Smoking linked to ‘new’ causes of death

BY MARY ANN MOON
Frontline Medical News

S
moking causes death from many diseases that until now have not been linked officially to tobacco use, including digestive disorders, liver cirrhosis, infections, renal failure, and breast and prostate cancers, according to a report published online Feb. 11 in the New England Journal of Medicine.

“Our results suggest that the number of persons in the United States who die each year as a result of smoking cigarettes may be substantially greater than currently estimated,” said Brian D. Carter of the epidemiology research program, American Cancer Society, Atlanta, and his associates.

The 2014 Surgeon General’s report estimated that smoking causes more than 480,000 deaths every year in the United States, based on mortality figures from 21 diseases that have been formally established as caused by smoking: 12 types of cancer, 6 types of cardiovascular disease, diabetes, chronic obstructive pulmonary disease, and obstructive pulmonary disease.

Medicare now covers CT for lung cancer screening

BY M. ALEXANDER OTTO
Frontline Medical News

E
ffective immediately, Medicare will cover annual lung cancer screening with low-dose CT for certain beneficiaries, according to a Feb. 5 national coverage determination.

To qualify, beneficiaries must be 55-77 years old, have a smoking history of at least a 30 pack-years, exhibit no signs or symptoms of lung cancer, and currently smoke or have quit within 15 years. They also must have a written screening order from their provider.

Coverage includes a counseling visit for shared decision making, so patients know beforehand the “benefits and harms of screening, follow-up diagnostic testing, over-diagnosis, false positive[s], and total radiation exposure,” among other things, according to the decision memo from the Centers for Medicare & Medicaid Services.

“Gradual smoking cessation

Varenicline for 24 weeks boosted quit rates in smokers, according to Dr. Jon O. Ebbert of the Mayo Clinic. See page 6, and watch the video at chestphysician.org.

Steroid cut CAP therapy failures

BY MARY ANN MOON
Frontline Medical News

A
5-day course of methylprednisolone reduced the rate of treatment failure in adults with severe community-acquired pneumonia and a high initial inflammatory response.

“If replicated, these findings would support the use of corticosteroids as adjunctive treatment in this clinical population,” said Dr. Antoni Torres of Institut Cliní del Torax, Hospital Clinic, Barcelona, and his associates.

Dr. Torres and his colleagues studied the use of corticosteroids in the subgroup of patients who present with severe disease and a proinflammatory profile characterized by a serum C-reactive protein level over 150 mg/dL – the patients most likely to benefit from anti-inflammatory therapies and least likely to be harmed by steroid-induced superinfection.

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Gradual smoking cessation

Medicare now covers CT for lung cancer screening

Steroid cut CAP therapy failures

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Reduce lung function decline

Delay IPF Progression with Esbriet

**Indication**

Esbriet® (pirfenidone) is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

**Select Important Safety Information**

**Elevated liver enzymes:** Increases in ALT and AST >3× ULN have been reported in patients treated with Esbriet. Rarely these have been associated with concomitant elevations in bilirubin. Patients treated with Esbriet had a higher incidence of elevations in ALT or AST than placebo patients (3.7% vs 0.8%, respectively). No cases of liver transplant or death due to liver failure that were related to Esbriet have been reported. However, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that could lead to death or the need for liver transplants in some patients. Conduct liver function tests (ALT, AST, and bilirubin) prior to initiating Esbriet, then monthly for the first 6 months and every 3 months thereafter. Dosage modifications or interruption may be necessary.

**Photosensitivity reaction or rash:** Patients treated with Esbriet had a higher incidence of photosensitivity reactions (9%) compared with patients treated with placebo (1%). Patients should avoid or minimize exposure to sunlight (including sunlamps), use a sunblock (SPF 50 or higher), and wear clothing that protects against sun exposure. Patients should avoid concomitant medications that cause photosensitivity. Dosage reduction or discontinuation may be necessary.

**Gastrointestinal disorders:** Gastrointestinal events of nausea, diarrhea, dyspepsia, vomiting, gastroesophageal reflux disease, and abdominal pain were more frequently reported in patients treated with Esbriet. Dosage reduction or interruption for gastrointestinal events was required in 18.5% of patients in the Esbriet 2403 mg/day group, as compared to 5.8% of patients in the placebo group; 2.2% of patients in the Esbriet 2403 mg/day group discontinued treatment due to a gastrointestinal event, as compared to 1.0% in the placebo group. The most common (>2%) gastrointestinal events that led to dosage reduction or interruption were nausea, diarrhea, vomiting, and dyspepsia. Dosage modifications may be necessary in some cases.

**Adverse reactions:** The most common adverse reactions (≥10%) were nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastroesophageal reflux disease, sinusitis, insomnia, weight decreased, and arthralgia.

**Drug interactions:** Concomitant administration with strong inhibitors of CYP1A2 (eg, fluvoxamine) significantly increases systemic exposure of Esbriet and is not recommended. Discontinue prior to administration of Esbriet. If strong CYP1A2 inhibitors cannot be avoided, dosage reductions of Esbriet are recommended. Monitor for adverse reactions and consider discontinuation of Esbriet as needed.
Concomitant administration of Esbriet and ciprofloxacin (a moderate inhibitor of CYP1A2) moderately increases exposure to Esbriet. If ciprofloxacin at the dosage of 750 mg twice daily cannot be avoided, dosage reductions are recommended. Monitor patients closely when ciprofloxacin is used.

Agents that are moderate or strong inhibitors of both CYP1A2 and CYP isoenzymes involved in the metabolism of Esbriet should be avoided during treatment.

The concomitant use of a CYP1A2 inducer may decrease the exposure of Esbriet, and may lead to loss of efficacy. Concomitant use of strong CYP1A2 inducers should be avoided.

**Specific populations:** Esbriet should be used with caution in patients with mild to moderate (Child-Pugh Class A and B) hepatic impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Esbriet as needed. The safety, efficacy, and pharmacokinetics of Esbriet have not been studied in patients with severe hepatic impairment. Esbriet is not recommended for use in patients with severe (Child-Pugh Class C) hepatic impairment.

Esbriet should be used with caution in patients with mild (CLcr 50-80 mL/min), moderate (CLcr 30-50 mL/min), or severe (CLcr less than 30 mL/min) renal impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Esbriet as needed. The safety, efficacy, and pharmacokinetics of Esbriet have not been studied in patients with end-stage renal disease requiring dialysis. Use of Esbriet in patients with end-stage renal disease requiring dialysis is not recommended.

Smoking causes decreased exposure to Esbriet, which may alter the efficacy profile of Esbriet. Instruct patients to stop smoking prior to treatment with Esbriet and to avoid smoking when using Esbriet.

**You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.**

**Please see Brief Summary of Prescribing Information on adjacent pages for additional important safety information.**

†Rank ANCOVA with lowest rank imputation for missing data due to death. Patients who died were counted in the ≥10% decline category.
‡Stable was defined as no decline in lung function.

**References:**
1. Esbriet full Prescribing Information. InterMune, Inc. October 2014.
ESBRIET® (pirfenidone)

Clinical Trials Experience
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 of pirfenidone has been evaluated in more than 1400 subjects with idiopathic pulmonary fibrosis (IPF) treated in 3 randomized, double-blind, placebo-controlled trials (Studies 1, 2, and 3) in which a total of 623 patients received 2403 mg/day of ESBRIET and 624 patients received placebo. Subjects ages ranged from 40 to 80 years (mean age of 67 years). Most patients were male (74%) and Caucasian (95%). The mean duration of exposure to ESBRIET was 62 weeks (range: 2 to 118 weeks) in these 3 trials.

At the recommended dosage of 2403 mg/day, 14.6% of patients on ESBRIET compared to 9.6% on placebo permanently discontinued treatment because of an adverse event. The most common (>1%) adverse reactions leading to discontinuation were rash and nausea. The most common (>3%) adverse reactions leading to dosage reduction or interruption were rash, nausea, diarrhea, and photosensitivity reaction.

The most common adverse reactions with an incidence of ≥10% and more frequent in the ESBRIET than placebo treatment group are listed in Table 1.

| Table 1. Adverse Reactions Occurring in ≥10% of ESBRIET-Treated Patients and More Commonly Than Placebo in Studies 1, 2, and 3 |
|---|---|---|
| Adverse Reaction | % of Patients (0 to 118 Weeks) |
| **ESBRIET 2403 mg/day** (N = 623) | **Placebo (N = 624)** |
| Nausea | 36% | 16% |
| Rash | 30% | 10% |
| Abdominal Pain† | 24% | 15% |
| Upper Respiratory Tract Infection | 27% | 25% |
| Diarrhea | 26% | 20% |
| Fatigue | 26% | 19% |
| Headache | 22% | 19% |
| Dyspepsia | 19% | 7% |
| Dizziness | 18% | 11% |
| Vomiting | 13% | 6% |
| Anorexia | 13% | 5% |
| Gastro-esophageal Reflux Disease | 11% | 7% |
| Sinusitis | 11% | 10% |
| Insomnia | 10% | 7% |
| Weight Decreased | 10% | 5% |
| Arthralgia | 10% | 7% |

† Includes abdominal pain, upper abdominal pain, abdominal distension, and stomach discomfort.

Adverse reactions occurring in ≥5 to <10% of ESBRIET-treated patients and more commonly than placebo are photosensitivity reaction (9% vs. 1%), decreased appetite (8% vs. 3%), pruritus (8% vs. 5%), asthenia (6% vs. 4%), dystonia (6% vs. 2%), and non-cardiac chest pain (5% vs. 4%)

Postmarketing Experience
In addition to adverse reactions identified from clinical trials the following adverse reactions have been identified during postapproval use of pirfenidone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency.

Blood and Lymphatic System Disorders
Agranulocytosis
Immune System Disorders
Angioedema
Hepatobiliary Disorders
Bilirubin increased in combination with increases of ALT and AST
### DRUG INTERACTIONS

#### CYP1A2 Inhibitors

Pirfenidone is metabolized primarily (70% to 80%) via CYP1A2 with minor contributions from other CYP isoenzymes including CYP2C9, 2C19, 2D6 and 2E1.

**Strong CYP1A2 Inhibitors**

The concomitant administration of ESBRIET and fluvoxamine or other strong CYP1A2 inhibitors (e.g., enoxacin) is not recommended because it significantly increases exposure to ESBRIET [see Clinical Pharmacology section 12.3 in full Prescribing Information]. Use of fluvoxamine or other strong CYP1A2 inhibitors should be discontinued prior to administration of ESBRIET and avoided during ESBRIET treatment. In the event that fluvoxamine or other strong CYP1A2 inhibitors are the only drug of choice, dosage reductions are recommended. Monitor for adverse reactions and consider discontinuation of ESBRIET as needed [see Dosage and Administration section 2.4 in full Prescribing Information].

**Moderate CYP1A2 Inhibitors**

Concomitant administration of ESBRIET and ciprofloxacin (a moderate inhibitor of CYP1A2) moderately increases exposure to ESBRIET [see Clinical Pharmacology section 12.3 in full Prescribing Information]. It ciprofloxacin at the dosage of 750 mg twice daily cannot be avoided, dosage reductions are recommended [see Dosage and Administration section 2.4 in full Prescribing Information]. Monitor patients closely when ciprofloxacin is used at a dosage of 250 mg or 500 mg once daily.

Concomitant CYP1A2 and other CYP Inhibitors

Agents or combinations of agents that are moderate or strong inhibitors of both CYP1A2 and one or more other CYP isoenzymes involved in the metabolism of ESBRIET (i.e., CYP2C9, 2C19, 2D6, and 2E1) should be discontinued prior to and avoided during ESBRIET treatment.

#### CYP1A2 Inducers

The concomitant use of ESBRIET and a CYP1A2 inducer may decrease the exposure of ESBRIET and this may lead to loss of efficacy. Therefore, discontinue use of strong CYP1A2 inducers prior to ESBRIET treatment and avoid the concomitant use of ESBRIET and a strong CYP1A2 inducer [see Clinical Pharmacology section 12.3 in full Prescribing Information].

#### USE IN SPECIFIC POPULATIONS

**Pregnancy**

Teratogenic Effects: Pregnancy Category C.

There are no adequate and well-controlled studies of ESBRIET in pregnant women. Pirfenidone was not teratogenic in rats and rabbits. Because animal reproduction studies are not always predictive of human response, ESBRIET should be used during pregnancy only if the benefit outweighs the risk to the patient.

A fertility and embryo-fetal development study with rats and an embryo-fetal development study with rabbits that received oral doses up to 3 and 2 times, respectively, the maximum recommended daily dose (MRDD) in adults (on mg/m² basis at maternal doses up to 1000 and 300 mg/kg/day, respectively) revealed no evidence of impaired fertility or harm to the fetus due to pirfenidone. In the presence of maternal toxicity, acyclic/irregular cycles (e.g., prolonged estrous cycle) were seen in rats at doses approximately equal to and higher than the MRDD in adults (on a mg/m² basis at maternal doses of 450 mg/kg/day and higher). In a pre- and post-natal development study, prolongation of the gestation period, decreased numbers of live newborn, and reduced pup viability and body weights were seen in rats at an oral dosage approximately 3 times the MRDD in adults (on a mg/m² basis at a maternal dose of 1000 mg/kg/day).

**Nursing Mothers**

A study with radio-labeled pirfenidone in rats has shown that pirfenidone or its metabolites are excreted in milk. It is not known whether ESBRIET is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue ESBRIET, taking into account the importance of the drug to the mother.

**Pediatric Use**

Safety and effectiveness of ESBRIET in pediatric patients have not been established.

**Geriatric Use**

Of the total number of subjects in the clinical studies receiving ESBRIET, 714 (67%) were 65 years old and over, while 231 (22%) were 75 years old and over. No overall differences in safety or effectiveness were observed between older and younger patients. No dosage adjustment is required based upon age.

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**ESBRIET® (pirfenidone)**

**Hepatic Impairment**

ESBRIET should be used with caution in patients with mild (Child Pugh Class A) to moderate (Child Pugh Class B) hepatic impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of ESBRIET as needed [see Dosage and Administration section 2.2 in full Prescribing Information]. The safety, efficacy, and pharmacokinetics of ESBRIET have not been studied in patients with severe hepatic impairment. ESBRIET is not recommended for use in patients with severe (Child Pugh Class C) hepatic impairment [see Clinical Pharmacology section 12.3 in full Prescribing Information].

**Renal Impairment**

ESBRIET should be used with caution in patients with mild (CLcr, 50–80 mL/min), moderate (CLcr, 30–50 mL/min), or severe (CLcr, less than 30 mL/min) renal impairment [see Clinical Pharmacology section 12.3 in full Prescribing Information]. Monitor for adverse reactions and consider dosage modification or discontinuation of ESBRIET as needed [see Dosage and Administration section 2.3 in full Prescribing Information]. The safety, efficacy, and pharmacokinetics of ESBRIET have not been studied in patients with end-stage renal diseases requiring dialysis. Use of ESBRIET in patients with end-stage renal diseases requiring dialysis is not recommended.

**Smokers**

Smoking causes decreased exposure to ESBRIET [see Clinical Pharmacology section 12.3 in full Prescribing Information], which may alter the efficacy profile of ESBRIET. Instruct patients to stop smoking prior to treatment with ESBRIET and to avoid smoking when using ESBRIET.

**OVERDOSAGE**

There is limited clinical experience with overdosage. Multiple dosages of ESBRIET up to a maximum tolerated dose of 4005 mg per day were administered as five 257 mg capsules three times daily to healthy adult volunteers over a 12-day dose escalation.

In the event of a suspected overdose, appropriate supportive medical care should be provided, including monitoring of vital signs and observation of the clinical status of the patient.

**PATIENT COUNSELING INFORMATION**

Advising the patient to read the FDA-approved patient labeling (Patient Information).

**Liver Enzyme Elevations**

Advise patients that they may be required to undergo liver function testing periodically. Instruct patients to immediately report any symptoms of a liver problem (e.g., skin or the white of eyes turn yellow, urine turns dark or brown [tea colored], pain on the right side of stomach, bleed or bruise more easily than normal, lethargy) [see Warnings and Precautions].

**Photosensitivity Reaction or Rash**

Advise patients to avoid or minimize exposure to sunlight (including sunlamp) during use of ESBRIET because of concern for photosensitivity reactions or rash. Instruct patients to use a sunblock and to wear clothing that protects against sun exposure. Instruct patients to report symptoms of photosensitivity reaction or rash to their physician. Temporary dosage reductions or discontinuations may be required [see Warnings and Precautions].

**Gastrointestinal Events**

Instruct patients to report symptoms of persistent gastrointestinal effects including nausea, diarrhea, dyspepsia, vomiting, gastro-esophageal reflux disease, and abdominal pain. Temporary dosage reductions or discontinuations may be required [see Warnings and Precautions].

**Smokers**

Encourage patients to stop smoking prior to treatment with ESBRIET and to avoid smoking when using ESBRIET [see Clinical Pharmacology section 12.3 in full Prescribing Information].

**Take with Food**

Instruct patients to take ESBRIET with food to help decrease nausea and dizziness.

Manufactured for:

InterMune, Inc.

Brisbane, CA 94005 USA
Varenicline facilitates gradual smoking cessation

A 24-week course of varenicline improved quit rates among smokers who preferred to gradually reduce their use of cigarettes. In an industry-sponsored, randomized, double-blind, controlled trial, participants who were given varenicline showed higher quit rates at the end of treatment as well as 1 year later, compared with those given placebo, said Dr. Jon O. Ebbert of the Mayo Clinic, Rochester, Minn., and his associates.

Current U.S. clinical practice guidelines recommend that smokers set an immediate quit date and quit abruptly, “even though only 8% of smokers report being ready to do so,” Ebbert noted.

The study was performed at 61 medical centers in 10 countries during a 2-year period. The 1,310 participants would not quit abruptly, as is recommended, but were willing to reduce their smoking and make a quit attempt within the next 3 months. They were asked to reduce their smoking rate by 50% or more by week 4, to further reduce it by 75% or more by week 8, and to quit altogether by week 12.

Study participants, who smoked 10 or more cigarettes per day at baseline, were randomly assigned to receive varenicline (760 patients) or a placebo (750 patients) for 24 weeks. All received written materials and smoking cessation counseling focused on reduction techniques, problem solving, and skills training provided during 18 clinic visits and 10 telephone sessions of 10 minutes’ duration.

The primary efficacy endpoint was the continuous abstinence rate during weeks 15-24, which was self-reported by the participants and confirmed using exhaled carbon monoxide measurements. This rate was significantly higher for the varenicline group (32.1%) than for the placebo group (6.9%). The continuous abstinence rate remained significantly higher through 1 year of follow-up for varenicline (27%) than for placebo (9.9%).

The median time to abstinence was significantly shorter with varenicline (50 days) than with placebo (85 days). Results of sensitivity analyses confirmed those of the primary analysis, the investigators said (JAMA 2015 Feb. 17;313:687-94).

The percentage of participants who reported adverse events was higher with varenicline (82.3% vs. 72.5%), and the difference was largely accounted for by increases in nausea, abnormal dreams, insomnia, constipation, vomiting, and weight gain.

Rates of serious adverse events were similar between the two study groups, as were rates of treatment discontinuation (8.4% for varenicline and 7% for placebo). In particular, rates of suicidal ideation or behavior and depression scores were not significantly higher with varenicline.

The study findings indicate that prescribing varenicline “with a recommendation to reduce the number of cigarettes smoked per day, with the eventual goal of quitting, could be a useful therapeutic option for this population of smokers,” Dr. Ebbert and his associates said. A limitation of this study was that patients were excluded from participating if they had severe psychiatric, pulmonary, cardiovascular, or cerebrovascular disease, which hinders the generalizability of the results to a broader population of smokers.

In addition, study participants received significant counseling support that would not necessarily be available to patients in real-world clinical practice, so quit rates would be expected to be lower in actual practice.

This study was funded by Pfizer, maker of varenicline (Chantix). Pfizer also participated in the design and conduct of the study; the collection, analysis, and interpretation of the data; and manuscript preparation. Dr. Ebbert reported receiving grants from Pfizer, JHP Pharmaceuticals, and Orexigen, as well as personal fees from GlaxoSmithKline. His associates reported ties to industry sources.
CT screens
Medicare from page 1

deaths in the United States,” Dr. Patrick Conway, CMS chief medical officer, said in a statement. “We believe this final decision strikes an appropriate balance between providing access to this important preventive service and ensuring, to the best extent possible, that Medicare beneficiaries receive maximum benefit from a lung cancer screening program.”

The decision has been in the works for a while. In 2011, the National Cancer Institute–sponsored National Lung Screening Trial (NLST) showed that people aged 55-74 years with a history of heavy smoking are 20% less likely to die from lung cancer if they are screened with low-dose helical CT instead of standard chest x-ray (N. Engl. J. Med. 2011;365:395-409).

Previous studies had shown that screening with standard chest x-rays does not reduce mortality from lung cancer.

Results from NLST and other studies prompted the U.S. Preventive Services Task Force in 2013 to recommend annual low-dose CT screening for adults aged 55-80 years with a 30-pack-year history; the recommendation in turn led to formal requests to CMS for coverage. In proposing coverage, the

‘New’ causes of death
Smoking from page 1

and pneumonia. Mr. Carter and his associates pooled data from five large cohort studies to examine possible associations between smoking and an additional 31 cause-of-death categories. They now estimate that an additional 60,000-120,000 deaths each year can be attributed to smoking.

For their study, the investigators assessed 421,378 men and 532,651 women aged 55 years and older at baseline whose smoking status was carefully recorded and who were followed from 2000 to 2011 in the Cancer Prevention Study II Nutrition Cohort, the Nurses’ Health Study I, the Health Professionals Follow-Up Study, the Women’s Health Initiative, and the National Institutes of Health-AARP Diet and Health Study.

As expected, smokers had a twofold to threefold higher mortality from any cause, compared with nonsmokers. Smokers also had a markedly higher risk of death than nonsmokers from all 21 causes already established as attributable to tobacco use, such as lung cancer, oral cancer, ischemic heart disease, atherosclerosis, and stroke. But approximately 17% of smokers’ excess mortality was accounted for by several diseases that previously have not been attributable to tobacco use.

For example, the risk of death due to intestinal ischemia was approximately six times higher among smokers than among nonsmokers, a remarkably strong association that was also reported in the Million Women Study. “Smoking acutely reduces blood flow to the intestines, and evidence suggests that smoking causes risk factors that can often lead to intestinal ischemia, including atherosclerosis, platelet aggregation, and congestive heart failure,” Mr. Carter and his associates reported in the N. Engl. J. Med. 2015 Feb. 12 [doi:10.1056/NEJMsa140721].

In this study, smoking also more than doubled the risk of dying from other digestive diseases. Previous studies have suggested a link between smoking and digestive disorders such as Crohn’s disease, peptic ulcers, acute pancreatitis, paralytic ileus, bowel obstruction, cholecystitis, diverticulitis, and gastrointestinal hemorrhage. Although these diseases are not common causes of death, they account for millions of hospitalizations each year, the investigators noted.

The mortality risk from liver cirrhosis, after the data were adjusted for alcohol consumption, was more than three times higher in smokers. The latter association “is relevant for assessing the public health burden of smoking, since a considerable number of deaths in the United States are attributable to hypertensive heart disease,” according to Mr. Carter and his associates.

Smoking also was strongly associated with “multiple diseases too uncommon to examine individually.” This included all rare cancers combined, rare digestive diseases, and respiratory diseases other than those already known to stem from smoking.

In women, smoking raised breast cancer mortality, with a relative risk of 1.3. This association was strongly dose dependent. In men, smoking raised prostate cancer mortality, with a relative risk of 1.4.

This study was limited in that most of the participants were white and better educated than the general population, which may affect the applicability of the results to other populations.

VITALS

Key clinical point: Smoking is now thought to cause many deaths from infections, renal failure, liver cirrhosis; digestive diseases; and breast, prostate, and other cancers.

Major finding: Several diseases that previously have not been attributable to tobacco use accounted for 17% of smokers’ excess mortality.

Data source: An analysis of pooled data from five large cohort studies involving 954,029 people aged 55 years and older followed for 12 years to examine associations between smoking and 52 possible causes of death.

Disclosures: This study was supported by the American Cancer Society, Mr. Carter reported having no financial disclosures; one of his associates reported receiving grant support from Novo Nordisk.

Dr. Vera A. DePalo, MBA, FCCP, comments: We have long known of the health complications of chronic lung disease, cancer, and heart disease related to smoking. In an American Cancer Society–supported analysis of pooled data from a number of large cohort studies, not only is it clear that the burden of tobacco use has been underestimated, but a number of diseases not previously thought to be associated with tobacco use have now been linked to smoking.
One variable involved with mechanical ventilation – driving pressure – may predict mortality in adult respiratory distress syndrome. Research suggests that scaling ventilator tidal volumes ($V_T$) to patients’ body weight will minimize ventilator-induced lung injury. But patients with ARDS have a marked decrease in the proportion of lung available for ventilation, as is indicated by their lower respiratory-system compliance ($C_{RS}$), which is not related to their body weight.

“Therefore, we hypothesized that normalizing $V_T$ to $C_{RS}$ and using the ratio as an index indicating the ‘functional’ size of the lung would provide a better predictor of outcomes in patients with ARDS than $V_T$ alone, said Dr. Marcelo B.P. Amato of the cardiopulmonary department, University of Sao Paulo (Brazil) Heart Institute, and his associates.

This ratio, also known as the driving pressure, is easily calculated at the bedside.

The researchers explored whether driving pressure or other variables related to mechanical ventilation, including variables set by the ventilator operator, could be statistically linked to survival outcomes and therefore serve as a risk predictor.

They first devised a survival-prediction model using data from a cohort of 336 ARDS patients participating in four randomized clinical trials examining different ventilation strategies.

They then tested their findings using a validation cohort of 861 patients from a single large trial, then...

Continued on following page
Poor inhaler use may lead to poor asthma control

Over 75% of patients make mistakes when using metered-dose inhalers

Inflammatory CAP

Therapy failures from page 1

In a randomized double-blind trial at three teaching hospitals in Spain, 120 such patients were randomly assigned to receive 5 days of either IV methylprednisolone (61 patients) at a dose of 0.5 mg/kg every 12 hours or a matching placebo (59 patients), in addition to antibiotics.

The most common cause of pneumonia in both study groups was Streptococcus pneumoniae, and the most frequent empiric antimicrobial treatment was a combination of ceftriaxone, levofloxacin, and azithromycin. As expected, CRP and IL-10 levels decreased more in patients who received the corticosteroid than in those who received placebo.

The primary endpoint was treatment failure, both within 72 hours (early) and at 72-120 hours (late) after initiation of therapy. This rate was significantly lower in patients who received methylprednisolone (8 patients, or 13%) than in those who received placebo (18, or 31%). This reduction was largely attributed to the prevention of radiographic progression and late septic shock.

However, there were no significant differences in the secondary outcomes of time to clinical stabilization, length of ICU stay, length of hospitalization, and in-hospital mortality, the investigators said (JAMA 2015 Feb. 17 [doi:10.1001/jama.2015.88]).

It is likely that the most feared adverse effect of corticosteroid therapy – immunosuppression leading to superinfection – wasn’t an issue in this study because of the short course of treatment and the relatively low dose of methylprednisolone used.

These findings are important because any efficacious adjunctive treatment may help reduce the high mortality associated with severe community-acquired pneumonia. It is estimated that despite effective antibiotic treatment, 12%-36% of patients admitted to an ICU with this disease will die within a short period, Dr. Torres and his associates noted.

A larger study is underway to confirm the results.

Continued from previous page

tested them again in a more recent validation cohort of 2,365 patients participating in four more randomized trials comparing different ventilation strategies.

Driving pressure was the only ventilation variable found to be strongly associated with survival. Higher driving pressures strongly predicted higher mortality: Every 1-standard deviation increase in driving pressure was related to increased mortality, with a relative risk of 1.41. Even in patients receiving lung-protective plateau pressures and low tidal volumes, higher driving pressure was associated with increased mortality, with a relative risk of 1.36, Dr. Amato and his associates said (N. Engl. J. Med. 2015 Feb. 19 [doi:10.1056/NEJMsa1410639]).

These findings can only suggest that driving pressure is a critical mediator of various ventilator strategies, since they are derived from a post hoc observational statistical analysis and cannot establish causality, the researchers said.

Now, prospective clinical trials are needed to determine whether adjusting ventilator settings to lower driving pressure will improve survival in ARDS.
LAS VEGAS – In the clinical opinion of Dr. Andi L. Shane, tuberculin skin testing and interferon gamma release assay diagnostics and surveillance for *Mycobacterium tuberculosis* infection are game changers in the ongoing effort to reduce TB infections.

“From 1982 to 2013, we’ve had a very nice decline in TB cases. However, we still have quite a bit of work to do,” Dr. Shane said at an update sponsored by the American Academy of Pediatrics California District 9.

Case rates are high in California, Nevada, Texas, Florida, New York, Washington, New Jersey, and the District of Columbia. Those under 5 years old and those aged 15-24 years are more likely to be affected.

“It’s really important to identify TB as soon as possible, especially in children,” said Dr. Shane of the department of pediatrics, division of infectious diseases, Emory University, Atlanta. “An interferon gamma release assay (IGRA) or a tuberculin skin test (TST) may be used in situations where assessment for MTB [M. tuberculosis] exposure is indicated. IGRA is preferred in persons who received BCG vaccine and who have low rates of test completion, while TST is preferred for testing of children younger than age 5.”

TB in people younger than age 15 years is a marker for transmission of TB, usually from an adult. “So when we identify a case of TB in children, that requires a contact investigation,” she said. “We’re more concerned with children under the age of 5 with TB because they are more likely to have disseminated disease.”

Latent TB means that the patient has been exposed to the disease but that his or her body has been able to control the infection; no systemic manifestations of infection are present. Identifying the difference between latent tuberculosis infection (LTBI) and actual tuberculosis disease is one of the most challenging aspects to explain to families. The reason is that children or adults who have LTBI are not infectious, whereas someone who has pulmonary or laryngeal TB is considered to be an infectious risk to other individuals.

Dr. Shane went on to discuss limitations of the TST. For one, the test may be placed incorrectly, resulting in an inflammatory response or no response, “and there is reader variability,” she said. “The reading needs...
to occur 48-72 hours after placement of the test. So, if you place it on a
Thursday, that means you really are not going to read it at the optimal
time unless the child comes to you
on a weekend or the test is read by
somebody else.”
As an alternative, two IGRA have
been developed that measure how
the immune system reacts to MTB.
One is QuantiFERON, which is wide-
ly used in the United States; the other
is the T-SPOT.TB test, which is wide-
ly used in Europe. A positive result
on either test indicates that there has
been interaction with MTB bacteria
but it does not differentiate between
LTBI and active TB disease.

“A negative IGRA tells you there
is no reaction to the test and MTB
is not likely, while an indeterminate
result is when you’re unable to in-
terpret the result due to low positive
[mitogen] or increased negative con-
trol [nil] compared to TB response,”
Dr. Shane said. “This usually indi-
cates that there’s some problem with
the assay itself. It can also indicate
that the individual may not have an
immune system that can respond to
and produce interferon gamma.”

Assessment of IGRA accuracy is
challenged by the lack of a standard
for the diagnosis of LTBI and active
TB. “We just don’t have a lot of good
data from resource-endowed set-
tings,” Dr. Shane explained. “We have
good data from areas where TB is
prevalent.” According to the Centers
for Disease Control and Prevention
and the AAP, IGRA are probably
reliable in children over the age of 5
years, but a TST is still recommend-
ed in children under the age of 5.
The IGRA’s specificity is much
higher than TSTs, Dr. Shane said.
“However, in some cases a TST
might be more sensitive for detecting
more remote MTB infections than
an IGRA, but IGRA may be better
at detecting a recent infection. Like
the TST, an IGRA also shows that
if you’re infected with TB you have
5-10% chance of developing active
TB in your lifetime.”

As a significant amount of blood
is required to perform an IGRA,
that might not always be optimal in
a young child, she said. “Low CD4
counts and other immunodeficien-
cies have also been associated with
false-negative TST and indetermi-
rate/false-negative IGRA results.”

For contact investigations, IG-
RA offer increased specificity, are
completed during a single visit, and
their response is not boosted if an
additional evaluation is needed 8-10
weeks after exposure. If the TST or
IGRA is positive, additional diagnos-
tic efforts are needed “to differenti-
te between LTBI and active MTB,” said
Dr. Shane, who recommended the
Curry International Tuberculosis
Center as a resource for clinicians
(www.currytbcenter.ucsf.edu/).

If the TST or IGRA is negative,
“it’s not sufficient to exclude MTB in-
fec tion. If you have a discordant TST
and IGRA result, consider history
and epidemiologic risk factors. Treat
with clinical suspicion or risk of a
poor outcome (those younger than
age 5 and those infected with HIV).”

---

To identify the symptoms of narcolepsy,
LOOK DEEPER

Cataplexy: A sudden, temporary loss of muscle tone triggered by strong emotions[2][3]
Hypnagogic Hallucinations: Vivid dream-like experiences that occur during the
transitions between wake and sleep[2][3]
Excessive Daytime Sleepiness: The inability to stay awake and alert during the day,
resulting in unintended lapses into drowsiness or sleep[2]
Sleep Paralysis: The temporary inability to move or speak while falling asleep
or waking up[2]
Sleep Disruption: The interruption of sleep by frequent awakenings[2][3]

C.H.E.S.S. is a useful mnemonic for recalling the 5 symptoms of narcolepsy,[1] although not all patients
experience all symptoms[2] Narcolepsy is primarily characterized by excessive daytime sleepiness and
catatonia.[2] All patients with narcolepsy have excessive daytime sleepiness.[2] The presence of cataplexy
is pathognomonic for narcolepsy.[2]

Narcolepsy is a Chronic, Life-Disrupting Neurologic Disorder[2][3]
Narcolepsy is a chronic, life-disrupting neurologic disorder in which the brain is unable to regulate
sleep-wake cycles normally, resulting in sleep-wake state instability.[4]

Narcolepsy is Underdiagnosed
It is estimated that approximately 50% or more of individuals with narcolepsy remain undiagnosed.[1]
Initial onset of symptoms typically occurs between the ages of 15-25,[5] although an accurate diagnosis
can take more than 10 years.[1]

Narcolepsy Symptoms Can Be Difficult to Recognize
Narcolepsy symptoms may overlap with those of other conditions, such as obstructive sleep apnea
and depression.[1] The initial and presenting symptom is typically some manifestation of excessive
daytime sleepiness such as tiredness, fatigue, difficulty concentrating, or mood changes.[2][3] Individual
symptoms should be evaluated carefully to determine whether they are due to narcolepsy or another
condition. Looking deeper at the symptoms can help healthcare professionals establish a differential
diagnosis.

To get a Deeper Look, at www.NarcolepsyLink.com

Narcolepsy Link contains resources to help
identify narcolepsy symptoms and facilitate
communications with your patients.

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1.2,3

1

1-4

1,2

1,2,5

Individual

1

1-4

1,2

1,2,5
SLEEP STRATEGIES: Multilevel surgical approach to OSAS

BY DR. BORIS CHERNOBILSKY

Despite significant technological, diagnostic, and therapeutic advancements, obstructive sleep apnea syndrome (OSAS) remains difficult to treat. The surgical “gold standard” for the treatment of severe OSAS remains tracheotomy. While completely bypassing all sites of upper airway obstruction, this treatment entails a significant alteration in lifestyle, may not be palatable to patients, and has cultural implications. The noninvasive “gold standard” has been positive airway pressure (PAP). When properly titrated and fitted, PAP is curative of OSAS provided the patient is compliant with therapy. Unfortunately, studies demonstrate noncompliance rates in the 40% to 54% range, which significantly drop to 84% at 1 year of use (Terri et al. Proc Am Thoracic Soc. 2008;5(2):171).

Alternate treatments have been proposed. These include mandibular advancement devices (MAD) and upper airway surgery. Surgery has been proposed as both adjunctive treatment to PAP and as a potential curative alternative, which does not require “maintenance” on the part of the patient but requires long-term follow-up and observation, especially in the event of symptom recurrence or major fluctuations in body mass index (BMI).

The challenge of surgical treatment is patient selection, as well as proper surgical procedure selection for each patient. OSAS is a complex disease process composed of both fixed and fluctuating variables. In brief, it is a complex interplay of static factors such as craniofacial anatomy, cephalometrics and nasal anatomy with soft tissue fluctuations dependent on weight, age (tonsil and adenoid size, palatal length), syndromes (macroglossia, palatal function), and varying distribution of fat in the three tongue fat pads and visceral vs peripheral body fat distribution. Couple this with conditions that affect muscle tone, cardiopulmonary function, “tracheal tug,” and even normal nightly variations in tone with the onset of REM and physiologic transitions that occur from one sleep stage to another, one begins to understand that the patient with OSAS requires an individualized multidisciplinary approach.

Proper understanding of the patient’s physiology and anatomy is crucial to success with treatment. The physical examination starts with inspection of the face: does the patient appear syndromic, have significant hemifacial microsomia, major maxillary or mandibular hypoplasia (or both)? These factors can lead to significant difficulty in fitting a PAP mask or MAD. Options for correction include maxillary-mandibular advancement (MMA) or isolated mandibular advancement / reconstruction. MMA is an oromaxillofacial procedure that shifts the entire maxilla and mandible forward; the soft palate, base of the tongue, and, to an extent, the larynx move forward, resulting in multilevel correction. It has the added benefit of potentially improving a patient’s occlusion and cosmetic appearance, as the chin and cheek bones advance to a more favorable position. While this is a major procedure for the patient, success rates have been reported upwards of 90% (Lei et al. Sleep Breath. 2000;4:137).

The nasal exam is crucial. While we start off as obligate nose breathers in infancy, this preference never goes away. Studies demonstrate that PAP requirements between nasal and oronasal masks are equivalent, but patient preference weighs heavily toward nasal masks where leak is significantly reduced (Bakker et al. Sleep Breath. 2012;16(3):709).

The exam should start with the external nose looking for dorsal deviations (congenital or traumatic), a significant proboscis, or lateral nasal wall collapse. Repair of the nasal valve or even functional rhinoplasty are the procedures of choice for these problems.

The internal nasal exam consists of evaluation for turbinate hypertrophy, significant nasal septal deviation, widening of the middle turbinates from concha bulla, the presence of nasal edema due to infection, extensive crusting from nasal dryness or septal perforation, significant nasal polyposis or even a nasal tumor. Initiation of PAP therapy is very often a “one-shot deal” and patients who were otherwise motivated to use PAP failed because their nasal obstruction was not diagnosed. Ideally, the exam should include nasal endoscopy.

Intrasal surgical techniques include septoplasty, turbinate resection, polypectomy, and functional endoscopic sinus surgery. While AHI is usually not significantly affected by nasal surgery, there are major improvements in quality of life scores and PAP compliance (Poirier, et al. Laryngoscope. 2014;124[1]:317). Rare patients, especially those with complete obstruction, can be treated in mild to moderate cases. In most, it is an important adjunct to the treatment of the patient with OSAS.

The exam should then proceed to the oral cavity and oropharynx. Careful note should be taken of the dentition and occlusion class, arching of the hard palate (especially in children), tongue size (Friedman or Mallampati class), length of soft palate, and uvula and tonsil size. In children and young adults, adenotonsillectomy or tonsillectomy alone can be curative as a first line therapy. Compliance issues with PAP are especially problematic in these populations. High arched palates in children can be managed with rapid maxillary expansion which can significantly broaden both the nasal and oral airway. MMA for retro/micrognathia was discussed previously.

The patient should next have a flexible laryngoscopic exam, usually a continuation of the nasal endoscopy. The nasopharynx is inspected for adenoid hypertrophy, polyps, cysts, and tumors. The palate is inspected from above. The exam proceeds to the level of the pharynx and hypopharynx with attention paid to the pharyngeal and lingual tonsils and the base of tongue position. Finally, the larynx is inspected for position of the epiglottis, laryngeal masses, vocal fold immobility, laryngomalacia, and arytenoid redundancy and prolapse with inspiration. A drug-induced sleep endoscopy (DISE) should be performed at a later date to assess these same structures dynamically in a state mimicking sleep to help guide appropriate surgical technique. DISE was reviewed in a previous issue and will not be discussed in detail.

Nasopharyngeal lesions are treated with surgical excision. The velopharynx is usually addressed with uvulopalatopharyngoplasty which often, but not always, includes the tonsils. Various techniques have been developed to address circumferential vs anteroposterior (AP) collapse of the palate and uvula. Present practices favor soft tissue/muscle rearrangement over soft tissue ablation. One such technique preferred by the author is expansion sphincter pharyngoplasty. Lingual tonsillectomy addresses large lingual tonsils, if present.

Many operations exist to address the tongue base, and consensus as to best practice is yet to be reached. Generally, two broad categories exist: suspensory or ablative. Suspension can be accomplished with sutures along the base of tongue, hyoid fixated to the anterior mandible or thyroid cartilage, and genioglossus advancement. A novel technology recently FDA-approved shows immense promise. Upper-airway stimulation uses electrodes on the hypoglossal nerve to protrude the tongue, timing it with each respiration through an intercostal muscle sensor lead (Strollo Jr et al. STAR Trial Group. N Engl J Med. 2014;370[2]:139).

Ablation can be accomplished by reducing the base of tongue through the delivery of energy, such as use of radiofrequency or excising tissue through techniques such as the Greenfield laser. This can be accomplished both directly and with robot-assisted techniques using the daVinci system transorally (TORS).

Laryngeal techniques include epiglottopexy or epiglottectomy in cases where the epiglottis retroflexes and obstructs the airway on inspiration. Laryngeal lesions are generally addressed with excision. Vocal fold paralysis in the midline can be addressed with cordotomy or arytenoidectomy. Prolapsing redundant tissue can be tightened using a laser. Laryngomalacia can be addressed surgically, as well.

Finally, the neck should be examined. Masses, tracheal deviation, evidence of prior tracheotomy, hyoid position, circumference, and lymphadenopathy should all be noted. Masses, especially goiters, can compress the internal jugular veins leading to laryngeal and pharyngeal swelling.

Sleep strategies continued on page 13.
CORONADO, CALIF. – Some patients with treatment-refractory obstructive sleep apnea may be candidates for upper airway stimulation, though those with complete concentric palatal collapse may not respond, according to Dr. Marion Boyd Gillespie.

“There’s been sound research showing that patients with obstructive sleep apnea have reduced neural tone,” Dr. Gillespie, who directs the snoring clinics at the Medical University of South Carolina, Charleston, said at the Triological Society’s Combined Sections Meeting. “During these apneic events, there’s a reduction in the neural tone of the genioglossus muscle, which is the main dilator of the upper airway. With upper airway stimulation, we’re trying to account for that loss of neural tone by providing more neural impulse to these muscle groups that perform the dilator functions.”

In 2014, the Food and Drug Administration cleared an upper airway stimulation system manufactured by Inspire Medical Systems, a pacemaker-like device that’s implanted in the subclavicular space. The system features a stimulator lead that attaches to the right hypoglossal nerve and a sensing lead that goes between the external and internal intercostal muscles to detect breathing.

Surgical removal of the mass is the treatment of choice.

In summary, OSAS is a complex disease that often requires multiple therapeutic modalities. Proper patient selection and a thorough physical exam are crucial to proper treatment choice. Surgery can be both adjunctive and curative. Patients often have multiple levels of airway obstruction that can be treated simultaneously or staged. Careful follow-up and involvement of a multidisciplinary care team will result in the highest success rates for these patients with complex disease.

Dr. Chernobilsky is Director of Sleep and Airway Surgery, Mount Sinai Beth Israel, Assistant Professor of Otolaryngology-Head and Neck Surgery, Icahn School of Medicine at Mount Sinai, New York, New York.

Editor’s comments
Although positive airway pressure is the gold standard treatment for obstructive sleep apnea, poor compliance with this modality provides the impetus for alternative treatments that are both effective and acceptable to patients. Upper airway surgery is a viable alternative for select patients, either as a primary treatment modality or as adjunctive therapy. In this installment of sleep strategies, Dr. Boris Chernobilsky discusses and clarifies, from a surgical perspective, the surgical techniques available, as well as the systematic approach, in the evaluation of the patient with sleep apnea.

Dr. Jeremy A. Weingarten, FCCP
Indication
Striverdi® Respimat® (olodaterol) Inhalation Spray is a long-acting beta2-agonist indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

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WARNING: ASTHMA-RELATED DEATH
Long-acting beta2-adrenergic agonists (LABA) increase the risk of asthma-related death. Data from a large, placebo-controlled US study that compared the safety of another long-acting beta2-adrenergic agonist (salmeterol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of LABA, including olodaterol, the active ingredient in STRIVERDI RESPIMAT. The safety and efficacy of STRIVERDI RESPIMAT in patients with asthma have not been established. STRIVERDI RESPIMAT is not indicated for the treatment of asthma.

All LABAs are contraindicated in patients with asthma without use of a long-term asthma control medication. STRIVERDI RESPIMAT should not be initiated in patients with acutely deteriorating COPD, which may be a life-threatening condition, or used as rescue therapy for acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled short-acting beta2-agonist.

STRIVERDI RESPIMAT should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medications containing long-acting beta2-agonists as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

STRIVERDI RESPIMAT may produce paradoxical bronchospasm that may be life threatening. If paradoxical bronchospasm occurs, STRIVERDI RESPIMAT should be discontinued immediately and alternative therapy instituted.

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- With the exception of other LABAs, all pulmonary medications were allowed as concomitant therapy (24% tiotropium, 25% ipratropium, 45% inhaled corticosteroids, and 16% xanthines)
- Mean increase in FEV1 of 110 mL at 5 minutes after the first dose compared to placebo (range: 100 to 120 mL)
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FEV1, forced expiratory volume in 1 second.

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There’s been sound research showing that patients with OSA have reduced neural tone.

DR. GILLESPIE

Continued from previous page

Dr. Gillespie, professor of otolaryngology–head and neck surgery at the university. “The sensing lead detects the respiratory wave, and the stimulatory lead starts stimulation at the end of expiration, because that’s when the airway is in its most collapsible state. It continues about two-thirds of the way through the inspiratory cycle to keep the airway open.”

Titration of the device is very similar to continuous positive airway pressure, he continued. Once implanted, the patient “will go back to the sleep lab where a tech who’s trained in the device will ramp up stimulation until observed apneas and hypopneas are adequately reduced. You would think that isolated stimulation of the hypoglossal nerve would only open up the airway at the level of the tongue. However, our initial investigation showed that there is dilation at the velopharynx...
as well,” Dr. Gillespie said. By moving the tongue out of the posterior airway, “you’re moving the dorsum of the tongue away from the velopharynx. You’re also getting active traction on the palatoglossal fold,” he added.

Results of the initial trial of the system in 126 patients with a mean body mass index of 28.4 kg/m² were published last year (N. Engl. J. Med. 2014;370:139-49). At 12 months of follow-up, patients experienced a 68% overall reduction in their apnea-hypopnea index (AHI) score, from a preoperative mean of 29 to a postoperative mean of 9. In addition, patients had a 70% overall reduction in their oxygen desaturation index (ODI). The researchers also observed normalization of patient-based outcomes, with improvement in the Functional Outcomes of Sleep Questionnaire score and reduction of the Epworth Sleepiness Scale score to a level of 10 on average. “We also saw a

Continued on following page

To learn more about STRIVERDI RESPIMAT, visit www.STRIVERDI.com

Please see Brief Summary of full Prescribing Information, including boxed WARNING for STRIVERDI RESPIMAT on adjacent page.

References:
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Continued from previous page
duction of snoring,” said Dr. Gillespie, who was a member of the research team. “Snoring went from 72% of patients having severe, an-
noying snoring to the point where a bed partner leaves the room 15% postoperatively.” Even so, 96% of patients who had a previous his-
tory of uvulopalatopharyngoplasty (UPPP) or laser-assisted uvulopal-
atoplasty (LAUP) still had tongue-
based collapse after 12 months of follow-up. “But we found that their response to this therapy was just as good as people who had an UPPP or LAUP,” Dr. Gillespie said at the meeting, jointly sponsored by the Triological Society and the American College of Surgeons. “So it seems like patients who have failed UPPP are still good candi-
dates for upper airway stimulation therapy.”

Dr. Gillespie noted that selection criteria for the trial were limited to patients with a BMI of less than 32 kg/m² and to those who did not have complete circumferential collapse at the level of the soft palate did not respond to upper airway stimulation (J. Clin. Sleep Med. 2013;9:433-8).

Dr. Gillespie is a consultant for and has received research support from Inspire Medical Systems, Olympus, and Surgical Specialties. He is also a consultant for Medtronic.

Published online: October 17, 2015

Non-Potassium-Sparing Diuretics: The ECS changes and hypo-
kalaeia that may result from the administration of non-potassium-
sparing diuretics can be safely reversed by beta-agonists, especially when the recommended dose of these effects is not known, caution is advised in the co-administration of beta-agonists with non-potassium-sparing diuretics. Modern Blood Inhibitor, Fibrotic Antidotes, 687, Proximally

Dr. SPEER / HEINZL / Raul	

Dr. David A. Schlump, FCCP, comments: The data present-
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scribed issues with continuous positive air-
way pressure (CPAP) adherence and the less-

of currently available CPAP alternatives, patients with obstructive sleep apnea and their providers have long awaited access to hypoglossal nerve stimulators to add to the armamentum of options for manage-
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tribute to the soft palate). While upper airway stimulation therapy is not likely the first-line OSA treatment for the majority of patients, it is an important step forward for those unwilling or unable to use CPAP.

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Panel backs antifungal for invasive aspergillosis

BY ELIZABETH MECHCATIE
Frontline Medical News

SILVER SPRING, MD. – A novel treatment for invasive aspergillosis and invasive mucormycosis gained the support of a Food and Drug Administration advisory panel, although members were ambivalent about the mucormycosis indication, based on the small study size.

The FDA’s Anti-Infective Drugs Advisory Committee voted 11-0 that isavuconazonium, an antifungal prodrug, was safe and effective for the treatment of invasive aspergillosis. A phase III study compared isavuconazonium to voriconazole, the standard of care, in more than 500 patients.

The panel voted 8-2, with one abstention, that there was substantial evidence that isavuconazonium, an antifungal prodrug of isavuconazole, is safe and effective for treating patients with invasive mucormycosis, with panelists citing concerns about a study size of only 37 patients and historical controls. If approved for mucormycosis, the panel said that the manufacturer, Astellas, should be required to conduct a phase IV trial further evaluating treatment in this population.

Isavuconazonium is a prodrug of isavuconazole, a triazole antifungal, and would be available as an oral capsule and as a powder formulation reconstituted for intravenous administration through an in-line filter.

For aspergillosis, “I do believe that this drug provides a reasonable alternative ... without additional toxicities,” said panelist Dr. Paige Waterman of the Global Emerging Infections Surveillance and Response System at the Walter Reed Army Medical Center, Silver Spring, Md. Labeling should make clear that the drug should not be used in people under age 18 years or in pregnant women, and that a filter should be used with IV administration. Also, labeling should state a risk of hepatotoxicity, which appears in the labeling of other drugs in the same class.

Because isavuconazonium has been associated with a shortened QT interval, Dr. Waterman said that screening ECGs should be recommended. There should be extra caution when prescribing the drug to those of Asian descent, since drug concentrations were higher in those patients.

For treatment of invasive mucormycosis, those voting in favor of approval cited the significance of the condition and the reasonable efficacy results. Panelists also noted that more clinical data are clearly needed and that the lack of data directly comparing isavuconazonium to amphotericin B – the only FDA-approved drug for this indication – was problematic. Isavuconazonium “really does fill an unmet need; I have high hopes that it is at least as good as amphotericin. But I do think we need more data to confirm that,” said Dr. Michael Neely, chair of antimicrobial stewardship at Children’s Hospital, Los Angeles, who voted for this indication.

If approved, isavuconazonium would provide an alternative to voriconazole for treating aspergillosis. Further, the IV formulation of isavuconazonium does not contain cyclodextrin, which is present in the IV formulation of voriconazole and limits its use in patients with moderate to severe renal dysfunction, according to Astellas. Safety concerns include QT-segment shortening and particulate formation in the IV formulation, according to the FDA.

The randomized, double-blind, international, noninferiority study compared treatment with isavuconazonium to voriconazole in 316 adults with invasive aspergillosis. In the randomized study, 11% of patients were in the United States and Canada, 20% had had an allogeneic bone marrow transplant, and 70% had an uncontrollable malignancy (Infect. Drug Resist. 2013;6:16374). The primary effectiveness endpoint, all-cause mortality through day 42, was 19% in those on isavuconazonium, compared with 20% in those on voriconazole. There were fewer events in those on isavuconazonium requiring discontinuation of the drug (14% vs. 23%). Decreases in the QT segment occurred in 7.5% of those on isavuconazonium, compared with 4.5% of those on voriconazole, but were not associated with events.

The prospective, open-label, single-arm study evaluated isavuconazonium in 37 patients with proven or probable mucormycosis infections; 59% had a hematologic malignancy, and about 40% were neutropenic at baseline. All-cause mortality at day 42 was 38%, which was similar to the mortality rate for amphotericin in the literature, according to Astellas. Besides voriconazole, drugs approved for aspergillosis include amphotericin, itraconazole, and caspofungin. Astellas will market isavuconazonium as Cresemba if approved.

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ABIM responds to criticism, makes changes to MOC

BY ALICIA GALLEGOS
Frontline Medical News

In a frank announcement, the American Board of Internal Medicine has apologized to doctors for a Maintenance of Certification program that “clearly got it wrong,” and pledged to make the program more consistent with internists’ practice and values.

Among the immediate changes: updates to its internal medicine exam; suspension of the practice assessment, patient voice, and patient safety requirements for at least 2 years; and MOC enrollment fees set at or below the 2014 levels through at least 2017.

Dr. David A. Fleming, president of the American College of Physicians (ACP), called the move monumental and historic.

“This turnaround has occurred in the face of mounting pressure and discontent expressed by a growing number of U.S. internists concerned about the MOC process,” Dr. Fleming said in an interview. “With the newly announced changes, internists are still being held accountable and responsible for maintaining professional competence, but by removing the practice assessment and patient [safety] requirements that are not well supported by evidence, we go a long way in taking the pressure off very busy physicians who already feel burdened by many layers of regulatory and administrative reporting that many view as burdensome and a barrier to our first duty – caring for patients.”

In a statement, ABIM President and CEO Richard J. Baron said it was clear that aspects of the program were not meeting physicians’ needs.

“We got it wrong and sincerely apologize,” Dr. Baron said in the statement. “We are sorry. ABIM is changing the way it does its work so that it is guided by, and integrated fully with, the medical community that created it. The goal is to co-create an MOC program that reflects the medical community’s shared values about the practice of medicine today and provides a professionally created and publicly recognizable framework for keeping up in our discipline.”

As part of the newly announced changes, ABIM will make its internal medicine exam more reflective of physician practice, with changes to be incorporated in fall 2015, according to the announcement. The decision to suspend the practice assessment, patient voice, and patient safety requirements means internists who have not completed activities in these areas will not have their certification status changed. Diplomates who are currently uncertified but who have satisfied all requirements for MOC except for the practice assessment requirement will be issued a new certificate this year. Within the next 6 months, ABIM will also change the language used to publicly report a diplomate’s MOC status on its website from “meeting MOC requirements” to “participating in MOC.”

By the end of 2015, ABIM said it will ensure new and more flexible ways for internists to demonstrate self-assessment of medical knowledge by recognizing most forms of Accreditation Council for Continuing Medical Education–approved continuing medical education. An online FAQ provides more information on the changes.

ABIM initially revamped its certification policies beginning in January 2014, shortening the time physicians had to earn MOC points and publishing online whether doctors were meeting requirements. The actions meant that every 2 years physicians certified by ABIM had to earn at least some points by completing some of the educational activities approved for MOC credit, and at the 5-year mark, earn 100 points. Previously, physicians were given 10 years to earn 100 points. Physicians were also listed publicly as either “certified, meeting maintenance of certification requirements” or “certified, not meeting MOC requirements.”

The changes were met with almost immediate backlash. Doctors expressed frustration that the requirements were burdensome, expensive, Continued on following page
October start favored for ICD-10

BY GREGORY TWACHTMAN
Frontline Medical News

WASHINGTON – The transition to the ICD-10 coding set should take place as planned on Oct. 1, witnesses testified at a hearing of the House Energy and Commerce Committee’s Subcommittee on Health.

The message was welcome to committee leadership, who invited testimony almost solely from experts who support that position.

Subcommittee members from both sides of the aisle expressed a desire to not delay the implementation any further, though some at the Feb. 11 hearing questioned whether the Centers for Medicare & Medicaid Services was ready for the transition.

Subcommittee member Rep. Michael Burgess (R-Tex.), an ob.gyn., said he had no questions about the readiness of Medicare contractors and insurance companies for the transition, but “all roads eventually lead to the Centers for Medicare & Medicaid Services. And if you will pardon me, that does appear to be a weak link in the chain because from HealthCare.gov to the Sunshine Act reporting website, when CMS flips a switch, something breaks.”

NOW APPROVED

For the treatment of idiopathic pulmonary fibrosis (IPF)

Boehringer Ingelheim has long been committed to developing effective medications for people living with lung diseases. This heritage continues with the approval of OFEV (nintedanib) for the treatment of IPF. Start your appropriate patients with IPF on OFEV today—visit www.OFEV.com to download the OFEV Prescription Form.

- Once the prescription form is completed, fax it to one of our 4 partnering specialty pharmacies listed below:
  - Acro Pharmaceutical Services
    - Phone: 800-306-7798
    - Fax: 855-439-4768
  - Advanced Care Scripts
    - Phone: 855-252-5715
    - Fax: 866-679-7131
  - Orsini Healthcare
    - Phone: 800-372-9581 (option 3)
    - Fax: 888-975-1456
  - Walgreens
    - Phone: 800-420-3228
    - Fax: 866-889-1510

- For additional information or assistance, you and your patients can contact OPEN DOORSTM, our patient support program, at 866-OPENDOOR (673-6366)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Elevated Liver Enzymes

The safety and efficacy of OFEV has not been studied in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment. Treatment with OFEV is not recommended in patients with moderate or severe hepatic impairment.

In clinical trials, administration of OFEV was associated with elevations of liver enzymes (ALT, AST, ALKP, GGT) and bilirubin. Liver enzyme increases were reversible with dose modification or interruption and not associated with clinical signs or symptoms of liver injury.

Conduct liver function tests (ALT, AST, and bilirubin) prior to treatment with OFEV, monthly for 3 months, and every 3 months thereafter, and as clinically indicated. Dosage modifications, interruption, or discontinuation may be necessary for liver enzyme elevations.

Gastrointestinal Disorders

Diarrhea

Diarrhea was the most frequent gastrointestinal event reported in 62% versus 18% of patients treated with OFEV and placebo, respectively. Most patients, the event was of mild to moderate intensity and occurred within the first 3 months of treatment. Diarrhea led to permanent dose reduction in 11% of patients treated with OFEV compared to 0 placebo-treated patients. Diarrhea led to discontinuation of OFEV in 5% of the patients compared to <1% of placebo-treated patients. Dosage modifications or treatment interruptions may be necessary in patients with adverse reactions of diarrhea. Treat diarrhea at first signs with adequate hydration and antidiarrheal medication (e.g., loperamide), and consider treatment interruption if diarrhea continues. OFEV treatment may be resumed at the full dosage (150 mg twice daily), or at the reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage. If severe diarrhea persists despite symptomatic treatment, discontinue treatment with OFEV.

Nausea and Vomiting

Nausea was reported in 24% versus 7% and vomiting was reported in 12% versus 3% of patients treated with OFEV and placebo, respectively. In most patients, these events were of mild to moderate intensity. Nausea led to discontinuation of OFEV in 2% of patients. Vomiting led to discontinuation of OFEV in 1% of the patients.

Please see additional Important Safety Information on next page and accompanying brief summary.
While no representative from the CMS testified, a report from the Government Accountability Office suggested that the agency is positioned to make the transition to ICD-10 by the Oct. 1 deadline, although continued testing is warranted. That report was commissioned by the Senate Finance Committee, which also expressed support for an Oct. 1 start date for ICD-10.

Kristi Matus, chief financial and administrative officer for Athena- health, testified to the general readiness of the health IT community to make the switch to ICD-10. The government should “maintain the current date for ICD-10 implementation or cancel it once and for all. Pull the trigger or pull the plug,” Ms. Matus said.

Dr. William J. Terry Sr., a urologist from Mobile, Ala., testified on behalf of the American Urological Association and expressed concern that not all physicians are ready. He suggested that a transition period might allow physicians and other providers to run ICD-9 and ICD-10 simultaneously to ensure that physicians do not inadvertently lose any payments because of coding errors that might occur as they learn the new system.

gtwachtman@frontlinemedcom.com

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (cont’d)

For nausea or vomiting that persists despite appropriate supportive care including anti-emetic therapy, dose reduction or treatment interruption may be required. OFEV treatment may be resumed at the full dosage (150 mg twice daily), or at the reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage. If severe nausea or vomiting does not resolve, discontinue treatment with OFEV.

Embryofetal Toxicity

OFEV is Pregnancy category D. It can cause fetal harm when administered to a pregnant woman. If OFEV is used during pregnancy, or if the patient becomes pregnant while taking OFEV, the patient should be advised of the potential hazard to a fetus. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with OFEV and to use adequate contraception during treatment and at least 3 months after the last dose of OFEV.

Arterial Thromboembolic Events

Arterial thromboembolic events have been reported in patients taking OFEV. In clinical trials, arterial thromboembolic events were reported in 2.5% of patients treated with OFEV and 0.8% of placebo-treated patients. Myocardial infarction was the most common adverse reaction under arterial thromboembolic events, occurring in 1.5% of OFEV-treated patients compared to 0.4% of placebo-treated patients. Use caution when treating patients at higher cardiovascular risk including known coronary artery disease. Consider treatment interruption in patients who develop signs or symptoms of acute myocardial ischemia.

Risk of Bleeding

Based on the mechanism of action (VEGFR inhibition), OFEV may increase the risk of bleeding. In clinical trials, bleeding events were reported in 10% of patients treated with OFEV and in 7% of patients treated with placebo. Use OFEV in patients with known risk of bleeding only if the anticipated benefit outweighs the potential risk.

Gastrointestinal Perforation

Based on the mechanism of action, OFEV may increase the risk of gastrointestinal perforation. In clinical trials, gastrointestinal perforation was reported in 0.3% of patients treated with OFEV, compared to 0 cases in the placebo-treated patients. Use caution when treating patients who have had recent abdominal surgery. Discontinue therapy with OFEV in patients who develop gastrointestinal perforation. Only use OFEV in patients with known risk of gastrointestinal perforation if the anticipated benefit outweighs the potential risk.

ADVERSE REACTIONS

- Adverse reactions reported in ≥5% of patients treated with OFEV and more commonly than in patients treated with placebo include diarrhea (62% vs. 18%), nausea (24% vs. 7%), abdominal pain (15% vs 6%), liver enzyme elevation (14% vs 3%), vomiting (12% vs 3%), decreased appetite (11% vs 5%), weight decreased (10% vs 3%), headache (8% vs 5%), and hypertension (5% vs 4%).
- The most frequent serious adverse reactions reported in patients treated with OFEV, more than placebo, were bronchitis (1.2% vs 0.8%) and myocardial infarction (1.5% vs 0.4%). The most common adverse events leading to death in patients treated with OFEV, more than placebo, were pneumonia (0.7% vs. 0.6%), lung neoplasm malignant (0.3% vs 0%), and myocardial infarction (0.3% vs 0.2%).

In the predefined category of major adverse cardiovascular events (MACE) including MI, fatal events were reported in 0.6% of OFEV-treated patients and 1.8% of placebo-treated patients.

DRUG INTERACTIONS

P-glycoprotein (P-gp) and CYP3A4 Inhibitors and Inducers

Coadministration with oral doses of a P-gp and CYP3A4 inhibitor, ketoconazole, increased exposure to nintedanib by 60%. Concomitant use of P-gp and CYP3A4 inhibitors (e.g., erythromycin) with OFEV may increase exposure to nintedanib. In such cases, patients should be monitored closely for tolerability of OFEV. Management of adverse reactions may require interruption, dose reduction, or discontinuation of therapy with OFEV. Co-administration with oral doses of a P-gp and CYP3A4 inducer, rifampicin, decreased exposure to nintedanib by 50%. Concomitant use of P-gp and CYP3A4 inducers (e.g., carbamazepine, phenytoin, and St. John’s wort) with OFEV should be avoided as these drugs may decrease exposure to nintedanib.

Anticoagulants

Nintedanib is a VEGFR inhibitor, and may increase the risk of bleeding. Monitor patients on full anticoagulation therapy closely for bleeding and adjust anticoagulation treatment as necessary.

USE IN SPECIFIC POPULATIONS

Nursing Mothers

- Excretion of nintedanib and/or its metabolites into human milk is probable. Because of the potential for serious adverse reactions in nursing infants from OFEV, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Hepatic Impairment

- Monitor for adverse reactions and consider dose modification or discontinuation of OFEV as needed for patients with mild hepatic impairment (Child Pugh A). Treatment of patients with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment with OFEV is not recommended.

Smokers

- Smoking was associated with decreased exposure to OFEV, which may alter the efficacy profile of OFEV. Encourage patients to stop smoking prior to treatment with OFEV and to avoid smoking when using OFEV.

Please see accompanying brief summary on next page.
OFEV® (nintedanib) capsules, for oral use
BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see package insert for full Prescribing Information, including Patient Information
INDICATIONS AND USAGE: OFEV is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

DOSAGE AND ADMINISTRATION:
Testing Prior to OFEV Administration: Conduct liver function tests prior to initiating treatment with OFEV (see Warnings and Precautions, Contraindications, and Precautions and Adverse Reactions). Dose modifications or interruptions may be necessary for liver enzyme elevations. For separate alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥3 times the upper limit of normal (ULN) with signs of severe liver damage, impairment of treatment or reduce OFEV to 100 mg twice daily. Once liver enzymes have returned to baseline values, treatment with OFEV may be reintroduced at a reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage. If a patient does not tolerate 100 mg twice daily, discontinue treatment with OFEV (see Warnings and Precautions and Adverse Reactions). Dose modifications or interruptions may be necessary for liver enzyme elevations. For separate alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥3 times the upper limit of normal (ULN) with signs of severe liver damage, impairment of treatment or reduce OFEV to 100 mg twice daily. Once liver enzymes have returned to baseline values, treatment with OFEV may be reintroduced at a reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage (150 mg twice daily) (see Warnings and Precautions and Adverse Reactions). Discontinue OFEV for AST or ALT elevations ≥5 times ULN or ≥3 times ULN with signs or symptoms of severe liver damage.

CONTRAINDICATIONS: None
WARNINGS AND PRECAUTIONS: Elevated Liver Enzymes: The safety and efficacy of OFEV have not been studied in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment (see Use in Specific Populations). In clinical trials, administration of OFEV was associated with elevations of liver enzymes (ALT, AST, ALKP, GGT). Liver enzyme increases were reversible with dose modification or interruption and not associated with clinical signs or symptoms of liver injury. The majority (84%) of patients with ALT and/or AST elevations had elevations <5 times ULN. Administration of OFEV was also associated with elevations of bilirubin. The majority (95%) of patients with ALT and/or AST elevations had elevations <2 times ULN (see Use in Specific Populations). Conduct liver function tests (ALT, AST, and bilirubin) prior to treatment with OFEV, monthly for 3 months, and every 3 months thereafter, and as clinically indicated. Dose modifications or interruption may be necessary for liver enzyme elevations. Gastrointestinal Disorders: Diarrhea: Diarrhea was the most frequent gastrointestinal adverse reaction (≥5% and more frequent in OFEV-treated patients versus placebo). Diarrhea was reported in 62% versus 18% of OFEV-treated patients and placebo, respectively. Diarrhea led to discontinuation of OFEV in 1% of patients. Use caution when treating patients at higher cardiovascular risk including known coronary artery disease. Consider treatment interruption in patients who develop signs or symptoms of acute myocardial ischemia. Risk of Bleeding: Based on the mechanism of action (VEGFR inhibition), OFEV may increase the risk of bleeding. In clinical trials, bleeding events were reported in 10% of patients treated with OFEV and in 7% of patients treated with placebo. Use OFEV in patients with known risk of gastrointestinal perforation. Only use OFEV in patients with known risk of gastrointestinal perforation if the anticipated benefit outweighs the potential risk.

ADVERSE REACTIONS: The following adverse reactions are discussed in greater detail in other sections of the labeling: Liver Enzyme and Bilirubin Elevations (see Warnings and Precautions). Gastrointestinal Perforation: Based on the mechanism of action, OFEV may increase the risk of gastrointestinal perforation. In clinical trials, gastrointestinal perforation was reported in 0.3% of patients treated with OFEV, compared to 0 cases in the placebo-treated patients. Use caution when treating patients who have had recent abdominal surgery. Discontinue therapy with OFEV in patients who develop gastrointestinal perforation.

Table 1 Adverse Reactions Occurring in ≥5% of OFEV-Treated Patients and More Commonly Than Placebo in Studies 1, 2, and 3

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Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal and abdominal tenderness.

Includes gamma-glutamyltransferase increased, hepatic enzyme increased, alanine aminotransferase increased, aspartate aminotransferase increased, hepatitis function abnormal, liver function test abnormal, transaminase increased, bilirubin increased, lipase increased, alanine aminotransferase abnormal, aspartate aminotransferase abnormal, gamma glutamyltransferase abnormal.

Includes hypertension, blood pressure increased, hypertensive crisis, and hypertensive cardiomyopathy.

Includes gamma-glutamyltransferase increased, hepatic enzyme increased, alanine aminotransferase increased, aspartate aminotransferase increased, hepatitis function abnormal, liver function test abnormal, transaminase increased, bilirubin increased, lipase increased, alanine aminotransferase abnormal, aspartate aminotransferase abnormal, gamma glutamyltransferase abnormal.

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Includes hypertension, blood pressure increased, hypertensive crisis, and hypertensive cardiomyopathy.
the President’s health care debacle has only made things worse,” Sen. Burr said in a statement. “The Patient CARE Act repeals Obamacare and addresses the fundamental cost drivers that Obamacare failed to address. We can lower costs and expand access to quality coverage and care by empowering individuals and their families to make their own health care decisions.”

The Patient CARE Act outlines some federal medical liability reforms, including a cap on non-economic damages and limits on attorneys’ fees. It also seeks to encourage new models for resolving disputes on the state level, such as expert panels to evaluate injury claims and administrative health courts.

The proposal offers a more limited range of consumer insurance protections than does the ACA, including:

- Adopting an age rating ratio of 5:1 for premiums, which would limit plans from charging older individuals any more than five times what

Dr. Michael E. Nelson, FCCP, comments: With a new Congress controlled by Republicans, and given the prior attempts to overturn the Patient Protection and Affordable Care Act (a.k.a. “Obamacare”), it is not surprising that early in this legislative session an alternative plan has been proposed. One could argue some of the points of the proposal but not the accuracy of the statement made by one of the bill’s authors that “our nation’s health care system was broken before Obamacare.” While this bill does address some issues of importance to physicians, it is certainly disappointing that this bill does not address the Sustainable Growth Rate formula (SGR). This looming threat of a 20% or more cut in physician reimbursement will do more harm to patient access and care than any other aspect addressed in this bill. Unfortunately, physicians rarely advocate at the federal level for themselves or their patients. Perhaps, with the introduction of this bill, it is the time to start.

Dr. Michael E. Nelson, FCCP

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**USE IN SPECIFIC POPULATIONS**:

**Pregnancy**: Pregnancy Category D. [See Warnings and Precautions]. The use of OFEV is not recommended during pregnancy. Advise pregnant women to avoid becoming pregnant while receiving treatment with OFEV. Smoking when using OFEV may increase risks to the fetus and to avoid becoming pregnant while receiving treatment with OFEV. Advise females of childbearing potential to use effective contraception during treatment, and for at least 3 months after taking the last dose of OFEV. Advise females to notify their doctor if they become pregnant during therapy with OFEV. [See Warnings and Precautions].

**Breastfeeding**: Advise females of childbearing potential of the potential hazard to a fetus and to avoid becoming pregnant while receiving treatment with OFEV. Advise females of childbearing potential to use effective contraception during treatment, and for at least 3 months after taking the last dose of OFEV. Advise females to notify their doctor if they become pregnant during therapy with OFEV. [See Warnings and Precautions].

**Use in Specific Populations**: Pregnancy: Counsel patients on pregnancy planning and prevention. Advise females of childbearing potential of the potential hazard to a fetus and to avoid becoming pregnant while receiving treatment with OFEV. Advise females to notify their doctor if they become pregnant during therapy with OFEV. [See Warnings and Precautions].

**Disorders of Bleeding**: Bleeding events have been reported. Advise patients to avoid smoking when using OFEV. Administration: Instruct patients to swallow OFEV capsules whole with liquid and to avoid smoking while using OFEV. [See Warnings and Precautions].

**OVERDOSAGE**: In the trial, one patient was inadvertently exposed to a dose of 600 mg daily for a total of 21 days. A non-serious adverse event (nosopharyngitis) occurred and resolved during the period of incorrect dosing, with no onset of other reported events. Overdose was also reported in two patients in oncology studies who were exposed to a maximum of 600 mg twice daily for up to 8 days. Adverse events reported were consistent with the existing safety profile of OFEV. Both patients recovered. In case of overdose, interrupt treatment and initiate general supportive measures as appropriate.

**PATIENT COUNSELING INFORMATION**: Advise the patient to read the FDA-approved patient labeling Patient Information. Liver Enzyme and Bilirubin Elevations: Advise patients to report signs and symptoms of myocardi...
One of the most satisfying roles of a leader is to see the hard work of dedicated individuals pay off with a successful event or product. I find this particularly gratifying when the work is the result of collaboration among key groups who bring different perspectives and, by virtue of combining forces, make a greater impact on important issues.

Recently, I had the honor of being one of several representatives of our organization to the annual business meeting of the Forum of International Respiratory Societies (FIRS), in Cape Town, South Africa. CHEST is one of seven founding professional societies that represent all regions of the world—from the Pan African Thoracic Society (PATS) to the Asia Pacific Society of Respirology (APSR) and the European Respiratory Society (ERS)—all “united for lung health.” Established in 2001, the Forum is dedicated to controlling respiratory disease worldwide and promotes advocacy in matters of respiratory health. CHEST leaders have played prominent roles in FIRS activities that help influence international health policy and contribute to better care of patients worldwide. For example, CHEST Past President Darcy Marciniuk chaired and was lead author of the recent sentinel FIRS document, Respiratory Diseases in the World: Realities of Today—Opportunities for Tomorrow, which draws attention to the magnitude and opportunities for improving management of the five main global respiratory diseases: COPD, asthma, TB, respiratory infections, and lung cancer.

Among its list of activities to promote lung health, FIRS develops position statements that influence key organizations like the World Health Organization and United Nations in important areas, with recent examples of statements on e-cigarettes and on Ebola virus disease. Additionally, FIRS and member organizations actively support greater awareness of important respiratory conditions, and lung cancer screening for practitioners of all specialties. The “Choosing Wisely” campaign is dedicated to addressing common but overutilized tests and treatments, aiming to eliminate low-value but expensive care. With four professional societies, CCSC represents the largest collaborative group to contribute to the Choosing Wisely series and the first to include a professional nursing society (AACN) in its recommendations for clinicians through evidence-based clinical practice guidelines. A recent notable example is the comprehensive set of recommendations for the Prevention of Acute Exacerbation of Chronic Obstructive Pulmonary Disease developed in collaboration with the Canadian Thoracic Society (CTS) and published in CHEST (Feb. 2014). Similarly, CHEST recently collaborated with the ATS to publish a combined CHEST and ATS policy statement on high-quality lung cancer screening, also published in CHEST (Dec. 2013;147[2]:295). In addition to providing practical information necessary for high-quality lung cancer screening for practitioners and institutions, this important evidence-based document was highly influential in guiding CMS to make recent changes in coverage.

Finally, collaboration can assume the form of guidance and assistance in development of new programs. In 2013, leaders and experts in graduate medical education from CHEST, in collaboration with leaders from the Chinese Thoracic Society (CTS), developed and initiated a plan to create the first formal Pulmonary and Critical Care Medicine (PCCM) fellowship training programs in China. Leaders from major teaching hospitals in China were recruited, curricula developed, and the first class of PCCM fellows enrolled. The challenges and the magnitude of the task require dedication and true collaboration that include genuine appreciation for differences in culture, in expectations, and ongoing mutual respect. It is exciting to anticipate the results of this collaboration with the graduation of the first class of PCCM fellows coinciding with CHEST World Congress 2016 in Shanghai.

The Forum of International Respiratory Societies develops position statements that influence key organizations...
Make Plans Now to Attend CHEST 2015

October 24-28
Montréal, Canada

Montreal is a lively city with multicultural influences that make the city tick. What better place for CHEST 2015, where we’ll connect a global community in clinical chest medicine? As always, our program will deliver current pulmonary, critical care, and sleep medicine topics, presented by world-renowned faculty using innovative instruction formats—like hands-on simulation and interactive case discussions—to offer popular options for learning. Take advantage of these opportunities now:

Call for Abstracts
Submission Deadline: April 1
Submit an abstract of your original investigative work for presentation at the meeting. Accepted abstracts will be published in an online supplement to CHEST. Three types of abstracts will be considered:
• Slide presentations
• Poster presentations
• Poster discussions
Learn more and submit at chestmeeting.chestnet.org.

Call for Case Reports
Submission Deadline: April 1
Submit case reports for presentation during special sessions. Accepted case reports (excluding clinical case puzzles) will be published in an online supplement to CHEST. Four types of case reports will be considered:
• Affiliate case reports
• Medical student/resident case reports
• Global case reports
• Clinical case puzzles
Learn more and submit at chestmeeting.chestnet.org.

The CHEST Foundation 2015 Grants Program
Application Deadline: April 30
The CHEST Foundation tradition of recognizing and rewarding health-care professionals for scholarly projects and research continues. Grants for both leaders in chest medicine and young investigators are available, including:
• CHEST Foundation and the Alpha-1 Foundation Research Grant in Alpha-1 Antitrypsin Deficiency - $25,000 1-year grant
• CHEST Foundation Research Grant in Women’s Lung Health - $10,000 1-year grant
• CHEST Foundation Research Grant in Pulmonary Fibrosis - $30,000 1-year grant
• CHEST Foundation Research Grant in Chronic Obstructive Pulmonary Disease - $50,000 1-year grant
• CHEST Diversity Committee Minority Investigator Research Grant - $25,000 1-year grant
• Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP - up to $15,000 1-year grant
• CHEST Foundation Research Grant in Pulmonary Arterial Hypertension - $50,000 1-year grant
• Eli Lilly and Company Distinguished Scholar in Critical Care Medicine - $150,000 for 3 years
See which grants you are eligible for, and apply today at chestnet.org/grants.

Play CHEST Challenge
Game Ends: May 30
CHEST affiliate members, play CHEST Challenge to test your knowledge of pulmonary, critical care, and sleep medicine while competing for prizes. The three top-scoring programs will compete in the CHEST Challenge Championship at CHEST Annual Meeting 2015. All championship players will receive:
• Airfare and registration to CHEST Annual Meeting 2015 in Montréal, Canada
• Complimentary hotel
• Cash prizes
Game on! Learn more at chestchallenge.org.

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Meet ABIM’s Pulmonary Disease Board

BY DR. SERPIL C. ERZURUM
Chair, ABIM Pulmonary Disease Board

As you have likely heard, the American Board of Internal Medicine (ABIM) has recently introduced a number of changes to its Maintenance of Certification (MOC) program, but what you may not know is that its governance structure has also undergone some important changes, including the formation of new specialty boards.

In the past, the specialty boards or test writing committees were charged with developing new exam questions, and due to the amount of time and effort involved in this process, they had little time to weigh in on specialty-specific issues related to certification and MOC.

One of the major criticisms of the MOC program is that certain requirements do not have options relevant to specific specialties or that on-the-ground physicians were not engaged in the process. In direct response to that criticism, ABIM established these specialty boards so they could:

- Define, refine, and set standards for certification and MOC in the discipline;
- Perform oversight/review of performance assessments in the discipline; and to
- Build partnerships with societies and other organizational stakeholders.

The secure examination will continue to be developed by a separate, dedicated group of physicians but will now be referred to as exam committees, ie, Pulmonary Disease Board Exam Committee.

As the Chair of the ABIM’s Pulmonary Disease Board, I am excited to take this opportunity to introduce the role of this newly formed specialty board, as well as introduce its members.

The ABIM Pulmonary Disease Board, along with nine other specialty boards, held their inaugural meetings this fall. Each of the specialty boards consist of practicing ABIM Board-Certified physicians, an intraprofessional team member, and a patient representative.

Members of the ABIM Pulmonary Disease Board include:

Dr. Serpil C. Erzurum, Chair, Cleveland, OH
Dr. Kevin M. Chan, FCCP, Ann Arbor, MI
Dr. John Allen Cooper, Birmingham, AL
Dr. Dean R. Hess, PhD, RRT, FCCP, Boston, MA
Dr. Lynn T. Tanoue, FCCP, New Haven, CT
Dr. Michael E. Nelson, FCCP, Shawnee Mission, KS
Dr. Stanton T. Siu, Oakland, CA

Tommye Lambert, MBA, MDIV, Hoover, AL

Ms. Lambert, our patient representative, is a leader in the caregiver community who focuses on patient-doctor communication and collaboration and was primary caregiver for 28 years to her daughter who suffered with cystic fibrosis. Ms. Lambert earned her MDIV at Beeson Divinity School, Samford University, and her Executive MBA from the University of Alabama.

Dr. Michael E. Nelson, FCCP, Shawnee Mission, KS
Dr. Siu, who is board-certified in Internal Medicine, Pulmonary Disease, and Critical Care Medicine, is a practicing physician in Shawnee Mission, Kansas, and Medical Director of the Sleep Laboratory of the Shawnee Mission Medical Center.

Dr. Lynn T. Tanoue, FCCP, New Haven, CT
Dr. Tanoue, who is board-certified in Internal Medicine, Pulmonary Disease, and Critical Care Medicine, is Professor of Medicine and Clinical Chief of the Section of Pulmonary, Critical Care, and Sleep Medicine, and Vice-Chair for Clinical Affairs in the Department of Internal Medicine at Yale School of Medicine. As a long-time member and current Chair of ABIM’s Pulmonary Disease Board Exam Committee, Dr. Tanoue works closely with me in planning and carrying out the work of the Pulmonary Disease Board.

I am honored to lead such a diverse group of professionals from across the spectrum of pulmonary disease and look forward to sharing updates with you as we embark on our work of ensuring the relevancy of MOC to pulmonary disease physicians across the country.

Further information about ABIM’s new governance structure may be found via the ABIM website: www.abim.org/about/governance.

This Month in CHEST: Editor’s Picks

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

Platelet Count Mediates the Contribution of a Genetic Variant in LRRC16A to ARDS Risk. By Dr. Y. Wei et al.

Impact of COPD on the Mortality and Treatment of Patients Hospitalized With Acute Decompensated Heart Failure: The Worcester Heart Failure Study. By Dr. K. A. Fisher et al.

The Prognostic Value of Undetectable Highly Sensitive Cardiac Troponin I in Patients With Acute Pulmonary Embolism. By Dr. E. U. Hakemi et al.

Treatment of Alveolar-Pleural Fistula With Endobronchial Application of Synthetic Hydrogel. By Dr. H. J. Mehta et al.

COMMENTARY
Evolution in Reimbursement for Sleep Studies and Sleep Centers. By Dr. J. M. Parish et al.

EVIDENCE-BASED MEDICINE
NAMDRC Roundtable on ‘Respiratory Compromise’

BY DR. DENNIS E. DOHERTY, FCCP
NAMDRC President

PHIL PORTE
NAMDRC Executive Director

NAMDRC brought together representatives of key medical societies, including CHEST, ATS, AARC, SCCM, AACN, SHM (hospitalists), PPAHS (patient safety), and ACEP (emergency physicians) to address respiratory compromise, that cascade of events that moves from respiratory insufficiency to respiratory failure to respiratory arrest. Recognizing that respiratory compromise occurs in various settings, the conference, Feb 26-27 in Orlando, Florida, focused on the hospital setting.

In addition to society representatives, the NAMDRC leadership, in consultation with recognized experts, also invited key opinion leaders to participate, including physicians, respiratory therapists, and nurses.

There were several challenges facing the participants, perhaps paramount was to define the concept of “respiratory compromise.” Some have signaled, “I know it when I see it,” but the expectation was to formulate a specific clinical definition of the respiratory deterioration, and devise a recognition pathway that can easily be used in the hospital setting to identify patients earlier in the course of this cascade.

How to identify high risk patients is critical to the discussion, because it is generally believed that this is where resources need to be focused, both from a personnel and monitoring perspective. Can consensus be drawn to determine which patient characteristics can reliably classify that patient into a high risk for respiratory compromise, and, if so, those characteristics should be delineated. The corollary challenge is to identify the low risk patients so that inappropriate resources are not focused where efforts might not be necessary.

Individual hospital policies are integral to this issue, as the relative value of rapid response teams appears to vary greatly. Add to the equation a recent Wall Street Journal article (http://online.wsj.com/search/term.html?KEYWORDS=Heart%20attack) that highlighted the success of managing heart attacks outside the hospital but the notable challenges of managing those events when they occur within the inpatient population.

Another key challenge facing roundtable participants was to focus their discussions on what clinical parameters should be monitored and which, if any, should be put on the back burner. There was a relatively wide variation of views regarding what should be monitored, what thresholds are problematic and indicative of a declining patient, and what actions need to be taken, and how swiftly, to abate the downward cascade of respiratory compromise. A related challenge facing participants was, “should the industry be moving toward refinement of their monitoring technologies to give physicians and the health-care team more valuable and more timely information? Are we monitoring the right parameters, or are we monitoring what the technology allows us to monitor? Are there gaps that can be addressed?”

It is likely that not only will the proceedings be documented for submission for publication, but this may very well lead to other conferences that focus on respiratory compromise in other settings. Both the skilled nursing facility and long-term care for a spectrum of pulmonary/ventilator patients, and the characteristics of their potential cascade of deterioration may or may not be the same as in an acute care hospital.

The challenges are similar, but solutions may be different – a subject for further discussion.

This conference was just one example of NAMDRC’s approach to a range of pulmonary-related clinical issues. While NAMDRC’s broad mission is to “improve access to quality care for patients with respiratory disease by removing regulatory and legislative barriers to appropriate treatment,” the roundtable does fit Respiratory Compromise continued on page 30
PULMONARY/CRITICAL CARE PHYSICIAN

Gundersen Health System is seeking a BC/BE Pulmonary/Critical Care physician. Join a well-established group of board certified pulmonary and critical care physicians. Opportunity for critical care only is also available. Practice highlights:

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Kalah Haug (608)775-1005, khaug@gundersenhealth.org
Gundersenhealth.org/MedCareers
EEO/AA/Veterans/Disabilities
About the Opportunity:
Memorial Healthcare System is seeking two critical care physicians, dedicated to night shifts, to join the critical care team. Successful candidates will have excellent clinical skills, a broad knowledge base in critical care and be dedicated to providing high quality, evidence-based care. Applicants must be BC/BE in critical care medicine. Previous experience in managing cardiac surgery patients is a plus, but not a requirement. Physician(s) would have exposure to all aspects of the care of cardiac surgery patients, including mechanical devices, advanced heart failure patients, ECMO and transplant.

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Inpatient Pulmonary/Critical Care Position in Maine:
Join a vibrant Inpatient Pulmonary and Critical Care group of five in beautiful Maine. Central Maine Medical Center (CMMC) is seeking a BC/BE Pulmonary/Critical Care Physician to help provide pulmonary and critical care services to medical, surgical, trauma, and cardiac patients.

CMMC is a 250 bed, full service regional referral center with busy trauma, cardiothoracic, interventional radiology, vascular, and neurosurgical programs. We have a state-of-the-art 15 bed ICU and a separate 16 bed cardiothoracic unit.

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Interested applicants: submit CV to Julia Lauer, Medical Staff Recruiter, Central Maine Medical Center, 300 Main Street, Lewiston, ME 04240. Email: jlauer@cmmc.org. Fax: 207-795-5696. Call: 800-445-7431. Visit our website, www.cmmc.org.

For Deadlines and More Information, Contact:
John Baltazar
Tel: (917) 488-1528
jbaltazar@americanmedicalcomm.com

Chesterfield, Virginia

Colorado Health Medical Group is seeking a Pulmonologist/Critical Care trained physician. Sleep Medicine training desirable but not required. Will rotate in two hospitals and our Loveland based clinic. Call is 1:11 nights and 1:5-6 weekends. Physician will be doing general Pulm/CC procedures and read sleep studies from outlying facilities.

If interested, email your CV to
Brian.Leone@uchealth.org
CHEST PREP – Disease-State Education for Industry

BY LISA STANICK, MBA
Director, PREP Operations

Did you know the American College of Chest Physicians (CHEST) has provided disease-state-specific education for pharmaceutical and medical device representatives for over 12 years? The CHEST Professional Representative Education Program, or PREP, is an unbranded disease-state clinical immersion program. The PREP Team works with pharmaceutical and medical device companies to understand their learning objectives and the educational needs of their representatives. A customized program to address those specific needs is then developed.

Each program uses different learning methods – problem-based case studies, patient testimony, simulation, and faculty-led workshops – to create a dynamic learning environment that increases interaction and develops deeper comprehension. The PREP curriculum is based on evidence-based clinical practice guidelines and consensus statements. Each program is created by clinical thought leaders and delivered by expert faculty, typically drawn from our CHEST membership. PREP courses are held at leading hospitals and academic medical centers throughout the country, as well as at the CHEST Innovation, Simulation, and Training Center in Glenview, Illinois.

Participants who complete the course objectives, including the post-course knowledge assessment, are awarded a Certificate of Completion valid for a 3-year period. More importantly, they gain the most current, in-depth clinical information needed to engage with health-care professionals knowledgeably, confidently, and meaningfully. This translates to better-educated representatives who interact with you as you make clinical decisions that enhance patient outcomes.

CHEST has trained over 4,000 sales representatives over the past 2 years. Not only has CHEST conducted PREP programs for disease states such as atrial fibrillation, venous thromboembolism, and COPD, PREP programs are also available for women’s health, oncology, and interventional radiology through strategic agreements with the American Congress of Obstetricians and Gynecologists (ACOG), the American Society of Clinical Oncology (ASCO), and the Society of Interventional Radiology (SIR). The PREP Team recently conducted a Prostate Cancer PREP course at Huntsman Cancer Institute in Salt Lake City, Utah. This course is the first of four to be conducted over the next months at academic medical centers around the country. Over 100 sales representatives will participate in this PREP, which was developed and is being conducted through CHEST’s agreement with ASCO. The PREP Team continues to expand its offerings. If you would like to develop curriculum content or participate as faculty for a PREP course or to receive more information about how your hospital or medical center can become a course site, please contact me at listanick@chestnet.org or 224/521-9518.

NAMDRC
Respiratory Compromise from page 27

into the mission because of growing concerns that we are facing challenges that are solvable if we take the initiative to address solutions to these challenges. Another broad challenge facing NAMDRC is its belief that the growing area of home mechanical ventilation is being shaped by archaic and outdated legislation and regulation. In a discussion with Marilyn Tavenner, CMS Administrator (and critical care nurse by training) last August, she conceded that the laws and regulations have not kept pace with innovations as basic as noninvasive mechanical ventilation. The idea that mechanical ventilation involves intubation or tracheostomy is universally recognized as archaic. As archaic is the concept that, by definition, ending mechanical ventilation leads to imminent death. Amending the existing laws and regulations in this area may become a high priority for NAMDRC over the next few years.

For membership information, visit the NAMDRC website at www.namdrc.org or call 703/752-4359.

CLASSIFIEDS
Also available at MedJobNetwork.com

PROFESSIONAL OPPORTUNITIES

Overton Brooks VA Medical Center in Shreveport, LA is seeking full-time BE/BC staff physicians in the following areas:

Pulmonary/Sleep Medicine or Sleep Medicine Position
Applicant must be BC/BE in Pulmonary and Sleep Medicine OR Sleep Medicine alone. Position involves teaching students, residents and Pulmonary & Sleep fellows. Duties include hospital consultations, clinic responsibilities, and proficiency in pulmonary and sleep diagnostic procedures. Experience in EBUS and Ultrasonography would be desirable if trained in Pulmonary.

Key requirements: BC in Internal Medicine and BE/BC in Pulmonary and Sleep Medicine, US citizenship, proficiency in English, full & current unrestricted licensure. Applicant must also qualify for an appointment with LSU Health Center, Shreveport.

Pulmonary/Critical Care or Critical Care Position
Applicant must be BC/BE physician in either Pulmonary/Critical Care or Critical Care alone teaching students, residents and Pulmonary & Critical Care fellows while at the VA. Duties include hospital consultations, clinic responsibilities, and proficiency in pulmonary and critical care procedures as appropriate. Experience in EBUS and Ultrasonography would be desirable if trained in Pulmonary. Experience in ultrasonography would be desirable. Experience in extracorporeal modalities a plus.

Key requirements: BC in Internal Medicine and BE/BC in Pulmonary/Critical Care or Critical Care Medicine, US citizenship, proficiency in English, full & current unrestricted licensure. Applicant must qualify for an academic appointment with LSU Health Center, Shreveport.

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Networks: Outbreak research, social media, lung transplant, OSA

Disaster Response
Chasing the tail of Ebola’s epi curve: Outbreak research


The initial aim was for this supplement to be evidence-based; however, due to the paucity of high quality evidence in the field of outbreak response and disaster management, ultimately, consensus-based guidelines were developed.

Today, as the world has faced its largest outbreak of Ebola costing upwards of tens of thousands of lives, once again, we find ourselves in a situation where just when research efforts are ramping up, the tail of the epidemiologic curve for the outbreak is rapidly falling off. While this is excellent news for those living in the affected countries, it unfortunately means that similar to efforts during SARS and H1N1, the potential to advance our clinical management and treatment options through research is likely to fall short of both the potential and need to do so.

Conducting research during disasters and outbreaks is fraught with challenges ranging from the sudden and, arguably, unpredictable nature of these events, through to the time required for ethics approval (Cook et al. Crit Care Med. 2010;38:e138) and execution of the studies. Despite these challenges, we must not accept failure and work to ensure the research is an essential component of the public health emergency response (Lurie et al. N Engl J Med. 2013;368[13]:1251).

A promising effort is now underway through a collaboration between the International Federation of Acute Care Trialsists [InFACT] (Lancet. 2010;375[9708]:11) and the International Severe Acute Respiratory and Emerging Infection Consortium [ISARIC] (https://www.isaric. tghn.org/) to put in place a “sleeper study” to be tested annually on severe acute respiratory infections but will otherwise lie in wait ready to spring into action at the onset of the next emerging infection. This holds promise for potentially enabling a true rapid research response.

Dr. Mike Christian, MSc (Public Health), FCCP
NetWork Vice-Chair
Chief Safety Officer
Niagara Health System

Critical Care & Infectious Diseases
Attending Physician
Corporate Services

Practice Operations
Why Your Practice Should Be Involved in Social Media

Social media has been taking on an increasingly important role in medicine. Patients use social media to learn and share information, while medical establishments use it to help build their brands. Yet, as individual practitioners, we have been slow to adapt to the expanding role of social media in our profession.

There are three key reasons why we need to be more involved in using social media tools.

First, more patients are getting health-care information through it. Connections that are made through social media tend to be more valued than other sources. Practitioners know all too well that medical advice obtained through social media may be as highly regarded as their own advice to their patients. This provides an important opportunity. Using social media, we can provide useful information and contradict false information. For example, using your practice’s Facebook page, you could provide information about sleep apnea or dispel vaccine myths.

Second, patients use social media to choose health-care providers. One in six patients now post online reviews about their health-care encounters. Inviting patients to give you positive reviews now can help counteract negative reviews later. In addition, registering at rating sites can elevate your Google profile and allows you to educate prospective patients about the services you offer.

Third, social media is where our patients are. It’s time we were there, too.

Dr. Pradeep Ramachandran
Steering Committee Member
Social Media Co-Editor, CHEST

Transplant
What is the skinny on weight in adult lung transplant?

More than two-thirds of American adults are overweight (body mass index [BMI] 25 kg/m² or greater) (Ogden et al. JAMA. 2014;311[8]:806).

Trends in patients presenting for initial lung transplant evaluations are only slightly better, with 55% of candidates categorized as overweight (Chandrasekaran et al. J Heart Lung Transplant. Nov 17, 2014; epub ahead of print).

This raises the question—does increased weight confer increased risk in lung transplantation?

Kanasy and colleagues first described a possible mortality risk posed by excess weight in lung transplant candidates in 2002 (Chest. 2002;121[2]:401).

Subsequently, obesity was also associated with an increased risk of primary graft dysfunction (Lederer et al. Am J Respir Crit Care Med. 2011;184[9]:1055).

Recently, Singer and colleagues demonstrated that class II or III obesity (BMI greater than 35 kg/m²) was associated with an increased risk of death in lung transplant, but class I obesity (BMI between 30 and 34.9 kg/m²) was not (Am J Respir Crit Care Med. 2014;190[9]:1012).

Last month, the International Society for Heart and Lung Transplant published updated lung transplant candidate selection guidelines that now list obesity class II or III as absolute contraindications to lung transplantation (Weill et al. J Heart Lung Transplant. 2015;34[1]:1). Obesity class I remains a relative contraindication.

Interestingly, Chandrasekaran and colleagues showed that weight loss in the overweight and class I obesity group was associated with improved mortality, suggesting ongoing weight loss should be encouraged.

The clinical bottom line: all overweight lung transplant candidates should be encouraged to lose weight. Those with a BMI greater than 35 should be deferred from transplant listing until weight loss is achieved.

Dr. Cassie Kennedy, FCCP
Steering Committee Member

Women’s Health
How prevalent is sleep apnea in women? It’s how you slice and dice it.

More than 90% of women with OSA are reportedly undiagnosed (Young et al. Sleep. 1997;20[9]:705).

There, of course, many factors that contribute to this. One less apparent reason is how we define and measure sleep apnea. More and more, there is an attempt to phenotype sleep apnea; an aim to be able to use the multitude of data gathered from overnight polysomnography to better prognosticate cardiovascular, mental, and other health outcomes.

For example, there is evidence to suggest respiratory event-related arousals (RERAs) worsen fatigue and depression and result in greater use of hypnotics, antidepressants, and stimulants (Guilleminault et al. J Psychiatr Res. 2006;40[3]:273).

A greater proportion of women than men are likely to have RERAs than frank apneas. As a result, the inclusion of RERAs into the hypopnea definition in the 2012 American Academy of Sleep Medicine scoring guidelines may lead to a greater proportion of women being diagnosed with OSA, as well as with more severe OSA.

A study from the Wisconsin Sleep Cohort demonstrated that AHII in REM sleep (but not in NREM sleep) confers a dose-dependent risk of hypertension (Mohlesi et al. Am J Respir Crit Care Med. 2014;190[1]:1158).

The clinical implication is that women, particularly younger premenopausal women who are more prone to REM-related OSA (O’Connor et al. Am J Respir Crit Care Med. 2000;161[5]:1465), may not be adequately treated since current standards quality treatment based on total AHII, which is often driven by NREM AHII.

Meanwhile, we are moving more toward home sleep testing where arousals and sleep stages are often not measured. When the way we measure disease is moving dichotomously from our attempts to more precisely define and characterize OSA, we are challenged to consider how this impacts the diagnosis of sleep apnea in women.

Dr. Christine Won
Steering Committee Member
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