**Sildenafil Found Beneficial in Pediatric PAH**

**BY DOUG BRUNK**

**Elsevier Global Medical News**

HONOLULU – The use of oral sildenafil helped improve oxygen delivery and exercise capacity in children with pulmonary arterial hypertension, results from a randomized, multicenter trial showed.

The study, which employed cardiopulmonary exercise testing— including assessment of ventilation to carbon dioxide (Ve/VCO2) slope — confirmed our suspicion that ventilatory efficiency, as measured by Ve/VCO2, appears to be a sensitive measurement to assess exercise ability in pediatric pulmonary arterial hypertension as long as the children are old enough and developmentally able to exercise reliably,” lead investigator Dr. Robyn J. Barst, FCCP said in an interview in advance of CHEST 2011, where the study was presented. Using such measures may allow future trials to determine drug effectiveness and safety with fewer study participants, thus shortening time to approval for new drugs, she said.

The STARTS-1 study included 234 treatment-naive children with pulmonary arterial hypertension (PAH), who were aged 1-17 years and weighed 8 kg or more. Participants were randomized to receive placebo or low, medium, or high doses of oral sildenafil three times a day at a 1:32 history of 16 countries including the United States. Doses were based on weight groups – 8-20 kg, 20-45 kg, and more than 45 kg — with the doses ranging from 10 to 80 mg t.i.d. Sildenafil is approved in the European Union for children with PAH at a dose of 10 mg t.i.d. for children who weigh less than 20 kg and 20 mg t.i.d. for children over 20 kg, but is not currently approved in childhood. The results were presented at CHEST 2011, where Dr. Barst was the lead author of the study.

**See Sildenafil • page 13**

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**CFRD Is Not Your Typical Diabetes**

**BY KERRI WACHTER**

**Elsevier Global Medical News**

Baltimore – Cystic fibrosis-related diabetes differs from type 1 and 2 diabetes and requires different management.

“Screening early and knowing which patients are at risk is really important,” Amanda Leonard said at a meeting on pediatric nutrition sponsored by Johns Hopkins University. Pulmonary function begins to decline several years before diagnosis of cystic fibrosis-related diabetes (CFRD), so identifying and treating patients with CFRD can have a big impact on life expectancy, said Ms. Leonard, a senior pediatric clinical dietician at the Johns Hopkins Cystic Fibrosis Center. Although CFRD is very different from type 1 and type 2 diabetes, “it does share some components,” she said. She summarized the highlights of the clinical care guidelines for CFRD issued by the American Diabetes Association and the Cystic Fibrosis Foundation (Diabetes Care 2010;33:2697-708). CFRD is associated with
CFC-Free Inhaler for COPD Approved

An inhalation spray containing ipratropium bromide and albuterol sulfate has been approved for patients with COPD, according to a statement by the Food and Drug Administration.

The product, marketed as Combivent Respimat inhalation spray, does not contain chlorofluorocarbons (CFCs) and “is a suitable alternative for patients who are currently using Combivent (ipratropium bromide and albuterol sulfate) inhalation aerosol,” according to the statement, issued by the Division of Drug Information (DDI) in the FDA's Center for Drugs, Evaluation and Research (CDER). Combivent inhalation aerosol, which contains CFCs, will not be available after Dec. 31, 2013. Like other inhalers that contain CFCs that deplete the ozone layer, the inhaler is being phased out because of the Montreal Protocol on Substances that Deplete the Ozone Layer, which makes it illegal to sell or make substances that deplete the ozone layer.

Ipratropium is an anticholinergic bronchodilator, and albuterol is a selective beta-2 adrenergic bronchodilator. Combivent inhalers are indicated for people with COPD on a regular bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator.

PAH Risk Seen With Dasatinib

Treatment with the leukemia drug dasatinib has been linked with an increased risk for pulmonary arterial hypertension, which can occur at any time after starting treatment, the FDA announced. None of the cases were fatal, and PAH “may be reversible” if treatment is discontinued, according to the statement.

Dasatinib, a kinase inhibitor marketed as Sprycel by Bristol-Myers Squibb, is approved for treating adults with Philadelphia chromosome-positive chronic myeloid leukemia (CML) or acute lymphoblastic leukemia (ALL). Since dasatinib was approved in 2006, the BMS global pharmacovigilance database has identified cases of PAH in treated patients, the statement said. In 12 of these cases, right heart catheterization confirmed the diagnosis, and dasatinib was considered “the most likely cause,” the FDA said. These patients had developed symptoms at various intervals after starting treatment, including more than 12 months afterward, and they were often taking other medications or had comorbidities, so “there may be a combination of factors contributing to the development of PAH” in patients taking dasatinib, the FDA said.

Because dyspnea, fatigue, hypoxia, fluid retention, and other PAH symptoms overlap with those of other conditions, “a diagnosis of Sprycel-associated PAH should be considered” if other causes have been ruled out in symptomatic patients, the FDA advises. Health care professionals should also evaluate patients for signs and symptoms of underlying cardiopulmonary disease before and during treatment. The drug should be permanently discontinued if a diagnosis of PAH is confirmed. Improvements in pulmonary hemodynamics and clinical parameters were observed following discontinuation in some patients, the FDA statement said.

Risks Added to Bevacizumab Label

A warning about the risk of ovarian failure in premenopausal women has been added to the label for bevacizumab, along with additional data about venous thromboembolic events and new postmarketing data identifying osteonecrosis of the jaw as an “adverse reaction,” the FDA said.

Bevacizumab—marketed as Avastin by Genentech—is a vascular endothelial growth factor inhibitor approved in 2004 for the treatment of lung and several other cancers. (Approval for use in breast cancer was revoked by the FDA on Nov. 18.)

Information about the increased risk of VTEs and bleeding associated with bevacizumab in patients receiving anti-coagulation therapy after a first VTE event has also been added in the section on Clinical Trial Experience, the FDA said. A randomized, prospective four-arm study of 1,401 patients found that in those in the bevacizumab-containing arms, the incidence of a first VTE was 13.5%, compared with 9.6% among the patients in the chemotherapy-only arms.

The potential for ovarian failure associated with bevacizumab treatment is new information. The label now states that the long-term effects of exposure to bevacizumab on fertility are unknown and that women of reproductive potential should be informed about the risk of ovarian failure before starting treatment.

The label also now includes a statement about postmarketing reports of osteonecrosis of the jaw (ONJ) in patients treated with bevacizumab who have not been treated with bisphosphonates. (ONJ has been reported in patients on bisphosphonates.)

Septic Shock Drug Pulled Off Market

The failure of Xigris to show an effect on mortality in a clinical trial of patients with septic shock has prompted the manufacturer to withdraw the drug from the United States and other countries where it is approved, Eli Lilly announced.

Xigris (drotrecogin alfa [activated]), a recombinant form of human activated protein C, was approved in the United States in 2001 for the reduction in mortality in adults with severe sepsis who have a high risk of death.

The PROWESS-SHOCK study showed that treatment with Xigris did not meet the primary end point, a significant reduction in 28-day all-cause mortality in patients with septic shock, Lilly announced in a statement.

“While there were no new safety findings, the study failed to demonstrate that Xigris improved patient survival and thus calls into question the benefit-risk profile of Xigris and its continued use,” Dr. Timothy Garrett, senior vice president and chief medical officer at Lilly, said. Xigris should be stopped in patients currently being treated with it, and the drug should not be used in new patients.

—Elizabeth Mechanic
Lung Transplantation Beneficial in Select CF Patients

BY SUSAN LONDON
Elsvier Global Medical News

DENVER – “Lung transplantation for cystic fibrosis can be performed successfully, with survival benefit and quality of life benefit,” Dr. Keith C. Meyer, FCCP, told attendees at the International Conference of the American Thoracic Society.

The median survival of patients with cystic fibrosis (CF) has increased dramatically, from 0.5 years in 1940 to 37 years in 2006, according to data from the Cystic Fibrosis Foundation. “We see more and more adults in clinics with time, and actually about 47% of patients have now reached adulthood at age 18;” he noted. However, many of them have severe lung dysfunction by the time they reach adulthood.

When it comes to referring patients for transplantation, “you have to weigh things very carefully and make sure you are providing benefit to your patient,” noted Dr. Meyer, codirector of the Adult Cystic Fibrosis Program at the University of Wisconsin Hospital and Clinics in Madison. “Not only the success of the disease must be compared with the risks of transplantation.

As for the timing of transplantation, patterns suggest that patients go through three disease phases during which they are too well for transplantation, one during which they experience a rapid decline in their condition, and one during which they are too ill. The middle phase is where you want to catch them, a window of opportunity,” he said.

Current guidelines recommend that referral for lung transplantation be based on the individual patient, the referring physician’s estimation of functional and quality of life, and the patient’s desire for information (J. Heart Lung Transplant. 2006;25:745-55).

The guidelines also outline criteria for referring patients to a transplant center and for placing them on the wait list for lung transplantation. The main trigger for referral, in addition to clinical events signaling rapid deterioration, is a forced expiratory volume in 1 second (FEV1) that has dropped below 30% of that predicted or has declined rapidly. The triggers for listing are oxygen-dependent respiratory failure, hypercapnia, and pulmonary arterial hypertension.

You have to evaluate your patient very well,” Dr. Meyer noted. “We do a thorough psychosocial evaluation at our center, as well as our full cardiopulmonary evaluation. Other testing, as required, and an infection-specific evaluation – we have all our patients hooked up with an infectious disease specialist before transplant.”

AMONG ALL LUNG TRANSPLANT RECIPIENTS WITH VARIOUS CONDITIONS, PATIENTS WITH CYSTIC FIBROSIS HAVE THE BEST SURVIVAL.

For example, “if they are colonized with Aspergillus, we still will do the transplantation,” explained Dr. Meyer. “Of course, over half of our patients with CF are colonized with Aspergillus. We just want to make sure that there are not perhaps some other complications along with the Aspergillus.

The lung allocation score, adopted in 2005, “has changed things a little bit. We tend to transplant patients at the right time because we are better able to match them with donors,” he said. Patients with CF and patients with idiopathic pulmonary fibrosis are given priority.

The lung allocation score “rises with disease progression,” Dr. Meyer noted. The mean score for patients with CF who are candidates for transplantation is among the highest of all candidates for lung transplantation, at approximately 35 (Am. J. Transplant. 2006;6:1212-27).

“Bilateral lung transplant is the procedure of choice,” he said. Adults with CF now make up a quarter of all adults undergoing bilateral lung transplantation (J. Heart Lung Transplant. 2010;29:1083-141). As of 2009, roughly 200 patients with CF were undergoing lung transplantation annually.

Among all lung transplant recipients with various conditions, patients with CF have the best survival (J. Heart Lung Transplant. 2010;29:1083-141). This is “probably partially due to the fact that they are younger and maybe because with all this tremendous pulmonary inflammation they had over time, maybe their immune rejection response is somewhat blunted.”

A total of 72 patients with CF have undergone lung transplantation at his center, and their 1-year survival rate is 67%.

“Things are often rocky in the first few months. If they can make it out to 1 year and things are going pretty well, they tend to do well over time,” he said. Dr. Meyer reported having no conflicts of interest related to his presentation.
Steroids May Help if Given Early

ALI-ARDS

From page 1

Dr. Pastores, who is also a professor of medicine concluded that moderate-dose glucocorticoids should be considered in patients with early severe ARDS (PaO₂/FiO₂, of less than 200) and before day 14 in patients with unresolved ARDS (Crit. Care Med. 2008;36:1937-49). “We could not come to a definitive conclusion or recommendation on patients with less severe ALI,” said Dr. Pastores, who was a member of the task force. “Keep in mind that the recommendation is based on level 2B evidence for a mortality benefit. It’s a weak recommendation because the quality of the evidence was moderate; it wasn’t very strong because we didn’t have enough good randomized, controlled trials. For reduction in duration of mechanical ventilation, however, the evidence is strong (1B), with the aggregate of data showing a doubling of extubation, in comparison to controls, by days 7 and 14.”

He noted that physicians should give steroids in conjunction with infection surveillance, “avoiding neuromuscular blockers if you can, and being concerned about the phenomenon of rebound inflammation if you stop steroids abruptly.”

Inhaled nitric oxide has also been studied in ALI/ARDS. A Cochrane review of 13 randomized, controlled trials involving 1,303 patients found no significant effect with this approach in overall mortality, but did show a transient improvement in oxygenation in the first 24 hours. The review also found that inhaled nitric oxide had no significant effect on duration of ventilation, ventilator-free days, and ICU and hospital length of stay. An increased risk of renal impairment among adults was also noted (Cochrane Database Syst. Rev. 2010 Oct. 23 [doi:10.1002/14651858.CD002782.pub2]).

The conclusion from this meta-analysis was that there was no mortality benefit, and in fact [nitric oxide] might even be harmful,” Dr. Pastores said.

Intriguing findings on the use of neuromuscular blockers in severe, early ARDS was presented in 2010 after a multicenter trial of 340 patients who were randomized to IV cisatracurium infusion or placebo for 48 hours (N. Engl. J. Med. 2010;363:1107-16). The primary outcomes were 90-day mortality and ventilator-free days.

Patients in the treatment group had lower 90-day mortality and more ventilator-free days, compared with those in the placebo group. “Neuromuscular blockers may facilitate lung protective ventilation in this patient population by improving patient-ventilator synchrony,” Dr. Pastores said. “They may also improve chest wall compliance and reduce oxygen consumption, and possibly cause a decrease in lung or systemic inflammation.”

The study’s limitations were that “it only involved cisatracurium and therefore may not apply to other neuromuscular blockers. There were also no data on conditions known to antagonize or potentiate neuromuscular blockers,” he added.

Another treatment strategy for ALI/ARDS – the routine use of aerosolized beta₂-agonists – cannot be recommended at this time because of the results of a recent trial in which patients were randomized to 5 mg aerosolized albuterol or saline placebo every 4 hours for up to 10 days. The primary outcome was ventilator-free days.

“The trial had to be stopped for futility because there was no improvement in ventilator-free days,” Dr. Pastores said. “In fact, there was a suggestion of a slight trend of increasing morbidity among patients in the treatment group. The investigators theorized that the lung-protective ventilation and conservative fluid management reduced lung injury and water to the extent that additional lung fluid clearance with beta₂-agonists had no additional beneficial effect,” he said.

The role of pharmacomutrition has also been studied in this patient population. According to Dr. Pastores, three previous trials of continuous omega-3 enteral feeds showed improved PaO₂/FiO₂ ratio, shorter ventilator time and ICU stay, and fewer organ failures and lower mortality. However, a more recent randomized, controlled trial of 272 adults found that twice-daily administration of omega-3 fatty acids plus antioxidant supplementation did not improve ventilator-free days or other clinical outcomes (JAMA 2011;306:1574-81). “There was some suggestion that perhaps it was harmful to these patients,” Dr. Pastores said. For example, 60-day hospital mortality was higher among the patients in the treatment group, compared with those in the placebo group (27% vs. 16%, respectively, P = 0.05).

Future nonventilatory therapies that might hold promise for patients with ALI/ARDS, he said, include inhaled protein C, tissue factor inhibition, statins, and the extended use of steroids in severe community-acquired pneumonia.

Dr. Pastores disclosed that he has received grant support from Altor Bioscience Corp. and from Spectral Diagnostics Inc.
Long-Term Impairments Common in ALI/ARDS

THE PACE OF RECOVERY IS PROTRACTED AND LIKELY INCOMPLETE IN THE CURRENT PARADIGM OF CARE.

BY DOUG BRUNK
Elsiver Global Medical News

HONOLULU – Although large numbers of patients are surviving acute lung injury/adult respiratory distress syndrome, long-term impairments are common and “striking for their relationship to neuropsychiatric dysfunction,” Dr. Jesse Hall, FCCP, said at CHEST 2011, the annual meeting of the American College of Chest Physicians.

“The pace of recovery is protracted and likely incomplete in the current paradigm of care,” said Dr. Hall, professor of medicine, anesthesia, and critical care at the University of Chicago. “Interventions including those begun at the onset of critical illness will hopefully improve these outcomes.”

According to the best epidemiologic study on the topic, an estimated 191,000 cases of acute lung injury (ALI) and 141,500 cases of adult respiratory distress syndrome (ARDS) occur each year in the United States, causing a combined 133,500 deaths annually (N. Engl. J. Med. 2005;353:1685-93). Implementation of low-tidal-volume ventilation over the past decade has led to an improvement in survival among this patient population. Dr. Hall said, but “we are just beginning to understand through descriptive studies what the path is for these patients down the road. We really lack many prospective trials in that arena.”

One study of 109 ARDS patients who were followed for 1 year found that most developed a restrictive lung lesion that improved in the first 6-12 months (N. Engl. J. Med. 2003;348:681-93). “The most consistent pulmonary function test abnormality tends to be low diffusion capacity that often resolves over time,” Dr. Hall said. Some of their general functional limitation correlates to their pulmonary dysfunction, “but much of it does not,” he said. “In fact, it’s not what the patients report. They start to have a very low functional status 6, 12, and more months out, and they don’t ascribe it primarily to their lung dysfunction.”

Residual areas of fibrosis are not unusual on follow-up CT scans of ALI/ARDS patients, and many of these patients develop airway abnormalities such as bronchiectasis associated with their lung injury, said Dr. Hall, who is also section chief of pulmonary and critical care medicine at the University of Chicago.

The 2003 study of 109 ARDS patients found that all subjects reported poor function due to loss of muscle bulk, proximal weakness, and fatigue. Some (12%) reported persistent pain at the chest tube site, 7% reported entrapment neuropathies, 7% had tracheotomy site problems, 5% had large joint enlargement/immobility from heterotopic osseous formation, and 4% had immobility in the form of contracted fingers or frozen shoulders. “It can be up to a year before patients regain their body weight after this episode,” Dr. Hall said.

Neuromuscular sequelae may include myopathy, peripheral neuropathy, or deconditioning. “Any given patient can have any combination of those,” he said. “Some of these disorders are reasonably strongly associated with some of our therapies. Most of our patients have a combination of peripheral neuropathies and problems that may by themselves be modest but are attended by extreme deconditioning. The neuromuscular sequelae of critical illness are variable in terms of recovery over months and years, and some patients seem to never fully recover.”

The impact of neuropsychiatric sequelae can be significant. One study of 55 ARDS patients found that 100% had cognitive and affective impairments at hospital discharge, and 30% had generalized cognitive decline 1 year later (Am. J. Respir. Crit. Care Med. 1999;160:50-60). In the 2003 study, only 49% of the ARDS patients who had been employed were back to work at 1 year. “This is an astounding economic and financial consequence for the patient and the family,” Dr. Hall c o n f i r m e d. “Scoring on the Short Form-36 were below normal in all eight domains at 3-, 6-, and 12-month follow-up from ICU discharge. There were improvements in most SF-36 categories, but almost none were back to normal.”

Dr. Hall said that changes in the current health care system are needed to improve outcomes for ALI/ARDS patients. Currently, “it’s difficult for those in our discipline to figure out how to become a change agent, or help our patients acquire what they need to optimize their recovery,” he explained. “It’s not likely, in fact, to be done by critical care doctors down the road.”

One study from the United Kingdom sought to determine if giving patients a self-help rehabilitation manual would affect their general functional status and “therefore their psychiatric axes as well,” Dr. Hall said. “We may even make them more functional,” Dr. Hall said. For the study, patients in the control group received ward visits, three telephone calls at home, and clinic appointments at 8 weeks and 6 months, whereas patients in the intervention group received the same plus a 6-week self-help rehabilitation manual. At the end of 6 weeks, patients in the intervention group had significantly better physical function scores, compared with controls (Crit. Care Med. 2003;31:2456-61). Unfortunately, such benefits were not seen in another recent prospective trial.

In a recent trial conducted by a group of researchers that included Dr. Hall, 104 critical care patients who required ventilation were randomized to either early physical and occupational therapy during periods of daily interruption of sedation, or to no daily interruption of sedation with therapy as ordered by the primary care team (Lancet 2009; 373:1874-82). Compared with controls, patients who received early physical and occupational therapy had a faster return to independent functional status at hospital discharge (59% vs. 35%, respectively) and less ICU delirium (2 days vs. 4 days).

Dr. Hall concluded by noting that the brain and the neuromuscular and musculoskeletal systems “are likely the last to recover after ALI/ARDS, and may not recover fully to the status patients had before. We don’t know what matters most for long-term recovery. It’s reasonable to think that shortening ICU and mechanical ventilation time would be beneficial.”

Dr. Hall disclosed that he receives honoraria from the American College of Chest Physicians and the American Thoracic Society.

Adverse Effects Discourage Imatinib for Treatment of SSc

THE PACE OF RECOVERY IS PROTRACTED AND LIKELY INCOMPLETE IN THE CURRENT PARADIGM OF CARE.

VITALS

Major Finding: Five of the 20 patients treated with imatinib discontinued treatment due to adverse side effects. Improvements of 1.74% in the estimated FVC % predicted, 4.17% in the TLC % predicted, and 1.46% in the DLCO % predicted were seen over a 1-year period.

Data Source: The study was conducted on 20 SSc patients at two sclerodema centers in the United States.

Disclosures: The researchers reported no relevant financial disclosures. Novartis Pharmaceuticals provided the study drug and partial support for the study.

The study subjects met the American College of Rheumatology criteria for systemic sclerosis (SSc). The mean disease duration was less than 10 years, their mean forced vital capacity (FVC) was less than 85% of predicted, their dyspnea on exertion was at least grade 2 on the modified Rodman skin thickness score (MRSS) was assessed every 3 months, according to Dr. Dinesh Khanna of the University of California at Los Angeles.

Imatinib treatment increased FVC by 1.74%, though this was not statistically significant. In addition, the MRSS increased by 3.9 units. The total lung capacity increased by 4.17% over predicted and the diffusion capacity for carbon monoxide improved by 1.46% versus predicted, according to the investigators (Arthritis Rheum. 2011;63:1340-6).

One of the 20 who participated, 5 did not complete the study due to adverse events that were caused by the treatment itself. A further two dropped out due to adverse events caused by SSc, and one was lost due to follow-up. The rest completed the study.

Some of the common adverse events the participants experienced were fatigue, swelling of the face and/or lower extremities, nausea and vomiting, diarrhea, generalized rash, and new-onset proteinuria.

Because of its efficacy, the authors suggest further research with smaller doses of imatinib so as to reduce adverse effects while maintaining the positive effects.

Dr. Jeana O’Brien, FCCP, comments: This small study regarding treatment with imatinib in patients with systemic sclerosis-associated interstitial lung disease (ILD) revealed no significant improvements in objective pulmonary function and only very modest gains on the Mahler dyspnea index. This dose of imatinib unfortunately also produced significant adverse effects resulting in a high discontinuation rate. While additional study with lower doses of the medication may show fewer adverse effects – and is reasonable to perform given the limited therapeutic options – these results cast doubt as to the overall ultimate benefit of imatinib for SSc-associated ILD.
Most Smokers Want to Quit, but Few Get Help

BY PATRICE WENDLING
Elsevier Global Medical News

M ost smokers in the United States want to quit, but when they try, they do so without medications or formal counseling from health professionals, according to a new study in the Centers for Disease Control and Prevention’s National Health Interview Survey. In 2010, 69% of adult cigarette smokers said they wanted to quit, and 52.4% had recently tried to do so for more than 1 day. Still, 68.3% of current smokers who tried to quit did so without using evidence-based cessation counseling or medications, and fewer than half (48.3%) of those who saw a health professional in the past year reported receiving advice to quit (MMWR 2011 Nov 11;60:1513-9).

“What this means is that there’s significant room for improvement in this arena because use of these treatments can double or triple success rates,” Dr. Tim McAfée, director of the Office of Smoking and Health, said during a press briefing on the report.

Among those who visited a health professional in the year, women (51.7%) were more likely than men were (44.8%) to have received a health professional’s advice to quit. More than half of those aged 65 years and older (57%) received such advice.

Among racial groups, Hispanics were the least likely to have received advice, at 34.7%, compared with 50% of whites and 46% of blacks, according to the study, which was based on 2001-2010 National Health Interview Survey data. When asked by reporters how the overall 46% counseling rate stacks up with previous years, Dr. McAfée said it’s lower than in their previous surveys, but added that the current survey had changed and that an earlier question on tobacco use had been removed.

“We’re not sure if this is a real trend or an artifact in the way the survey questions were administered,” he said. Ann Malarcher, Ph.D., lead author of the study, said other national data sets that examine whether smokers receive advice to quit are showing no change over time. Those data sets show counseling rates as high as 60%.

One of the more troubling findings in the report is that non-Hispanic blacks had the highest level of interest in quitting and the most quit attempts in the past year, but also the lowest rate of successfully quitting, at 3.3% vs. 6.0% for whites and 9.5% for Hispanics.

The lower success rate for those aged 65 years and older, even those who made a quit attempt, was 6.2% of smokers reported stopping smoking. It’s hard to say how this compares with previous years because other surveys didn’t typically ask this, although it is a new measure required for the Healthy People 2020 objective, Dr. Malarcher said.

“Why we added that measure for these objectives is that we really want to look at recent success,” she said. “We hope to move the needle and get more people to quit each year.”

“Of those who made a quit attempt, just under one-third received counseling and medication,” Dr. McAfée said. He acknowledged the controversy over the use of varenicline (Chantix) and advised smokers to ask their physician. He added that the smoking cessation drugs are effective and that data on the reported neuropyschiatric effects are mixed. Notably, a study reported last week that varenicline was eight times more likely to be linked with suicidal behavior or depression than were other nicotine replacement products (PLOS One 2011 Nov 2; [doi:10.1371/journal.pone.0027016]), while two recent Food and Drug Administration-revised studies found no relationship between varenicline use and the risk of psychiatric hospitalization.

Finally, Dr. McAfée said the study is not without its shortcomings: He noted that it shows that the 45.3 million Americans (19.3%) who still smoke are as interested in quitting as they were 10 years ago. “What we’re concerned about, honestly, is that society has been losing its enthusiasm for supporting smokers’ in their quit attempts, he said. “We’ve seen a degradation in funding by the states over the last 3 years that is deeply concerning, especially considering the increasing amount of money they are bringing in through taxes and the [Tobacco] Master Settlement.”
INDICATIONS AND USAGE
DALIRESP is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. DALIRESP is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

Please see Important Safety Information and Brief Summary of full Prescribing Information on the following pages and at www.DALIRESP.com.

COPD=chronic obstructive pulmonary disease.
IMPORTANT SAFETY INFORMATION

Contraindications
DALIRESP is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C).

Warnings and Precautions
• DALIRESP is not a bronchodilator and should not be used for the relief of acute bronchospasm.
• Prescribers should advise patients, their caregivers, and families to be alert for the emergence or worsening of insomnia, anxiety, depression, suicidal thoughts or other mood changes, and if such changes occur, to contact their healthcare provider. Prescribers should carefully evaluate the risks and benefits of continuing treatment if such events occur. Before using DALIRESP in patients with a history of depression and/or suicidal thoughts or behavior, prescribers should carefully weigh the risks and benefits of treatment with DALIRESP.
  – Treatment with DALIRESP is associated with an increase in psychiatric adverse reactions. In controlled clinical trials 5.9% of patients treated with DALIRESP reported psychiatric adverse reactions vs 3.3% treated with placebo. The most common psychiatric adverse reactions were insomnia (2.4% vs 1.0%), anxiety (1.4% vs 0.9%), and depression (1.2% vs 0.9%).
  – Three patients treated with DALIRESP experienced suicide-related adverse reactions (one completed suicide and two suicide attempts) compared to one patient (suicidal ideation) treated with placebo.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages and at www.DALIRESP.com.
For patients with severe COPD associated with chronic bronchitis and a history of exacerbations

TREAT NOW WITH DALIRESP®

The first and only selective PDE4 inhibitor to reduce the risk of COPD exacerbations¹,²

- Reduces moderate or severe exacerbations by 17% vs placebo¹,³,⁴
- Effective alone or in combination with a bronchodilator¹,³
- Effective in older and younger patients (>65 and 40-65 years)¹,³
- Statistically significant increase in lung function (pre-bronchodilator FEV₁) of 48 mL vs placebo¹,⁴
  - DALIRESP is not a bronchodilator; this increase was not clinically significant¹,³
- The first class of drugs approved for COPD in 25 years²,⁵

• Patients should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated and treatment discontinuation considered.
  - In addition to weight loss being reported as a common adverse reaction (7.5% of patients treated with DALIRESP vs 2.1% placebo), weight was prospectively assessed in two 1-year clinical trials. In these studies that compared DALIRESP to placebo, 20% vs 7% experienced moderate weight loss (5-10% of body weight) and 7% vs 2% experienced severe weight loss (>10% body weight).
  - During the follow-up period after discontinuing DALIRESP, the majority of patients regained some of the weight they had lost.
- Use with strong cytochrome P450 enzyme inducers (eg, rifampicin, phenobarbital, carbamazepine, phenytoin) is not recommended, as they decrease the exposure and may reduce the therapeutic effectiveness of DALIRESP.
For patients with severe COPD associated with chronic bronchitis and a history of exacerbations

DALIRESP significantly reduces exacerbations

Study design: A pre-specified pooled analysis from 2 identical, 52-week, double-blind, placebo-controlled trials in patients with severe COPD associated with chronic bronchitis and a history of exacerbations (N=3091). Median patient age was 64 years; 76% male, 84% Caucasian. LABAs or short-acting anticholinergics were allowed as concomitant treatment. The reduction in the rate of moderate (requiring treatment with systemic glucocorticosteroids) or severe (resulting in hospitalization and/or leading to death) exacerbations and change in lung function (pre-bronchodilator FEV₁) were co-primary endpoints. Each study met both co-primary endpoints.

- Moderate exacerbations were defined as those requiring treatment with systemic corticosteroids¹
- Severe exacerbations were defined as resulting in hospitalization and/or death¹

INDICATIONS AND USAGE
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For patients with severe COPD associated with chronic bronchitis and a history of exacerbations

Effective with LABAs or short-acting anticholinergics

**In the same studies:**

**DALIRESP** significantly reduced the rate of exacerbations vs placebo in patients using a bronchodilator

**Study design:** A pre-specified pooled analysis from 2 identical, 52-week, double-blind, placebo-controlled trials in patients with severe COPD associated with chronic bronchitis and a history of exacerbations (N=3091). Median patient age was 64 years; 76% male, 84% Caucasian. LABAs and short-acting anticholinergics were allowed and were used by 44% and 35% of patients treated with DALIRESP and 45% and 37% of patients treated with placebo, respectively. The reduction in the rate of moderate (requiring treatment with systemic glucocorticosteroids) or severe (resulting in hospitalization and/or leading to death) exacerbations and change in lung function (pre-bronchodilator FEV₁) were co-primary endpoints. Each study met both co-primary endpoints.

- The effect with concomitant LABAs or short-acting anticholinergics was similar to that seen in the overall population

**IMPORTANT SAFETY INFORMATION**

**Warnings and Precautions**

- Patients should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated and treatment discontinuation considered.

**Adverse Reactions**

In clinical trials the most common adverse reactions (≥2% and greater than placebo) were diarrhea (9.5% vs 2.7%), weight loss (7.5% vs 2.1%), nausea (4.7% vs 1.4%), headache (4.4% vs 2.1%), back pain (3.2% vs 2.2%), influenza (2.8% vs 2.7%), insomnia (2.4% vs 1.0%), dizziness (2.1% vs 1.1%), and decreased appetite (2.1% vs 0.4%).

Please see additional Important Safety Information on the previous pages and Brief Summary of full Prescribing Information on the following page and at [www.DALIRESP.com](http://www.DALIRESP.com).
DALRESP™ (roflumilast) tablets
Rx Only
Brief Summary of full Prescribing Information
Initial U.S. Approval: 2011
INDICATIONS AND USAGE
DALRESP™ is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.

Dalrespons is not a bronchodilator and should not be used for the relief of acute bronchospasm.

CONTRAINDICATIONS
The use of DALRESP is contraindicated in the following conditions:
- Moderate to severe liver impairment (Child-Pugh B or C) [see Clinical Pharmacology (12.3) and Use in Special Populations (8.6)].

Warnings and Precautions
- Treatment of Acute Bronchospasm
DALRESP is not a bronchodilator and should not be used for the relief of acute bronchospasm.

- Psychiatric Events Including Suicidality
Treatment with DALRESP is associated with an increase in psychiatric adverse reactions. In 8 controlled clinical trials 5.9% (263) of patients treated with DALRESP 500 mcg daily reported psychiatric adverse reactions compared to 3.3% (137) treated with placebo. The most commonly reported psychiatric adverse reactions were insomnia, anxiety, and depression which were reported at higher rates in those treated with DALRESP 500 mcg daily (2.4%, 1.4%, and 1.2% for DALRESP versus 1.0%, 0.9%, and 0.9% for placebo, respectively) [see Adverse Reactions (6.1)]. Instances of suicidal ideation and behavior, including completed suicide, have been observed in clinical trials. Three patients experienced suicide-related adverse reactions (one completed suicide and two suicide attempts) while receiving DALRESP compared to one patient (suicide ideation) who received placebo.

Before using DALRESP in patients with a history of depression and/or suicidal thoughts or behavior, prescribers should carefully weigh the risks and benefits of treatment with DALRESP in such patients. Patients, their caregivers, and families should be advised of the need to be alert for the emergence of worsening of insomnia, anxiety, depression, suicidal thoughts or other mood changes, and if such changes occur to contact their healthcare provider. Prescribers should carefully evaluate the risks and benefits of continuing treatment with DALRESP if such events occur.

- Weight Decrease
Weight loss was a common adverse reaction in DALRESP clinical trials and was reported in 7.5% (321) of patients treated with DALRESP 500 mcg once daily compared to 2.1% (89) treated with placebo [see Adverse Reactions (6.1)]. In addition to being reported as adverse reactions, weight was prospectively assessed in two placebo-controlled clinical trials of one year duration. In these studies, 29% of patients receiving roflumilast experienced moderate weight loss (defined as between 5-10% of body weight) compared to 7% of patients who received placebo. In addition, 7% of patients who received roflumilast compared to 2% of patients receiving placebo experienced severe (>10% body weight) weight loss. During follow-up after treatment discontinuation, the majority of patients with weight loss regained some of the weight they had lost while receiving DALRESP in these trials.

- Drug Interactions
A major step in roflumilast metabolism is the N-oxidation of roflumilast to roflumilast N-oxide by CYP3A4 and CYP1A2. The administration of the cytochrome P450 450 enzyme inducer rifampicin resulted in a reduction in the plasma exposure of DALRESP. The coadministration of DALRESP with drugs that induce cytochrome P450 450 enzymes should be avoided.

- Pregnancy and Lactation
Roflumilast is not indicated in pregnant or lactating women. There are no adequate and well controlled studies in pregnant women. In animal reproduction studies, DALRESP produced no evidence of fetal toxicity when given to rats and rabbits in doses up to 34 times the MRU on a mg/m² basis, 10 times the MRU on a mg/kg basis, and 34 times the MRU on a mg/m² basis to maternal and fetal tissues, respectively.

- Nursing Mothers
Roflumilast and its metabolites are excreted into the milk of lactating rats. Excretion of roflumilast and/or its metabolites into human milk is probable. There are no human studies that have investigated the effects of DALRESP on breast-fed infants. DALRESP should not be used by women who are nursing.

- Pediatric Use
DALRESP does not currently occur in children. The safety and effectiveness of DALRESP in pediatric patients have not been established.

- Geriatric Use
The safety and effectiveness of DALRESP were reduced in older subjects and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Based on available data for roflumilast, no adjustment of dosage in geriatric patients is warranted [see Clinical Pharmacology (12.3)].

- Hepatic Impairment
Roflumilast 250 mcg once daily for 14 days was studied in subjects with mild-to-moderate hepatic impairment compared to healthy volunteers (2 subjects in each group). The AUCs of roflumilast and roflumilast N-oxide were increased by 51% and 24%, respectively in Child-Pugh A subjects and by 92% and 77%, respectively in Child-Pugh B subjects compared to healthy subjects. The Cmss of roflumilast and roflumilast N-oxide were increased by 3% and 26%, respectively in Child-Pugh B subjects and by 26% and 40%, respectively in Child-Pugh B subjects, as compared to healthy subjects. Roflumilast 500 mcg has not been studied in subjects with severe or greater liver impairment. DALRESP is not recommended for use in patients with moderate or severe liver impairment (Child-Pugh B or C) [see Contraindications (4) and Clinical Pharmacology (12.2)].

- Renal Impairment
In twelve subjects with severe renal impairment administered a single dose of 500 mcg roflumilast, the AUCs of roflumilast and roflumilast N-oxide were decreased by 21% and 7%, respectively and Cmss were reduced by 16% and 12%, respectively. No dosage adjustment is necessary for patients with renal impairment [see Clinical Pharmacology (12.3)].

OVERDOSAGE
- Human Experience
No case of overdose has been reported in clinical studies with DALRESP. During the Phase I studies of DALRESP the following symptoms were noted at a single oral dose of 250 mcg and a single dose of 5000 mcg: headache, gastrointestinal disorders, dizziness, palpitations, lightheadedness, claustrophobia and arterial hypotension.

- Management of Overdose
In case of overdose, patients should seek immediate medical help. Appropriate supportive medical care should be provided. Since roflumilast is highly protein bound, drug elimination analysis is not likely an efficient method of drug removal. It is not known whether roflumilast is dialyzable by peritoneal dialysis.

Manufactured by:
Nycor GmbH
Production Site Dranenburg
Lehnitzstrasse 70 – 98
16155 Dranenburg
Germany
Manufactured for:
Gerson Pharmaceuticals, Inc.
Sub-Contractor of Forest Laboratories, Inc.
St. Louis, MO 631045, USA
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Rev 2/2001
84-1009598-BS-T-RMCl17137-EBF-21
Please also see all Prescribing Information at www.dalresp.com.
Drug May Help Kids With PAH

Sildenafil • from page 1

Diabetes A Risk in Cystic Fibrosis

CFRD • from page 1

PEDIATRIC CHEST MEDICINE

Colistin Risky but Essential for Some Critically Ill Kids

BY DIANA MAHONEY
Elsvier Global Medical News

BOSTON – Despite limited data on the safety and efficacy of colistin in children, the polymyxin antimicrobial has been used increasingly in high-risk pediatric patients as salvage therapy for serious infections caused by multidrug-resistant gram-negative bacteria, according to Dr. Pia S. Pannaraj.

“The escalating impact of antimicrobial selective pressure in high-risk pediatric populations has limited the therapeutic options available for the treatment of multidrug-resistant (MDR) gram-negative bacilli, which in turn has led to renewed interest in colistin, despite the known nephrotoxic and neurotoxic risks,” she reported at the annual meeting of the Infectious Diseases Society of America. In a study designed to review risk factors for acquiring multidrug-resistant gram-negative bacteria requiring colistin treatment and the adverse effects of such treatment in pediatric patients, Dr. Pannaraj of Children’s Hospital Los Angeles and colleagues reviewed their experience with colistin in pediatric patients admitted to their hospital between Jan. 1, 2005, and Oct. 31, 2010. Based on pharmacy records for that period, 53 children were treated with intravenous or nebulized colistin for treatment or suppressive therapy of an infection caused by MDR bacteria. Of the 53 children, 14 received 18 courses of the drug and were included in the analysis, she said. Control patients with matching underlying conditions were chosen from the medical records database.

MDR was defined as resistance to at least three classes of antibiotics, Dr. Pannaraj said. The underlying conditions reported in the 14 study patients included cystic fibrosis in 8, non-cystic fibrosis chronic lung disease in 3, and malignancy in 1, she said, noting that “2 of the patients were previously healthy.” Analysis showed that the children with an MDR isolate requiring colistin had more hospital days during the previous calendar year, compared with their matched controls, at 101.0 days vs. 27.2 days, respectively. Dr. Pannaraj reported. Those with MDR isolates also received more types of antibiotic than did the matched controls (6.6 vs. 4.2) for longer durations (191.0 vs. 53.8 antibiotic days).

Four gram-negative bacteria were isolated, including 16 Pseudomonas aeruginosa, 6 Acinetobacter baumannii, 3 Klebsiella pneumoniae, and 1 Alcaligenes species, with more than one pathogen isolated in seven children, she said. The indications for treatment with colistin included pulmonary exacerbation, wound infection, and bacteremia/sepsis.

Creatinine levels doubled in two children, Dr. Pannaraj reported. Two of the children developed neurololgic symptoms, including perioral tingling in one and headache in another; symptoms resolved after the drug course was completed.

“We need more studies on the dosing and safety of colistin to optimize it for the treatment of high-risk children,” Dr. Pannaraj said.
**Hia Infection Emerging in Alaskan Native Children**

BY MITCHEL L. ZOLER

BOSTON – A small but concerning recent surge in cases of invasive infection with Haemophilus influenzae serotype a among Native Alaskan children appears to be an ‘emerging’ infection, reported epidemiologists from the Centers for Disease Control and Prevention.

CDC epidemiologists first identified an Alaskan invasive infection by *H. influenzae* serotype a (Hia) in 2002, and by mid-October 2011 the tally stood at 27 cases in children younger than 5 years old and still rising, with 15 of the cases clustered in 2010 and 2011. Dr. Michael Bruce said at the annual meeting of the Infectious Diseases Society of America. Most of the cases have been in children younger than 5 years old and in Alaskan Native children, and most have been clustered in a specific region of western Alaska. Over the past 2 years, the Hia incidence rate among all Alaskan Native children younger than 5 years has been 15.4 cases/100,000, and among these children specifically in the western area the rate has approached about 200 cases/100,000, “comparable to Haemophilus influenzae type b [Hib] in the prevaccine era,” he said.

“It’s alarming to us that we have this many cases. It is particularly alarming because these children are quite ill,” Dr. Bruce said in an interview. “It is particularly alarming because these children are quite ill. Their symptoms are very similar to what we saw in the past with Hib.” The most common presentation of invasive disease has been meningitis (41%), followed by pneumonia with bacteremia (26%) and septic arthritis (22%). Hospitalization was required for 89% of the 27 cases he reviewed since 2002, and two children died (a third recent death was not included in this series), he said.

“This is a serious disease, similar to Hib,” said Dr. Bruce, epidemiology team leader in the Arctic Investigations Program of the CDC in Anchorage. But “I don’t think these [Hia cases] are temporally related to use of the Hib vaccine” which virtually eliminated Hib as a cause of invasive infections since its introduction 20 years ago.

The patients had an average age of 0.7 years (range 4 months to 2.4 years), and 63% were boys. Alaskan Native children accounted for 25 (93%) of the cases, and 93% of the patients had been appropriately vaccinated for Hib. Twenty-three (85%) of the 27 cases occurred in western Alaska.

Physicians in Alaska have generally been treating invasive Hia infections as they would invasive infections by Hib, and roughly half of the Alaskan physicians who have managed the invasive Hia cases have dispensed preventive antibiotics to close contacts, following the old Hib recommendations. So far, epidemiologic investigations in Alaska failed to identify any episodes of secondary Hia infections transmitted from an index case, Dr. Bruce said.

Recent reports of Hia clusters have come from a handful of other North American locations. “Testing for Hia in children with invasive bacterial infections is a good idea, especially because it is being identified in more and more places,” Dr. Bruce said. “It looks to me like we did not have any cases of invasive Hia in Alaska until 2002.”

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**Preventing exacerbations**

The impact of COPD exacerbations

Patients who experience frequent exacerbations have:

- A faster decline in lung function1,2
- A decline in lung function that can take up to several weeks to return to baseline1,2
- A poorer quality of life1,2
- A higher mortality rate2

The 30-day mortality rate for COPD exacerbations is approximately 3 times greater than for acute myocardial infarction3,4

One exacerbation can lead to the next

A common trigger for exacerbations is infection.1 It is thought that tobacco smoke and other noxious agents impair certain immune responses, leaving patients increasingly susceptible to infection.1 The increased incidence of infection may lead to even further inflammation, precipitating an exacerbation.2-4 Patients may end up in a cycle of recurring exacerbations, leading to progression of their disease as well as decrease in health status.2,5

This inflammatory process of COPD involves a variety of cells, including neutrophils, macrophages, and fibroblasts.5 The role played by neutrophils is especially significant. In a study of 64 patients with moderate to severe COPD, neutrophils accounted for approximately 70% of the inflammatory cells in patients’ sputum.10
New Formulation of Flu Vax Found Effective in Children

BY MARY ANN MOON

A primary goal of COPD management

Severe COPD patients are at a higher risk

Patients with severe and very severe COPD and a history of exacerbations are at greater risk for hospitalizations due to an exacerbation

Preventing exacerbations is a primary goal of COPD management


VITALS

Major Finding: A novel formulation of the flu vaccine that augments 86% efficacy against all strains and 89% efficacy against vaccine-matched strains in a pediatric population.

Data Source: A phase III field trial comparing the efficacy of a special formulation of the flu vaccine and the standard formulation during two flu seasons in 4,707 children in Germany and Finland.

Disclosures: This study was funded by Novartis Vaccines. Novartis employees also designed and conducted the study and analyzed the data. Dr. Vesikari and his associates reported ties to Asta Zenecea, GlaxoSmithKline, MedImmune, Merck, Pfizer, Sanofi Pasteur, SPMSD, and Wyeth.

A n adjuvant trivalent inactivated influenza vaccine in an oil-and-water emulsion that augments the immune response was found to be effective in a field trial of 4,707 German and Finnish children.

The novel vaccine showed 86% efficacy against all circulating viral strains of influenza during the 2 years of the trial, and 89% efficacy against vaccine-matched strains. In contrast, efficacy rates for the standard trivalent inactivated flu vaccine, which is known to be poorly immunogenic in children, were 43% and 45%, respectively, said Dr. Timo Vesikari of the University of Tampere (Finland) and his associates.

The oil-in-water emulsion (MF59), which enhances the immune response when combined with vaccine antigens, has been used since 1997 in the influenza vaccine for older adults, and has been licensed in 27 countries. In an earlier study, Dr. Vesikari and his colleagues reported that it induced a greater immune response in children aged 6-36 months than did the standard vaccine formulation.

They now report the results of a phase III trial in 654 children in Germany in year 1, as well as 2,104 children in Germany and 1,949 in Finland during year 2. These study subjects were 6-71 months old. The study participants were randomly assigned to one of three groups: the novel vaccine group (1,941 patients), those receiving the standard subunit trivalent inactivated vaccine that is poorly immunogenic in children (1,773 patients), or a control group receiving non-influenza vaccine (993 patients).

The vaccines were administered in two doses, 1 month apart.

The absolute efficacy of the novel vaccine for both influenza seasons was 86% against all strains and 89% against vaccine-matched strains and the H3N2 virus. In contrast, the standard vaccine had an efficacy of 43% against all strains and 45% against vaccine-matched strains and the H3N2 virus.

When the data were broken down by patient age, the novel vaccine showed efficacy against 64% of all strains and 68% of matched strains among children aged 6-35 months, and against 86% of all strains and 91% of matched strains among children aged 36-71 months, the investigators said (N. Engl. J. Med. 2011;365:1406-16).

Moreover, the study subjects frequently showed an immune response after the first dose of the novel vaccine, unlike with the standard or control vaccines. At ages 6-35 months, rates of seroprotection against influenza A (H1N1) and H3N2 strains after one dose were 92% and 95%, respectively, with the novel vaccine. The corresponding rates of sero-protection after one dose of the standard vaccine were 20% and 12%, respectively.

In children aged 36-71 months of age, these proportions after one dose were 100% and 97% for the novel vaccine, compared with 63% and 66% for the standard vaccine.

Vaccine-related adverse events were generally mild to moderate and were similar across the three vaccine groups in the younger patients. In older patients aged 36-71 months, “systemic reactions, including mild fever, were slightly more frequent after receipt of the [novel] vaccine, as compared with the other vaccines, but these reactions were mostly mild and of short duration,” Dr. Vesikari and his associates said.
Fostering Meaningful Communication at Life’s End

BY DOUG BRUNK
Elsevier Global Medical News

HONOLULU — What do patients in the ICU want at the end of life? Research has shown that pain control typically ranks at the top of the list, “but they also want to avoid inappropriate prolongation of dying,” Dr. Richard Mularski, FCCP, said at the annual meeting of the American College of Chest Physicians.

Patients “want to achieve a sense of control at the end of life,” continued Dr. Mularski, a pulmonologist who is a clinical investigator with the Center for Health Research at Kaiser Permanente Northwest, Portland, Ore. “They don’t want to be a burden on their family. We have to offer professional help, which primarily comes from talking with our patients and providing opportunities to strengthen relationships with loved ones. This might mean backing off on sedatives and pain medications so that patients and loved ones can interact before withdrawal of life support.”

Dr. Mularski highlighted four key points from a 2009 consensus statement he helped to create on pain management during the palliative and end of life experience in the ICU (Chest 2009; 135:1360-9). The first point reads that all ICU patients “experience opportunities for discomfort and suffering regardless of prognosis or goals, thus palliative therapy is a requisite approach for every patient, of which pain management is a principal component.”

According to the second, third, and fourth key points, “for those dying in the ICU, an explicit shift in management to comfort-oriented care is often warranted and may be the most beneficial treatment the health-care team can offer; communication and cultural sensitivity with the patient-family unit is a principal approach for optimizing palliative and pain management as part of comprehensive ICU care, [and] ethical and legal misconceptions about the escalation of opiates and other palliative therapies should not be barriers to appropriate care, provided the intention of treatment is alleviation of pain and suffering.”

Communicating effectively with the patient and family about prognosis in the critical care setting can be difficult “because we’re often limited by what treatments of life we can make,” Dr. Mularski said. “This creates a certain tension: Patients have a widespread and deeply held desire not to be dead. We have to try to focus on that desire and acknowledge our limitations. Data show we don’t really prognosticate when death will occur very well.”

The limited options for treatment are only part of the problem. A trial conducted in a university-affiliated ICU found that 54% of families fail to comprehend a diagnosis, a prognosis, or treatment options (Crit. Care Med. 2000;28:3044-9).

“We also know that family members experience a fair amount of moderate to severe posttraumatic stress,” Dr. Mularski added. “This stress is increased when we provide inadequate information. We have to be careful not to use phrases that

**Important safety information**

Because of the risks of liver injury and birth defects, Tracleer may be prescribed and dispensed only through the Tracleer Access Program (T.A.P.), a restricted distribution program, by calling 1-866-228-3546. Only prescribers and pharmacies registered with T.A.P. may prescribe and distribute Tracleer. Tracleer may be dispensed only to patients who are enrolled in and meet all conditions of T.A.P.

**Liver injury**

Elevations of liver aminotransferases (ALT, AST) and liver failure have been reported with Tracleer. In a setting of close monitoring, rare cases of liver failure and unexplained hepatic cirrhosis were observed after prolonged treatment. In general, avoid using Tracleer in patients with elevated aminotransferases (>3 × ULN). Measure liver aminotransferases prior to initiation of treatment and then monthly. Discontinue Tracleer if aminotransferase elevations are accompanied by signs or symptoms of liver dysfunction or injury or increases in bilirubin >2 × ULN.

**Teratogenicity**

Based on animal data, Tracleer is likely to cause major birth defects if used during pregnancy. Exclude pregnancy before and during treatment. To prevent pregnancy, females of childbearing potential must use 2 reliable forms of contraception during treatment and for 1 month after stopping Tracleer unless the patient has a tubal sterilization or Copper T 380A IUD or LNG-20 IUS inserted, in which case no other contraception is needed. Monthly pregnancy tests should be obtained.

**Contraindications**

Tracleer is contraindicated with cyclosporine A, gliburide, in females who are or may become pregnant, or in patients who are hypersensitive to bosentan or any component of Tracleer.

**Warnings and precautions**

In clinical trials, Tracleer caused ALT/AST elevations (>3 × ULN) in 11% of patients accompanied by elevated bilirubin in a few cases. The combination of hepatocellular injury (increases in aminotransferases of >3 × ULN) and increases in total bilirubin (>3 × ULN) is a marker for potential serious liver injury. Liver aminotransferase levels must be measured prior to initiation of treatment and then monthly. Avoid using Tracleer in patients with moderate or severe liver impairment (defined as ALT/AST >3 × ULN).

If clinically significant fluid retention develops, with or without associated weight gain, the cause, such as Tracleer or underlying heart failure, must be determined. Patients may require treatment or Tracleer therapy may need to be discontinued.

Preclinical data and an open-label safety study (N=25) showed a decline in sperm count of ≥50% in 25% of Tracleer-treated patients after 3 or 6 months. After 6 months, sperm count remained in normal range, with no changes in sperm morphology or motility, or hormone levels. Endothelin receptor antagonists such as Tracleer may adversely affect spermatogenesis.

Treatment with Tracleer can cause a dose-related decrease in hemoglobin (Hgb) and hematocrit. Hgb should be checked after 1 and 3 months, and then every 3 months. Upon marked decrease in Hgb, determine the cause and need for specific treatment.

If signs of pulmonary edema occur, the possibility of associated pulmonary vaso-occlusive disease should be considered. Tracleer should be discontinued.

**Adverse events**

In Tracleer pivotal trials, the most common adverse events occurring more often in Tracleer-treated patients than in patients taking placebo (≥2%) were respiratory tract infection, edema, hypotension, sinusitis, arthralgia, liver function test abnormal, palpitations, and anemia.
Indication
Tracleer is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominantly patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital systemic-to-pulmonary shunts (18%). Patients with WHO class II symptoms showed reduction in the rate of clinical deterioration and a trend for improvement in walk distance. Physicians should consider whether these benefits are sufficient to offset the risk of liver injury in WHO class II patients, which may preclude future use as their disease progresses.

Please see accompanying brief summary of prescribing information, including BOXED WARNING about liver injury and pregnancy, on following pages.

Patients ineligible for the Tracleer Patient Coupon Program include any patients whose prescriptions are paid for by the government, Medicare, Medicaid, VA/DoD (Tricare), or Indian Health Service, patients in Massachusetts and Puerto Rico, or where prohibited by law.

www.Tracleer.com
SAN FRANCISCO - A simple question can pick up obstructive sleep apnea in psychiatric patients, according to a small study. Screening is rare in psychiatric patients at present, but it’s important to diagnose obstructive sleep apnea (OSA) because it can make mental illness worse, contribute to depression and possibly to the risk of manic episodes. Symptoms can mimic mental illness as well, making patients irritable and tired, and OSA makes the use of benzodiazepines and other restless legs problems problematic, said lead investigator Dr. Vanita Jain, a psychiatry department resident at the University of Utah, Salt Lake City. “Sleep problems are so integral to psychiatric problems, [and] we want to make sure that along with the psychiatric disorders, we were treating obstructive sleep apnea, too,” she said.

The researchers screened 85 adult community mental hospital psychiatric patients with the STOP-Bang questionnaire, which is typically used as a presurgery screen and takes less than 2 minutes to fill out. The name refers to the survey’s eight yes/no questions: Do you snore loudly? Do you often feel tired, fatigued, or sleepy during daytime? Has anyone observed you stop breathing during your sleep? Do you have or are you being treated for high blood pressure? Body mass index (BMI) ≥ 30 kg/m²? Are you a smoker? Do you have a family history of heart disease? Do you have or have you had high blood pressure (systolic blood pressure > 140 mmHg)? Do you have diabetes? If yes to any of the above questions, patients were referred for sleep studies.

Of 85 psychiatric inpatients, 14 were ultimately diagnosed with obstructive sleep apnea.

Data Source: Screening study of adult community hospital psychiatric inpatients.

Disclosures: Dr. Jain said she has no disclosures.

Use in Females of Childbearing Potential

Initiate treatment in female of child-bearing potential only after a negative pregnancy test and only in females who are using two reliable methods of contraception. Females who have had a tubal ligation or a Copper T 380A IUD or Mirena 20 IUS inserted, in which case no other contraception is needed. Use with Cyclosporine A

Co-administration of cyclosporine A and bosentan resulted in markedly increased plasma concentrations of bosentan. Therefore, concomitant use of Tracleer and cyclosporine is contraindicated (see Drug Interactions).

Use with Glyburide

Increased an risk of liver injury were observed in patients receiving glyburide concurrently with bosentan. Therefore co-administration of glyburide and Tracleer is contraindicated (see Drug Interactions).

Hypersensitivity

Tracleer is contraindicated in patients who are hypersensitive to bosentan or any component of the product. Observed reactions include rash and angioedema (see Adverse Reactions).
more than 35 kg/m²? Age over 50 years? Neck circumference greater than 40 cm? Gender male? Most of the 85 subjects were white, and more than half were men. In all, 46 of the subjects answered yes to at least three of the eight questions, which is considered a positive screen.

Those patients who had positive pulse oximetry monitoring, 26 desaturated more than 10 times per hour. Fifteen of the 26 – most of the rest had been discharged after normal additional testing – underwent a polysomnography sleep study. Fourteen were ultimately diagnosed with OSA; three had more than 30 apneic episodes per hour. They would have gone undiagnosed if it were not for the questionnaire, Dr. Jain said at the American Psychiatric Associ-

If clinically significant fluid retention develops, with or without associated weight gain, further evaluation should be undertaken to determine the cause, such as Tracleer or underlying heart failure, and the possible need for treatment or discontinuation of Tracleer therapy.

Decreased Spontaneous Cough

An open-label, multicenter, safety study evaluated the effect on tachylocic cough of Tracleer 125 mg twice daily for 4 weeks, followed by 150 mg twice daily for 5 months. Twenty-five male patients with WHO functional class III and IV PHTN and neither baseline serum creatinine were enrolled. Twenty-three completed the study and 2 discontinued due to adverse events not related to tachylocic cough. There was no decline in tachylocic cough at least 20% of the patients after 4 or 6 months of treatment with Tracleer. Spontaneous cough remained within the normal range in all 22 patients with data after 4 months and did not change in spontaneous cough, serum creatinine, or tumor markers. None were observed. One patient developed a marked oliguria and two months the spontaneous cough remained low with 2-follow-up measurements over the subsequent 6 weeks. Tracleer was discontinued and after two months the cough returned to baseline levels. Based on these findings and practical data from medically respectable patient, it can be concluded that endothelin receptor antagonists such as Tracleer have an adverse effect on spontaneous cough.

Decrease in Hemoglobin and Hematocrit

Treatment with Tracleer can cause a dose-related decrease in hemoglobin and hematocrit. It is recommended that hemoglobin concentrations be checked after 1 and 3 months, and every 3 months thereafter. If a decrease in hemoglobin concentration occurs, further evaluation should be undertaken to determine the cause and need for specific treatment. The overall mean decrease in hemoglobin concentration for bosentan-treated patients was 8.5 g/L (change to end of treatment). Most of these decrease in hemoglobin concentration was not observed in the first 3 months of treatment, and hemoglobin levels stabilized by 4–12 weeks of bosentan treatment. In placebo-controlled studies of all uses of bosentan, marked decreases in hemoglobin (≥ 10% increase from baseline lasting in excess of 11 g/L) were observed in 4% of bosentan-treated patients and 3% of placebo-treated patients. In patients with PHTN treated with doses of 125 and 250 mg twice daily, marked decrease in hemoglobin occurred in 3% compared to 1% in placebo-treated patients. A decrease in hemoglobin concentration by at least 6 g/L was observed in 12% of bosentan-treated patients compared to 29% of placebo-treated patients. In 80% of these patients whose hemoglobin decreased by at least 6 g/L, the decrease occurred during the first weeks of bosentan treatment. As a result of treatment, the hemoglobin concentration remained within normal limits in 80% of bosentan-treated patients compared to 76% of placebo-treated patients. The explanation for the change in hemoglobin is not known, but dose not appear to be hepatomegaly or thrombocytopenia.

Pulmonary Venous–Occlusive Disease

Should signs of pulmonary edema occur when Tracleer is administered, the possibility of associated pulmonary venous–occlusive disease should be considered and Tracleer should be discontinued.

Prescribing and Distribution Program for Tracleer

Because of the risk of liver injury and birth defects, Tracleer is available only through a special distribution program called the Tracleer Access Program (TAP). Only prescribes and pharmacies participating in TAP may prescribe and dispense Tracleer to Tracleer patients. Tracleer may be dispensed only to patients who are enrolled in and meet all conditions of TAP. Information about Tracleer and TAP is available by calling 1-888-228-3466.

To enroll in TAP, prescribes must complete the TAP Tracleer (Eloratin and Renewal Program (see TAP Program Enrollment and Renewal Form for full prescribing physician agreement) including agreement to:

- Review and understand the educational materials and instructions for prescribing the rates of Tracleer.
- Review and discuss the Tracleer Medication Guide and the risk of bosentan (including the risk of teratogenicity) and hepatic injury with every patient prior to prescribing Tracleer.
- Review pretreatment liver function tests (AST/ALT/bilirubin) and, for females of childbearing age, review pretreatment pregnancy tests.
- Agree to order and monitor monthly liver function tests and for females of childbearing potential, pregnancy testing.
- Ensure all patients are on TAP and review patients’ enrollment annually thereafter.
- Educate and counsel females of childbearing potential to use reliable contraception, as defined on the Tracleer Enrollment and Renewal Form, during treatment with Tracleer and for one month after treatment discontinuation.
- Counsel patients who fail to comply with the program requirements.
- Notify AstraZeneca Pharmaceuticals US, Inc. of any adverse events, including liver injury, and report any pregnancy during Tracleer treatment.

Thorough treatment within one month after stopping Tracleer, females of childbearing potential may use two reliable methods of contraception unless the patient has a tubal sterilization or Copper IUD as birth control and for females of childbearing potential, including the oral contraceptive pill, for contraceptives, including any oral (contraцептив), transdermal, and intrauterine contraceptives should not be used as the sole means of contraception because they may be ineffective in patients receiving Tracleer.

ADVERSE REACTIONS

The following important adverse reactions are described elsewhere in the labeling:

- Aortic valve regurgitation
- Baseline hypothyroidism
- Fluid retention (see Warnings and Precautions)

Clinical Studies Experience

Safety data on bosentan were obtained from 13 clinical studies (9 placebo-controlled and 4 open-labeled) in 815 patients with pulmonary arterial hypertension and other diseases. Doses up to 800 mg bosentan as a 24-hour single dose (400 mg in the morning and 400 mg in the evening) was administered for a variety of durations. The exposure to bosentan in these trials ranged from 1 day to 1.7 years (N=172 patients in placebo-controlled studies of all uses of bosentan). During the first day of concomitant administration, trough concentrations of bosentan were increased 2.8–6 fold by about 30-fold. The mechanism of this interaction is most likely inhibit transport protein by cyclosporine. Steady-state exposure: combination of a CYP2C9 inhibitor and a strong or moderate CYP3A inhibitor (e.g., amprenavir or ritonavir) will likely lead to large increases in plasma concentrations of bosentan. Co-administration of such combinations of a CYP2D6 inhibitor plus a strong or moderate CYP3A inhibitor with Tracleer is not recommended.

Commentary

This study supports the view of Fleck and colleagues. This additional strength of this study was the absence of a placebo arm, the large number of patients, and the long duration of follow-up.

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Dr. Jane Fleck, FACC, comments: This study supports the view of Fleck and colleagues. This additional strength of this study was the absence of a placebo arm, the large number of patients, and the long duration of follow-up.

Dr. Emily Fleck, FACC, comments: This study supports the view of Fleck and colleagues. This additional strength of this study was the absence of a placebo arm, the large number of patients, and the long duration of follow-up.
The prognosis for patients with infections caused by Enterobacteriaceae that harbor KPC pneumonia is poor. Among patients with infections due to these resistant pathogens, the 30-day mortality rate in the study of 39 patients was 13% – or roughly half to a third of that seen in previous studies – researchers reported at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Moreover, 41% of the patients did not even receive an antibiotic active against KPC-positive pathogens.

There has been a really high mortality associated with this population, which, in many cases may in part explain the disparate findings, she speculated. “Maybe in other studies reporting such high mortality rates, it’s just that patients at baseline are really sick, and it’s not necessarily attributing to having the KPC.”

The investigators studied 39 patients with bloodstream infections due to KPC-harboring Enterobacteriaceae between May 2009 and December 2010. Study results were reported in a poster session at the meeting, which was sponsored by the American Society for Microbiology.

The patients were 62 years old, on average; 54% were male and 36% were white. They had been hospitalized for a mean of 27 days, and their mean APACHE II score was 12.4.

The most common source of the bacteria was abdominal (39%), followed by urinary (26%) and pulmonary (15%). In terms of the specific pathogens, 61.9% of patients had Klebsiella species, 36% had Escherichia coli, and 2.5% had Enterobacter aerogenes.

Overall, 13% of the patients died in the 30 days after diagnosis. In a multivariate analysis, patients with an APACHE II score of 17 or higher were more likely to die (odds ratio, 4.5; *P* = .013), whereas the mean death rate fell with advancing age (OR, 0.9; *P* = .038).

“Surprisingly, a lot of these patients didn’t even receive any therapy that was active against the KPC, but they cleared their bloodstream infection [anyway],” noted Dr. Hirsch.

Specifically, 16 patients did not receive any KCP-active therapy. In this subset, the most common source of bacteremia was urinary (44%) and the 30-day mortality rate was the same as that in the cohort overall (13%).

Given the high prevalence of a urinary source in this group, “if the urinary death rate fell with advancing age, that is the group that was probably improving,” Dr. Hirsch said.

Molecular analyses in the overall cohort identified 14 unique clones among the Klebsiella isolates and 7 unique clones among the E. coli isolates.

“Since we found the same rate of mortality (though previously reported), we are kind of wondering what the virulence is associated with these isolates,” Dr. Hirsch concluded. “So that’s the next step – we are going to do some analyses of the isolates to see really how virulent they are.”
The index (the ratio of heart rate divided by systolic blood pressure) is a simple calculation that can help fuel or allay suspicion of septic shock, he said. A normal ratio is 0.5-0.7, while 1.0 or greater may predict uncompensated shock.

The second step in SAVE is to act by perfusing the patient and giving the right antibiotics.

Fill the patient’s “tank” by aggressively giving fluids in serial 500- to 1,000-mL boluses of normal saline, he said. Often, 50-60 mL/kg are needed. “The fluids are about a liter every 30 minutes, if you think you’ve got someone with severe sepsis or septic shock. Four to six liters is not unusual before you fill the tank.”

Early goals in perfusion should be a mean arterial pressure greater than 65 mm Hg, urine output greater than 0.5 mL/kg per hour, and signs of clinical improvement such as waking up.

Tighten the patient’s perfusion “hose” by administering pressors when the “tank” is full and central venous pressure measurement such as filling the tank.”

When intensivists and ED physicians work in concert, patients’ risk of dying can be substantially reduced. ICU and hospital days can be shortened, and posthospital recovery can be faster and more complete.

When intensivists and ED physicians work in concert, patients’ risk of dying can be substantially reduced. ICU and hospital days can be shortened, and posthospital recovery can be faster and more complete.
FROM THE DESK OF THE PRACTICE MANAGEMENT COMMITTEE

PMC Year in Review and New ICD-9-CM, CPT Codes for 2012

By Dr. Robert DeMarco, FCCP, Chair; Donna Knapp, MA, FACMP, Vice-Chair; and Diane Krier-Morrow, MBA, MHP, CCS-P, ACCP Coding and Reimbursement Consultant

In 2011

December 2011 • CHEST PHYSICIAN

The November issue published two articles, one on new and deleted pulmonary function testing (PFT) codes and the other on bronchoscopy with the new tracking codes for bronchial thermoplasty.

For 2012, there are major diagnostic code changes with 54 new ICD-9-CM codes that may be of interest to providers in the practice, 10 deleted PFT codes replaced by 4 new codes and significantly expanded introductory language, new Bronchial Thermoplasty Category III tracking codes and new introductory language and definitions for the sleep family of codes in the AMA CPT® book.

ICD-9-CM Diagnosis Codes

There are several new diagnosis codes that drive and support medical necessity for the services and procedures you perform. In the September CHEST Physician, the ACCP provided a table of the 516.3-516.8 ICD codes, including the new 5th-digit codes for children, 516.61-516.69. The 793.11-793.19 pulmonary nodule codes were noted. (Other new codes are listed in the table at right, bottom.)

It is important to check that your entire practice is reporting new 4th and 5th digit diagnosis codes as of October 1, 2011, or your reimbursements will be denied. Again, official ICD-9-CM annual code revisions are referred to as addenda and the first volume of the addenda index is available from the National Center for Health Statistics (NCHS) Web site at www.cdc.gov/nchs/data/icd9/ICD-9-CMINDEXADDENDAfy12.pdf. The tabular list of diseases addenda (Volume II) can be reviewed at www.cdc.gov/nchs/data/icd9/ICD-9-CM%20TABULAR ADDENDAfy12.pdf. When you review the source addenda, check both the Diagnoses Index and the Tabular List for selection of the appropriate codes to report.

PFTs

CPT added a new header: “Pulmonary Diagnostic Testing and Therapies” to the PFT section of CPT. The 10 CPT PFT codes deleted are: 97274 to 97276, 94240, 94260, 94300, 94360, 94370, 94720 and 94725. The rationale for this change, by a directive from Medicare to bundle the PFT codes through the AMA RUC process, was that certain codes had duplicative reimbursement for pre-service and post-service times included in the payment. If your practice reports any of these deleted codes on a claim in 2012, the claim will not be processed, which will negatively affect cash flow in your practice.

New PFT Lung Volumes will be reported by the equipment used – 94726 plethysmography, 94727 gas dilution/washout or 94728 oscillometry. +94729 is an add-on code for diluting capacity. CPT 94726, 94727, and +94729 may be reported with spirometry (94010, 94060 or 94375).

PFT Introductory Notes in CPT 2012

Codes 94010-94799 include laboratory procedure(s) and interpretation of pulmonary function test results. If a separate identifiable Evaluation and Management service is performed, the appropriate E/M service code may be reported in addition to 94010-94799. Spirometry (94010) measures expiratory airflow and volumes and forms the basis of most pulmonary function testing. When spirometry is performed before and after administration of a bronchodilator, report 94060. Measurement of vital capacity (94150) is a component of spirometry and is only reported when performed alone. The flow-volume loop (94375) is used to identify patterns of inspiratory and/or expiratory obstruction in central or peripheral airways.

Spirometry (94010, 94060) includes maximal breathing capacity (MBC), or maximal voluntary ventilation (MVV) (94200) and flow-volume loop (94375), when performed.

Measurement of lung volumes may be performed using plethysmography or gas dilution. Plethysmography (94726) is utilized to determine total lung capacity, residual volume, functional residual capacity, and airway resistance. Nitrogen washout or helium dilution (94727) may be used to measure lung volumes, distribution of ventilation and closing volume. Impulse oscillometry (94728) assesses airway resistance and may be reported in addition to gas dilution techniques. Spirometry is not reported in addition to oscillometry. Spirometry (94010,
New CPT Codes for 2012

94060) and bronchial provocation (94729) is most commonly performed in conjunction with lung volumes or spirometry and is an add-on code to 94060-94728, 94010, 94060, 94070, and 94375. Pulmonary function tests (94011-94013) are reported for measurements in infants and young children through 2 years of age. Pulmonary function testing measurement reports are actual values and as a percent of predicted values by age, gender, height, and race.

2012 New Sleep Introductory Language

Sleep medicine services include procedures that evaluate adult and pediatric patients for a variety of sleep disorders. Sleep medicine testing services are diagnostic procedures using in-laboratory and portable technology to assess physiologic data and therapy. All sleep services (95800-95811) include recording, interpretation and the written report. (Report with modifier 52 if less than 6 hours of recording for 95800, 95801-95811, and 95806-95811, and if less than four nap opportunities are recorded for 95805).


Overutilization of 99214

The most common problem seen by Medicare is the overutilization of 99214 with documentation supporting a 99213. PMC suggests that you review your records for the last several weeks/months and see if you believe you would withstand an audit of your documentation supporting your reported 99214 E/M visits. Pulmonologists generally report all levels of evaluation and management (E/M) of the established office/outpatient visit codes, with levels 4 and 5 being the most frequent. 2010 Medicare data show the following national percentage distribution for pulmonary medicine reporting established patient E/M codes compared to all the other medical specialties: 99211 0.77% (of 8,515,467), 99212 0.59% (of 19,291,310), 99213 1.81% (of 102,237,982), 99214 2.55% (of 79,920,491), 99215 2.84% (of 10,112,992). It would be beneficial to review your E/M reporting for established patients in the office/outpatient setting to see if you and other providers in the practice have a distribution across all five codes (and check that the level is supported by medical necessity, ie, an ICD-9-CM code).

New COPD Measures Group

In addition to the existing two measures groups on Community Acquired Pneumonia and Asthma (ages 5 to 50 years of age), a new COPD Measures Group will be effective on January 1, 2012. This measures group will include the two existing COPD measures (unique #51 Spirometry evaluation and #52 Bronchodilator therapy) and two existing immunization/vaccine measures (#110 influenza and #111 pneumococcal pneumonia) and the new 2011 combined tobacco use: screening and cessation intervention, measure #226. The COPD measures group individual measures may also be reported individually. We do not expect any significant specification changes to the five individual performance measures.

This will be significantly easier for pulmonologists to report in that usually only one or two G codes will replace the reporting of six to seven individual codes. Watch for updates in the weekly Newsbrief.

New Sleep Apnea Measures Group

For 2012, there is also a new sleep apnea measures group that will include assessment of sleep symptoms, severity assessment at initial diagnosis, positive airway pressure therapy prescribed, and assessment of adherence to positive airway pressure therapy. This sleep measures group is reportable through registry-based reporting only. See the diagram of the historical improper payment rates for Medicare Fee-For-Service (facing page, bottom left).

New Telehealth, Smoking Cessation, and Critical Care

There are new smoking and tobacco cessation counseling codes: G0436, G0437 for telehealth services for asymptomatic patients; G0416 Smoking and tobacco cessation counseling visit for the asymptomatic patient; intermediate, greater than 3 minutes, up to 10 minutes

G0437 Smoking and tobacco cessation counseling visit for the asymptomatic patient; intensive, greater than 10 minutes

As a reminder, for critically ill patients and telehealth services, you would need to report Telehealth Consultation codes – G0426, G0427 for an initial encounter and G0406- G0408 for follow-up encounters. Existing 99291, 99292 were not approved for Telehealth reporting.

Pulmonary Rehabilitation

The Hospital Outpatient Payment Rule (OPPS-CMS-1525-FC) proposed a reduction from $62 to $38 for the bundled code, G0424 Pulmonary Rehabilitation for patients with COPD. Other patients are reported with the, 15 minutes G0237, G0238 or group code, G0239. Robert DeMarco, MD, FCCP represented ACCP at the W/24/1 meeting with CMS. A joint ACCP/ATS/AACVPR/AARC/ NAMDRC letter was filed requesting that this proposed lowered payment be reconsidered. The Final rule published that G0424 will be paid at $37 per hour.

New CPT Modifier 33 Preventive Services

In response to the Patient Protection and Affordable Care Act (ACA), health plans need to begin covering immunizations and preventive services without any cost sharing. Modifier 33 has been added to CPT to identify a service as preventive. If a CPT code descriptor identifies a code as preventive, such as preventive medicine counseling, the modifier should not be used.

Questions

For coding and practice management questions, contact ACCP staff, Marla Brintha at mbrintha@chestnet.org or at (847) 498-8364.

This Month in CHEST: Editor’s Picks

BY DR. RICHARD S. IRWIN, MASTER FCCP

Lectin-Like Oxidized Low-Density Lipoprotein Receptor-1 Modulates Endothelial Apoptosis in Obstructive Sleep Apnea.

By Dr. M. E. Akintusi et al.

The Effect of Weight Loss and Exercise Training on Flow-Mediated Dilatation in Coronary Heart Disease: A Randomized Trial.

By Dr. P. A. Ates et al.


By Dr. R. Mada et al.

Percutaneous Catheter Decompression in the Treatment of Elevated Intraabdominal Pressure.

By Dr. M. L. Chastain, and Mr. K. Safaii.

Venous Oxygen Saturation as Goals of Early Severe Sepsis and Septic Shock Therapy?

By Dr. A. J. Jones.

N. Dys, E. P. Riviera, R. Elkin; and C. M. Cannon.
Postoperative Complications in Patients Undergoing Thoracic Surgery

Lung cancer is on the rise with the number of reported cases up from approximately 200,000 in 2007 to an estimated 220,000 in 2011. The advent of CT scanning has allowed more of these tumors to be diagnosed early. In turn, earlier detection of tumors has shown that they are more likely to be resectable. As such, more patients are undergoing pulmonary resections. Major complications occur in approximately 10% of patients undergoing pulmonary resections, and cardiopulmonary complications occur in more than 50% of these patients. Thus, it behooves the nonthoracic intensivist to become familiar with the common postoperative issues in patients who have undergone lung resection.

Nonoperative Complications

Patients are prone to developing atelectasis and pneumonia after thoracic surgery. It is important that these patients are able to clear their own secretions. Three complementary approaches are used, which are adequate pain control, chest physiotherapy, including early mobility, and bronchoscopy. Pain control in a patient following thoracic surgery can be achieved with systemic opioids, nonsteroidal antiinflammatory agents, intercostal blocks, paravertebral blocks, epidural analgesia, and interpleural analgesics. A meta-analysis (Joshi et al. Anesth Analg. 2008;107[3]:1026) suggests that a thoracic epidural with local anesthetic plus an opioid is the most effective approach; however, thoracic paravertebral block with local anesthetic is a comparable alternative.

Regardless of the pain management strategy, the crucial element is the ability of patients to comfortably generate a good cough and clear their own secretions.

Chest physiotherapy, a vital adjunct in minimizing respiratory complications, includes incentive spirometry, coughing, chest percussion and vibration, and postural drainage. When performed by specialized therapists, the rates of pulmonary morbidity have been reported to improve from 15.5% to 4.7% (Novoa N et al. Eur J Cardiothorac Surg. 2011;40[1]:130).

However, patients must have adequate pain control in order to be motivated to undergo chest physiotherapy and be out of bed in a chair and ambulating on postoperative day one. For those patients who are unable to effectively clear their own secretions with noninvasive means, bronchoscopy may be warranted.

Postoperative acute lung injury (ALI) occurs in up to 7% of patients who undergo pulmonary resection, and the mortality rate is approaching 50%. Primary ALI occurs within 3 days of surgery, and its etiology is not well established. Risk factors are mostly unmodifiable and are thought to include preoperative alcohol abuse, large resection, transfusions, and increased intraoperative airway pressures. Secondary ALI occurs 3 days after surgery and results from identifiable causes such as pneumonia or aspiration. The primary perioperative risk factor that is modifiable is fluid management. Evidence shows that increased perioperative fluid administration increases the incidence of postoperative ALI.

One study (Alam N et al. Ann Thorac Surg. 2007;84[4]:1085) suggests that, for every 500-mL increase in perioperative fluids, there is an odds ratio of 1.17 for developing ALI. A proposed guideline suggests administering a maximum of 20 mL/kg of fluid in the first 24 h after surgery. Urine output of 0.5 mL/kg/h is acceptable in this period, and vaso-pressors may be used if tissue perfusion is inadequate (Slinger: J Cardiothorac Vasc Anesth. 1995;9[4]:442). Diuresis can be considered after the second postoperative day. Renal failure may occur from such fluid restriction, but this condition is usually reversible.

Atrial fibrillation is a common complication following pulmonary resections. The incidence increases with the greater extent of resection and the increasing age of the patient. Atrial fibrillation usually occurs within 2 to 3 days postoperatively and increases the hospital length of stay. The immediate therapeutic goal is rate control. Beta-blockade is usually the first-line treatment; however, calcium-channel blockers and digoxin have also been used. Good results have been observed with amiodarone, but some surgeons are wary of its use for the treatment of postoperative atrial fibrillation due to the risk of pulmonary toxicity in approximately 5% of patients. In fact, some surgeons do not use it in patients following a pneumonectomy for fear of harming the remaining lung.

Operative Complications

Bleeding is always a concern after surgery. The chest tube drainage system offers an excellent tool to monitor for postoperative hemorrhage. A rate of >100 mL/h for more than 2 h is cause for concern. Thick, red fluid is more concerning than thin, pink fluid. Checking a pleural fluid hemocrit can be performed; however, it is not indicated if clinical suspicion is high for postoperative bleeding. In fact, it may delay definitive treatment. Any coagulopathy should be corrected. Sometimes the chest tube may become clotted and stop draining effectively. In these cases, the radiograph will show a dramatic increase in pleural effusion. If there is no decrease in chest tube output or if a large effusion appears on chest radiograph despite functioning drainage catheters, the patient may need to undergo reexploration. (Fig 1).

Lobar torsion following thoracic surgery is a rare entity; however, the outcome may be fatal if left undiagnosed. Most cases involve the middle lobe following a right upper lobectomy. Patients can have fever, tachycardia, dyspnea, and diminished breath sounds. A high index of suspicion is required for this diagnosis. Chest radiograph shows a homogeneous consolidation in the suprmediastinal right lung field. Bronchoscopy should be performed immediately, and if there is difficulty passing the scope into the middle lobe bronchus, the patient should be emergently reexplored.

Depending on the promptness of reexploration, mortality is high. Occasionally, the torsion can be corrected during reexploration, and patients can recover without needing a lobectomy. However, if torsion cannot be corrected, a lobectomy is required.

Fig 1. Left: Immediate postoperative chest radiograph after decortication. Right: Postoperative day 1 chest radiograph showing interval accumulation of hemotherax. Chest tube was noted to be clotted on reexploration.

Fig 2. Subcutaneous emphysema after right-sided wedge resection.

Fig 3. Left: Four-week postoperative chest radiograph after right-sided pneumonectomy showing near opacification of right-sided hemithorax with sterile fluid. Right: Five-week postoperative chest radiograph showing a decrease in the amount of fluid in the right-sided hemithorax with concomitant aspiration-like changes on the contralateral side.
Tyvaso is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Additional improvements in 6MWD when added to oral monotherapy are seen. The most common adverse events seen with Tyvaso in >4% of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical study were cough, headache, throat irritation/pharyngolaryngeal pain, nausea, flushing, and syncope.

**INDICATION**

Tyvaso is a prostanoid vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).

**IMPORTANT SAFETY INFORMATION**

- **Tyvaso** is intended for oral inhalation only. **Tyvaso** is approved for use only with the Tyvaso Inhalation System.
- The safety and efficacy of Tyvaso have not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease) and in patients under 18 years of age. Patients with acute pulmonary infections should be carefully monitored to detect any worsening of lung disease and loss of drug effect.
- **Tyvaso** may increase the risk of bleeding, particularly in patients receiving anti-coagulants.
- **Tyvaso** may cause symptomatic hypotension. The concomitant use of **Tyvaso** with diuretics, antihypertensives, or other vasodilators may increase the risk of symptomatic hypotension.
- **Hepatic or renal insufficiency may increase exposure to **Tyvaso** and decrease tolerability. **Tyvaso** dosage adjustments may be necessary if inhibitors of CYP3A4 such as gemfibrozil or inducers such as rifampin are added or withdrawn.

**For the treatment of PAH (WHO Group 1) to improve exercise ability**

**For your PAH patients on oral monotherapy, effective inhalated prostanoid add-on is CHEWABLE**

**Additional improvements in 6MWD when added to oral monotherapy**

**Four-times-daily dosing**

**Treatment timing can be adjusted for planned activities**

**Patient-friendly features with the lightweight, portable, handheld Tyvaso Inhalation System**

**The most common adverse events seen with Tyvaso in >4% of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical study were cough, headache, throat irritation/pharyngolaryngeal pain, nausea, flushing, and syncope.**

**Tyvaso should be used in pregnancy only if clearly needed. Caution should be exercised when **Tyvaso** is administered to nursing women.**

Please see brief summary of Full Prescribing Information on following page. For more information, please see Full Prescribing Information, Patient Package Insert, and the Tyvaso Inhalation System Instructions for Use manual. These items are available at www.tyvaso.com.

**NEWS FROM THE COLLEGE**

Dr. Dong-Seok Lee  
Assistant Professor  
Division of Thoracic Surgery  
and  
Dr. Raja M. Flores  
Ama Professor of Surgery  
Chief, Division of Thoracic Surgery  
The Mount Sinai Medical Center  
New York, NY

**For the treatment of PAH (WHO Group 1) to improve exercise ability**

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The following is a brief summary of the full prescribing information for TYVASO® (treprostinil) Inhaled Suspension. Please review the full prescribing information prior to prescribing TYVASO.

INDICATIONS AND USAGE

TYVASO is a prostanoid vasoconstrictor indicated for the treatment of pulmonary arterial hypertension (PAH) WHO Group III to improve exercise ability. Studies establishing effectiveness included predominantly patients with PAH due to connective tissue diseases, and included patients with diseases of the stretch reflex and of the stretch reflex, and patients with idiopathic PAH. The effectiveness of TYVASO was noted in patients with PAH due to connective tissue disease, and when used as supportive therapy in patients with PAH due to connective tissue disease. Therefore, the safety of TYVASO has not been adequately evaluated in patients with idiopathic PAH, PAH associated with HIV, and PAH due to heart failure due to connective tissue disease. Therefore, the safety of TYVASO has not been adequately evaluated in patients with idiopathic PAH, PAH associated with HIV, and PAH due to heart failure due to connective tissue disease.

DRUG INTERACTIONS

Pharmacokinetic/pharmacodynamic interaction studies have not been conducted with inhaled treprostinil (TYVASO). However, some of these studies have been conducted with subcutaneous treprostinil (treprostinol) and subcutaneous treprostinil (treprostinol) (both Cmax and AUC) to treprostinil. Co-administration of the CYP3A inhibitor, ketoconazole, increases the exposure to treprostinil, resulting in an increased incidence of angina and syncope during the open-label experience. There were three serious episodes of hematoma (venous hemato ma) noted during the open-label experience.

ADVERSE REACTIONS

The following fatal adverse reactions are described in Table 1:

- Over 500 attendees interacting with presenters and obtaining information
- About how to replicate best practices at their own institutions as part of the new Centers of Excellence
- Nine hundred guests enjoying traditional Hawaiian hospitality, including a lei greeting, Hawaiian cuisine, live music, and dancing, at the sold-out One Breath Luau™ hosted by The CHEST Foundation.

The only one meeting where all of these events could occur—a launch of a remarkably successful CHEST 2011, October 22-26, in Honolulu, Hawaii. And mahalo to the ACCP leaders, faculty, and staff who made this premiere event possible, with a special thanks to Dr. Kevin Chan, FACC Chair of the CHEST 2011 Program Committee.

Additional CHEST 2011 Highlights

Registration for CHEST 2011 was up 5% from last year, particularly noteworthy given the meeting location and current financial climate. US and international registrations both exceeded the previous year.

A mobile-ready version of the meeting planner was available for attendees this year, and free Wi-Fi was available on-site.

Some of our leading medical experts visited several Hawaii hospitals, participating in grand rounds and critical care team debriefings, along with educating primary care physicians on COPD.

We expanded the global focus of the meeting to feature an international opening session and a chance to review unique cases from around the world during the first-ever global case reports session.

As part of the international opening session, Dr. Chen G. Wang, FACC, provided insights on how China addresses issues of lung health and what the world can learn from China’s experience.

Additional speakers discussed tobacco and lung health from global- and population-based perspectives.

Newer members learned about ACCP leadership opportunities at the first-ever Affiliate and Leadership Reception. The “speed dating with a twist” format allowed affiliates to visit roundtables representing various leadership areas within the College, including the Board of Regents, ACCP Committees, NetWorks, US/Canadian Governors, International Regent, and The CHEST Foundation. At each table, relevant ACCP leaders shared their leadership experiences, explained how to get involved in their respective areas, and answered College-related questions.

New Research Presented

Autism and autistic spectrum disorders are currently diagnosed primarily through subjective observation of autistic behaviors. New research presented at CHEST 2011 suggests that a physical abnormality in the airway...
may be a prominent indicator for autism and autistic spectrum disorders, making it a possible diagnostic marker for this disease. The potential association between autism and airway structure is intriguing; however, additional studies are needed to determine the genetic factors that may lead to airway abnormalities.

Sleeping less than 8 hours a night may be linked to weight gain in teens, according to a new study presented at CHEST 2011. In this study, obesity was linked to short sleep duration in teenage boys, with the fewest hours slept linked to the highest BMI levels.

Wish You Were Here
Unable to attend CHEST 2011 or stop by presentations of interest? You can access research that was presented in the October 2011 abstract supplement at chestjournal.chestpubs.org. More than 80% of the sessions presented at CHEST 2011 were recorded and are available for purchase. A significant discount is available for CHEST 2011 attendees. To receive the discount price, CHEST attendees should first register with OnlineEvent at http://onlineevent.com/OE_NewUser.aspx. Once registered, attendees can log in to receive the discounted price.

CHEST 2012
Looking ahead, we’ll build on our commitments to integrating technology to enhance patient care and maximize the attendee experience, as well as cultivating our members as health-care leaders—themes for next year’s annual meeting. See y’all in Atlanta for CHEST 2012.

PS. Best wishes for a healthy and happy New Year from all of us at your ACCP.

COE and Touchdown Stations

On October 23, 2011, the American College of Chest Physicians hosted the presentations by the following 10 Centers of Clinical Excellence (COE) and three companies recognized for their support of the medical community. The inaugural event was visited by 500 to 700 CHEST 2011 attendees who were able to view the outstanding demonstrations and take home educational resources. The grand opening on Monday included a ribbon-cutting (Figure) by then ACCP President, Dr. David D. Guterman, FCCP (center), with Dr. Ken Torrington, FCCP, Medical Director of the COE (right); and Dr. Sam Evans, ACCP Governor for Hawaii (left), assisting. Descriptions of the COE and touchdown stations will appear in the January and subsequent issues of CHEST Physician. If you wish to apply for participation in the COE for CHEST 2012, contact Dr. David H. Eubanks, FCCP(Hon), at deubanks@chestnet.org.

Centers of Excellence
- Hanuola ECMO Program of Hawaii
- Klingensmith HealthCare
- NorthShore University Health System
- Not One More Life
- Promise Hospital
- REMEO® Ventilation and Weaning Centers
- The Queen’s Medical Center
- Tripler Army Medical Center & 13th Air Force
- UMass Memorial Medical Center
- University of Hawaii

Touchdown Stations
- Boehringer Ingelheim Pharmaceuticals, Inc.
- Genentech
- Novartis Pharmaceutical Corp.

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Mediastinal masses are relatively rare and encompass a wide variety of diagnoses from the purely benign to the extremely malignant. The three anatomic mediastinal compartments are clinically notable because specific lesions characteristically arise in certain locations, making the compartment of origin integral to the differential diagnosis. Greater than half of mediastinal masses occur in the anterior/superior compartment. Thymic neoplasms, lymphomas, thyroid masses, and germ cell tumors make up the classic differential. Management strategies for these tumors are diverse and depend strongly on the histologic diagnosis and extent of disease. The rarity of these masses has led to an unstructured approach to their workup, with a diversity of choices and indications for histologic diagnosis.

CT scan, MRI, and FDG-PET are the main imaging modalities used to evaluate anterior mediastinal masses. CT scanning provides a reliable evaluation of mediastinal anatomy and relationship of the lesion to adjacent structures. CT scan findings that help differentiate tumor histology include the presence of fat, cysts, and calcifications, contrast enhancement, invasion of adjacent structures, and associated mediastinal lymphadenopathy. Of these criteria, the presence of fat and associated mediastinal lymphadenopathy are the most useful. Presence of fat density on CT scan has a 75% sensitivity, 99% specificity, and 90% positive predictive value (PPV) for the diagnosis of a germ cell tumor, while associated mediastinal lymphadenopathy has a 75% sensitivity, 93% specificity, and 67% PPV for lymphoma (Totanaranong et al. J Med Assoc Thai. 2010;93(4):488).

While a definitive diagnosis cannot be made by CT scan alone, there are constellations of CT findings that assist with diagnosis. Lymphomas are heterogeneous but rarely cystic. They may invade contiguous structures and have associated pleural or pericardial effusions. Only 5% of lymphomas occur solely in the mediastinum; therefore, extrathoracic lymphadenopathy is typically present. Teratomas can be smooth or lobulated but with smooth margins. Most are very heterogeneous with fluid, soft tissue, fat, and calcium. Seminomas are typically bulky, projecting out both sides of the mediastinum but rarely invade contiguous structures. They are homogeneous and have mild enhancement. Nonseminomatous germ cell tumors are large and inhomogeneous with areas of necrosis and hemorrhage, frequently invading or compressing adjacent structures, with resultant signs of obstruction. Subternal thyroid goiters can be traced in continuity to the cervical thyroid and have prolonged contrast enhancement. They can be definitively diagnosed by CT scan. Thymomas are typically well-defined and symmetric, draping along one side of the heart. They can be homogeneous or heterogeneous based upon presence of hemorrhage, necrosis, and cyst formation, which are soft indicators for more invasive histologic status. Thymic carcinomas are similar in appearance to thymomas but have more irregular contour, necrotic or cystic components, heterogeneous enhancement, and evidence of great vessel invasion. They may also present with findings suggestive of metastatic spread.

MRI can provide additional information with regard to separation from bronchial and vascular structures. MRI is more accurate than CT scanning in assessing invasion into vessels and adjacent structures. T1-weighted images are best for anatomic assessment, while T2-weighted images are preferred for tissue characterization. FDG-PET can be useful in predicting grade of malignancy in thymic epithelial tumors and serves as a useful adjunct for assessment of extrathoracic lymphadenopathy in lymphomas.

The precise histologic state of an anterior mediastinal mass cannot be determined without tissue, but a reasonable diagnosis can frequently be made considering the radiographic findings, age of the patient, the presence or absence of symptoms, associated systemic disease, and biochemical markers. Thymomas account for 70% of anterior mediastinal masses in patients over 50 when one excludes the easily recognizable substernal goiters (Dettberbeck et al. Thorac Surg Clin. 2011;21(1):59). In this age group, one can be confident that a mass with the typical appearance of a thymoma is a thymoma. Conversely, thymomas are relatively uncommon, and less than 20 clinical features are generally sufficient to guide treatment in this age group, but tissue is almost always required if the mass does not have the appearance of a mature teratoma. In the 20-40 year age group, the precise workup can be less clear. Thymomas in this age group are usually associated with myasthenia gravis or an indolent presence of lymphomas, on the other hand, typically present with B symptoms and a rapid progression of chest symptoms.

Since the introduction of video-assisted thoracoscopic surgery (VATS), the threshold for resection of mediastinal lesions without precise histologic diagnosis has been lowered. In patients who present with typical radiographic signs of mature teratomas, or in an older patient with a typical radiographic appearance for a thymoma, one can be confident in the diagnosis. In a recent survey of current practices among members of the European Society of Thoracic Surgeons, 91% of centers reported that they did not routinely look for a histologic diagnosis when presented with a small, resectable, encapsulated lesion, where the clinical presentation and CT scan characteristics are not suggestive of lymphoma (Ruffini et al. J Thorac Oncol. 2011;6(3):614). The presence of myasthenia gravis also helps in securing the diagnosis. Frozen section confirmation at the time of resection is difficult and not recommended unless unexpected intraoperative findings are encountered. There is no harm in performing a needle or incision biopsy of a small thymoma, if needed. The fear of tumor spread as a result of biopsy is not supported in the literature.

Making a precise diagnosis without tissue for poorly demarcated tumors of the anterior mediastinum is more difficult. A large thymoma, thymic carcinomas, seminomas, nonseminomatous germ cell tumors, and lymphomas can have a similar radiographic appearance. Tissue diagnosis is particularly important if there is a high index of suspicion for a lymphoma or germ cell tumor, as these are not treated surgically. A variety of anterior mediastinum biopsy techniques are available, including CT-guided percutaneous needle biopsy, parasternal anterior mediastinotomy (Chamberlain procedure), VATS, and open surgical approaches. None of these procedures are universally accepted, either because of low diagnostic yield or associated morbidity. Core needle biopsy is preferred by some due to its ease, patency, comfort, and low morbidity. Unfortunately, an accurate diagnosis by core biopsy is dependent upon tissue retrieval without extensive necrosis, on-site cytologic examination, and an experienced pathologist. Immunohistochemistry enhances the diagnostic accuracy because of its utility in identifying and classifying lymphomas. In a recent comparison of core needle biopsy to mini mediastinotomy in a series of 40 large unresectable anterior mediastinal masses, the diagnostic yield of mini mediastinotomy was 83.7%, significantly higher than that of core needle biopsy at 41.7% (Fang et al. Chin Med J (Engl). 2007;120(8):675).

Extensive necrosis was cited as most frequent reason for inability to make a diagnosis. Throughout the literature, sensitivity of needle biopsy is approximately 60%, while that of surgical biopsy is 90%. The perceived fear of pleural seeding during transsthoracic core needle biopsy is also not substantiated in the literature. Many surgeons recommend surgical biopsy when histologic status is needed. In the recent European Society of Thoracic Surgeons survey, most respondents stated that they preferred surgical biopsy by VATS or anterior mediastinotomy when histologic status is required. During anterior mediastinotomy, efforts should be made to avoid the internal mammary artery and to stay out of the pleural space. These biopsies are typically done under general anesthesia but have been reported in awake patients. VATS approaches are preferred by many, and awake biopsy by this approach has also been reported (Pompeo et al. Thorac Surg Clin. 2010;20(2):225). These are rare occasions when minimally invasive approaches are insufficient to obtain tissue, and sternotomy or thoracotomy is indicated. This is most common with the diagnosis of Hodgkin’s disease, due to its dense fibrotic capsule.

Tumors of the anterior mediastinum generate substantial interest, typically due to their large size and the diversity of the diagnosis and associated treatment plans. The threshold for biopsy prior to definitive resection is based on numerous factors, including size, encapsulation, respectability, patient age, and associated clinical scenario. Since resectability is an important component of this decision, appropriate diagnostic workup is best determined by a team that includes a thoracic surgeon. Mode of biopsy is highly dependent on institutional expertise, but surgical biopsy provides the greatest chance for adequate diagnosis with minimal associated morbidity and mortality.

Dr. Marilyn G. Foreman, FCCP
Editor, Pulmonary Perspectives

Dr. Loren J. Harris, FCCP
Deputy Editor, Pulmonary Perspectives
Supreme Court Takes Up Health Reform

T
he U.S. Supreme Court has agreed to hear arguments in a challenge to the constitutionality of the Affordable Care Act, with a decision likely to come in June.

On Nov. 24, the high court announced that it would consider arguments related to a well-publicized challenge to the health-reform law that was originally filed in Florida. The case, which was brought by a coalition of Republican attorneys general and governors from 26 states along with the National Federation of Independent Business, maintained that the federal government violated the Tenth Amendment when it established the individual mandate.

The coalition of states also objected to the law’s broad expansion of Medicaid.

They argued that requiring states to invest billions of dollars in an enlarged Medicaid program violated state sovereignty.

The Supreme Court has agreed to hear arguments related to the constitutionality of both the individual mandate and the Medicaid expansion. The justices also said that if the individual mandate is declared unconstitutional, they will determine whether the law can stand without it or must be struck down completely.

Opponents of the Affordable Care Act cheered the Supreme Court’s decision to accept the case.

Greg Abbott, the attorney general for Texas, which is part of the case being considered by the high court, said the court’s decision to accept the case means the law is just one step closer to being tossed out.

But White House officials also think they can win the case. “We know the Affordable Care Act is constitutional and are confident the Supreme Court will agree,” White House communications director Dan Pfeiffer said in a statement.

Families USA, a consumer advocacy group and supporter of the ACA, issued a statement saying it is “surprised and troubled” that the Supreme Court chose to review the expansion of Medicaid.

“It is particularly disingenuous for the states bringing this case to object to this expansion of Medicaid as ‘coercive,’ because the Affordable Care Act specifies that between 90% and 100% of the costs of this expansion will be paid by the federal government,” Families USA executive director Ron Pollack said in a statement.

“Striking down this Medicaid expansion would jeopardize health care for millions of low-income Americans at a time when they can least afford it,” he said.

The first decision in the Florida case came January when U.S. District Court Judge Roger Vinson ruled that the individual mandate was unconstitutional and voided the entire law. However, he did not agree with the states’ argument that the law’s Medicaid expansion was unconstitutional.

Next, the 11th Circuit Court of Appeals in Atlanta took up the case, agreeing with Judge Vinson that the individual mandate violated the Commerce Clause of the Constitution.

But in a 2-1 ruling on Aug. 12, the appeals court ruled that the individual mandate could be separated from the rest of the Affordable Care Act, allowing that law to stand.

Both the federal government and the plaintiffs in the Florida case petitioned the Supreme Court to take up the case.

Court watchers had expected the justices to consider the Affordable Care Act in its current term since there have been conflicting rulings from the appeals courts on the law.

While the 11th Circuit ruled against the individual mandate, other appeals courts have dismissed challenges to the law.
Final 2012 Fee Cut Is 27%, Not 29%

If current law stands, physician fees will be cut by 27% in 2012, not the 29% originally projected, according to the final payment rule issued Nov. 1 by the Centers for Medicare and Medicaid Services.

The slight decrease is due to lower-than-expected Medicare cost growth, CMS officials said in a statement. Unless Congress steps in, the reduction will go into effect Jan. 1 as mandated by Medicare’s Sustainable Growth Rate (SGR) formula.

Both President Obama, in his budget, and CMS officials have called for an overhaul of the SGR. The agency repeated that call with the issuing of the fee rule. “This payment rate cut would have dire consequences that should not be allowed to happen,” CMS Administrator Donald Berwick said in a statement. “We need a permanent SGR fix by the end of the year what the final outcome will be. Stay tuned!”

Dr. Stuart Garay, FCCP, comments: Any physician that left a condition untreated for a decade would be viewed as completely irresponsible. It is widely agreed that the SGR formula is flawed. Yet for a decade, Congress has failed to fix the problem. The final payment rule issued by CMS on Nov. 1 stated that there will be a 27% reduction in Medicare physician fees, instead of the originally projected 29%.

The smaller reduction in Medicare rates is attributed to lower Medicare utilization. So the impact of the cut could potentially be greater. As utilization decreases, so does reimbursement into the health care system, which further reduces physicians’ income. Now add the reduced Medicare rates. Don’t fret! Congress has the last word. We will know by the end of the year what the final outcome will be. Stay tuned!

Dr. Stuart Garay, FCCP

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Staff Physician (Pulmonary/Critical Care/Sleep)

The New Mexico VA Health Care System and the Division of Pulmonary, Critical Care & Sleep Medicine at the University of New Mexico are seeking full time faculty members to join the section at the New Mexico VA Health Care System (NMVAHCS), which is undergoing major expansion. Available positions in the clinician educator track include one with the leadership role of ICU Director and clinical operation for that section, sleep specialists for the new sleep medicine program, pulmonologist and intensivists to staff the pulmonary and ICU services. Positions are also available for physician scientists with startup package and protected time for research.

The NMVAHCS is a tertiary referral center, the sole VA system in the state. The Section evaluates and treats patients with a wide variety of pulmonary diseases and sleep disorders through an inpatient pulmonary consultation service and several outpatient clinics, and provides attending physician coverage for an ICU. There are ample opportunities to participate in scholarly activities including educational programs, clinical outcomes, translational and basic science research. Major research areas in the Division include lung cancer and chemoprevention, heat shock protein biology, asthma, COPD, cystic fibrosis, sleep medicine and epithelial cell biology. Research collaborations are also available through the NCI - designated Cancer Research and Treatment Center at UNM and the NIEHS -funded UNM Center for Environmental Health Sciences. The Division maintains strong ties with the Lovelace Respiratory Research Institute, a non-profit research organization focused on bench, translational, and clinical research in respiratory diseases.

The VA positions carry faculty appointment at UNM, competitive, market-based salary and full benefit package. Faculty rank will be determined based on qualifications, publication record, and experience.

Minimum qualifications: 1) M.D. degree, 2) BC/BE in Pulmonary and Critical Care.

Desirable: active research interests, BC/BE in sleep medicine. Evidence of extramural funding.

Interested applicants must apply online at www.usajobs.gov. Inquiries may be made to the Human Resources Management Service at the NMVAHCS, (505) 256-2760; or 505-265-1711, ext. 2244 regarding the application process. For information regarding the positions, please contact (505)-265-1711, ext. 4552. This position may be eligible for Recruitment Incentive. This is a VA designated Drug Testing Position, EEO/AA. Applicants may be subject to criminal records screening and random drug testing with UNM in accordance with New Mexico law. Positions will be open until filled.

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For Deadlines and More Information Contact:
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