and feeling better with nebulized therapy.

This year’s dinner will kick off the ACCP’s 75th anniversary celebration. There will be a 75th anniversary display at the venue that correlates with an interactive trivia game that will be played by everyone attending the dinner. So, make sure you take the opportunity to look the display over during the reception.

This is the 11th year that The Foundation will confer the newly named D. Robert McCaffree, MD, Master FCCP Humanitarian Award to deserving projects supported by ACCP members’ expertise and volunteer time. This year, $50,000 will be awarded to six winning projects, including one Ambassadors Group Humanitarian Recognition Award. Each of these projects exemplify best practices of care and serve families worldwide who otherwise would be unable to access or afford medical care.

Another exciting part of the celebration that evening will be the announcement of the Al and Norine Lever Honorary Endowment Fund. This endowment will continue the Lever’s practice of mentoring others by developing leaders in the field and strategic leadership initiatives that will transform pulmonary, critical care, and sleep medicine.

The ACCP Industry Advisory Council will also present their annual monetary award to the Community Outreach Event partner, Santee School District Foundation, which will benefit Sycamore Canyon Elementary School.

Dinner invitations will be mailed after Labor Day. We hope that you will be able to join your colleagues and friends for an evening of celebration and fun. Ticket price is $150 per person ($25 of ticket price is tax-deductible), and online registration is available for those purchasing a ticket at www.chestfoundation.org. Making a Difference Society members at the $1,000 level are eligible for two complimentary tickets, and annual donors at the $500 level are eligible for one complimentary ticket, upon request. Contact Teri Ruiz at truiz@chestnet.org or (847) 498-8308 to obtain more information.

The CHEST Foundation’s 11th Annual Making a Difference Awards Dinner sponsors, to date, are: AstraZeneca, LP; Boehringer Ingelheim Pharmaceuticals, Inc.; Holland & Knight, LLP; Merck & Co., Inc.; Nymcom, Inc.; Pfizer, Inc; and sanofi-aventis.

ACCP members and CHEST faculty have been generously donating their honoraria to The CHEST Foundation for many years. This method of contributing has proven to be an easy way for donors to give to The Foundation while they enjoy the professional interaction with their peers at ACCP educational programs and pharmaceutical focus groups. Those contributing their honoraria to The CHEST Foundation are supporting The Foundation’s four areas of focus: tobacco prevention, clinical research, humanitarian service, and critical care/end-of-life care.

This fall, ACCP members can direct their honoraria to a new campaign developed by Dr. Jay I. Peters, FCCP – Physicians Speaking for Humanity or PS4H. PS4H is an appeal to physicians who lecture and/or attend pharmaceutical focus groups to donate their honorariums to The CHEST Foundation to support the pro bono service of ACCP members through The Foundation’s Humanitarian Service Program.

Prior to CHEST 2009, CHEST faculty members can indicate online that all or a portion of their honoraria should be made payable to The CHEST Foundation. The designated amount will automatically be given to The Foundation as a charitable contribution in their name, and any remainder due will be processed and mailed by the ACCP.

This donation clearly benefits The Foundation and may be a benefit to you by reducing your annual income at year-end. Canadian members donating in this way are allowed to donate US income and claim the eligible amount of the gift allowed on a US tax return, up to 75% of the net US income on a Canadian tax return.

If you are interested in donating honoraria received as faculty at CHEST 2009 or at outside pharmaceutical engagements to The CHEST Foundation’s annual fund or the PS4H campaign, contact Teri Ruiz at truiz@chestnet.org or (847) 498-8308.
A number of medical specialty society-driven patient registries and databases exists. The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) registry has been successful in establishing practice benchmarks among participating hospitals. The American College of Cardiology National Cardiovascular Data Registry (NCDR) has established nationally recognized indicators to measure quality care, and The Society of Thoracic Surgeons National Database realized a milestone when The Society was successful in attaining higher reimbursement rates for certain procedures.

The American College of Chest Physicians (ACCP) now offers the ACCP Quality Improvement Registry, Evaluation, and Education (AQuIRE) to assist the chest physician to meet increasing demands placed upon them by the public, credentialing bodies, regulatory agencies, payers, and the institutions in which they practice. AQuIRE combines data collection, quality and data reporting, and pathways to targeted education to increase knowledge and performance in deficient areas. Participation provides evidence of ongoing self-assessment, benchmarking with peers and the national experience, access to clinically and technically experienced support, and development of practices.

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The need for IRB approval to participate in a quality improvement registry is at the discretion of your individual IRB. AQuIRE is HIPAA-compliant and is for the purpose of receiving feedback about your clinical performance and, therefore, patients’ personal health information is not required in either of the bronchoscopy registries. Furthermore, a business associate agreement has been developed for participating sites and must be agreed to before data entry is permitted.

How Do I Enroll?

To enroll, contact Joyce Bruno Reitzner, MBA, MIPH, at jbruno@chestnet.org or by calling (847) 498-1120.
Global Pulmonary Vascular Disease, Lung Donor Pools

The supplement will be followed by a special symposium held at the CHEST 2010 meeting in Vancouver, BC, Canada. The discussion will address the challenges of recognizing and treating pulmonary vascular disease in the Third World, where PH-specific therapies are either not approved or prohibitively expensive.

The Pulmonary Vascular Disease NetWork hopes to bring readers of the CHEST journal and attendees of the CHEST meeting an international view of disease and mortality in PH.

Dr. Kamal Mubarak, FCCP
Pulmonary Vascular Disease NetWork Chair

Thoracic Oncology

This has been another productive year for the Thoracic Oncology NetWork. The NetWork completed a project that explored the variation in experts’ beliefs about lung cancer growth, progression, and prognosis. This brief report appeared in the Journal of Thoracic Oncology in April 2008. A second phase of this study surveyed Thoracic Oncology NetWork members about their understanding and perceptions of cancer growth and outcomes in lung cancer.

Dr. John (Jack) Buckley, FCCP
Affiliate NetWork Chair

Pulmonary Vascular Disease

The Pulmonary Vascular Disease NetWork is collaborating with the Pulmonary Vascular Research Institute (www.pvri.info), and several projects have been envisioned. The first is a special supplement to the CHEST journal to be published in 2010. This supplement will present a global perspective on pulmonary vascular diseases and, more specifically, pulmonary hypertension (PH). Physicians in the United States often assume that idiopathic PH and collagen-vascular disease cause the majority of pulmonary vascular disease in the world. However, recent statistical estimates indicate that the majority of pulmonary vascular disease in the world is caused by schistosomiasis and other entities, such as hemolytic anemias.

This special supplement will focus on causes of PH commonly seen around the world, especially in less industrialized countries. These causes include schistosomiasis, congenital heart disease, high altitude and hypoxia, COPD, HIV, and hemolytic-induced pulmonary vascular disease. Special reports will be included from Pulmonary Vascular Research Institute task forces in China, India, the Middle East, and Latin America.

The discussion will address the challenges of recognizing and treating pulmonary vascular disease in the Third World, where PH-specific therapies are either not approved or prohibitively expensive.

The Pulmonary Vascular Disease NetWork hopes to bring readers of the CHEST journal and attendees of the CHEST meeting an international view of disease and mortality in PH.
beliefs of the biology of lung cancer and how it may affect the way they manage patients. The results of this survey are currently being analyzed for publication.

The NetWork also has been busy assembling the content for the CHEST 2009 program. Some of the scheduled topics are “Early-Stage Lung Cancer: Moving Beyond TNM Staging in the Era of Molecular Prediction and Prognosis,” “Five Papers That Will Change How You Practice,” and “Thoracic Oncology Interactive Tumor Board.” Dr. W. Michael Alberts, FCCP, will chair the lung cancer guidelines update session, “What’s Stage III?” In addition, a post-graduate course on lung cancer will be lead by the immediate past chair of the Thoracic Oncology NetWork, Dr. Gerald Silvestri, FCCP. The Thoracic Oncology NetWork open meeting will be held on Monday, November 2, 2009, at 8:00 AM and include a presentation by Dr. Farhood Farjah titled, “Outcomes-Based Research in Lung Cancer.” In addition, the Thoracic Oncology NetWork is currently collaborating with the Society of Thoracic Surgeons on a project to develop a consensus statement, “Management of High-Risk Stage I NSCLC Patients.”

If you have ideas for topic submission for CHEST 2010, please contact any of the steering committee members via our NetWork Web site at www.chestnet.org/networks. To find out more about how to become involved with the Thoracic Oncology NetWork, contact Jenny Nemkovich at nemkovich@chestnet.org.

Dr. John A. Howington, FCCP Thoracic Oncology NetWork Chair

Transplant Expanding the Donor Pool: Lung Transplant From Non-Heart-Beating Donors

Donor shortage is a major problem for all solid organ transplantation, especially lung transplantation, which continues to have the highest waiting list mortality compared with other organ transplants (Christie et al. J Heart Lung Transplant 2008; 27:957). In order to expand the pool of potential donors, a growing number of transplant centers are beginning to use non-heart-beating donors or donation after cardiac death (DCD), particularly for abdominal transplantation (Bernat et al. Am J Transplant 2006; 6:281).

Although the first lung transplant surgery performed in 1963 originated from non-heart-beating donors (Hardy et al. JAMA 1963; 186:1065), it was not until recently that DCD donors have been more widely considered for lung transplantation. Most of the lung donors used in the last 3 decades were traditional brain-dead donors, and the use of DCD lungs has been slow to gain widespread acceptance.

Over the last several years, a few transplant centers around the world have begun to use controlled DCD (Maastricht category III) donors, who have a grave neurologic prognosis but do not meet the strict definition of brain death. In 2002, only one lung transplant in the United States was from a DCD donor; however, the number of centers using DCD donors has progressively increased since that time. In 2008, 20 lung transplants were performed using DCD donors. The numbers continue to rise, as 13 DCD lung transplants were performed in the first 4 months of 2009, according to data from the United Network for Organ Sharing (UNOS) Registry.

The outcomes from DCD donation have primarily been series of case reports, which have been encouraging, with at least equivalent short-term outcomes compared with traditional brain-dead donors. Mason and colleagues (Mason et al. J Thorac Cardiovasc Surg 2008; 136:1061) recently reviewed the US experience with outcomes from 36 DCD lung donors and reported a 1-year survival of 94% and a 2-year survival of 87%. Data presented at The International Society for Heart and Lung Transplantation meeting in April 2009 (Kang et al. J Heart Lung Transplant 2009; 28:S149) demonstrated that bronchoalveolar lavage fluid from DCD donors compared with traditional brain-dead donors had lower levels of inflammatory cytokines, which may be associated with better short-term clinical outcomes after transplantation.

Overall, the early experience from the use of DCD donors in lung transplantation has shown that results are at least as good as those attained with conventional donors. Increased use of DCD donors has the potential to ameliorate the organ shortage and further decrease the number of deaths on the lung transplant waiting list.

Dr. David Zaas, FCCP Transplant NetWork Steering Committee Member

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Women’s Health NetWork Luncheon and Open Meeting

The Women’s Health NetWork invites CHEST 2009 attendees to attend the WHN Luncheon on Tuesday, November 3, 2009, at 11:45 AM to 1:00 PM, and the WHN Open Meeting immediately following from 1:00 PM to 2:15 PM.

Keynote speaker Dr. Michael Zack, FCCP, will present Poetry and Medicine: “Etiology, and Pathogenesis.

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SLEEP MEDICINE

Sleep Disturbances May Provide Entry Into PTSD Care

BY SUSAN LONDON
Elsevier Global Medical News

SEATTLE — Returning military veterans with post-traumatic stress disorder often also have sleep disturbances that may provide an alternative, stigma-free entry into medical care, Anne Germain, Ph.D., said at the annual meeting of the Associated Professional Sleep Societies. Approximately 1.6 million people have been deployed to Afghanistan and Iraq as part of the current combat operations in those countries, noted Dr. Germain, an assistant professor of psychiatry at the University of Pittsburgh.

Roughly one-third of these people have been deployed multiple times. “We know that the risk of PTSD increases with each deployment,” said Dr. Germain. “So whatever estimates that we have right now for PTSD, we are likely to see an increase with the number of deployments and duration of tours.”

Deployment has been associated with an increased prevalence of PTSD. Dr. Germain noted. For example, 5% of Army personnel meet criteria for PTSD before deploying to Iraq, compared with almost 13% after their return, according to a study published in the New England Journal of Medicine (2004;351:13-22). In addition, it is known that three other psychiatric disorders—anxiety, depression, and alcohol misuse—become more prevalent after deployment. “All of these disorders are associated with stigma,” Dr. Germain observed.

Despite the military’s best effort to desegregate mental health disturbances post-deployment, a lot of people will refuse or be very hesitant to seek care for these conditions,” she noted.

However, all the disorders are also associated with sleep disturbances, including insomnia, irregular sleep-wake schedules, and hypersomnia. “Sleep disturbances may actually provide an entry into care that is not stigmatizing, that is more socially acceptable, that gets people to seek help first,” she said.

“And once they are in treatment, maybe we can address these other psychiatric difficulties.”

When it comes to the pathogenesis of PTSD and sleep disturbances in returning military personnel, research has implicated both physical and psychological exposures during deployment, according to Dr. Germain.

Her team is specifically investigating the role of blast exposure in a new study that has thus far enrolled a total of 25 military veterans returning from Iraq or Afghanistan who reported having sleep difficulties.

Preliminary analyses have shown that the returnees had an average age of 28 years, and 92% were men. Forty percent had been exposed to a blast during deployment.

The prevalence of PTSD was higher in the group that was exposed to blasts than in the nonexposed group (90% vs. 67%).

The groups had nearly equal, moderate levels of insomnia as measured by mean scores on the Insomnia Severity Index, or ISI (16.5 vs. 16.0), and they also had the same poor sleep quality as measured by mean scores on the Pittsburgh Sleep Quality Index, or PSQI (10.7 vs. 10.7).

“These veterans are well within the realm for clinically significant sleep disturbance,” Dr. Germain observed.

“The levels of sleep disturbances that we treat.”

However, the blast-exposed military veterans had a higher level of disruptive nocturnal behaviors, such as nightmares and traumatic event or dream enactments involving kicking or punching, as measured by mean scores on the PSQI Addendum (PSQI-A), a test which assesses sleep disturbances associated with PTSD (6.6 vs. 3.9).

“What these sleep disturbance findings mean is unclear at this time,” she commented.

“These findings are definitely something that we want to follow up, because the treatments for these types of sleep disturbances are very different from those that we typically use for insomnia, for example.”

Both blast-exposed and nonexposed returnees were similar in terms of sleep diary and polysomnography measures.

However, she noted, the polysomnography data might have been confounded by the high prevalence of PTSD. “When veterans with PTSD sleep in the sleep lab, they sleep much better. They feel safe; there is somebody watching them,” Dr. Germain explained.

ALL POSTDEPLOYMENT MENTAL DISORDERS ARE TIED TO SLEEP DISTURBANCES, INCLUDING INSOMNIA, IRREGULAR SLEEP-WAKE SCHEDULES, AND HYPERSOMNIA.

“So usually they catch up on sleep a little bit, and their sleep efficiency is better.”

Dr. Germain cautioned that definitive study results will require a larger sample size, as well as follow-up to assess the course of the sleep disturbances and PTSD.

A comparison of treatment outcomes in the blast-exposed and nonexposed groups also will be needed, Dr. Germain said. “I’m especially interested in looking at how sleep may play a role in the development of some of those mental health difficulties or adjustment difficulties—not just PTSD but other difficulties, too, such as depression—and in looking at the role of sleep in recovery as well,” she said.

Dr. Germain reported that she had no conflicts of interest in association with her presentation.

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Vaccines, in particular, have been shown to be highly effective in preventing infections. In a study of children, vaccination was associated with a 50% reduction in the risk of hospitalization for pneumonia. In another study, vaccination was associated with a 70% reduction in the risk of death from pneumonia. In a third study, vaccination was associated with a 90% reduction in the risk of death from pneumonia.

The benefit of a vaccine may be greater in populations with a higher baseline risk of infection, such as children, the elderly, and the immunocompromised. In addition, vaccination may be more effective in preventing severe illness and death from pneumonia than in preventing mild illness. Therefore, vaccination should be considered for all age groups at risk of pneumonia.

References:

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ZYVOX is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms:

- Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-resistant and -susceptible) or Streptococcus pneumoniae (including multiresistant strains [MDRSP]).
- Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-resistant and -susceptible) or Streptococcus pyogenes, or Streptococcus agalactiae. ZYVOX has not been studied in the treatment of decubitus ulcers.
- ZYVOX should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g., phentolamine, isocarboxazid) or within 2 weeks of taking any such product.

Unless patients are monitored for potential increases in blood pressure, ZYVOX should not be administered to patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis, and/or patients taking any of the following directly or indirectly acting sympathomimetic, vasopressors, and dopaminergic agents.

- ZYVOX has no clinical activity against Gram-negative pathogens and is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected.

Clostridium difficile-associated diarrhea has been reported with use of nearly all antibacterial agents, including ZYVOX, and may range in severity from mild diarrhea to fatal colitis.

Lactic acidosis has been reported with the use of ZYVOX. Patients receiving ZYVOX who develop recurrent nausea, vomiting, unexplained acidosis, or a low bicarbonate level should receive immediate medical evaluation.

Peripheral and optic neuropathy have been reported primarily in patients treated with ZYVOX for longer than the maximum recommended duration of 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended.

Conclusions have been reported in patients treated with ZYVOX. In some of these cases, a history of seizures or risk factors for seizures was reported.

The most commonly reported adverse events in adults across phase 3 clinical trials were diarrhea, nausea, and headache.

*MDRSP = multiresistant Staphylococcus aureus

References:

Please see brief summary of prescribing information on adjacent page.