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Courtesy Vanderbilt University Medical Center

"Our nurses love the trophic feeds. Starting at 10-20 cc/hr and running it for 6 days is a lot less hassle than worrying about trying to ramp it up and get to goals," Dr. Todd W. Rice said.

ALI Patients Do Well With Trophic Feeding

BY DIANA MAHONEY
Elsevier Global Medical News

HOUSTON – Restricting the amount of initial enteral intake in mechanically ventilated patients who have acute lung injury neither reduces the duration of mechanical ventilation nor improves mortality relative to full enteral feeding, but the nutritional strategy may be slightly easier on the stomach, according to a study reported at the annual congress of the Society of Critical Care Medicine.

The importance of nutrition support in critically ill patients with acute lung injury (ALI) is well accepted as a means of maintaining gut integrity, modulating both stress and the systemic immune response, and attenuating disease severity, but conflicting data regarding the timing, formulation, and amount of enteral nutrition have contributed to uncertainty about the optimal feeding protocol, said Dr. Todd W. Rice, FCCP, of Vanderbilt University Medical Center in Nashville, Tenn.

"How much nutrition we need to promote the protective benefits, we don't know. Providing a little bit of nutrition – called trophic feeding – has been shown to decrease intestinal intolerances, compared with full-calorie feeds, but it may do so at the risk of malnutrition, worse immune function, and loss of muscle strength," he said. Full-calorie feeding, on the other hand, may lead to more intolerances, may cause hyperglycemia and other imbalances, may increase septic complications, and may fuel the inflammatory fire, he added.

In the current study, which was published simultaneously in JAMA, Dr. Rice and colleagues in the EDEN (Early vs.

See **ALI** • *page 4*

Home Sleep Apnea Testing Gaining Favor

Insurers like the lower price tag.

BY M. ALEXANDER OTTO
Elsevier Global Medical News

PHOENIX – Sleep medicine doctors need to get ahead of the curve on home sleep apnea testing or risk being put out of business, according to Dr. Charles W. Atwood Jr., FCCP, director of the Sleep Disorders Program at the Veterans Affairs Pittsburgh Healthcare System.

Those "who can integrate this are going to survive, and [those] who can't integrate this are not going to do as well," said Dr. Atwood, who is also an associate professor of medicine at the University of Pittsburgh.

Home sleep apnea testing (HSAT) is gaining traction among U.S. insurers because, among other things, it costs a lot less than traditional sleep lab apnea screening. Physician reimbursement is generally in the range of $180, compared with $700 or so for polysomnography. The Centers for Medicare and Medicaid Services is on board, as well, and has begun reimbursing for HSAT.

HSAT patients hook themselves up before bed to one of several HSAT devices on the market. The monitors typically measure airflow, respiratory effort, and heart rate, and include pulse oximetry. Results are later interpreted in the doctor's office.

HSAT has only about 10% of the U.S. sleep study market at the moment, "quite small despite all the attention it gets," but with a lower price tag and studies showing that it is a viable alternative to polysomnography, the market is "likely to continue to increase. Most private [insurance] companies are going to want you do to this," Dr. Atwood said at a meeting on

See **Apnea** • *page 2*

INSIDE

Adult Asthma Phenotypes No Help in Kids

BY PATRICE WENDLING
Elsevier Global Medical News

KEYSTONE, COLO. – Adult asthma phenotypes offer little guidance in the identification and management of severe, therapy-resistant asthma in children.

Cluster analysis was recently used to identify two subgroups with discordance between symptom expression and eosinophilic airway inflammation specific to refractory adult asthma (Am. J. Respir. Crit. Care Med. 2008; 178:218-24). In addition, a treatment strategy based on minimizing eosinophilic inflammation proved superior to standard care in reducing exacerbation frequency (Lancet 2002;360:1715-21).

Recent efforts to replicate the findings in severe pediatric asthma, however, met with disappointing results, study coauthor Dr. Andrew Bush said at a meeting on allergy and respiratory diseases.The ability to identify asthma phenotypes that exhibit differences in clinical response could enable

See **Asthma** • *page 15*

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Wake-Up Call for Sleep Docs

Apnea • *from page 1*

sleep medicine held by the American College of Chest Physicians.

Sleep medicine physicians "need to think about companies that want to contract with primary care providers or insurance companies and get an exclusive contract that bars you from doing this kind of work. That has happened in certain markets, and it's really devastated traditional sleep labs," Dr. Atwood said.

Forestalling that means "getting to your insurance companies first and saying, 'Look, we know this is coming. This is something that we can do. You'll be happy with our services. Let's talk,' " he said.

In the meantime, "network with your primary care and other referrers to make sure that they know you are doing this. They will want to know who's going to take care of these patients if they can't get a traditional sleep study," he said.

Overall, home sleep apnea testing "is not that hard," said Dr. Atwood, who researches HSAT and is a consultant for companies that make the devices.

Pick one system and get to know it well, and start with the easiest, least-complicated patients. Give some thought to who is going to teach patients how to use the devices – how-to videos are available for many – and how to get the devices back after patients are done with them. FedEx and UPS are options.

"You'll also need to think about what to do with negative studies," he noted. You could take them at face value, repeat the test, or send patients to sleep labs for follow-up.

Home tests won't work in about 10%-15% of patients, mostly because they will be noncompliant or will slip the pulse oximeter off while asleep. Also, because home testing generates fewer signals than does polysomnography, "you have to get comfortable making decisions with less information," Dr. Atwood said.

Nonetheless, he and his colleagues found that HSAT patients had no worse 3-month functional outcomes and continuous positive airway pressure (CPAP) adherence than did patients whose sleep apnea was diagnosed in a lab (Am. J. Respir. Crit. Care Med. 2011;183:1238-44).

Dr. Atwood receives commercial research support from Philips Respironics, Resmed, Embla, and Vapotherm. He is a consultant to Carecore, Resmed, and Philips Respironics. ■

COMMENTARY

Dr. Paul Selecky, FCCP, comments: Wise advice in these changing times in sleep medicine reimbursement. Resisting the changes is folly. Better that our professional organizations help us adapt before the payers demand what kind of study we can order.

APAP a Good Alternative to CPAP for Uncomplicated Apnea

BY M. ALEXANDER OTTO
Elsevier Global Medical News

PHOENIX – For uncomplicated, moderate to severe obstructive sleep apnea, autoadjusting positive airway pressure is as effective as continuous positive airway pressure titrated in a sleep laboratory, according to Dr. Neil Freedman, FCCP, a sleep medicine specialist and pulmonologist in Bannockburn, Ill.

Randomized controlled trials that compared lab-titrated continuous positive airway pressure (CPAP) to autoadjusting positive airway pressure (APAP) in unattended settings have shown similar compliance, apnea-hypopnea index (AHI), and daytime sleepiness improvements (Sleep 2010;33:267-71).

That raises the possibility of sending uncomplicated OSA patients home with APAP machines to see how they do, instead of to a sleep lab. With insurance companies, among others, interested in that option, "in the near future patients who need CPAP – if they have uncomplicated sleep apnea – are going to get an unattended APAP trial whether they're going to be treated long-term with it or they are going to be pushed to CPAP," Dr. Freedman said at a meeting on sleep medicine held by the American College of Chest Physicians.

APAP machines don't provide continuous pressure, but instead detect and respond to changes in upper airway flow or resistance patterns; the idea is to use the minimal effective pressure needed to maintain airway patency, which can change for various reasons, even body position.

Initially, machines are typically set to a minimum pressure of 4 cm H_2O and a maximum pressure of 20 cm H_2O. Dr. Freedman starts on the higher side with obese patients and those with worse symptoms, and includes heated humidification and a gradual ramp-up to therapeutic pressures at the start of sleep. "The overwhelming majority" of patients are going to need pressure of 8-12 cm H_2O. If patients need more than 14 cm H_2O, "there's probably something else going on."

Despite APAP's effectiveness, the machines use different technologies and algorithms to treat events, so data from one APAP study is specific to the device used and cannot be generalized to other machines.

Dr. Freedman said he had no relevant disclosures. ■

IN THIS ISSUE

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Dr. W. Michael Alberts, FCCP, is Medical Editor in Chief of CHEST PHYSICIAN.

CHEST PHYSICIAN

IMNG MEDICAL MEDIA

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Budget: Medicare, Medicaid to Help Reduce Deficit

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

President Obama is asking Congress to enact a budget that would cut more than $360 billion from Medicare, Medicaid, and other federal health programs over the next decade.

The president's fiscal year 2013 budget proposal seeks to shrink the growth in federal spending in the Medicare and Medicaid programs, in part by reducing payments to providers to cover patients' unpaid copayments and deductibles, by requiring drug manufacturers to provide the same drug rebates for Medicare Part D as they do for Medicaid, and by reducing payments to inpatient rehabilitation facilities for conditions that can be treated in skilled nursing facilities. The proposal also seeks to cut payments for certain advanced imaging modalities.

Through a package of reductions in provider payments, the Health and Human Services department estimates that the federal government would save more than $5 billion in fiscal year 2013 and about $267 billion by 2022.

The 2013 budget proposal includes many of the same health care policies President Obama presented to Congress last September as part of his deficit reduction plan. That plan called for $320 billion in cuts to federal health programs. This time around, the proposed savings projections are higher in part because the budget forecast has shifted forward by 1 year and in part due to increased fraud prevention activities.

The 2013 budget proposal continues implementation of the Affordable Care Act. Officials at the Centers for Medicare and Medicaid Services (CMS) are asking Congress for $574 million in new funds to begin certifying state-based insurance exchanges and begin work on the exchanges that will be run by the federal government. The proposal also would cut about $4 billion from the health law's Prevention and Public Health Fund over 10 years, starting in 2014.

Rep. Paul Ryan (R-Wis.), chairman of the House Budget Committee, called the proposal "irresponsible" and said the plan would spend, tax, and borrow too much. He also accused the administration of using budget gimmicks to overstate the level of deficit reduction by counting savings that have already been enacted.

Overall, the HHS 2013 budget proposal totals $940.9 billion, with $76.7 billion in discretionary spending. It includes $829.4 billion in funding for the CMS, up about $72 billion from 2012. Proposed funding for National Institutes of Health is level at $30.9 billion. The proposal would increase funding for the Food and Drug Administration by about 17% to $4.5 billion in 2013. The bulk of that increase would be funded through new industry user fees, some of which are currently pending in Congress. The president also requested $11.2 billion for the Centers for Disease Control and Prevention, an increase of $39 million from 2012.

The administration's budget proposal also reaffirms support for finding a permanent replacement for the Sustainable Growth Rate (SGR), the formula used in setting Medicare payments to physicians. The proposal sets aside $429 billion over the next decade to account for adjusting the SGR to prevent significant Medicare physician pay cuts. ■

COMMENTARY

Dr. Stuart M. Garay, FCCP, comments: The President's proposed 2013 budget calls for $360 billion in targeted cuts. In addition, the budget supports a permanent solution to Medicare's Sustainable Growth Rate (SGR) without specifying how to finance it. Despite the proposal and the ensuing rhetoric from both sides of Congress, actual funding for specific programs will be decided by the Senate and House appropriations committees – independent of these proposals. Indeed, an attempt to fix the SGR problem is not expected until after the elections. Then, who knows what will happen?

Prehospitalization Steroids Don't Reduce Risk of ALI

Prehospital use of systemic corticosteroids did not affect the need for ventilation or overall mortality.

BY DIANA MAHONEY
Elsevier Global Medical News

HOUSTON – Prehospital use of systemic corticosteroids does not prevent the development of acute lung injury in at-risk patients, according to data reported at the annual congress of the Society of Critical Care Medicine.

In the first study to specifically evaluate the prophylactic value of prehospital systemic corticosteroids in patients with at least one risk factor for acute lung injury (ALI), Dr. Lioudmila Karnatovskaia of the Mayo Clinic in Jacksonville, Fla., and colleagues found a statistically similar incidence of ALI among at-risk patients who were and were not taking systemic corticosteroids at the time of hospitalization. The investigators also determined that prehospital use of systemic corticosteroids did not affect the need for mechanical ventilation or overall mortality – a finding that appears to contradict previous studies that have linked preventive steroids in at-risk patients with increased rates of ALI and acute respiratory distress syndrome, Dr. Karnatovskaia said.

The study was a planned exploratory subgroup analysis of the Lung Injury Prediction Score cohort of the U.S. Critical Illness and Injury Trials Group, which prospectively enrolled 5,584 patients who were admitted to 22 acute care hospitals and who had predisposing conditions for ALI, including sepsis, shock, pancreatitis, pneumonia, aspiration, high-risk trauma, and high-risk surgery. The primary outcome was the development of ALI, and secondary outcomes were need for invasive ventilation and ICU and hospital mortality, Dr. Karnatavskaia said, noting that the data were analyzed using univariate, logistic regression, and propensity score–based analyses.

For the propensity analysis, "the propensity score balanced all of the covariates. Of the 458 patients on systemic corticosteroids, 443 were matched up 1:4 to those not on systemic corticosteroids, for a total of 1,332 matched patients," she said. "We calculated adjusted risk for acute lung injury, invasive ventilation, and in-hospital mortality from the propensity score–matched sample using a conditional logistic regression model."

Of the 5,584 patients, 458 were on systemic corticosteroids at the time of hospitalization and 5,126 were not. Among the systemic corticosteroid group, 34 (7.4%) developed ALI, compared with 343 (6.7%) of those not taking them, Dr. Karnatovskaia reported. In the systemic corticosteroid group, 104 patients (23%) required mechanical ventilation and 35 patients (8%) died, compared with 1,752 (34%) and 172 (3%) of those not taking systemic corticosteroids, she said.

On univariate analysis, systemic corticosteroid patients were more likely to be older, to be white, and to have diabetes, chronic obstructive pulmonary disease, malignancy, or previous chest radiation, Dr. Karnatovskaia said, noting that they were also more likely to have a lower body mass index and to be on a statin drug, inhaled steroid, inhaled beta-agonist, proton pump inhibitor, ACE inhibitor, angiotensin receptor blocker, or insulin and were less like likely to abuse alcohol or smoke tobacco.

VITALS

Major Finding: In hospitalized patients, 7.4% of those on systemic corticosteroids at admission developed ALI vs. 6.7% of those not on systemic corticosteroids – a statistically similar percentage.

Data Source: A planned exploratory subgroup analysis was done of the Lung Injury Prediction Score cohort of the U.S. Critical Illness and Injury Trials Group comprising 5,584 patients with at least one risk factor for ALI admitted to 22 acute care hospitals.

Disclosures: Dr. Karnatovskaia reported having no relevant financial disclosures.

After adjustment for significant covariates, systemic corticosteroid use was not independently associated with the development of ALI or the need for invasive ventilation, but did appear to be an independent predictor of ICU and hospital mortality, Dr. Karnatovskaia said. The latter association fell away, however, in the propensity score–based analysis. "Following propensity score–based analysis with matching, the association of prehospital systemic corticosteroids with mortality no longer remained significant," she said.

The findings are limited by the lack of data on the indication for systemic corticosteroid therapy, its duration, "and even whether it was continued throughout the hospital stay," as well as the fact that patients on prehospital systemic corticosteroids appeared to have worse functional status, which might have influenced their outcomes, according to Dr. Karnatovskaia. Although using the propensity score with matching addressed this as well as other hidden biases, "the potential for unmeasured effects remains," she said.

The study's strengths include the large number of patients at risk for ALI enrolled from different centers and regions in the United States, as well as two hospitals in Turkey, and the use of comprehensive propensity score–based analysis with matching in addition to traditional logistic regression, Dr. Karnatovskaia said.

Ideally, the finding that prehospital use of systemic corticosteroids does not mitigate the development of ALI would be validated in a randomized controlled trial to best address any causal relationship, "but such a study would not be practical," Dr. Karnatovskaia said. ■

EDEN: Less Is Fine

ALI • *from page 1*

Delayed Enteral Nutrition in ALI) trial, sought to examine the relative advantages of restricting the amount of initial enteral intake in mechanically ventilated ALI patients. Specifically, the prospective, randomized, open-label trial compared the effect on clinical outcomes and survival of initial trophic enteral feeding – approximately 25% of the full target feeding – with initial full-calorie feeding for the first 6 days of mechanical ventilation in ALI patients. "We hypothesized that reduced trophic feeding during the first [6 days] would increase ventilator-free days and reduce instances of gastrointestinal intolerances compared with the conventional full enteral nutrition strategy," he said.

The study's primary end point was ventilator-free days through day 28; secondary end points were daily percentage of goal enteral feeding, frequency of gastrointestinal intolerances, 60-day mortality before hospital discharge with unassisted breathing, ICU- and organ failure–free days, and new infections (JAMA 2012 Feb. 5 [doi:10.1001/jama2012.137]).

The multicenter study population comprised 1,000 patients, from January 2008 through mid-April 2011, who were initiated on mechanical ventilation within 48 hours of developing ALI. Within 6 hours of randomization, enteric nutrition was initiated in 508 patients assigned to trophic nutrition and 492 assigned to full feeding, and was continued until death, extubation, or day 6, Dr. Rice explained. Per standard protocol, enteral nutrition in the full-feeding group began at 25 mL/hr and advanced to goal weights (25-30 kcal/day of nonprotein calories and 1.2-1.6 g/kg per day of protein) as quickly as possible; gastric residual volumes were checked every 6 hours while enteral feeding was increased. In the trophic group, enteral feeding was initiated at 10-20 kcal/hr and gastric residual volumes were checked every 12 hours. After 6 days, patients in the trophic group who still required mechanical ventilation were advanced to the full-energy feeding rates, he said.

Baseline characteristics of the two groups were similar, Dr. Rice noted. "The primary etiologies of lung injury in both groups of patients were pneumonia and sepsis, and the average APACHE III [Acute Physiology and Chronic Health Evaluation III] score was approximately 92. These were sick patients," he said. For the first 6 days, the full- and trophic feeding groups received 1,300 kcal/day and 400 kcal/day, respectively.

With respect to the primary end point (28 days), the average number of ventilator-free days in both groups was similar, at 14.9 in the trophic group and 15.0 in the full-feeding group. "There were also no differences in 60-day mortality, organ failure–free days, ICU-free days, or the incidence of infection between groups," he said. Similarly, with respect to body mass index category or lung injury severity, "there were no between-group differences in ventilator-free days or survival."

The full-feeding group did have a higher number of gastrointestinal intolerances on any one day, and statistically significant increases on days 2 and 3, but the overall percentages of intolerances were low, Dr. Rice said. There were no differences in albumin and protein levels between the groups over the first 7 days, he said.

Regarding the immediate clinical relevance of the findings, Dr. Rice stressed that the study wasn't designed as an equivalence trial, "so I can't tell you both feeding strategies are similar, but you can look at the results." In fact, he said, although the study did not show a benefit other than improved gastrointestinal tolerance, his group has moved toward trophic feeds because of the ease of administration. "Our nurses love the trophic feeds. Starting at 10-20 cc/hr and running it for 6 days is a lot less hassle than worrying about trying to ramp it up and get to goals," he said.

"Looking ahead, there are a number of places to go" with this research, Dr. Rice said. "Some of the questions we've thought about are what role does this play in the [total parenteral nutrition] question, and whether we need to be feeding patients at all. Initially, we thought the idea of not feeding patients would be a hard study to sell, but with these data, it may not be an unreasonable thing to look at."

Dr. Rice disclosed no financial conflicts of interest. ■

COMMENTARY

Dr. Steven Q. Simpson, FCCP, comments: This large randomized, controlled trial should not be interpreted to show that "trophic" feedings are equivalent or noninferior to full caloric feeding, since that hypothesis was not tested and the study was underpowered to do so. However, in a practical sense, one may feel a bit more confident about those ALI patients in whom caloric goals are difficult to meet early in the ICU stay. Additionally, adopting a trophic feeding strategy, should intensivists so choose, may result in a more streamlined approach during the most acute segment of a patient's ICU stay, allowing nurses to prioritize their care on more time-sensitive issues.

Pages 4a—4b

ARDS Outcome Linked to Oxygenation at 48 Hours

VITALS

Major Finding: The mortality of patients with ARDS who failed to reach a threshold P/F ratio of at least 100 within 48 hours of initiation of high-frequency oscillatory ventilation was 75%, compared with a mortality of 24.3% among similar patients who achieved the ratio.

Data Source: A retrospective study comparing mortality in 58 surgical ICU patients with ARDS who received at least 48 hours of high-frequency oscillatory ventilation.

Disclosures: Dr. Tarras disclosed having no relevant conflicts of interest.

BY DIANA MAHONEY
Elsevier Global Medical News

HOUSTON – Failure to achieve threshold respiratory parameters within the first 48 hours after implementation of high-frequency oscillatory ventilation was linked to higher mortality in patients with severe acute respiratory distress syndrome.

This finding from a retrospective study suggests that the lack of sufficient early improvements in oxygenation in patients with the fulminant lung condition may justify a switch to an alternate ventilation strategy, said Dr. Samantha Tarras of the University of Michigan Health System, Ann Arbor.

Although high-frequency oscillatory ventilation (HFOV) is indicated as a rescue therapy for patients with severe acute respiratory distress syndrome (ARDS), specific threshold parameters predictive of outcome have not been described, contributing to uncertainty regarding its optimal application, she said at the annual congress of the Society of Critical Care Medicine.

In a retrospective investigation, Dr. Tarras and her colleagues evaluated the link between threshold oxygenation values and mortality in patients placed on HFOV in the University of Michigan extracorporeal membrane oxygenation (ECMO) referral surgical ICU during 2005-2011. Patients were excluded from analysis if their baseline PaO_2/FIO_2 (P/F) ratio was 100 or more; if they had ECMO support; or if transition to conventional ventilation, withdrawal of care, or death occurred within the first 48 hours.

Of 112 patients placed on HFOV as part of a standardized ARDS treatment algorithm, 58 met entry criteria. "Most of the patients were male, young, and critically ill. The median number of days on mechanical ventilation prior to HFOV was 3, and the largest risk factors for ARDS were pneumonia followed by sepsis," Dr. Tarras said. The mean P/F ratio at baseline of the patients included in the analysis was 58.4, the mean oxygenation index at baseline was 51.5, and in-hospital mortality was 41.3%, she said.

In univariate analyses, the mortality of patients who failed to reach a threshold P/F ratio of at least 100 within 48 hours was 75%, three times higher than the 24.3% observed in patients who achieved the threshold ratio, Dr. Tarras reported. The sensitivity and specificity of this threshold for predicting survival were 82.4% and 62.5%, respectively, and the positive and negative predictive values were 75.7% and 71.4%, respectively. "Similarly, a significant mortality rate was identified at a threshold oxygenation index of 25 at 48 hours," she said.

The findings are limited by the lack of information on patients' cause of death, Dr. Tarras acknowledged. Even so, "the results tell us that for patients whose oxygenation is not improving after 48 hours of HFOV, clinicians should start thinking about other rescue strategies as well as referral to an ECMO center." ■

COMMENTARY

Dr. Carl Kaplan, FCCP, comments: This is an important early report of an interesting study and findings from a single center of excellence. As we move forward in readdressing the role of ECMO in ARDS, we must approach these preliminary retrospective findings with caution. We need a prospective randomized, controlled trial.

Air Pollution Linked With Strokes, Reduced Cognition

BY HEIDI SPLETE
Elsevier Global Medical News

Levels of air pollution that fall within the amounts deemed safe in current U.S. standards for air quality were associated with a significant increase in the risk for acute ischemic stroke after short-term exposure and accelerated cognitive decline after long-term exposure in two separate studies.

Previous studies of the effects of ambient fine particulate matter air pollution, defined as particulate matter less than 2.5 mcm in diameter ($PM_{2.5}$), on ischemic stroke risk have not provided unequivocal results. Studies of the effects of air pollution on cognitive decline are even rarer, and none have assessed the longitudinal effects of $PM_{2.5}$ on cognition, according to the authors of the reports.

Gregory Wellenius, Sc.D., of Brown University, Providence, R.I., and his colleagues reviewed data from patients admitted to Beth Israel Deaconess Hospital, Boston, with ischemic stroke between 1999 and 2008. They used a time-stratified case-crossover study design to examine the association between ischemic stroke risk and $PM_{2.5}$ levels in the hours and days before each stroke (Arch. Intern. Med. 2012;172:229-34).

Overall, a 24-hour period of exposure to "moderate" air quality (as defined by the Environmental Protection Agency Air Quality Index) raised the odds of having a stroke by 34%, compared with a 24-hour period of "good" air quality. The estimated odds ratio of ischemic stroke was 1.11 for each interquartile range increase in pollution levels (defined as 6.4 mcg/m^3).

The increased stroke risk was highest within 12-14 hours of exposure to $PM_{2.5}$ and was most strongly linked with traffic-related pollution, the researchers noted.

Although the observed relative risk of stroke was modest, the findings suggest that "if the association between stroke and pollution is causal and a linear dose-response occurs, a 2-mcg/m^3 reduction in mean $PM_{2.5}$ levels (approximately 20%) during this time might have averted approximately 6,100 of the 184,000 stroke hospitalizations observed in the U.S. Northeast region in 2007 alone."

In a related finding, Jennifer Weuve, Sc.D., of Rush University Medical Center, Chicago, and colleagues found that long-term exposure to both coarse and fine PM was significantly associated with faster cognitive decline in older adults. They reviewed data from 19,409 women aged 70-81 years in the Nurses' Health Study Cognitive Cohort and used geographic information to estimate short-term exposure (1 month) and long-term exposure (7-14 years) before the women underwent baseline cognitive testing.

Overall, the 2-year cognitive decline as measured by a global score was 0.020 standard units worse per 10-mcg/m^3 increment of exposure to coarse PM, defined as particles 2.5-10 mcm in diameter ($PM_{2.5-10}$), and 0.018 standard units worse per 10-mcg/m^3 increment of exposure to $PM_{2.5}$, the researchers said. The average age at the time of baseline cognitive assessment was 74 years (Arch. Intern. Med. 2012;172:219-27).

"Decline in the individual cognitive domains generally was more strongly predicted by long-term than recent exposure to $PM_{2.5}$," the investigators wrote. The associations with cognitive decline were observed in women with levels of PM exposure typical in many areas of the United States, the researchers said. ■

VITALS

Major Finding: The odds of having a stroke were 34% higher after a 24-hour period of "moderate" air quality exposure, compared with a 24-hour period of "good" air quality, in a study of hospitalized stroke patients.

Data Source: Review of data from 1,705 adults hospitalized with stroke between 1999 and 2008, and data from 19,409 women aged 70-81 years in the Nurses' Health Study.

Disclosures: Dr. Wellenius' study was funded by the National Institutes of Health and the Environmental Protection Agency. Dr. Weuve's study was funded by the National Institute of Environmental Health Sciences and the EPA. The Nurses' Health Study is separately funded by the National Cancer Institute. None of the authors had relevant financial disclosures.

PCV13 May Cut Pneumococcal Disease Burden More

BY MARY ANN MOON
Elsevier Global Medical News

The pneumococcal conjugate vaccine, PCV13, may be better in adults than the pneumococcal polysaccharide vaccine, PPSV23, at reducing disease burden because of its potential effectiveness against nonbacteremic pneumococcal pneumonia, a study has shown.

PPSV23 covers 23 serotypes while PCV13 covers only 13. However, PPSV23 doesn't appear to consistently prevent nonbacteremic pneumococcal pneumonia, while PCV13 is more likely to do so, based on preliminary experience.

Because nonbacteremic pneumococcal pneumonia is much more common than invasive pneumococcal disease and is responsible for much more morbidity and mortality, PCV13, despite its narrower serotype coverage, should prevent more pneumococcal disease, reported Dr. Kenneth J. Smith of the section of decision sciences and clinical systems management, University of Pittsburgh, and associates.

VITALS

Major Finding: Substituting PCV13 for PPSV23 would cost $28,900 per quality-adjusted life-year, while staying with PPSV23 would cost $34,000 per quality-adjusted life-year.

Data Source: Analysis of statistical models predicting the effectiveness and costs of enacting six different vaccination strategies in identical hypothetical cohorts of adults aged 50 and older.

Disclosures: The study was supported by the National Institute of Allergy and Infectious Diseases. No relevant financial disclosures were reported by the study's authors.

The question of which pneumococcal vaccine to use in adults came to the fore when the Food and Drug Administration recently approved the use of PCV13 in patients aged 50 years and older. Dr. Smith and his colleagues used decision statistical modeling techniques to estimate the cost effectiveness of six different possible pneumococcal vaccine strategies in identical hypothetical cohorts.

The six strategies were no vaccination, the present U.S. Advisory Committee on Immunization Practices recommendation to vaccinate all adults with PPSV23 at age 65, substituting PCV13 for PPSV23 and vaccinating according to the ACIP recommendations, vaccinating with PCV13 at age 50 and with PPSV23 at age 65, vaccinating with PCV13 at ages 50 and 65 years, and vaccinating with PCV13 at ages 50 and 65, then with PPSV23 at age 75.

The models took into consideration the potential effects of herd immunity, different levels of patient risk of contracting pneumococcal disease, different levels of vaccine effectiveness based on patient age and comorbidity, and three different outcomes after pneumococcal infection: death, disability, or recovery.

"Our analysis favors vaccinating adults with PCV13 instead of PPSV23," chiefly because experts expect that PCV13 will be more effective against nonbacteremic pneumococcal pneumonia than PPSV23 appears to be, the researchers said.

Moreover, the data "suggest that PCV13 administered either as a substitute for PPSV23 [according to] current recommendations or [given] routinely at ages 50 and 65 years might reduce pneumococcal disease burden in an economically reasonable fashion," Dr. Smith and his colleagues wrote (JAMA 2012;307:804-12).

According to their models, substituting PCV13 for PPSV23 would cost $28,900 per quality-adjusted life-year, while staying with PPSV23 would cost $34,000 per quality-adjusted life-year. Even giving PCV13 at age 50 and again at age 65, which would cost $45,100 per QALY, would still be cost effective, they noted.

However, the study results would not hold true if PCV13's effectiveness against nonbacteremic pneumococcal pneumonia proves to have been overestimated. If it turns out that PCV13 is not very effective against nonbacteremic pneumococcal pneumonia, the current PPSV23 recommendations would be superior, the investigators said.

Similarly, the results of this study would not hold true if it turns out that childhood vaccination with PCV13, which has only recently begun, substantially changes herd immunity, reducing disease rates in adults. ■

Frequent Respiratory Infections? Think Bronchiectasis

BY PATRICE WENDLING
Elsevier Global Medical News

KEYSTONE, COLO. – Despite claims to the contrary, bronchiectasis is alive and unwell.

"One of the things that I hear time and time again is, 'I just don't see much bronchiectasis in my practice,' but I think it's because we're not looking," Dr. Gwen A. Huitt said at an allergy and pulmonary diseases meeting.

She said that if clinicians are prescribing antibiotics for respiratory exacerbations more than twice a year, and possibly even more than once a year, they should consider underlying bronchiectasis as a possible etiology. By the time bronchiectasis is suspected, the patient often has developed resistance to an antibiotic.

A noncontrast CT scan – and not a chest x-ray – is the method of choice to diagnosis bronchiectasis because it allows proper visualization of dilated bronchi and bronchioles, said Dr. Huitt, director of the adult infectious disease unit at National Jewish Health in Denver, which sponsored the meeting. Her service also screens all patients for cystic fibrosis (CF) and alpha-1-antitrypsin deficiency both for levels and phenotype because they've found that even phenotypic MZ heterozygotes do not clear infection well.

Once bronchiectasis has been determined, it is important to identify the etiology. In one study involving 150 adults with bronchiectasis, however, the cause was idiopathic in 53% (Am. J. Respir. Crit. Care Med. 2000;162:1277-84). That percentage has fallen only slightly since the study was published, she said.

Treatment goals should aim to reduce or eliminate the underlying host deficiency and improve secretion clearance. Secretions can be modified with nebulized hypertonic saline starting at 3%, and even nebulized normal saline can help get the heavy secretions out, Dr. Huitt said. Acetylcysteine (Mucomyst) and guaifenesin are also helpful, but dornase alfa (Pulmozyme) is not indicated in non-CF patients and was actually harmful in one study.

Clinicians also need to be diligent about controlling infections rationally. "If you have a gram-negative organism, don't keep throwing cipro [ciprofloxacin] at it because you are going to lose cipro after the fifth or sixth time you give it," she said. "These organisms are going to develop drug resistance. This is where using dual therapy with oral antibiotics and inhaled antibiotics, I think, is going to be the cornerstone."

Approval of inhaled ciprofloxacin is right around the corner, and clinical trials of inhaled mannitol and aztreonam are now underway in non-CF bronchiectasis. Inhaled tobramycin (TOBI), amikacin (Amikin), and colistin are established in clinical practice but can be difficult to obtain for non-CF patients, and the brand-name versions cost about $5,000 a month out of pocket, Dr. Huitt observed.

"When we have very difficult patients to manage and your back is against the wall, you're going to try some of these things if they are available to you," she said.

Although guidelines do not recommend obtaining sputum cultures in patients with acute exacerbations, she suggests this is for "garden variety" bronchiectasis. "Again, if someone is coming into your office two times or more a year with a respiratory tract infection, you should really do a sputum culture to see what you're dealing with," Dr. Huitt emphasized.

Inhaled corticosteroids and long-acting bronchodilators can be used for management, but azithromycin (Zithromax) should be used only if there are no nontuberculosis mycobacteria (NTM) on culture. "Azithromycin is being used like water today, and I think it is going to come back and haunt us in the future because we are seeing a huge rise in our service of macrolide-resistant nontuberculosis mycobacteria patients who have been on chronic macrolides as an anti-inflammatory that never had a culture done," Dr. Huitt said. "By the time we see them, they've lost the macrolide ... a cornerstone drug for the treatment of NTMs."

Finally, lung resection surgery should always be considered as an adjunctive treatment option in patients with very focal bronchiectasis. With a skilled surgeon, most resections can be accomplished with the video-assisted thoracopic approach, which avoids spreading the rib cage, reduces the risk of rib fractures, and minimizes postoperative pain, she said.

Dr. Huitt is an advisory board member for Hill-Rom. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: This summary of Dr. Huitt's presentation provides useful and practical guidance to physicians caring for patients with frequent respiratory infections regarding possible undiagnosed bronchiectasis. Establishing the diagnosis by chest CT is an important first step as management of these patients potentially requires a different approach, including rational antibiotic use and consideration of pulmonary hygiene therapy.

Postop Radiation No Boon for Elderly Lung Cancer Patients

BY M. ALEXANDER OTTO
Elsevier Global Medical News

Postoperative radiation therapy does not improve the survival of elderly patients following complete resection of stage III non–small cell lung cancer with N2 lymph node involvement, according to a retrospective study of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry linked to Medicare records.

VITALS

Major Finding: Postoperative radiation did not improve the survival of elderly patients following resection of stage III non–small cell lung cancer tumors with N2 lymph node involvement (hazard ratio, 1.11).

Data Source: Retrospective analysis of 1,307 patients in the SEER registry linked to Medicare records.

Disclosures: Dr. Wisnivesky has received a research grant from GlaxoSmithKline and lecture honorarium from Novartis. His coauthors reported no relevant conflicts of interest. The study was funded by the National Cancer Institute.

"Clinicians should refrain from widespread use of PORT [postoperative radiation therapy] in elderly patients with this cancer subtype until we know more," especially given its side effects, said Dr. Juan P. Wisnivesky of the Mount Sinai School of Medicine, New York, and coauthors.

Although the value of PORT in N2-positive disease has been uncertain, it's often used in these patients for whom the extent of lymph node involvement greatly affects prognosis. Long-term survival drops from 70% of patients without lymph involvement to 20%-35% of patients with microscopic N2 disease.

More than 54% (710) of the 1,307 patients diagnosed in 1992-2005 identified in the SEER-Medicare database received PORT. Patients who underwent limited resection, received preoperative chemotherapy or radiation therapy, or died within 30 days of surgery were excluded from this study (Cancer 2012 Feb. 13 [doi:10.1002/cncr.26585]).

Patients who received PORT tended to be younger and higher in income, but otherwise the groups were evenly matched for race, gender, and comorbidities. In the PORT group, 42% were aged 65-70 years, 34% aged 71-75, and 24% older than 75 years.

Tumor status, histology, and rates of lobectomy and pneumonectomy were similar between groups. Patients in the PORT group were more likely to receive adjuvant chemotherapy, however; 36% did so vs. 23% of the group not given PORT.

PORT did not improve 1- or 3-year survival in an unadjusted analysis or in a Cox model adjusting for propensity scores (HR, 1.11; 95% confidence interval 0.97-1.27). "Analyses limited to patients treated with or without chemotherapy" as well as "intermediate or high complexity [radiation therapy] planning … showed similar results," the researchers noted.

The SEER study "was powered to detect relatively small benefits of PORT," they said. "The generalizability of our results should be excellent"

SEER doesn't record disease recurrence, so "we were not able to assess whether PORT is associated with … increased disease-free survival or lower rates of local recurrence." Similarly, because the registry does not record total radiation dose or fractionation schedule, "we were not able to assess the impact of these factors on lung cancer survival," they cautioned.

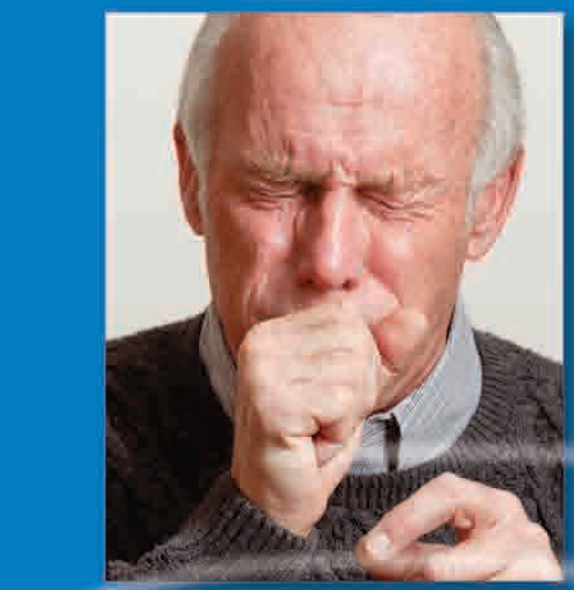
The results are consistent with the conclusions of the PORT Meta-Analysis Trialists Group, which recommended that PORT use be limited to clinical trials until more data are available, the authors wrote, adding that their results "highlight the importance" of enrolling patients in the ongoing phase III Lung Adjuvant Radiotherapy Trial, known as Lung ART. ■

COMMENTARY

Dr. Lary Robinson, FCCP, comments: Based on the findings of their retrospective review, Dr. Wisnivesky and associates caution clinicians about using PORT with elderly patients over 65 years old since it did not appear to impact overall survival in their analysis. However, in addition to its retrospective nature, this study suffers from several weaknesses associated with other SEER database reviews, including lack of information about local control, disease-free survivals, and radiation doses and fractionation. Their conclusions are somewhat at odds with recommendations from prior reviews and meta-analyses, including the PORT Meta-analysis Trialists Group study. The only randomized, prospective, multi-institutional adjuvant lung cancer trial (ANITA) did a post hoc subset analysis of the survival benefit of adding radiotherapy after adjuvant chemotherapy in their resected stage IIIA patients. Their results strongly suggested an advantage for PORT after chemotherapy, but the age groupings were not clearly defined. Likely this controversy about the advisability of PORT will be more directly answered once results of Lung ART are available.

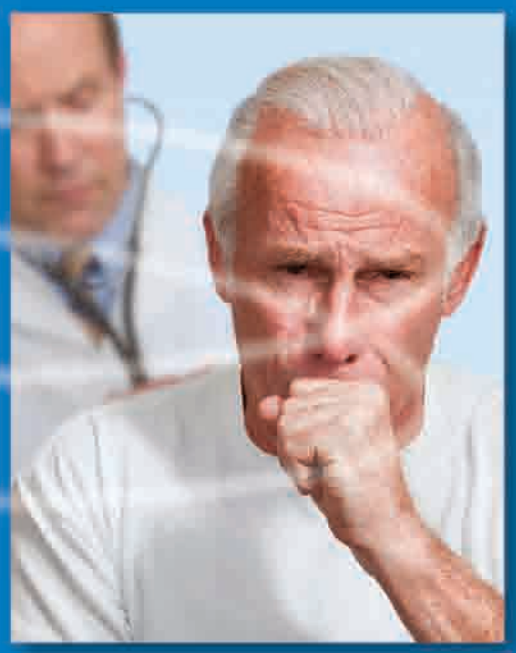
For patients with severe COPD associated with chronic bronchitis and a history of exacerbations

COPD EXACERBATIONS



are serious events...

Reducing Patient Risk Is Critical



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.

Daliresp®
(roflumilast) tablets
500 mcg

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 exacerbations[1,2]

- Reduces moderate or severe exacerbations by 17% vs placebo[1,3,4]
- Effective alone or in combination with a bronchodilator[1,3]
- Effective in older and younger patients (>65 and 40-65 years)[1,3]
- Statistically significant increase in lung function (pre-bronchodilator FEV_1) of 48 mL vs placebo[1,4]
  - DALIRESP is not a bronchodilator; this increase was not clinically significant[1,3]
- The first class of drugs approved for COPD in 25 years[2,5]

ONCE-DAILY
ORAL

Tablet shown not actual size.

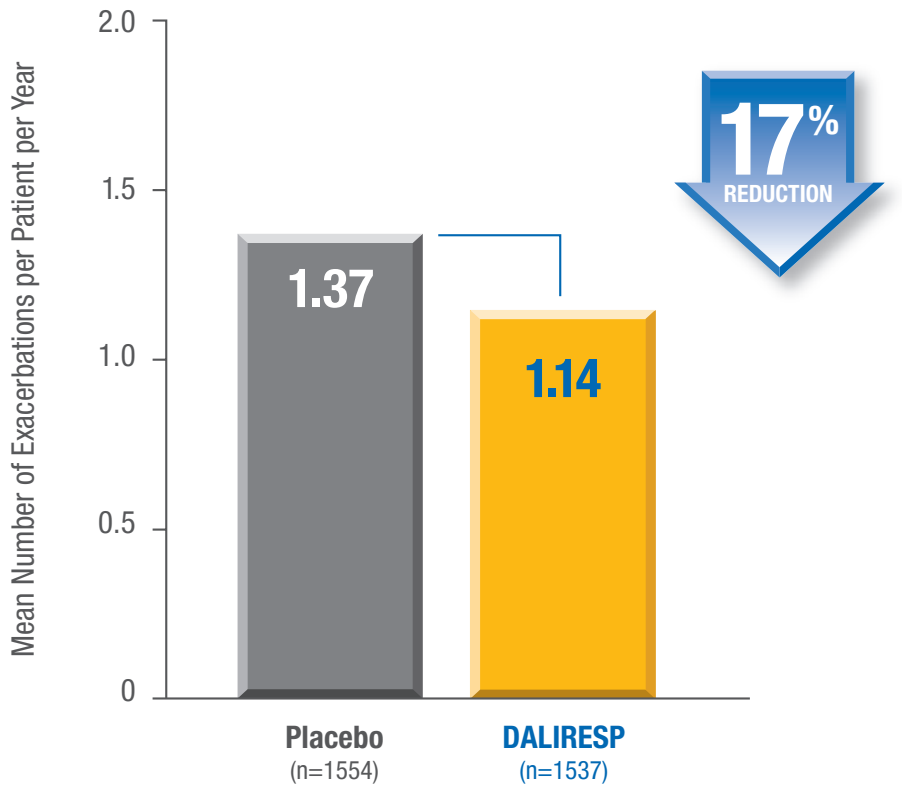
- Patients should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated and treatment discontinuation considered.
  - In addition to weight loss being reported as a common adverse reaction (7.5% of patients treated with DALIRESP 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.

Daliresp®
(roflumilast) tablets
500 mcg

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

DALIRESP significantly reduces exacerbations

REDUCTION IN THE RATE OF MODERATE OR SEVERE EXACERBATIONS[3,4]



P=0.0003 vs placebo

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 FEV_1) were co-primary endpoints. Each study met both co-primary endpoints.

- Moderate exacerbations were defined as those requiring treatment with systemic corticosteroids[1]
- Severe exacerbations were defined as resulting in hospitalization and/or death[1]

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.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- 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.

References: 1. DALIRESP (roflumilast) Prescribing Information. Forest Pharmaceuticals, Inc. St. Louis, MO. **2.** US Food and Drug Administration. FDA approves new drug to treat chronic obstructive pulmonary disease. March 1, 2011. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm244989.htm. Accessed October 19, 2011. **3.** Data on file. Forest Laboratories, Inc. **4.** Calverley PMA, Rabe KF, Goehring U-M, Kristiansen S, Fabbri LM, Martinez FJ; for the M2-124 and M2-125 study groups. Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials. *Lancet.* 2009;374:685-694. **5.** US Food and Drug Administration. Atrovent approval history (NDA 019085, 1986). Drugs@FDA. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed October 19, 2011.

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[1,3]

CONSISTENT EFFECT WITH A CONCOMITANT BRONCHODILATOR[1,3]

DALIRESP with LABAs (Long-acting $ß_2$ Agonists)	✓
DALIRESP with Short-acting Anticholinergics	✓

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 FEV_1) 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[1,3]

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.

Forest Pharmaceuticals, Inc.
Subsidiary of Forest Laboratories, Inc.
St. Louis, Missouri 63045

Daliresp® (roflumilast) tablets 500 mcg

 84-12000308Tr1 11/11

DALIRESP® (roflumilast) tablets **Rx Only**
Brief Summary of Full Prescribing Information

Initial U.S. Approval: 2011

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.

Limitations of Use

DALIRESP is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

CONTRAINDICATIONS

The use of DALIRESP 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

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

Psychiatric Events including Suicidality

Treatment with DALIRESP is associated with an increase in psychiatric adverse reactions. In 8 controlled clinical trials 5.9% (263) of patients treated with DALIRESP 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 DALIRESP 500 mcg daily (2.4%, 1.4%, and 1.2% for DALIRESP 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 DALIRESP compared to one patient (suicidal ideation) who received placebo.

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 in such patients. Patients, their caregivers, and families should be advised of the need 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 with DALIRESP if such events occur.

Weight Decrease

Weight loss was a common adverse reaction in DALIRESP clinical trials and was reported in 7.5% (331) of patients treated with DALIRESP 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, 20% 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 DALIRESP. Patients treated with DALIRESP should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated, and discontinuation of DALIRESP should be considered.

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 enzyme inducer rifampicin resulted in a reduction in exposure, which may result in a decrease in the therapeutic effectiveness of DALIRESP. Therefore, the use of strong cytochrome P450 enzyme inducers (eg. rifampicin, phenobarbital, carbamazepine, phenytoin) with DALIRESP is not recommended. [*see Drugs That Induce Cytochrome P450 (CYP) Enzymes (7.1) and Clinical Pharmacology (12.3)*].

ADVERSE REACTIONS

The following adverse reactions are described in greater detail in other sections:

- Psychiatric Events Including Suicidality *[see Warnings and Precautions (5.2)]*
- Weight Decrease *[see Warnings and Precautions (5.3)]*

Adverse Reactions in Clinical Studies

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below reflect exposure of 4438 patients to DALIRESP 500 mcg once daily in four 1-year placebo-controlled trials, two 6-month placebo-controlled trials, and two 6-month drug add-on trials *[see Clinical Studies (14.1)]*. In these trials, 3136 and 1232 COPD patients were exposed to DALIRESP 500 mcg once daily for 6 months and 1-year, respectively.

The population had a median age of 64 years (range 40-91), 73% were male, 92.9% were Caucasian, and had COPD with a mean pre-bronchodilator forced expiratory volume in one second (FEV_1) of 8.9 to 89.1% predicted. In these trials, 68.5% of the patients treated with DALIRESP reported an adverse reaction compared with 65.3% treated with placebo.

The proportion of patients who discontinued treatment due to adverse reaction was 14.8% for DALIRESP-treated patients and 9.9% for placebo-treated patients. The most common adverse reactions that led to discontinuation of DALIRESP were diarrhea (2.4%) and nausea (1.6%).

Serious adverse reactions, whether considered drug-related or not by the investigators, which occurred more frequently in DALIRESP-treated patients include diarrhea, atrial fibrillation, lung cancer, prostate cancer, acute pancreatitis, and acute renal failure.

Table 1 summarizes the adverse reactions reported by ≥ 2% of patients in the DALIRESP group in 8 controlled COPD clinical trials.

Table 1: Adverse Reactions Reported by ≥ 2% of Patients Treated with DALIRESP 500 mcg daily and Greater Than Placebo

	Treatment	
Adverse Reactions (Preferred Term)	**DALIRESP** (**N=**4438) n (%)	**Placebo** (**N=**4192) n (%)
Diarrhea	420 (9.5)	113 (2.7)
Weight decreased	331 (7.5)	89 (2.1)
Nausea	209 (4.7)	60 (1.4)
Headache	195 (4.4)	87 (2.1)
Back pain	142 (3.2)	92 (2.2)
Influenza	124 (2.8)	112 (2.7)
Insomnia	105 (2.4)	41 (1.0)
Dizziness	92 (2.1)	45 (1.1)
Decreased appetite	91 (2.1)	15 (0.4)

Adverse reactions that occurred in the DALIRESP group at a frequency of 1 to 2% where rates exceeded that in the placebo group include:

Gastrointestinal disorders - abdominal pain, dyspepsia, gastritis, vomiting

Infections and infestations - rhinitis, sinusitis, urinary tract infection,

Musculoskeletal and connective tissue disorders - muscle spasms

Nervous system disorders - tremor

Psychiatric disorders - anxiety, depression

DRUG INTERACTIONS

A major step in roflumilast metabolism is the N-oxidation of roflumilast to roflumilast N-oxide by CYP3A4 and CYP1A2 [*see Clinical Pharmacology (12.3)*].

Drugs That Induce Cytochrome P450 (CYP) Enzymes

Strong cytochrome P450 enzyme inducers decrease systemic exposure to roflumilast and may reduce the therapeutic effectiveness of DALIRESP. Therefore the use of strong cytochrome P450 inducers (e.g., rifampicin, phenobarbital, carbamazepine, and phenytoin) with DALIRESP is not recommended *[see Drug Interactions (5.4) and Clinical Pharmacology (12.3)]*.

Drugs That Inhibit Cytochrome P450 (CYP) Enzymes

The co-administration of DALIRESP (500 mcg) with CYP3A4 inhibitors or dual inhibitors that inhibit both CYP3A4 and CYP1A2 simultaneously (e.g., erythromycin, ketoconazole, fluvoxamine, enoxacin, cimetidine) may increase roflumilast systemic exposure and may result in increased adverse reactions. The risk of such concurrent use should be weighed carefully against benefit. *[see Clinical Pharmacology (12.3)]*.

Oral Contraceptives Containing Gestodene and Ethinyl Estradiol

The co-administration of DALIRESP (500 mcg) with oral contraceptives containing gestodene and ethinyl estradiol may increase roflumilast systemic exposure and may result in increased side effects. The risk of such concurrent use should be weighed carefully against benefit *[see Clinical Pharmacology (12.3)]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic effects: Pregnancy Category C: There are no adequate and well controlled studies of DALIRESP in pregnant women. DALIRESP was not teratogenic in mice, rats, or rabbits. DALIRESP should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

DALIRESP induced stillbirth and decreased pup viability in mice at doses corresponding to approximately 16 and 49 times, respectively, the maximum recommended human dose (MRHD) (on a mg/m^2 basis at maternal doses > 2 mg/kg/day and 6 mg/kg/day, respectively). DALIRESP induced post-implantation loss in rats at doses greater than or equal to approximately 10 times the MRHD (on a mg/m^2 basis at maternal doses ≥ 0.6 mg/kg/day). No treatment-related effects on embryo-fetal development were observed in mice, rats, and rabbits at approximately 12, 3, and 26 times the MRHD, respectively (on a mg/m^2 basis at maternal doses of 1.5, 0.2, and 0.8 mg/kg/day, respectively).

Nonteratogenic effects: DALIRESP has been shown to adversely affect pup post-natal development when dams were treated with the drug during pregnancy and lactation periods in mice. These studies found that DALIRESP decreased pup rearing frequencies at approximately 49 times the MRHD (on a mg/mg^2 basis at a maternal dose of 6 mg/kg/day) during pregnancy and lactation. DALIRESP also decreased survival and forelimb grip reflex and delayed pinna detachment in mouse pups at approximately 97 times the MRHD (on a mg/m^2 basis at a maternal dose of 12 mg/kg/day) during pregnancy and lactation.

Labor and Delivery

DALIRESP should not be used during labor and delivery. There are no human studies that have investigated effects of DALIRESP on preterm labor or labor at term; however, animal studies showed that DALIRESP disrupted the labor and delivery process in mice. DALIRESP induced delivery retardation in pregnant mice at doses greater than or equal to approximately 16 times the MRHD (on a mg/m^2 basis at a maternal dose of > 2 mg/kg/day).

Nursing Mothers

Roflumilast and/or 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 effects of DALIRESP on breast-fed infants. DALIRESP should not be used by women who are nursing.

Pediatric Use

COPD does not normally occur in children. The safety and effectiveness of DALIRESP in pediatric patients have not been established.

Geriatric Use

Of the 4438 COPD subjects exposed to DALIRESP for up to 12 months in 8 controlled clinical trials, 2022 were > 65 years of age and 471 were > 75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger 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 classified as Child-Pugh A and B (8 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 41%, respectively in Child-Pugh B subjects, as compared to age-, weight- and gender-matched healthy subjects. The C_{max} of roflumilast and roflumilast N-oxide were increased by 3% and 26%, respectively in Child-Pugh A subjects and by 26% and 40%, respectively in Child-Pugh B subjects, as compared to healthy subjects. DALIRESP 500 mcg has not been studied in hepatically impaired patients. Clinicians should consider the risk-benefit of administering DALIRESP to patients who have mild liver impairment (Child-Pugh A). DALIRESP is not recommended for use in patients with moderate or severe liver impairment (Child-Pugh B or C) *[see Contraindications (4) and Clinical Pharmacology (12.3)]*.

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 C_{max} 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 DALIRESP. During the Phase I studies of DALIRESP, the following symptoms were observed at an increased rate after a single oral dose of 2500 mcg and a single dose of 5000 mcg: headache, gastrointestinal disorders, dizziness, palpitations, lightheadedness, clamminess 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, hemodialysis is not likely to be an efficient method of drug removal. It is not known whether roflumilast is dialyzable by peritoneal dialysis.

Manufactured by:
Nycomed GmbH.
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Manufactured for:
Forest Pharmaceuticals, Inc.
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Please also see full Prescribing Information at www.daliresp.com.

Screen Open-Airway Surgery Patients for MRSA

BY MARY ANN MOON
Elsevier Global Medical News

Children who are to have open airway surgery should first be screened for methicillin-resistant *Staphylococcus aureus* colonization because the prevalence is particularly high in this patient group and treatment drastically reduces postoperative infections, graft loss, and wound dehiscence, researchers reported.

In a retrospective cohort study at a single tertiary pediatric medical center, the prevalence of MRSA colonization was 32.5% during a 2-year period among 175 children who underwent 197 open airway operations, a rate considerably higher than has been reported in patients undergoing other types of surgery, said Dr. Melissa McCarty Statham of the department of otolaryngology–head and neck surgery, Emory University, Atlanta, and her associates.

Because these MRSA-colonized patients were identified and treated appropriately, they did not develop any postoperative MRSA infections, graft losses, or cases of surgical site dehiscence, the investigators noted.

Dr. McCarty Statham and her colleagues studied this issue because, "in our experience, MRSA infection in open airway procedures can be a devastating complication." Such procedures include laryngotracheal reconstruction and grafting, correction of laryngotracheoesophageal clefts, repair of tracheoesophageal fistulas, and laryngotracheal separations.

VITALS

Major Finding: The overall rate of MRSA colonization was approximately 33%, but no MRSA infections developed in the screened and treated carriers; rates of any postoperative infection were comparable between colonized (15.9%) and noncolonized (17.4%) patients.

Data Source: Retrospective cohort study of 175 children who underwent 197 open airway surgeries at a single pediatric medical center in a 2-year period.

Disclosures: One of Dr. McCarty Statham's associates reported ties to Acclarent, Gyrus/Olympus, Boston Medical Products, Hood Laboratories, Bryan Medical, and Karl Storz.

These patients are at high risk for MRSA colonization because most are preterm; have been tracheotomized; and have serious comorbidities such as pulmonary, gastrointestinal, and cardiac disease. "We consider these factors to be proxies for frequent hospitalization and exposure to antibiotics," the researchers said.

They assessed the 175 patients who underwent such surgery (at a median age of 4 years) at the Cincinnati Children's Hospital Medical Center in the 2 years after a program of MRSA screening and treatment had been instituted there. Their purpose was to document the prevalence of MRSA colonization in this vulnerable patient population and to assess the effect of the program. Preoperatively, all patients were cultured for MRSA at the nares, perianal area, axila, gastrostomy tube (if present), and tracheotomy tube aspirate (if present).

Colonized patients were given double-strength trimethoprim-sulfamethoxazole empirically for 72 hours before surgery, with clindamycin as an alternative in patients who were allergic to sulfa drugs or were carrying organisms resistant to TMP-SMX. Patients with positive nasal cultures also received intranasal mupirocin twice daily. Perioperatively, colonized patients received either intravenous vancomycin or clindamycin. Postoperatively, they received the same antibiotic regimen for 14 days as they had been given before surgery.

No MRSA-associated infections developed in patients treated according to this protocol, Dr. McCarty Statham and her associates said (Arch. Otolaryngol. Head Neck Surg. 2012;138:153-7).

Postoperative rates of any infection were comparable between the patients colonized with MRSA and those not colonized. There were 10 infections in the MRSA-positive patients (a rate of 15.9%) and 23 infections in the noncolonized patients (a rate of 17.4%).

All 10 infections in the MRSA-colonized patients were caused by nosocomial non-MRSA organisms, as were 19 of the 23 infections in the noncolonized patients.

Three patients who had been MRSA-negative at screening nevertheless developed postoperative MRSA infections after surgery, suggesting that their MRSA was acquired during this hospitalization, the investigators said.

Overall, there were two failures of laryngotracheal reconstruction cartilage grafts and one case of surgical site dehiscence, but neither occurred in MRSA-positive patients. One graft failure was attributed to impaired wound healing as a result of corticosteroid use; the other to beta-hemolytic streptococcus infection. The dehiscence was caused by *Haemophilus influenzae* infection.

This finding suggests that "there is an inherent risk of graft loss and dehiscence in all patients who undergo airway surgery. Infections other than MRSA may be causative factors," Dr. McCarty Statham and her associates noted.

"In view of our results, we advise instituting MRSA screening and treatment protocols in patients undergoing airway surgery," they added. ■

COMMENTARY

Dr. Susan Millard, FCCP, comments: The kiddos who require "open airway" surgery are often our ex-preemies with subglottic stenosis and tracheotomies. The most important thing for these patients and families is to be successfully liberated from the tracheotomy, so understanding the importance of preoperative management is critical.

Pediatric Data Lacking

Asthma • *from page 1*

more targeted therapy and spare children unlikely to benefit from exposure to powerful anti-inflammatories like methotrexate and cyclosporine. The pediatric study did include an unvalidated post hoc analysis showing that a sputum normalization strategy in the first month after changing treatment may reduce asthma exacerbations (Thorax 2012;67:193-8).

Persistent airflow limitation is also a hallmark of severe, therapy-resistant asthma (STRA) in adults, and is typically defined using a postcorticosteroid trial, postacute bronchodilator response in forced expiratory volume in 1 second (FEV_1), and *z* scores. What is not known for children, however, is what dose, route of administration, and duration of steroids is best, or what dose of bronchodilator is most effective.

"There really is no good pediatric evidence," said Dr. Bush, professor of pediatric respirology at the Royal Brompton Hospital and Imperial College in London. "The point in finding this out is that if you really do have persistent airflow obstruction [in] a child, there is no point in flogging them with more and more medications, if in fact they're not going to open their airways."

Corticosteroid response is another cornerstone for identifying and managing STRA in adults. However, when Dr. Bush and his colleagues looked at corticosteroid response in a group of 50 children who had severe asthma by American Thoracic Society and American College of Surgeons criteria, 50% of the children had such good lung function that the adult definition of response, based on an FEV_1 of at least 80% or a 15% increase, could not be applied.

"The adult definition of corticosteroid response based on lung function does not work in kids," he said.

Clinical phenotypes such as female gender and obesity, which are associated with more severe asthma after childhood, have also proved unreliable. Another unpublished study by the group involving 40 boys and 36 girls (aged 6-19 years) with STRA found no sex differences; it also found that young people with STRA had an average body mass index of 19 kg/m^2, which was identical to the average BMI of a cohort of age-matched children with mild asthma and was lower than the mean of 20.4 kg/m^2 in age-matched controls.

The children with STRA had symptoms for an average of 2-6 years, an average of six steroid bursts (range, 1-30), and three hospital admissions (range, 0-21) in the previous year; 21% had ever been intubated because of their asthma.

Asthma Control Test scores were low in the children with STRA (average, 13.5), and lung function varied widely from an FEV_1 of 33% to 121% of predicted (average, 70%).

The children with STRA had a strong positive history of atopy (82%) and family history of atopy (84% in a first-degree relative), Dr. Bush noted.

"Indeed, if I see a child with alleged severe, therapy-resistant asthma who is not atopic, I take another further good hard look at the diagnosis," he said.

Getting the Basics Right

One of the most important steps in managing children with genuine STRA is to distinguish them from those with difficult asthma, in whom biologic therapies are not justified.

"In really severe childhood asthmatics, potentially reversible factors will be found in more than half of those not responding to treatment," Dr. Bush said at the meeting, sponsored by National Jewish Health.

The most important factors to look for are adherence, cigarettes, allergens, and psychosocial issues. He suggested that nurse-led home visits are particularly beneficial in identifying these factors. When nurses from Royal Brompton visited 71 "hard-core asthmatics," potentially modifiable factors were identified in 79%, and only 32 patients were thought to need further invasive investigation. A quarter could not produce a complete set of medications, a third were picking up fewer than half of their prescriptions, 38% did not have good inhaler technique despite multiple attempts at testing, and medication issues contributed to poor control in 48%.

"These guys know the nurses are coming; it's not like the nurses come at 3:00 in the morning and bang on the door and say show me your medications," he said.

Dr. Bush reported no relevant financial disclosures. ■

COMMENTARY

Dr. Burt Lesnick, FCCP, comments: Pediatric severe asthma differs from the phenotype seen in adults. This is an important consideration not only in treatment protocols, but also in designing studies to assess therapeutic effectiveness. For instance, pediatric investigations of new medications may need different inclusion criteria since FEV_1 is often normal even in children with severe asthma.

PRESIDENT'S CORNER

The Changing Health-care Landscape

Background

I work as division chief in an academic practice based at a 650-bed community hospital that serves as a major teaching facility in Brooklyn, New York. As full-time, salaried pulmonary, critical care, and sleep medicine attending physicians, my associates and I interact with our private practice colleagues on a daily basis. These interactions provide me a unique perspective about the concerns that both private practice and academic physicians harbor about the changing health-care landscape.

SUHAIL RAOOF, MBBS, FCCP

The Problem

Health-care reform has introduced a sense of insecurity and "fear of the unknown" in the minds of our ACCP members, especially those in private practice. These insecurities and fears complement our natural human tendency to resist change. However, regulatory agencies and payers are directing both physicians and hospitals alike to utilize outcomes-based performance improvement metrics, regularly report their performance and outcomes data, and, in instances, accept variations of an evolving, pay-for-performance reimbursement system that represents a culture of, and impetus for, change.

Most physicians agree that rising health-care costs need to be reigned in. The current iteration of health-care reform, however, makes the model of independent private practice extremely difficult to sustain. While academic practices will also be affected, the increased tracking of defined performance improvement measures, complications, and hospital-acquired events; the escalating potential liability under both the fraud and abuse statutes and various auditing contractors; and dwindling reimbursements are likely to affect clinical practitioners disproportionately. Even more so, the rising costs of routine clinical practice, added to the expenses of both investment in electronic health record implementation in their offices and electronic integration with the hospitals where they practice, disfavor private practice physician groups. Finally, private practice physicians face heightened competition from contracted groups for hospitalist, intensivist, and telemedicine (remote monitoring) services, as well as for diagnostic testing services.

Health-care Reforms

What are the major tenets of the Obama health-care reforms? These include seven major components:

▶ *Universal coverage*: Health-care insurance should be universal, ie, it should extend to include the estimated 50 million currently uninsured individuals. Dependent children can already stay on their parents' insurance until the age of 26 years, as a result of the health reform bill. Individuals or families will be mandated to select and purchase insurance by 2014, even if they are young and in good health. Subsidies to purchase insurance will be available to low income families.

▶ *Portability and limited coverage exclusions*: Health insurance coverage should be portable—people should not lose insurance if they change jobs. Additionally, individuals with preexisting conditions should not be entirely denied or offered only limited health care.

▶ *Affordable*: Health-care premiums should be affordable. This will require reductions in escalating administrative costs, unnecessary testing, unproven modes of treatment, and other inefficiencies in the health-care delivery system. The revamped system should protect families from bankruptcy in the event of a catastrophic illness.

▶ *Choice*: Individuals will have a choice of the hospital, clinic, doctor, and health services in their community. They will be able to retain their employer-based health plan if they so chose.

▶ *Quality:* The health-care delivery system should provide standardized care, predicated upon evidence-based principles, improving patient safety, and reducing variability from doctor to doctor or institution to institution. Such standardized, less variable care remains consonant with the principles of patient-centered, family-focused care. The use of electronic medical records and health information technology to develop patient data-banks, track outcomes, identify complications, and measure effectiveness of medical interventions will be provided incentives and will catalyze such care.

▶ *Preventive medicine:* Promote public health measures to improve wellness and prevent disease. Included in this category are vaccinations, tobacco education, smoking cessation programs, prevention of obesity, and others.

▶ *Sustainability:* The system should be self-sustaining with appropriate cost-sharing between individuals, employers, and public sources. Reform will center around insurance issues and much less on reimbursement issues.

Physician Perceptions About Health-care Reforms

General

In a survey carried out by Merritt Hawkins, on behalf of The Physicians Foundation, approximately 2,400 physicians responded with their perceptions about health-care reform. The main survey findings were as follows:

▶ The majority of physicians opposed the passage of health-care reform.

▶ Most physicians anticipated caring for a greater number of patients and, simultaneously, they felt less financially stable in their practices.

▶ More than half of the physician respondents planned to change their practices in a manner to limit access to new patients and to explore options of retirement or working part-time.

▶ The model of a full-time, independent physician engaged in private clinical practice is likely to be replaced by part-time, locum tenens and concierge practitioners.

ACCP Membership Perspectives

What do our members think of these health-care reforms? The following provides a sample of some membership views on this tough issue.

▶ Dr. Anthony Saleh, FCCP, a well established private practice colleague in pulmonary and critical care medicine at NY Methodist Hospital, where I lead our academic pulmonary practice, had the following comments to make: *"As a busy practitioner, I have to maximize my time management. The ACCP can play a pivotal role in keeping me informed of the changes coming down the pike. With all of its emphasis on education, the College can help streamline my efforts toward continuing my busy practice and allowing me to keep abreast of all of the newest innovations in pulmonary and critical care medicine. I also hope the College will be able to help me deal with the increased scrutiny that practitioners will be facing over the next 5 to 10 years."*

▶ Dr. Douglas J. Cohen, FCCP, a practicing pulmonologist at Pulmonary and Sleep Physicians of South Jersey, had this to say: *"I am a private practitioner for 30 years. It is an impossible environment to practice in and make a living. Payments for work are dropping (loss of consult code, decreased insurance payments), and hospitals are competing for pulmonary talent to cover the ICUs. Private practitioners cannot compete with hospitals for salary. We cannot recruit new physicians. Isn't anyone listening?"*

▶ Dr. Tom Russi, who runs a busy solo pulmonary and critical care medicine practice in Bayshore, Brooklyn, New York, when asked about his perceptions of how health-care reform will affect his private practice remarked: *"As a physician who is accustomed to following a mental process when confronted with a decision or problem, I find it frustrating more often than not when asked to make*

Continued on following page

Continued from previous page

a general, blanket statement about health-care reform, especially as it relates to the state of private practice. The usual process of evaluating data, filtering out relevant from irrelevant information, and generating a risk/benefit analysis seems to inevitably lead my brain to an uncomfortable mental hardwiring freeze. I believe this neuronal paralysis stems from the overwhelming amount of data and variables out there that have not yet been organized and packaged properly for practicing physicians to fully digest. In other words, I feel uncomfortable giving a prognosis when I am still uncertain of the diagnosis."

Hence, in order to stay afloat and remain engaged in delivering clinical care, many physicians I spoke with thought they will have to increase their patient load, sell their practices and join large financially solvent hospitals, start working part-time, or evolve to offer boutique medical services.

Analysis of the Problem

The changes proposed as part of health-care reform are not trivial and have far-reaching consequences. In analyzing the impact of these changes for our members, the following issues come to mind:

▶ *Excessive information to digest*: The health-care reform bill is 1,000 pages of fine print. Our physicians, already inundated with clinical responsibilities, do not have the time to read through this maze of legal terminology and prepare their practices for the imminent changes. Furthermore, this bill will engender many thousands of additional pages of regulations to achieve implementation.

▶ *Success of reform will depend upon physicians' participation and leadership*: Most experts agree that curbing spiraling costs is, to a great measure, in the hands of the medical profession. This is because doctors, generally engaging in shared decision making with their patients, determine the selection and timing of different medical resources. Paradoxically, at a time when physicians feel they are losing control, they should feel empowered!

▶ *Perceived conflict of interest under a fee-for-service structure*: A perception in the minds of many legislators and policy makers is that most doctors are paid on a fee-for-service basis. This payment methodology may lead physicians (especially specialists) to order tests, perform procedures, and suggest treatments that drive up costs, despite guidelines and evidence to the contrary. In fact, research has shown that even when clinical guidelines are available, they may not be applicable to a particular patient or not appropriate for complex patients with comorbidities. Consequently, guidelines may not be adhered to for a variety of patient and process characteristics rather than the failure of physicians to act responsibly. Furthermore, global payment methodologies associated with risk bearing may confront many of the problematic results and adverse consequences associated with full risk capitation in the past. Notably, practice patterns vary significantly across geographically disparate regions of the country and between different physician specialties caring for the same patients and problems; yet, at present, these variations are the subject of intense scrutiny and remain without full explanation. In addition, many hospitalizations are unnecessary and many errors preventable, although systematic, generalizable, scalable models to reduce such unnecessary hospitalizations and abolish medical errors remain in their infancy. Outcomes research institutes have been set up to conduct comparative effectiveness research to begin identifying which, among potentially many, seemingly effective therapies are actually the most effective or have the safest profile. Recently, the American College of Physicians has recommended physicians "practice effective and efficient health care and to use health-care resources responsibly." They coined the term, "parsimonious care," which urges physicians to utilize resources "wisely" in an attempt to ensure that "resources are equitably available." Regulating resource utilization may be possible through Accountable Care Organizations (ACOs). These ACOs are physician and hospital networks that share responsibility for providing care to patients, with opportunity for novel and blended payment models to avert the potential distortions created by either pure fee-for-service or full risk capitation environments. By integrating systems, rewarding favorable outcomes, and coordinating care of a large number of patients, ACOs may act as a model for "parsimonious care."

▶ *Greater scrutiny of physicians*: In an effort to enforce utilization of best practices, minimize variations in quality of care, improve outcomes, reduce costs incurred from unproven treatments, and lower complications, physicians will be under greater scrutiny by patients, regulatory agencies, and insurance companies. Physicians will be required to utilize electronic medical records; perform practice improvement modules (perhaps outside the auspices of the board certification process); initiate, if not demonstrate, and complete quality improvement projects; practice evidence-based medicine; and be subject to the incentives and disincentives of value-based purchasing. Physicians' complications and outcomes will be tracked and patients encouraged toward high "value" physicians (with lower cost, lower complications, better outcomes) by tiered copayments and other financial incentives.

▶ *Lack of commensurate limitations upon consumers' choices to treatments*: A critical missing link in this equation (to drive health-care costs down) is the absence of public commentary and engagement of our patients in the discussion of the impact of the consequences of health-care reform upon their treatment choices. Our society has not been educated about the possible specific restrictions imposed to limit access to, and choices in, medical diagnostic testing and potential therapeutic treatments. The comparative effectiveness findings from the Outcomes Research Institutes cannot be used to limit diagnostic tests and medical treatments from physicians if patients nonetheless demand such care. The concept that sometimes "less is more," in medical care has not been adequately conveyed to, or enforced with, our patients ("the consumers").

Moving Forward

The College, poignantly aware of its responsibility toward the members, has taken multiple steps in this era of health-care reform:

1. Setting up an infrastructure utilizing the Practice Management Committee, Chest Medicine Affairs Committee, the ACCP Governors, and staff who will work to provide education to the College on regulatory issues.
2. Expansion of AQuIRE-the College-maintained secure clinical database for its members. This database is developed by physicians, for physicians, and is more trusted by providers than clinical and administrative databases kept by regulatory agencies or insurance companies. Participating physicians are provided access to a secure, Web-based registry where they can easily enter the procedures they perform, the complications they encounter, and the practice improvement measures they utilize in their day-to-day work. These registries are associated with online educational activities that are targeted to the outcomes being assessed. The combination of these targeted educational activities and registries for practice assessment, called performance improvement modules (PIMs), are approved for awarding participants American Board of Internal Medicine (ABIM) Maintenance of Certification (MOC) part IV credit. Such resources have special utility for College members' recertification, licensure, and liability insurance.
3. Promoting the training of our physicians and other members in acquiring new skill sets, such as ultrasound, management of the difficult airway, performance of percutaneous tracheostomy, or advanced modes of mechanical ventilation through simulation courses offered throughout the year (www.chestnet.org/accp/education).
4. Planning dissemination of more information about health-care reform. Over the next 7 months, a series of articles entitled, "Health-care Reform: Is Anyone Listening?" will be published in *CHEST Physician*. The schedule of planned articles includes the following:

March: Inaugural article to introduce and explain the purpose of this series (this article).
April: Legislative and regulatory changes in health care
May: Apprehension about change, remodeling, and surviving in private practice.
June: The impact upon pulmonary, critical care, and sleep medicine of legislative and regulatory changes in the day-to-day practice of medicine (including ICD-10, adoption of electronic medical records, practice improvement modules, quality improvement, evidence-based medicine, value-based purchasing, and more.
July: The top 10 things a practitioner should do to prepare for impending change.
August: As health-care reform proceeds, what are the forthcoming, expected changes in the practice of sleep, critical care, and pulmonary medicine?
September: What are the available ACCP resources to help members prepare for the expected changes in health-care delivery?

Each article will present the relevant discussion in a concise and easily assimilated manner.

We will continue to monitor the changing health-care landscape and provide timely and useful information and suggestions to our members, so they can adapt and react appropriately and effectively. Change in health care is inevitable; let us work together to be as knowledgeable and well-equipped as possible to meet the challenges that confront us. ■

This Month in *CHEST*: Editor's Picks

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

▶ Refractory Asthma: Importance of Bronchoscopy to Identify Phenotypes and Direct Therapy. *By Dr. J. T. Good Jr et al.*

▶ Medication Chart Intervention Improves Inpatient Thrombo-embolism Prophylaxis. *By Dr. D. S. H. Liu et al.*

▶ Surveillance Tracheal Aspirate Cultures Do Not Reliably Predict Bacteria Cultured at the Time of an Acute Respiratory Infection in Children With Tracheostomy Tubes. *By Dr. J. M. Cline et al.*

▶ Obstructive Sleep Apnea: Effects of Continuous Positive Airway Pressure on Cardiac Remodeling as Assessed by Cardiac Biomarkers, Echocardiography, and Cardiac MRI. *By Dr. J. Colish et al.*

▶ Functional and Muscular Effects of Neuromuscular Electrical Stimulation in Patients With Severe COPD: A Randomized Clinical Trial. *By Dr. I Vivodtzev et al.*

▶ A Randomized Trial to Improve Communication About End-of-Life Care Among Patients With COPD. *By Dr. D. H. Au et al.*

You Should Know About...

OneBreath® New Contest, Plus Member Guest Bloggers Needed

A new Facebook contest began March 1 and focuses on the OneBreath® Family Activities Toolkit. It will encourage OneBreath fans and followers to explore and post about their favorite toolkit activities. A mobile-friendly version of the toolkit has been created.

Become a guest blogger on OneBreath. Blog postings, 200- to 300-word articles, are meant for a patient audience and, ideally, will coincide with monthly disease awareness initiatives. Suggestions for topics are welcome. If you are interested, please contact Kristi Bruno at kbruno@chestnet.org or (847) 498-8308. Like OneBreath on Facebook (www.facebook.com/onebreathorg) or follow OneBreath on Twitter (www.twitter.com/onebreathorg).

Health-care Reform: Is Anyone Listening?

A new series you will not want to miss. Read this month's President's Corner on pages 16-17 that announces Dr. Raoof's start-up of a new monthly series on health-care reform issues. ACCP members with expertise in many of these areas will be writing these "don't miss" columns.

CHEST Podcasts: ACCP Antithrombotic Guidelines, 9th ed

Listen to podcasts that feature discussions on methodology and key recommendations related to the newly released ACCP antithrombotic guidelines.

Access podcasts on the *CHEST* Web site at http://chestjournal.chestpubs.org or on iTunes®.

March Is DVT Awareness Month

The ACCP supports the Coalition to Prevent DVT in raising awareness of this commonly occurring medical condition and its potentially fatal complication—pulmonary embolism. Learn more (www.chestnet.org/accp/march-dvt-awareness-month) about ACCP resources to prevent, diagnose, and treat DVT. ■

Don't Miss These CHEST 2012 Opportunities

CHEST 2012

October 20 - 25
Atlanta, Georgia

Call for Abstracts and Case Reports

Submission Deadline: April 9

Be part of the CHEST 2012 program by submitting an abstract of your original investigative work or a case report for presentation at the meeting. The ACCP is now taking submissions for:

- Abstracts
- Affiliate Case Reports
- Medical Student/Resident Case Reports
- Global Case Reports
- Clinical Case Puzzlers

Submission is FREE, and both domestic and international submissions are invited. Accepted abstracts and case reports (excluding clinical case puzzlers) will appear online in a *CHEST* journal supplement. Be aware that the submission deadline is earlier than it has been for previous CHEST meetings. Submissions are due April 9. Learn more at accpmeeting.org.

The CHEST Foundation Awards Program

Application Deadline: May 4

Apply for awards to support volunteer work, leadership projects, or clinical research. Nearly 800 recipients have received more than $8 million worldwide from The CHEST Foundation Awards Program for outstanding work in chest and critical care medicine. In 2012, The Foundation will offer more than $500,000 in awards. The following will be conferred at CHEST 2012:

- Service Awards: multiple awards totaling $55,000
- Distinguished Scholar Award: $150,000 awarded over 3 years
- Clinical Research and Leadership Awards: multiple awards totaling $210,000

THE CHEST FOUNDATION®

See which awards you are eligible for and apply by May 4 at OneBreath.org. ■

Centers of Excellence at CHEST 2012

Exciting Preparations Now Underway

Preparation is in full swing for a grand presentation of the Centers of Excellence (COE) at CHEST 2012 in Atlanta, Georgia. This year, the COE will be the gateway for attendees entering the ACCP Clinical Resource Center (exhibit hall) and Experience ACCP. It will offer attendees an opportunity to interact with their colleagues in a clinically focused environment with 10 COEs (hospital and nonhospital based practices) and five touchdown stations (TDS) (supporting companies).

The hospital and nonhospital-based practices will be selected primarily from Atlanta and surrounding state areas, although COEs that offer innovations and best practices not found in those areas will be invited to present.

The five companies that occupy the TDSs will be selected based on unique contributions to medical practice and/or exceptional learning strategies. Both the COE and the TDS will offer attendees an opportunity to view and discuss the lessons learned from outstanding demonstrations and presentations with the experts and with their colleagues.

The COE will be open to all CHEST attendees Monday, October 22, through Wednesday, October 24. There will a special reception on Monday to recognize the participants and offer an opportunity for invited attendees to ask questions and discuss innovations with the presenters.

If you and other attendees wish to view innovation and best practices in a clinically focused environment, plan to visit the COE for a great learning experience and tasty refreshments.

For additional information and to request an application, please contact Dr. David Eubanks at deubanks@chestnet.org; or Kim Schrader at kschrader@chestnet.org.

Subsequent issues of *CHEST Physician* will present overviews of the COE and TDSs that will present at CHEST 2012.

The ACCP recognizes the following participants in last year's CHEST 2011 COE:

Boehringer Ingelheim Pharmaceuticals, Inc.
Genentech
Hanuola ECMO Program of Hawaii
Klingensmith HealthCare
NorthShore University HealthSystem
Not One More Life
Novartis Pharmaceutical Corp.
Promise Hospital
REMEO Ventilation and Weaning Centers
The Queen's Medical Center
Tripler Army Medical Center & 13th US Air Force
UMass Memorial Medical Center
University of Hawaii, John A. Burns School of Medicine ■

SLEEP STRATEGIES

Sleep, Metabolic Disturbance, and Diabetes Mellitus: Are They Linked?

It is being increasingly recognized that sleep has an important effect on glucose metabolism and regulation of body weight, suggesting that the lack of sufficient sleep worldwide may contribute to the global epidemic of obesity and diabetes. This brief review examines the current evidence that demonstrates the link between sleep loss (due to sleep restriction, sleep fragmentation, or insomnia) and these metabolic disturbances.

Sleep Quantity as a Risk Factor

Evidence demonstrating that sleep duration of less than 7 h is linked to an increased risk of glucose intolerance and diabetes comes from both experimental sleep restriction studies and epidemiologic studies.

Sleep Restriction Studies

One study (Spiegel et al. *Lancet*. 1999;354[9188]:1435) conducted in young healthy adults, restricted to 4 h of sleep for six consecutive nights, found a 40% reduction in glucose tolerance that reversed after two nights of recovery sleep. In a similar study, the same group also demonstrated an association between sleep restriction and reduced leptin and elevated ghrelin levels associated with increased hunger and appetite. Other studies have shown that modest sleep restriction of 5 to 6 h/night leads to a reduction in insulin sensitivity. These data suggest that sleep restriction, even to a short-term, modest degree, as experienced by healthy adults in everyday life, can lead to changes in glucose metabolism and weight gain that can further promote insulin resistance.

Epidemiologic Studies

A pooled meta-analysis of 10 prospective studies (Cappuccio et al. *Diabetes Care*. 2010;33[2]:414) with 107,756 study participants who were followed for a median duration of 9.5 years found that short sleep duration of less than 5 to 6 h/night was associated with a 28% increase in risk of developing diabetes. Interestingly, the risk of developing diabetes was 48% higher in individuals who reported sleeping more than 8 to 9 h/night. The risk of developing diabetes was also higher in individuals who reported difficulty in initiating sleep (57%) and maintaining sleep (84%). These studies suggest that both short and long sleep times with poor sleep quality are risks for developing diabetes, compared with the "optimum sleep time" of 7 to 8 h. The mechanism for developing diabetes in long duration sleepers is not known, though reported long sleep time may be associated with sleep fragmentation and subsequent excessive somnolence.

Sleep Quality as a Risk Factor

Slow wave sleep (SWS) has been linked to metabolic, hormonal, and neuroendocrine changes that modulate glucose metabolism. These changes include reduction in cerebral glucose utilization, increase in growth hormone, a reduction in cortisol secretion, and a decrease in sympathetic tone (Knutson et al. *Sleep Med Rev*. 2007;11[3]:163). An experimental study (Tasali et al. *Proc Natl Acad Sci U S A*. 2008;105[3]:1044) conducted in nine healthy lean subjects showed that selective interruption of SWS by acoustic stimuli for three nights led to a reduction in insulin sensitivity and glucose tolerance by 25%, despite maintenance of total sleep duration. Similar results were also noted in 11 healthy subjects (Stamatakis et al. *Chest*. 2010;137[1]:95), whose sleep was interrupted in all sleep stages for two consecutive nights. This suggests that selective loss of SWS or chronic fragmentation of sleep, as can be seen in patients with obstructive sleep apnea (OSA), may increase the risk for glucose intolerance and diabetes.

OSA as a Risk Factor

In addition to its effects on sleep fragmentation that may modulate glycemic control, OSA is characterized by repetitive collapse of the upper airway with resultant intermittent hypoxia and sleep fragmentation leading to activation of the sympathetic system and catecholamine excess that may contribute to glucose intolerance. Several cross-sectional epidemiologic studies have suggested a link between OSA and diabetes, though only two prospective longitudinal studies have been performed, yielding conflicting results. Reichmuth and colleagues (*Am J Respir Crit Care Med*. 2005;172[12]:1590) followed 987 subjects for 4 years and did not find an independent association between sleep apnea severity and diabetes after adjustment for abdominal girth. The other study (Botros et al. *Am J Med*. 2009;122[12]:) was performed in 544 nondiabetic subjects and showed a link etween severity of sleep apnea (divided into quartiles) and the risk of developing diabetes; every quartile increase in severity was associated with a 43% increase in the incidence of diabetes. Two additional studies show a link between severity of sleep apnea and the degree of alterations in glucose metabolism. In a study of 118 nondiabetic subjects (Punjabi et al. *Am J Respir Crit Care Med*. 2009;179[3]:235), severity of sleep apnea was linearly correlated with insulin resistance; individuals with mild, moderate, and severe sleep apnea showed 26%, 36%, and 43% reduction in insulin sensitivity, respectively, as compared with normal subjects. In a cross-sectional study of 60 diabetics (Aronsohn et al. *Am J Respir Crit Care Med*. 2010;181[5]:507), glycosylated hemoglobin levels worsened with increasing severity of sleep apnea, independent of age, sex, adiposity, and other confounders. Compared with subjects with no sleep apnea, the adjusted mean HbA1c increased by 1.49% in patients with mild OSA, 1.93% in moderate OSA, and 3.69% in severe OSA. Both of these studies showed a positive correlation between the degree of nocturnal oxygen desaturation and insulin resistance. While these data demonstrate a strong association between OSA and diabetes, causality cannot be proven without more prospective long-term studies.

Impact of CPAP Treatment on Glucose Metabolism and Diabetes

Although several uncontrolled studies have shown a beneficial effect of short-term CPAP (3 months) on glucose metabolism and glycemic control, the results from randomized controlled studies using sham-CPAP have shown conflicting results. West and colleagues (*Thorax*. 2007;62[11]:969) randomized 42 patients with known type 2 diabetes and newly diagnosed OSA to therapeutic CPAP or sham but were not able to demonstrate any difference in insulin resistance or HbA1c levels at 3 months between the groups. A second study (Lam et al. *Eur Respir J*. 2010;35[1]:138) randomized 61 Chinese male subjects with moderate-to-severe OSA to therapeutic CPAP or sham; at 12 weeks, insulin sensitivity improved in the therapeutic CPAP group only. This benefit was seen predominantly in patients with a body mass index of > 25 kg/m^2. It is possible that the higher therapeutic CPAP adherence rates in this study (average CPAP use 6.2 h vs 3.6 h in the West study) may explain the differences in the outcomes between the two studies. Additionally, the group randomized to therapeutic CPAP in the Lam study had a higher rate of adherence (average CPAP use 6.2 h vs 4.5 h in the sham group), though this difference in adherence rate was not seen in the West study. While this may suggest a benefit to CPAP, it may also mean that adherence to CPAP is also predictive of other behaviors that improve glycemic control; more studies are needed to better define the role of obesity and potential benefit of CPAP on glucose metabolism.

In summary, both quantity and quality of sleep are important, and loss of sleep either due to chronic sleep restriction or fragmentation can have an adverse impact on glucose metabolism, insulin resistance, and the risk for developing diabetes. OSA is very common in diabetics and may contribute to an increased risk for diabetes and poor diabetes control, suggesting a bidirectional link between the two disorders; treatment with CPAP may improve glycemic control in a manner related to the degree of adherence to therapy. Quality sleep of a 7- to 8-h duration may improve glucose metabolism, weight control, and yield a subsequent decrease in diabetes risk. ■

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Editor's Comment

The link between poor sleep and glycemic control has been well-described, and the spectre of causality is becoming increasingly more solidified. Based upon the available evidence, it seems that treatment of sleep disorders can restore sweet dreams and may mitigate the risk of the sweet tooth.

–Dr. David S. Schulman, FCCP

NETWORKS
Home Care, Practice Operations, Transplant

Home Care

Use of Simulation in the Teaching of Community/Family Caregivers Providing Complex Care in the Home

Use of simulation in the training of health-care professionals is emerging as an important adjunct to traditional education models (Gordon. *Chest*. 2012;141[1]:12). It exposes learners to a multitude of clinical scenarios, whereby they can experience clinical situations and be evaluated without risk to patients. This experiential, deliberate practice in a stress-free environment is very important in building learner confidence and in mastery learning (McGaghie. *Chest*. 2009;135[3]:62S).

It is these aspects of mastery learning and building confidence in a risk-free environment that make the use of simulation an interesting adjunct to the traditional teaching of community/family caregivers providing complex care in the home.

Techniques such as tracheotomy care, suctioning, ventilator management, and appropriate intervention in critical situations (ie, tracheal cuff leaks, mucus plugs, and ventilator alarm conditions) can be very stressful for community/family caregivers. Learning to recognize signs and symptoms of infection, oxygen desaturation, or respiratory distress is also challenging, since, traditionally, these scenarios can only be described and not simulated.

Addition of simulation to existing education programs allows community/family caregivers the opportunity to safely experience the event, recognize the problem, and intervene as required.

It also allows educators the opportunity to better evaluate the readiness of the community/family caregivers to assume care once the patient returns home.

This evaluation of caregiver readiness is crucial because concerns about patient safety often result in prolonged hospitalizations, insecurity, and frustration on both sides of the hospital/home care continuum.

In these exceptional cases, use of simulation, in combination with traditional teaching, facilitates safe patient transition to the home.

Rita Troini, RRT
Steering Committee Member

Practice Operations

Medical practices face great challenges as our health-care environment is undergoing significant changes. While physicians used to thrive on remaining independent, the number physicians employed by hospitals is rapidly escalating. Many established practices are seeking to either sell themselves or to integrate with hospitals through professional service agreements. The common theme of the future of health care involves the delivery of high quality, cost-effective care, where provider compensation is no longer linked to productivity measured by volume of delivered services. Electronic connectivity among all health-care providers (physicians, hospitals, pharmacies, insurers, extended care facilities, and others) will be key to these initiatives. Our immediate action plan should consider cost-cutting efforts, redesign of our delivery processes to improve efficiencies, and exploring opportunities to align with our hospital partners. Regardless of the business model, practices will optimize their value by developing the ability to measure quality metrics.

On April 20-21, the American College of Chest Physicians will conduct a Business of Medicine course that will address these issues, with the goal of helping the participants prepare for these challenges. The topics will include Health-care Macroeconomic Forces and Trends; Financial and Managerial Accounting: Getting Behind the Numbers; Key Drivers for Physician-Hospital Affiliations: Alignment and Clinical Integrations; Payer Contracting Strategies; Optimizing Technology to Reduce Costs and Increase Effectiveness; and Using EHRs in Your Practice. The participants will have time for networking and one-to-one discussions with an outstanding, well-informed faculty.

Dr. Edward J. Diamond, FCCP

Transplant

Adjunct Mediastinal Pexy in Posttransplant LVRS

Symptomatic native lung hyperinflation occurs in 5% of patients following single lung transplantation for emphysematous disease (Krishman et al. *Radiographics*. 2007;27[4]957). The

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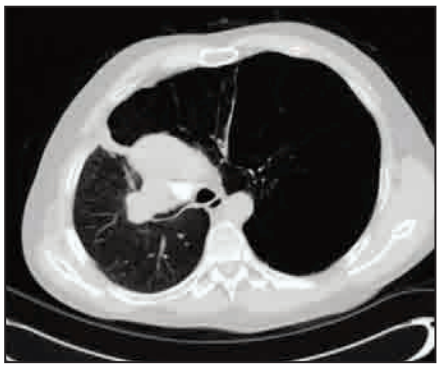


Fig 1. Preoperative CT scan showing mediastinal shift and graft compression.

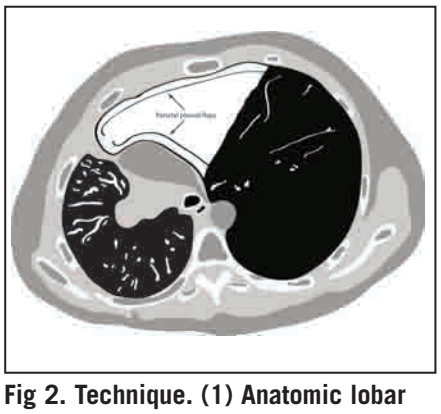


Fig 2. Technique. (1) Anatomic lobar resection of most hyperinflated lobe is done through an axillary muscle sparing thoracotomy; (2) medial anterior mediastinal parietal pleura is incised in a craniocaudal fashion, ideally from the apex to the diaphragm.

transplanted lung becomes restricted, but the overall physiology is obstructive-dominated by the native lung (Fig 1). Native lung volume reduction surgery (nLVRS) relieves graft compression and results in symptomatic and functional improvement (Reece et al. *J Thorac Cardiovasc Surg*. 2008;135[4]:931). However, this procedure carries increased morbidity due to prolonged air leak.

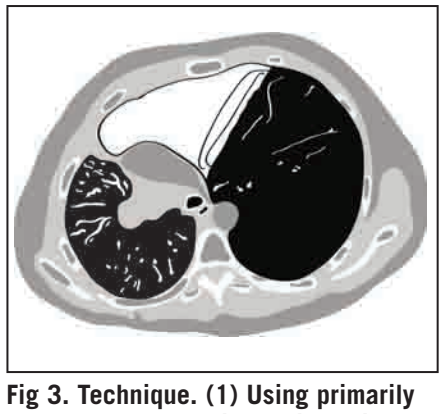


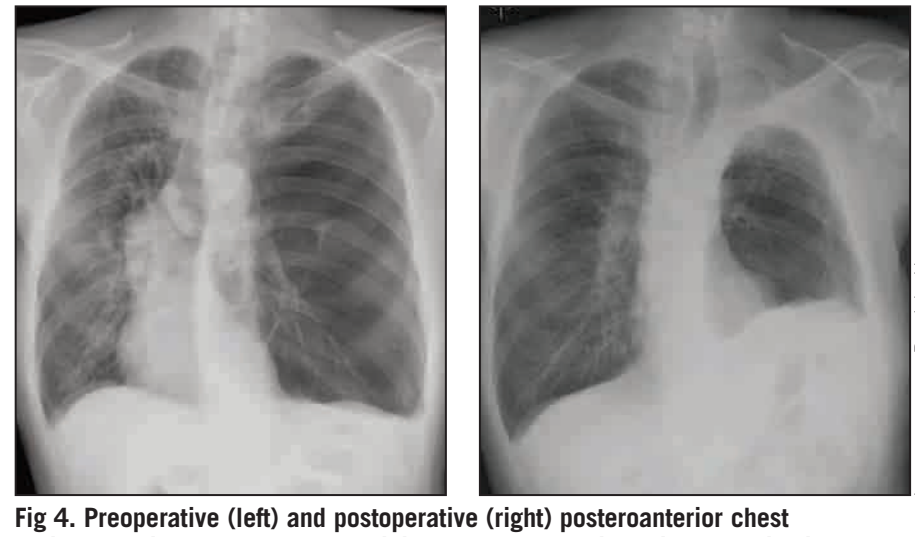
Fig 3. Technique. (1) Using primarily blunt, manually assisted dissection, generous pleural flaps are developed; (2) ideally. these flaps are dissected back to the edge of remaining lung (anterior flap) and to the medial hilum (posterior flap); and (3) pleural flaps are trimmed (if needed), overlapped (in whichever orientation seems most appropriate), and tacked in place with 3-0 braided, absorbable suture.

We have developed a technique of mediastinal pexy in conjunction with nLVRS in attempt to decrease such morbidity.

Anatomic lobectomy is performed via thoracotomy. The anterior mediastinal parietal pleura is incised longitudinally from apex to diaphragm (Fig 2). Using blunt manual dissection, generous pleural flaps are developed and dissected back to the remaining lung edge and hilum. The flaps are trimmed, overlapped, and tacked in place (Fig 3).

We have used this technique in four patients with no mortality and noted decreased morbidity with regards to chest tube duration and hospital length of stay (LOS). Mean LOS was 13 days. Mean increase in FEV_1 was 512 mL (59% increase in absolute milliliters). Mediastinal pexy promotes both reduction and fixation of the pleural space more effectively than can be achieved with standard pleural tenting or resection alone (Fig 4). We propose this could decrease frequency and severity of morbidity and encourage others to adopt or trial this technique.

Dr. J. L. Hermsen;
N. K. Strieter, RN, MSN; and
Dr. J. D. Maloney, FCCP
Steering Committee Member



IMAGES COURTESY DR. J. L. HERMSEN

Fig 4. Preoperative (left) and postoperative (right) posteroanterior chest radiographs in lung transplant recipient after nLVRS with adjunct mediastinal pexy.

New Membership Benefit Connects Members Virtually

Join the ACCP e-Community Today

Whether it's networking with members in your state, across the country, or even around the world, the new ACCP e-Community offers a private, secure platform for members to connect and share with other members virtually. Hundreds of ACCP members have already joined the e-Community, and initial member feedback has been positive. "This is going to be a great (and fun) interactive online tool and should make communication within the College a snap," said Dr. Francis J. Podbielski, FCCP, Vice-Chair, US and Canadian Governors. "I think it enhances ACCP membership by allowing us easy ways to connect and engage with other members."

Benefits of the e-Community

The e-Community utilizes a simple, user-friendly, secure format that allows members to:

- Share resources, such as slide sets, photos, videos, and links to journal articles
- Discuss clinical issues related to specific disease topics, practice management issues, or research interests
- Collaborate with members around the world on CHEST presentations, guideline development, case studies, and more
- Search for members by institution, specialty, or clinical interests
- Subscribe to content alerts and RSS feeds by topic
- Create and comment on simple polls

"By joining the ACCP e-Community, members can not only stay current on key clinical topics, but they can also build relationships across multiple disciplines and ask for input on everything from abstract development to difficult patient cases," said Dr. Jay I. Peters, FCCP, Council of NetWorks Chair.

Recent e-Community discussions relate to sepsis and critical care issues; ideas for effectively managing your practice; and the new ACCP anti-thrombotic guidelines. The e-Community also provides training resources, including answers to frequently asked questions and step-by-step videos, to help members learn how to use key features, such as uploading resources, searching for members, and starting and contributing to discussions.

Join the ACCP e-Community in Three Steps

All ACCP members have the opportunity to join the ACCP e-Community as part of their ACCP membership. To join, ACCP members will need to:

- **Join at least 1 of the 23 ACCP NetWorks.** ACCP members who join at least one ACCP NetWork, including those currently involved in the NetWorks, will be automatically enrolled in the ACCP e-Community. ACCP members can join NetWorks or change their NetWork affiliation by indicating their NetWork preferences within their ACCP profile on www.chestnet.org.
- **Respond to the e-Community e-mail invitation.** After joining a NetWork, ACCP members will receive an e-mail inviting them to participate in the ACCP e-Community. The e-mail will include information on how to access the e-Community website and how to login to the e-Community.
- **Start participating.** Once members receive their e-mail invitation and login to the e-Community, they can immediately upload their profile photo, set their personal preferences, and participate in discussions.

Learn more about the ACCP e-Community and NetWorks by visiting www.chestnet.org/networks. ■

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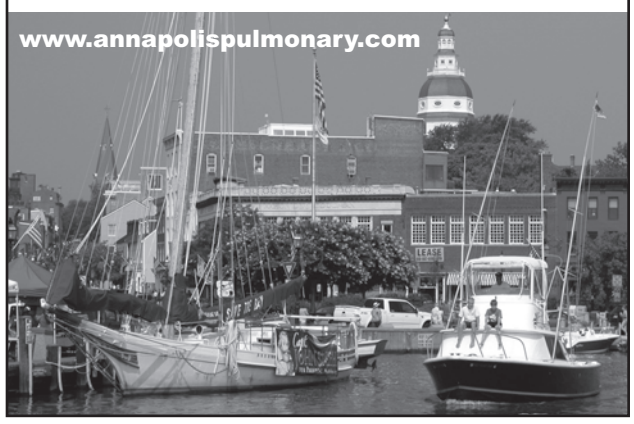

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FROM THE DESK OF THE PRACTICE MANAGEMENT COMMITTEE

ACCP Contractor Advisory Committee (CAC)

BY DR. ALAN BARKER, FCCP
Chair ACCP CAC

Each state or region is required by the Centers for Medicare & Medicaid Services (CMS) to have a Contractor Advisory Committee (CAC), composed of various physician specialties that submit claims to Medicare. Each CAC advises their sponsoring Medicare Administrative Contractor (MAC) regarding administrative issues. Most importantly, CACs review and offer advice on payment policies for new, emerging, or updated diagnostic tests or procedures that require a Local Coverage Decision (LCD). In the past year, MACs have been consolidated to 15 jurisdictional regions. Local coverage decisions are also circulated nationally among the MACs for additional review and comments, concerning payment policy for physician and other Medicare Part B services. Each CAC includes at least one representative (and alternates encouraged) of each specialty and subspecialty. Each CAC meets quarterly (in person or by conference call) and includes the physician members, consumer representatives (ie, Medicare beneficiaries), and administrative staff. CACs offer a voice and opportunity for physicians to effect Medicare payment decisions, which are then often followed by Medicaid and commercial insurance carriers.

The ACCP CAC, working with the Practice Management Committee and Governors, advocates on behalf of ACCP members and provides a forum to: (1) inform ACCP physicians in each state or region, and participate broadly in the review of LCD; (2) discuss and improve administrative policies within MAC discretion; (3) allow MACs to hear directly from the physician community; and (4) anticipate and communicate Medicare policy changes in one region that may quickly be implemented in other regions. The ACCP CAC meets quarterly by conference call and in person annually at CHEST, usually with a physician medical director of the hosting MAC region. The chair of the ACCP CAC is a nonvoting member of the Practice Management and Chest Medicine Affairs Committees. ACCP CAC members are encouraged to review pertinent issues with their respective ACCP Governor, disseminate information widely, and reflect ACCP member opinions. The ACCP CAC functions best when every state CAC has a pulmonary, sleep, or critical care representative so that regional issues can be addressed early and effectively. The ACCP CAC regularly communicates with ACCP leadership, practice administrative staff and consultants, and other committees and NetWorks. ACCP CAC members participate in educational sessions at CHEST, regional and national updates or meetings regarding the business of medicine, and related Medicare review organizations. Current pulmonary, sleep, and critical care representatives can be found at http://www.chestnet.org/practice//representatives.php.

In summary, the ACCP CAC is an advisory committee that is a voice and forum to disseminate, advise, and advocate on Medicare policy and administrative rules for pulmonary, sleep, and critical care physicians to ensure members are appropriately reimbursed for medically reasonable and necessary services provided to Medicare patients. Integral working relationships are fostered with other ACCP committees, leadership, and administrative staff, as well as one's own Medicare MAC.

The following states need ACCP CAC representatives:

Arizona, Idaho, Missouri, North Carolina, North Dakota, South Carolina, West Virginia, and Wyoming.

If you are interested in serving as the ACCP CAC representative for one of the states listed above, please contact Marla Brichta at mbrichta@chestnet.org. ■

For PAH (WHO Group 1) patients on oral monotherapy

TYVASO: the ONLY inhaled prostacyclin analogue approved for 4x-daily dosing[1]

Short treatment sessions: just 2 to 3 minutes each[2]

ONLY inhaled prostacyclin analogue approved as an add-on to oral PAH monotherapy[1]

- 52% of patients improved 6MWD by greater than 20 m[3]
- Improvement in 6MWD at peak (20 m) and trough (14 m) exposure[3]

Dosing regimen fits into patients' schedules

- Short treatment sessions: just 2 to 3 minutes, 4x daily[2]
- Set up once daily[1,2]
  - —One plastic ampule per day—no need to replace ampule for each treatment session[1]
  - —About 5 minutes a day for device preparation—once in the morning, and the device is ready to go all day[2]
- Treatment timing can be adjusted for planned activities[1]

Adverse events

- 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[1]

STUDY DESIGN: TRIUMPH I was a 12-week, randomized, double-blind, placebo-controlled, multicenter study of patients (N=235) with PAH who were receiving a stable dose of bosentan or sildenafil for 3 months before study initiation. Patients were administered either placebo or Tyvaso in 4 daily treatment sessions with a target dose of 9 breaths (54 mcg) per session over the course of the 12-week study. Primary endpoint was change in 6MWD at 12 weeks. Secondary endpoints included time to clinical worsening, Borg dyspnea score, NYHA functional class, trough 6MWD at week 12 (obtained at least 4 hours after study drug administration), peak 6MWD at 6 weeks, quality of life as measured by the MLWHF questionnaire, and PAH signs and symptoms.[3]

INDICATION

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

The effects diminish over the minimum recommended dosing interval of 4 hours; treatment timing can be adjusted for planned activities.

While there are long-term data on use of treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.

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 anticoagulants
- In patients with low systemic arterial pressure, 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 CYP2C8 such as gemfibrozil or inducers such as rifampin are added or withdrawn
- 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 (54% vs 29%), headache (41% vs 23%), throat irritation/pharyngolaryngeal pain (25% vs 14%), nausea (19% vs 11%), flushing (15% vs <1%), and syncope (6% vs <1%)
- 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.

6MWD=6-minute walk distance. MLWHF=Minnesota Living With Heart Failure. NYHA=New York Heart Association. WHO=World Health Organization.

References: 1. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2011. **2.** Tyvaso [patient package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2011. **3.** McLaughlin VV, Benza RL, Rubin LJ, et al. Addition of inhaled treprostinil to oral therapy for pulmonary arterial hypertension: a randomized controlled clinical trial. *J Am Coll Cardiol*. 2010;55(18):1915-1922.

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