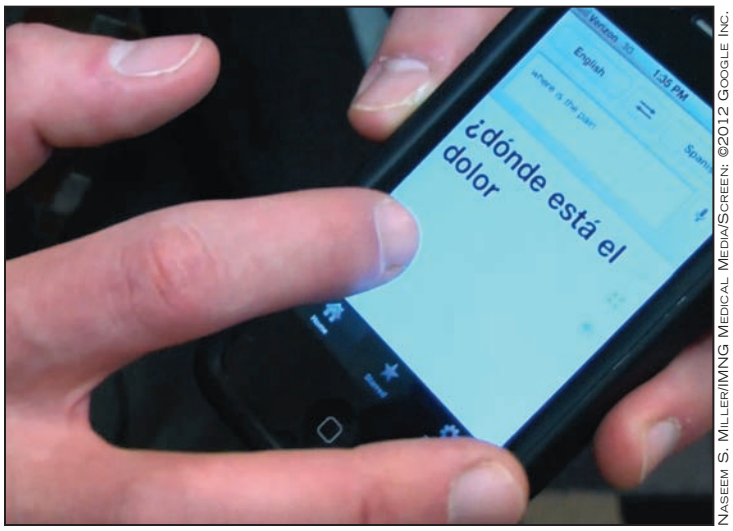
VOL. 7 • NO. 11 • NOVEMBER 2012

CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS



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Medical use of apps such as Google Translate is proliferating but so are worries over accuracy and privacy, as well as hygiene.

App Choices Grow, Along With Concerns

BY SHERRY BOSCHERT
IMNG Medical News

DENVER – Do you need a stethoscope, a blood pressure monitor, or a tool to study chest sounds? There are apps for that. In fact, by recent count there are more than 200,000 applications of technology – or "apps" – available for smartphones or tablet devices, and they're being used more and more for medical purposes.

Need a convenient way to look up drug interactions, pediatric dosing, or clinical decision rules from guidelines? Or how about a translator, a light to examine a finicky infant's throat, or a "white board" to draw a picture for your patient? Yup – they're all in apps, and chances are you already may be using some of these.

Dr. Joshua S. Broder expects an exponential increase in the use of apps in medicine as smartphones and tablets continue to proliferate, but their accuracy needs to be verified and potential problems need to be addressed, he said at the annual meeting of the American College of Emergency Physicians.

Apps will be used increasingly for bedside diagnosis and measurement of hemoglobin or other physiologic parameters. "Some of these tests may be taken over by smartphones in the near future," according to Dr. Broder of Duke University, Durham, N.C.

On the other hand, he cautioned, how do you sterilize a smartphone as you move from one hospital room or patient to another, so that you avoid transmitting infection? There are few independent studies so far testing the accuracy and reliability of medical apps, most of which were designed for lay consumers, not physicians.

The Food and Drug Administration is "very interested" in regulating any apps that might substitute for proven technologies such as stethoscopes or that physicians use as accessories to medical devices that already are regulated, he said. The FDA described its approach to deciding

See **Concerns** • *page 34*

Riociguat Promising for PAH Across End Points

Pluses seen for walk distance and more.

BY SHARON WORCESTER
IMNG Medical News

ATLANTA – The investigational drug riociguat significantly improved 6-minute walk distance in patients with symptomatic pulmonary arterial hypertension in the phase III PATENT-1 study.

Of 443 patients who participated in the randomized, double-blind trial, those who received active treatment with the novel oral soluble guanylate cyclase (sGC) stimulator experienced a 36-m improvement in 6-minute walk distance, compared with those who received placebo, after 12 weeks.

This "clinically meaningful as well as highly statistically significant" improvement was evident in both treatment-naive patients and pretreated patients, who each comprised about 50% of the study population, Dr. Hossein Ghofrani reported at the annual meeting of the American College of Chest Physicians.

Treatment also resulted in "significant and robust" improvements on several secondary end points, including pulmonary vascular resistance, N-terminal prohormone brain natriuretic peptide, World Health Organization functional class, time to clinical worsening, and Borg dyspnea score, said Dr. Ghofrani of University Hospital Giessen and Marburg in Giessen, Germany.

For pulmonary vascular resistance, for example, a 29% reduction was noted in the treatment group, compared with the placebo group. This translated into a 226-dyne reduction, with more than a half liter increase in cardiac output and a highly statisti-

See **PAH** • *page 16*

INSIDE

MRSA Rates Slashed by ICU Scrub Down

BY DOUG BRUNK
IMNG Medical News

SAN DIEGO – The use of antimicrobial soap and ointment on all patients admitted to intensive care units led to a 37% reduction in methicillin-resistant *Staphylococcus aureus* clinical isolates and a 44% reduction in bloodstream infections caused by all pathogens, results from a large multicenter study demonstrated.

"While earlier, smaller studies have suggested benefit from bathing with antibacterial soap and using nose ointment, this trial provides the first large-scale evaluation of this question and is anticipated to impact on best-practice guidelines for preventing hospital infections," lead researcher Dr. Susan S. Huang said in an interview prior to IDWeek 2012, where the research was presented.

Dr. Huang, medical director of epidemiology and infection prevention at the University of California, Irvine, and her associates randomized 43 hospitals

See **MRSA** • *page 7*

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Test Improves Diagnostic Yield of Bronchoscopy

New gene-expression test can lead to 22% lower false-negative rate, researcher says.

BY SHARON WORCESTER
IMNG Medical News

ATLANTA – The combined use of a novel bronchial airway gene-expression test and bronchoscopy improves the ability to rule out lung cancer in patients with benign disease, compared with bronchoscopy alone, according to findings from the prospective case-controlled AEGIS-1 trial.

Because bronchoscopy, which plays a central role in lung cancer diagnosis, has varying diagnostic yield based on factors such as the size and location of the lesion, the method used to collect cells, and pathological processing methods, the findings suggest that the test (BronchoGen) could minimize the need for additional invasive procedures in these patients, Duncan Whitney, Ph.D., said at the annual meeting of the American College of Chest Physicians.

The AEGIS-1 (Airway Epithelium Gene Expression in the Diagnosis of Lung Cancer 1) trial included more than 700 current or former smokers undergoing bronchoscopy for suspicion of lung cancer. It was designed to evaluate the diagnostic accuracy of the genomic test, which detects gene expression of cytologically normal bronchial airway epithelial cells.

The investigators collected mainstem bronchial airway brushings from 330 patients, including 240 with confirmed primary lung cancer and 90 controls, and performed microarray analysis. The sample set was then split into an independent training sample of 220 cases and a test set of 110 cases, and the gene-expression prediction model was optimized.

Next, reverse transcription polymerase chain reaction (RT-PCR) assays were developed for candidate biomarker genes, and a multivariate test algorithm was reoptimized using the RT-PCR data generated by a reanalysis of 153 of the samples from cancer patients and 64 of the samples from controls, explained Dr. Whitney.

The test, which ultimately focused on 30 genes, yielded a sensitivity of 77%, compared with 74% for bronchoscopy alone. The combined use of the test and bronchoscopy yielded a sensitivity of 96% and a specificity of 73%.

The negative predictive value of the combined test also was better than that of bronchoscopy alone (0.85 vs. 0.65, respectively), said Dr. Whitney.

"So in essence, we're reducing the false- negative rate from 26% down to 4%," he said.

The BronchoGen test was developed based on the airway "field of injury" principle, which refers to the common molecular response that occurs throughout the respiratory tract in current and former smokers with lung cancer, Dr. Whitney explained.

These changes are detected in a gene-expression signature from normal airway cells, even decades after smoking cessation, he noted.

Despite tremendous work done in this area, which has dramatically improved the diagnostic yield and sensitivity of bronchoscopy in the past few years, the procedure is either inconclusive or not diagnostic in up to 50% of cases, he said.

Thus, a "fairly large need" exists in the medical community, given that about 300,000 bronchoscopy procedures are performed each year for suspicion of lung cancer, he added.

Complete results from AEGIS-1, as well as clinical validation of the BronchoGen test, are expected to be released later this year. An additional 1,300 patients have been enrolled in the ongoing AEGIS-II trial.

Dr. Whitney is senior vice president for research, development, and technical operations of Allegro Diagnostics and is the study's director.

Allegro Diagnostics, which developed the BronchoGen test, reports that it plans to commercialize it for use with bronchoscopy beginning in 2013. ■

VITALS

Major Finding: The test, which focused on 30 genes, yielded a sensitivity of 77% for lung cancer, compared with 74% for bronchoscopy alone. The combined use of the test and bronchoscopy yielded a sensitivity of 96% and a specificity of 73%.

Data Source: This was a prospective case-controlled trial (AEGIS-1).

Disclosures: This study was sponsored by Allegro Diagnostics. Dr. Whitney is an employee of the company, and reported having no other relevant disclosures.

IN THIS ISSUE

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

CHEST PHYSICIAN

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

POSTMASTER: Send change of address (with old mailing label) to CHEST PHYSICIAN, Subscription Service, 151 Fairchild Ave., Suite 2, Plainview, NY 11803-1709.

CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609. Phone 973-206-3434, fax 973-206-9378.

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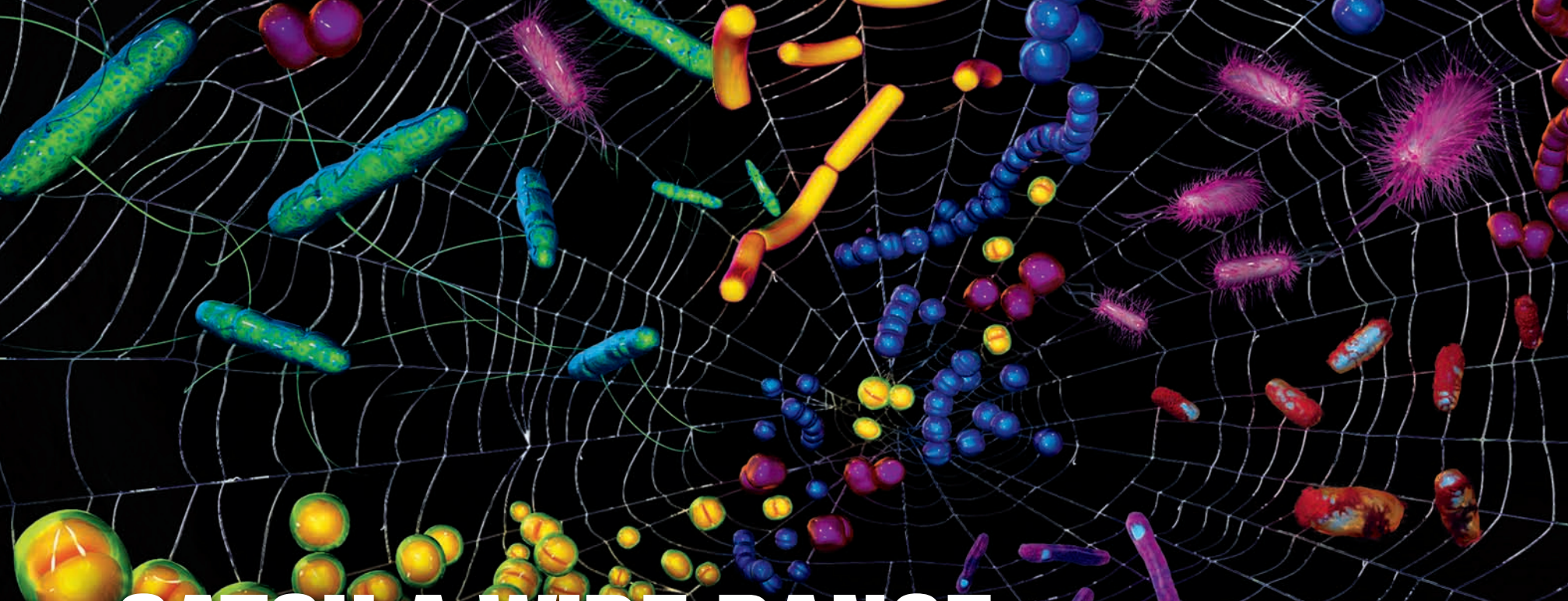

CATCH A WIDE RANGE OF PATHOGENS WITH TYGACIL

TYGACIL provides coverage of gram-positive (including MRSA*), gram-negative, anaerobic, and atypical pathogens. TYGACIL does not cover *Pseudomonas aeruginosa*.[1]

*Methicillin-resistant *Staphylococcus aureus.*

INDICATIONS—TYGACIL is indicated for the treatment of adults with:

cIAI

Complicated intra-abdominal infections caused by *Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Clostridium perfringens*, and *Peptostreptococcus micros*

cSSSI

Complicated skin and skin structure infections caused by *Escherichia coli, Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus agalactiae, Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Streptococcus pyogenes, Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Bacteroides fragilis*

CABP

Community-acquired bacterial pneumonia caused by *Streptococcus pneumoniae* (penicillin-susceptible isolates), including cases with concurrent bacteremia, *Haemophilus influenzae* (beta-lactamase negative isolates), and *Legionella pneumophila*

IMPORTANT SAFETY INFORMATION

- TYGACIL is contraindicated in patients with known hypersensitivity to tigecycline
- Anaphylaxis/anaphylactoid reactions have been reported with nearly all antibacterial agents, including tigecycline, and may be life-threatening. TYGACIL should be administered with caution in patients with known hypersensitivity to tetracycline-class antibiotics
- Isolated cases of significant hepatic dysfunction and hepatic failure have been reported in patients being treated with tigecycline. Some of these patients were receiving multiple concomitant medications. Patients who develop abnormal liver function tests during tigecycline therapy should be monitored for evidence of worsening hepatic function. Adverse events may occur after the drug has been discontinued
- The safety and efficacy of TYGACIL in patients with hospital-acquired pneumonia have not been established
- **An increase in all-cause mortality has been observed across Phase 3 and 4 clinical trials in TYGACIL-treated patients versus comparator-treated patients. In all 13 Phase 3 and 4 trials that included a comparator, death occurred in 4.0% (150/3788) of patients receiving TYGACIL and 3.0% (110/3646) of patients receiving comparator drugs. In a pooled analysis of these trials, based on a random effects model by trial weight, an adjusted risk difference of all-cause mortality was 0.6% (95% CI 0.1, 1.2) between TYGACIL and comparator-treated patients. The cause of this increase has not been established. This increase in all-cause mortality should be considered when selecting among treatment options**
- **TYGACIL may cause fetal harm when administered to a pregnant woman**
- **The use of TYGACIL during tooth development may cause permanent discoloration of the teeth**. TYGACIL should not be used during tooth development unless other drugs are not likely to be effective or are contraindicated
- Acute pancreatitis, including fatal cases, has occurred in association with tigecycline treatment. Consideration should be given to the cessation of the treatment with tigecycline in cases suspected of having developed pancreatitis
- *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including TYGACIL, and may range in severity from mild diarrhea to fatal colitis
- Monotherapy should be used with caution in patients with clinically apparent intestinal perforation
- TYGACIL is structurally similar to tetracycline-class antibiotics and may have similar adverse effects. Such effects may include: photosensitivity, pseudotumor cerebri, and anti-anabolic action (which has led to increased BUN, azotemia, acidosis, and hyperphosphatemia). As with tetracyclines, pancreatitis has been reported with the use of TYGACIL
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of TYGACIL and other antibacterial drugs, TYGACIL should be used only to treat infections proven or strongly suspected to be caused by susceptible bacteria. As with other antibacterial drugs, use of TYGACIL may result in overgrowth of nonsusceptible organisms, including fungi
- The most common adverse reactions (incidence >5%) are nausea, vomiting, diarrhea, infection, headache, and abdominal pain
- Prothrombin time or other suitable anticoagulant test should be monitored if TYGACIL is administered with warfarin
- Concurrent use of antibacterial drugs with oral contraceptives may render oral contraceptives less effective
- The safety and effectiveness of TYGACIL in patients below age 18 and lactating women have not been established

Please see brief summary on adjacent page.

REFERENCE: 1. TYGACIL® [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc; 2011.

Tygacil® tigecycline IV

e-Tests Catch Missed Vancomycin Resistance

BY M. ALEXANDER OTTO
IMNG Medical News

SAN FRANCISCO – Vancomycin and glycopeptide resistance detection e-tests are better than the automated microbiology systems used in many hospitals when it comes to detecting vancomycin-resistant *Staphylococcus aureus* infections, according to researcher Meghan Jeffres, Pharm.D

An associate professor of pharmacy practice at Roseman University of Health Sciences in Henderson, Nev., Dr. Jeffres reached her conclusion after testing 63 blood, 115 respiratory, and 29 cystic fibrosis sputum *S. aureus* isolates for vancomycin susceptibility using all three methods.

She reported that a GRD (glycopeptide resistance detection) e-test vancomycin MIC (minimum inhibitory concentration) of 8 mcg/mL or more, in conjunction with a vancomycin e-test MIC of 4 mcg/mL or less, is diagnostic of heteroresistant vancomycin-intermediate *S. aureus* (hVISA). By itself, a vancomycin e-test MIC of 1.5 mcg/mL or greater is associated with poor outcomes, and suggests the need for an alternative antibiotic, Dr. Jeffres said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The combined GRD and vancomycin e-tests found 10 hVISA isolates, all respiratory.

Ninety-three (45%) of the isolates, however, had vancomycin e-test MICs of 1.5 mcg/mL or more. Of those 93 isolates that vancomycin e-testing suggested needed a vancomycin alternative, the hospital's BD Phoenix Automated Microbiology System identified only one as being resistant to vancomycin, with an MIC of 2 mcg/mL; it reported the rest as having vancomycin MICs of 0.5 or 1 mcg/mL, suggesting susceptibility to vancomycin.

"Our automated system accurately identified 1 out of 93 isolates" as needing something other than vancomycin, she said. "As a clinician, when your isolates are 1 and 0.5, you treat it as a susceptible isolate." Ultimately, if those results come from automated testing, "it's a false sense of security. None of the [automated testing systems] are very good at reporting vancomycin MICs," Dr. Jeffres said.

'Dead people cost way more' than the tab for added testing for vancomycin resistance.

DR. JEFFRES

Because of that, many larger academic institutions have moved to e-testing, but other hospitals – such as the large community hospital in Las Vegas where Dr. Jeffres did her research – still rely heavily on automated vancomycin resistance testing.

That can have serious consequences. Dr. Jeffres' e-test results were not reported in patients' medical records, so clinicians at the hospital used the automated results to help make treatment decisions. All 10 of the hVISA isolates reported out of automated testing had vancomycin MICs of 0.5 or 1 mcg/mL, indicating vancomycin susceptibility.

Three of those patients were treated with vancomycin; they died. The rest were treated with linezolid – a vancomycin alternative – probably based on clinical hunches. Those patients lived, and were able to be sent home or to rehab.

"There is no statistical analysis" here, "but you can't help but to at least pause," given the results. Had even the [vancomycin] e-test alone been done by clinicians, "there's no way" the three patients would have gotten vancomycin, Dr. Jeffres said.

E-testing adds a bit to the cost of assessing vancomycin resistance; the GRD e-test costs about $5.39, the vancomycin e-test about $2.90, and the necessary blood agar about 79 cents. Alternative antibiotics are more costly than vancomycin, as well.

"However, dead people cost way more, from both economic and humanistic points of view," she said. E-testing will increase the pharmacy budget, especially if it leads to alternative antibiotics, but overall, the hospital budget should stay the same if not decrease, Dr. Jeffres said.

The conference was sponsored by the American Society for Microbiology. Dr. Jeffres disclosed research funding from Pfizer, the maker of linezolid. ■

For PAH (WHO Group 1) patients on oral monotherapy

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

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

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

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

Dosing regimen fits into patients' schedules

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

Adverse events

- The most common adverse events seen with Tyvaso in ≥4% of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical study were cough, headache, throat irritation/pharyngolaryngeal pain, nausea, flushing, and syncope[1]

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

INDICATION

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

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

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

IMPORTANT SAFETY INFORMATION

- Tyvaso is intended for oral inhalation only. Tyvaso is approved for use only with the Tyvaso Inhalation System
- The safety and efficacy of Tyvaso have not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease) and in patients under 18 years of age. Patients with acute pulmonary infections should be carefully monitored to detect any worsening of lung disease and loss of drug effect
- Tyvaso may increase the risk of bleeding, particularly in patients receiving anticoagulants
- In patients with low systemic arterial pressure, Tyvaso may cause symptomatic hypotension. The concomitant use of Tyvaso with diuretics, antihypertensives, or other vasodilators may increase the risk of symptomatic hypotension
- Hepatic or renal insufficiency may increase exposure to Tyvaso and decrease tolerability. Tyvaso dosage adjustments may be necessary if inhibitors of CYP2C8 such as gemfibrozil or inducers such as rifampin are added or withdrawn
- The most common adverse events seen with Tyvaso in ≥4% of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical study were cough (54% vs 29%), headache (41% vs 23%), throat irritation/pharyngolaryngeal pain (25% vs 14%), nausea (19% vs 11%), flushing (15% vs <1%), and syncope (6% vs <1%)
- Tyvaso should be used in pregnancy only if clearly needed. Caution should be exercised when Tyvaso is administered to nursing women

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

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

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

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PROSTACYCLIN MADE PRACTICAL

Physician Pay Rule Contains Good and Bad News

Maligned fee schedule includes SGR-based cuts along with new codes for coordination of care.

BY ALICIA AULT
IMNG Medical News

Medicare's physician fee schedule for 2013 contains both a 26.5% pay cut based on the Sustainable Growth Rate formula and pay increases for care coordination and for primary care provided under Medicaid.

Under current law, the Sustainable Growth Rate (SGR) formula will kick in Jan. 1 and lop one-fourth off doctors' pay under Medicare, unless Congress steps in to halt the cut.

In issuing the fee schedule final regulation on Nov. 1, the Obama administration noted that Congress has reversed the mandated cut every year since 2003.

The administration "is committed to fixing the SGR update methodology and ensuring these payment cuts do not take effect," according to a statement. "Predictable, fiscally responsible physician payments are essential for Medicare to sustain quality and lower health care costs over the long term."

The American Medical Association decried the SGR cut.

"Eliminating this failed formula will allow us to enter a period when physicians can begin transitioning to new payment and delivery models to help meet the overall goal of improving patient care and moving to a higher performing Medicare program," Dr. Ardis D. Hoven, AMA president-elect, said in a statement.

The fee schedule final rule also includes changes to the value-based modifier program, designed to pay physicians based on the quality of care they deliver.

In a proposed rule issued earlier this year, physicians in groups of 25 or larger would have been subject to the new pay plan in 2015. The final rule increases the size of the group to 100 initially.

In addition, the final rule creates a new set of codes to pay physicians for care coordination in the 30 days after a patient is discharged from a hospital or nursing home. Those codes were initially proposed as G codes, but now will be full-fledged codes in the AMA Current Procedural Terminology (CPT). Physicians will be rewarded for patient interactions that are not face to face, such as phone consults, chart reviews, and email communications.

'Eliminating this failed formula' would allow transition to new payment and delivery models.

DR. HOVEN

In another final rule issued Nov. 1, the CMS announced that, as expected, it will pay certain providers the Medicare pay rate for certain primary care services provided under Medicaid in 2013 and 2014.

As called for under the Affordable Care Act, the CMS will pay Medicare rates for evaluation and management codes between 99201 and 99499 when they are used by physicians who are board certified by the American Board of Medical Specialties, the American Osteopathic Association, and the American Board of Physician Specialties.

The codes cover not just primary care, but also hospital observation and consultation for inpatient services provided by nonadmitting physicians, emergency department services, and critical care services.

The final rule does not, however, allow emergency physicians or obstetricians to be compensated at the Medicare level for services under Medicaid, according to the consulting firm Washington Analysis.

The CMS estimated that increasing the Medicaid pay will cost $5.6 billion in 2013 and $5.7 billion in 2014.

The rules will be published in the Federal Register on Nov. 16 and comments will close on Dec. 31. Both rules take effect Jan. 1, 2013. ■

Pages 6a—6b

Universal Scrub Down Wins in ICU

MRSA • *from page 1*

in 16 states to one of three ICU strategies for reducing bloodstream infections: nasal MRSA screening followed by isolation if positive (group 1); targeted decolonization by treating patients who tested positive with chlorhexidine baths and mupirocin for 5 days (group 2); or universal decolonization by elimination of all screening and administration of mupirocin for 5 days and daily chlorhexidine baths for the duration of ICU stay (group 3).

TREATING ALL ICU PATIENTS WITH 5 DAYS OF NASAL MUPIROCIN AND DAILY CHLORHEXIDINE BATHS CUT MRSA RATES BY 37%.

The study, known as the REDUCE MRSA Trial, included a 1-year baseline period and an 18-month intervention period that ended in September 2011.

"Until this trial, there has been debate about whether bathing with antibacterial soap and using nose ointment prevent infections in these high-risk settings," Dr. Huang said. "There has also been debate whether such bathing, if it is helpful, should be used for all ICU patients or only for patients who can be shown to have MRSA on their skin or nose."

Dr. Huang reported results from 48,390 ICU admissions in the baseline period and 74,256 in the intervention period. Between the two time periods, MRSA rates among ICU patients fell by 37% in group 3, compared with a 25% drop in group 2 and an 8% drop in group 1. The difference between groups reached statistical significance (*P* less than .01).

A similar association was seen when the researchers compared the effect of all interventions on the rate of all bloodstream infections caused by all pathogens.

Between the two time periods, the rates of bloodstream infections among ICU patients fell by 44% in group 3, compared with a 22% drop in group 2 and a 1% drop in group 1. The difference between groups reached statistical significance (*P* less than .00001).

"This trial was almost entirely based in community hospitals and the results are therefore likely to be applicable to nearly all U.S. hospitals," Dr. Huang said at the combined annual meetings of the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the HIV Medicine Association, and the Pediatric Infectious Diseases Society. "This is in contrast to prior research, which mainly involved large academic centers that may not be representative of usual medical care."

She went on to note that, until now, it was unclear which strategy – directing prevention strategies at patients who harbor highly resistant organisms or at entire high-risk patient groups – would yield better results.

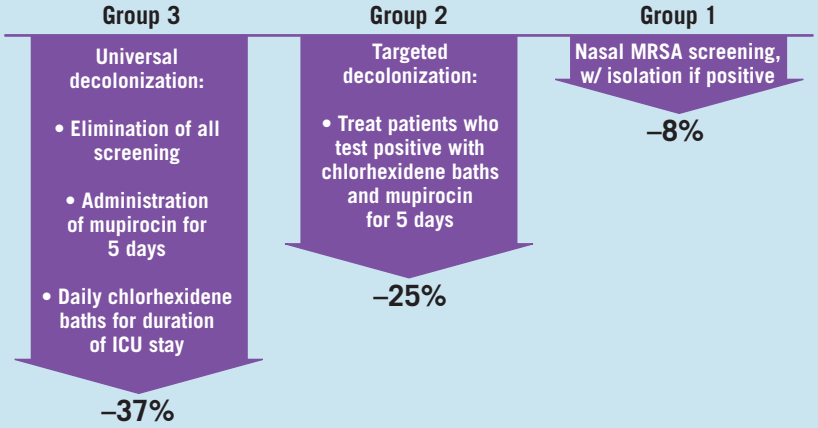
"This has been a key area of debate among infection prevention experts," she said. "We are pleased to find that the results support a strategy that will benefit more people and prevent more infections than those just due to MRSA."

Dr. Huang acknowledged certain limitations of the study, including the fact that it was conducted exclusively in ICUs. "We do not know the effects of this strategy in other settings."

"Formal cost analyses have yet to be done to understand the cost of product compared to the reduction in infection risk. In addition, we have yet to analyze whether wide use of these products caused resistant bacteria to emerge. Even if it did not, continued vigilance for emerging resistance will be required if it is widely implemented," she said.

The study was sponsored by Harvard Pilgrim Health Care and supported by funding from the Agency for Healthcare Research and Quality, the CDC, and Hospital Corporation of America.

Dr. Huang had no relevant financial conflicts. ■



Note: Based on 48,390 ICU admissions at 43 hospitals in the baseline period (1 year) and 74,256 in the intervention period (18 months).
Source: Dr. Huang

IMNG Medical Media

COMMENTARY

Dr. Stephen Simpson, FCCP, comments: MRSA infections, including bloodstream infections, continue to rise in incidence and represent a significant danger to our ICU patients. Chlorhexidine bathing is a simple means to reduce these potentially deadly infections. As is frequently the case, adhering to fundamentally simple concepts, in this instance skin decontamination via a simple technique, can and does alter important outcomes. The observed reduction in infections very likely translates to shorter ICU and hospital lengths of stay and to reduced mortality.

Linezolid Predicted MRSA Pneumonia Treatment Success

BY DOUG BRUNK
IMNG Medical News

SAN FRANCISCO – In a national cohort of patients with methicillin-resistant *Staphylococcus aureus* pneumonia, treatment with linezolid was the only modifiable variable in predicting clinical success.

"Pneumonia is the No. 1 cause of infectious disease–related deaths in the United States yet there are limited treatment options for pneumonia caused by MRSA," Aisling R. Caffrey, Ph.D., said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy. "Identification of independent predictors of clinical success can optimize patient care."

In an effort to identify independent predictors of clinical success in MRSA pneumonia, Dr. Caffrey, assistant professor of pharmacoepidemiology at the University of Rhode Island College of Pharmacy, and her associates conducted a retrospective cohort study of Veterans Affairs hospital admissions between January 2002 and September 2010 with diagnosis codes for MRSA and pneumonia. They used pharmacy records to identify initiation of linezolid or vancomycin during admission, with at least 3 days of therapy as dosed per protocol.

Patients who died or were discharged within 3 days of treatment initiation with either agent were excluded from the study, as were those whose treatment was initiated in a nursing home and those who were exposed to more than 2 consecutive days of antibiotic therapy with MRSA activity within 3 days prior to initiation of linezolid or vancomycin or during treatment with either agent.

Clinical success was defined as discharge from the hospital or intensive care unit by day 14 after treatment initiation, in the absence of death, therapy change, or intubation. Nonsuccess was defined as therapy change, intubation, discharge, and readmission, or death between treatment initiation and day 14. They also investigated numerous potential predictors of clinical success, including treatment with linezolid or vancomycin, demographics and admission characteristics, and comorbidities and medical history.

Dr. Caffrey reported data from 231 patients who received linezolid and 3,501 patients who received vancomycin. Their mean age was 70 years and most (98%) were male. Predictors of clinical success included treatment with linezolid (odds ratio 1.53) and having a previous complication of an implant or graft (OR 1.55). Factors associated with nonsuccess included dialysis (OR 0.54), intravenous line (OR 0.76), having three or more inpatient procedures (OR 0.53), inpatient surgery (OR 0.48), urinary tract infection (OR 0.82), previous coagulopathy (OR 0.74), previous endocarditis (OR 0.24), and previous amputation procedure (OR 0.72).

Dr. Caffrey acknowledged certain limitations of the study, including the reliance on diagnostic codes to ascertain the number of MRSA pneumonia cases. "We're probably only capturing 20%-40% of MRSA diagnoses by using the diagnosis codes," she said at the meeting sponsored by the American Society for Microbiology.

Low generalizability of the findings to other patient populations is another limitation, she said.

She concluded that patients with MRSA pneumonia "are often complex, and identifying predictors of success is useful in maximizing clinical decision making."

The study was supported by the Department of Veterans Affairs and Pfizer. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: This retrospective cohort study suggests patients treated with linezolid for MRSA pneumonia who also had an implant or graft had improved outcomes compared with those treated with vancomycin. The use of claims data may have significantly limited this analysis. Further investigation of this potential benefit in complex patients would be useful in helping to select patients who may benefit more from this therapy over the more conventional IV vancomycin treatment.

SERAPHIN: Lower Mortality in PAH With Macitentan

BY SHARON WORCESTER
IMNG Medical News

ATLANTA – Macitentan, a novel dual endothelin receptor antagonist with enhanced tissue penetration, significantly improves morbidity and mortality in patients with pulmonary arterial hypertension, according to findings from the industry-sponsored, randomized controlled phase III SERAPHIN trial.

Macitentan treatment reduced the risk of occurrence of combined morbidity and mortality events by 30% in 250 patients randomized to receive 3 mg once daily and by 45% in 242 patients randomized to receive 10 mg once daily, compared with 250 patients who received placebo, Dr. Lewis Rubin, FCCP, reported at the annual meeting of the American College of Chest Physicians.

Existing PAH therapies have been based only on short-term trials.

DR. RUBIN

The differences were highly significant for both macitentan doses, and the effect of treatment on this novel primary end point was observed irrespective of background therapy, which consisted mainly of phosphodiesterase type-5 (PDE-5) inhibitors.

Among patients using background therapy, risk was reduced by 17% and 38% for the 3 mg and 10 mg groups, respectively; in treatment-naive patients, the risk was reduced by 47% and 55% in the dosage groups, respectively, said Dr. Rubin of the University of California, San Diego.

The findings hold promise for improved long-term outcomes in patients with pulmonary arterial hypertension (PAH), Dr. Rubin said. "This primary morbidity/mortality end point captures clinically relevant events that reflect true disease progression," he noted, explaining that the end point included time to death, atrial septostomy, lung transplantation, initiation of intravenous/subcutaneous prostanoids, or worsening of PAH.

To meet the criteria for PAH worsening, participants had to experience a confirmed 15% or greater decrease in 6-minute walk distance and worsening of symptoms as defined by either a worsening in functional class, worsening symptoms of right heart failure, need for a new PAH treatment, or need for an intravenous diuretic. The majority of events contributing to achievement of the primary end point were associated with worsening of PAH, rather than death, he noted.

In addition to improvements with respect to the primary end point, macitentan treatment also was associated with improvement on the secondary end point of the composite of mortality or hospitalization due to PAH, with risk reduction of 33% and 50% in the 3-mg and 10-mg groups, respectively, compared with placebo, Dr. Rubin said.

Macitentan was well tolerated, with both the treatment group and the placebo group experiencing similar incidences of elevated liver aminotransferases and peripheral edema, although headache, nasopharyngitis, and anemia all occurred more frequently in the treatment groups.

Participants in the double-blind, event-driven SERAPHIN (Study With an Endothelin Receptor Antagonist in Pulmonary Arterial Hypertension to Improve Clinical Outcome) were individuals aged 12 years or older with PAH. Randomization began in May of 2008, and study end was predefined as the occurrence of 285 morbidity/mortality events, which occurred as of March 2012.

The findings are notable because existing PAH therapies, including bosentan and ambrisentan, have been approved based only on short-term trials with exercise capacity as the primary end point, and have potential for adverse events that can limit tolerability, Dr. Rubin said.

"So an endothelin receptor antagonist that has a better tolerability profile would be potentially desirable," he said.

The SERAPHIN trial was sponsored by Actelion, the maker of macitentan. Dr. Rubin disclosed that he has received payment for consulting and/or serving on speaker bureaus or advisory committees for Actelion, Pfizer, United Therapeutics, Lung LLC, Gilead, GlaxoSmithKline, Bayer, and GeNo. ■

Kids' Outcomes Good at Pediatric, Adult Trauma Sites

VITALS

Major Finding: In-hospital mortality for children aged 0-14 years was twice as high for those treated at mixed centers as for those treated at pediatric centers (2% vs. 1%), but this difference was not significant.

Data Source: The data come from the National Trauma Database for 2007-2008, and included 33,327 patients treated at pediatric centers and 12,605 patients treated at mixed centers.

Disclosures: Dr. Villegas reported having no financial conflicts of interest.

BY HEIDI SPLETE
IMNG Medical News

CHICAGO – Outcomes for children seen at pediatric trauma centers were not significantly different than for children seen at adult trauma centers, according to a review of more than 45,000 pediatric injuries.

The finding "has significant policy implications because it means that emergency medical services do not have to triage patients according to specialty care centers," and informs discussions about pediatric access to trauma care, said researcher Dr. Cassandra Villegas of the University of Arizona in Tucson.

Trauma accounts for approximately one-third of all pediatric mortality, but there are only 170 pediatric-specific trauma centers in the United States, which "means that the vast majority of pediatric patients that are injured are actually managed and evaluated at adult trauma centers," Dr. Villegas said at the annual clinical congress of the American College of Surgeons.

Nonetheless, data on pediatric outcomes for children treated at pediatric vs. adult trauma centers have not been conclusive, and most previous studies have focused on metropolitan or state pediatric centers, she said.

Dr. Villegas and her colleagues reviewed data from the National Trauma Database for 2007-2008 that included 27 pediatric trauma centers and 30 adult (mixed care) centers that had pediatric beds. Most (90%) of the 30 mixed care centers provided all acute pediatric services, while 10% shared these services with another medical center. All of the pediatric centers and 90% of the mixed care centers had pediatric intensive care units. The pediatric centers were significantly more likely to be university hospitals than were the mixed centers (85% vs. 53%).

THIS FINDING SUGGESTS THAT 'EMERGENCY MEDICAL SERVICES DO NOT HAVE TO TRIAGE PATIENTS ACCORDING TO SPECIALTY CARE CENTERS.'

The researchers analyzed outcomes for children aged 0-14 years, including 33,327 patients treated at pediatric centers and 12,605 patients treated at mixed centers.

After controlling for multiple variables including injury characteristics, Dr. Villegas and her associates found that in-hospital mortality – the primary outcome – was twice as high at mixed centers as at pediatric centers (2% vs. 1%), but this difference was not significant. The median length of stay was 2 days at all centers, although intensive care unit admission rates were higher at mixed centers versus pediatric centers (26% vs. 14%).

Approximately one-third of the patients seen at either type of center had an Injury Severity Score (ISS) in the 9-15 range, said Dr. Villegas. Falls were the most common type of injury, accounting for 49% of cases at pediatric centers and 37% of cases at mixed centers.

The patients at mixed centers were more likely than those at pediatric centers to be hypotensive (18% vs. 10%), she reported.

The study was limited by several factors, including the low incidence of pediatric mortality, the lack of uniform coding for death on arrival, and differences in intensive care unit admission practices, said Dr. Villegas.

However, the findings suggest that there are no differences in outcomes for children treated at pediatric vs. mixed care centers, she said. ■

Aspirin Cuts Recurrence of Vascular Events, VTEs

The rate of a composite outcome including VTE, MI, stroke, major bleeding, or death was reduced by 33%.

BY HEIDI SPLETE
IMNG Medical News

A 100-mg daily dose of aspirin reduced by one-third the rate of recurrent major vascular events for patients who had one acute unprovoked venous thromboembolism and were switched from anticoagulant therapy to either aspirin or placebo after 3 months of anticoagulant therapy.

Patients with one episode of unprovoked VTE often discontinue anticoagulant therapy due to inconvenience and the risk of bleeding, said Dr. Timothy A. Brighton of the University of Sydney, Australia, and his colleagues. For those patients, 100 mg of aspirin per day appears to be a safe alternative.

Dr. Brighton and his colleagues reported the findings based on combined data from the ASPIRE (Aspirin to Prevent Recurrent Venous Thromboembolism) study and the WARFASA (Warfarin and Aspirin) study. The findings of ASPIRE were simultaneously published in the New England Journal of Medicine and presented at the annual meeting of the American Heart Association in Los Angeles. The findings of WARFASA were previously published in the same journal.

ASPIRE examined the effect of a 100-mg daily dose of aspirin in patients who had a history of a first-ever unprovoked VTE and had completed initial anticoagulation therapy. The study population included 822 adults who were randomized to a placebo or aspirin at 56 sites in five countries from May 2003 and August 2011. Roughly half of the patients were men; 56% had a proximal deep-vein thrombosis as an index event; 29% had a pulmonary embolism as an index event, and 14% had both conditions as an index event (N. Engl. J. Med. 2012 Nov. 4 [doi: 10.1056/NEJMoa1210384]).

Overall, VTE recurred in 57 patients (14%) in the aspirin group, compared with 73 patients (18%) in the placebo group (rates of 5% and 7% per year, respectively, a nonsignificant difference).

However, the rates of two secondary composite outcomes were significantly reduced in patients who took aspirin compared with those on placebo, the researchers noted.

The rate of a composite outcome including VTE, myocardial infarction, stroke, or cardiovascular death was reduced by 34% in aspirin patients (5% per year for aspirin vs. 8% per year for placebo). The rate of a composite outcome including VTE, myocardial infarction, stroke, major bleeding, or death from any cause was reduced by 33% in aspirin patients (6% per year for aspirin vs. 9% per year for placebo).No significant differences in serious adverse events or in the rates of major or clinically relevant nonmajor bleeding were observed between the aspirin and placebo groups, researchers noted.

The findings were limited by the low number of patients in the study, however. The ASPIRE data alone were not adequately powered to show a significant reduction in the recurrence of VTE.

To address the issue, researchers combined the ASPIRE data with data from a similar population of 402 patients in the WARFASA (Warfarin and Aspirin) study (N Engl J Med 2012; 366:1959-67). In this multicenter, double-blind study, patients with first-ever unprovoked venous thromboembolism completed 6-18 months of oral anticoagulant treatment and were randomly assigned to aspirin, 100 mg daily, or placebo for 2 years.

VTE recurred in 28 of the 205 patients who received aspirin and in 43 of the 197 patients who received placebo (6.6% vs. 11.2% per year; hazard ratio, 0.58). One patient in each treatment group had a major bleeding episode. Adverse events were similar in the two groups.

Using the combined data from both studies, the researchers found "a highly significant reduction of 32% in the rate of recurrence of venous thromboembolism and a reduction of 34% in the rate of major vascular events with no excess of bleeding." Therefore, the combined results of the two studies support the use of low-dose aspirin to prevent both recurrent VTE and major vascular events in patients who have had a first episode of unprovoked VTE, the researchers said.

The study was supported by grants from the National Health and Medical Research Council (Australia), the Health Research Council (New Zealand), the National Heart Foundation of Australia, Bayer HealthCare (Germany), and the Australasian Society of Haematology and Thrombosis. ■

VITALS

Major Finding: The combined results of the ASPIRE and WARFASA trials showed significant reductions of 32% in the rate of recurrence of venous thromboembolism and 34% in the rate of major vascular events among patients given 100 mg of aspirin daily compared with a placebo.

Data Source: The data come from 822 adults in the ASPIRE trial and 402 adults in the WARFASA trial.

Disclosures: Dr. Brighton disclosed serving as a consultant for Pfizer, GlaxoSmithKline, and other companies.

COMMENTARY

Dr. Theodore Warkentin comments: Anticoagulants may trump aspirin in efficacy for preventing VTE after surgery, but the findings from the ASPIRE and WARFASA studies support a clinical role for aspirin in preventing VTE.

Dr. Warkentin noted the long-term risk of a recurrence of venous thromboembolism in patients who have had a first unprovoked VTE.

"Could aspirin represent a reasonable intermediate option between the extremes of indefinite anticoagulation and no ongoing anticoagulation, particularly from the additional perspective of concomitant prevention of arterial thrombosis?" he asked.

The combined data from the WARFASA and ASPIRE studies suggest that aspirin has the double benefit of significantly reducing not only the rate of venous thromboembolism recurrence, but also the rate of a composite of major vascular events, Dr. Warkentin said.

On the basis of the findings, Dr. Warkentin explained how aspirin could fit into clinical practice.

"Before physicians consider prescribing aspirin for patients who have had acute unprovoked venous thromboembolism, it is important that they treat the patients with effective anticoagulation for at least 3 months, to avoid the high risk of early recurrence," he said.

"For patients who then wish to stop anticoagulation, a switch to aspirin at a dose of 100 mg daily will reduce by one-third the risk of recurrent venous thromboembolism, as well as of arterial cardiovascular events, and may also attenuate the early burst of thrombosis recurrence after cessation of oral anticoagulation," he said.

Aspirin has the added benefits of being cost effective, requiring no monitoring, and not accumulating in patients with renal insufficiency, Dr. Warkentin added.

DR. WARKENTIN *is a professor of pathology and molecular medicine at McMaster University in Hamilton, Ont. He also has served as a consultant for GlaxoSmithKline and as a speaker for Pfizer Canada, and he has received grants from Bayer. These remarks were taken from his accompanying editorial (N. Engl. J. Med. 2012 Nov. 4 [doi: 10.1056/NEJMe1211480]).*

Despite Ban, 18% of Smokers Light Up in Hospitals

BY MARY ANN MOON
IMNG Medical News

More than 18% of smokers who were inpatients at a large urban teaching hospital reported that they smoked during their stay, even though smoking was prohibited in the hospital buildings, according to a report in the Archives of Internal Medicine.

Receiving nicotine replacement therapy at admission delayed but did not prevent these patients from smoking eventually, said Susan Regan, Ph.D., of the tobacco research and treatment center at Massachusetts General Hospital, Boston, and her associates.

Virtually all hospitals now prohibit smoking indoors, but many permit smoking outdoors on the hospital grounds. "The fact that patients may go outside to smoke, especially without supervision or in inclement weather, raises safety concerns," the researchers said. Further, inpatients who duck outside to smoke "deprive themselves of an opportunity to initiate a quit attempt in a supportive, smoke-free environment."

Inpatient smoking was studied during a 3-year period at the hospital, where smoking is banned indoors but allowed at two outdoor shelters. The study subjects were 2,185 adult inpatients who were referred to the facility's tobacco treatment service at admission, which facilitated the ordering of nicotine replacement therapy and provided a bedside counselor to assist in managing nicotine withdrawal.

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The counselor also gave brief (5 minutes or less) advice on quitting smoking, as well as longer (20 minutes) cessation counseling for patients who expressed interest in quitting. The counseling included motivational interviewing, plus discussion of behavioral strategies and the use of medications to maintain smoking abstinence.

Patients' in-hospital smoking was assessed by self-report during their hospital stays and telephone follow-up in the 2 weeks after discharge. Median length of stay was 5 days, and 62% of the subjects received nicotine replacement therapy; one-third received the therapy on the first day of their stay. The mean patient age was 53 years, and 58% of the study subjects were men.

Overall, 18.4% of these patients reported that they smoked at some time during their hospital stay. Patients were more likely to report such smoking if they were younger, had longer hospitalizations, and had no plans to quit.

Patients who received nicotine replacement therapy on admission were less likely to smoke early in their hospital stay, but they resumed smoking later in their stay at the same rate as did patients who never received the treatment. "Patients with longer stays might require increasing nicotine dose or supplementation of patch with shorter-acting forms of nicotine replacement therapy" such as nicotine gum or lozenges, researchers said (Arch. Intern. Med. 2012;doi:10.1001/2013.jamainternmend.300).

The number of cigarettes that subjects typically smoked was not as predictive of smoking during hospitalization as was the intensity of their cigarette cravings.

"Routine ongoing assessment of cigarette craving, although more time-consuming, might be a more effective means of identifying patients who will have difficulty remaining abstinent during their hospital stay and assist in titrating nicotine dose for patients already receiving nicotine replacement therapy," researchers said. ■

COMMENTARY

Dr. Steven A. Schroeder comments: The study by Dr. Regan and her associates reminds us that many smokers will find a way to smoke during a hospitalization. Perhaps extending the prohibition to the entire hospital campus might further cut down on the 18% who do.

Even if a hospital cannot have a tobacco treatment service like the one at Massachusetts General, "at the very least there should be a health professional group (e.g., physicians, nurses, respiratory therapists, pharmacists, behavioral psychologists, or some combination of these) that can work with smokers to prevent nicotine withdrawal symptoms and help them quit. Referral to a toll-free telephone quit line, available in every state, can be accomplished by fax or telephone (1-800-QUITNOW)," he wrote.

DR. SCHROEDER *is with the department of medicine at the University of California, San Francisco. He reported no financial conflicts of interest. These remarks were adapted from his invited commentary accompanying Dr. Regan's report (Arch. Intern. Med. 2012;doi:10.1001/2013.jamainternmed.308).*

Pneumonia Prevalence Among Highest of HAIs

BY DOUG BRUNK
IMNG Medical News

SAN DIEGO – The overall prevalence of health care–associated infections among inpatients in the United States stands at 4%, with the most common types of infections being a combination of pneumonia and lower respiratory infections.

Those are key preliminary findings from the Centers for Disease Control and Prevention's first large-scale health care–associated infection (HAI) prevalence survey in more than 30 years, Dr. Shelley S. Magill reported during IDWeek 2012, the combined annual meetings of the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the HIV Medicine Association, and the Pediatric Infectious Diseases Society.

The data "can help us better understand the factors that influence HAI prevalence," said Dr. Magill of the division of health care quality promotion at the Centers for Disease Control and Prevention, Atlanta. "We can also clarify the burden of different HAI types and pathogens across the hospital, which can suggest areas to target for prevention."

The phase 3 survey was conducted in 2011 in 183 hospitals in 10 states. Dr. Magill reported results from 11,282 patients who were surveyed in the 183 hospitals. Of these, 452 patients had HAIs, for a prevalence of 4%.

The researchers identified 504 HAIs in the 452 patients. Of these, the highest proportion (26%) were pneumonia or lower respiratory infections. "Of the pneumonia events, 39% were ventilator-associated infections," Dr. Magill said.

Dr. Magill also reported that 56% of HAIs were attributed to non-ICU locations in the hospital while 53% were not directly associated with a device or with a procedure.

After multivariable regression analysis, patients with the following factors were at higher risk of having HAIs: Older age (risk ratio, 4.60 for patients > age 77 vs.< 3 months) ; inpatient in a hospital with 400 or more beds (RR, 1.24);inpatient in a critical care unit (RR ,1.96 vs. with all other units);i npatient for > 2 weeks at the time of the survey (RR, 26.09 vs. with patients in the hospital for 3 days or fewer).

Pathogens were reported for 372 of the 504 HAIs. *Clostridium difficile* was the most common pathogen, accounting for 12% of all HAIs that were identified. *Staphylococcus aureus* was the second most common pathogen (11%; about half of these cases were methicillin-resistant *S. aureus*), followed by *Klebsiella pneumoniae* and *Klebsiella oxytoca* (10%).

Dr. Magill acknowledged certain limitations of the survey, including the fact that a small number of patients surveyed in each hospital "make results of limited use to individual facilities," she said. " This survey method provides a single snapshot of HAIs based on a retrospective review of medical record data, which are sometimes not complete. ■

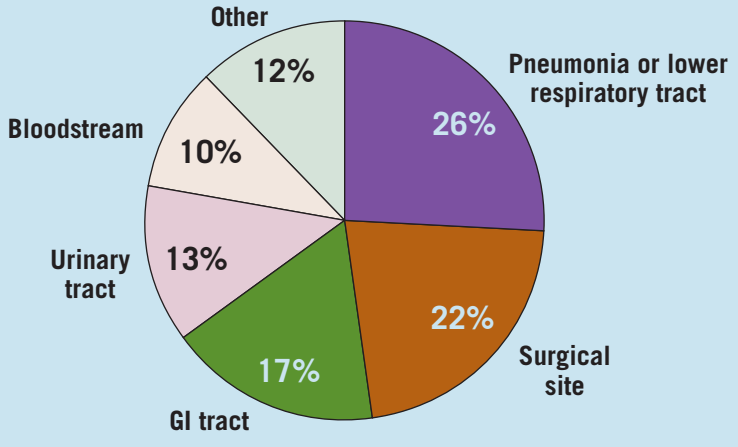
VITALS

Major Finding: The overall prevalence of health care–associated infections among hospitalized patients nationwide was 4%.

Data Source: Preliminary results were obtained from a 2011 survey of 11,282 inpatients at 183 hospitals located in 10 states.

Disclosures: The study was conducted by the CDC. Dr. Magill said she had no relevant financial conflicts to disclose.

Location of Health Care–Associated Infections



Note: Based on data for 504 infections in 452 patients.
Source: Dr. Magill

IMNG MEDICAL MEDIA

Perceived Dyspnea May Affect COPD Outcomes

BY SHARON WORCESTER
IMNG Medical News

ATLANTA – The perception of dyspnea among patients with chronic obstructive pulmonary disorder plays a bigger role in quality of life, functional status, and depression than do objective measures of disease severity, according to findings from cross-sectional study involving 158 patients.

The findings suggest that assessing and addressing dyspnea in COPD patients could play an important role in improving quality of life outcomes, Dr. Sandra Adams reported at the annual meeting of the American College of Chest Physicians.

The patients included in this analysis are part of the CASCADE study, a 2-year longitudinal observational study of genes and depression in COPD. They completed spirometry, the modified Medical Research Council (mMRC) dyspnea scale, questions related to exacerbation risk within the last year, the Chronic Respiratory Questionnaire (CRQ), a nine-item depression interview, the Personal Health Questionnaire (PHQ-9), and a 6-minute walk test at baseline.

Study participants had a mean age of about 67 years, about 25% were women, 40% were on supplemental oxygen, and the mean forced expiratory volume in 1 second (FEV_1) percent predicted was 43%. Exacerbations were self-reported.

More than 60% had a self-reported physician diagnosis of depression.

About 20% of the patients were found to be grade A patients, based on the revised Global Initiative for Chronic Obstructive Lung Disease (GOLD) released in December 2011, about 10% were grade B patients, about 20% were grade C patients, and about 50% were grade D patients, said Dr. Adams of the University of Texas Health Science Center, San Antonio.

Patients with grade A disease have mild disease severity, airflow limitation, and few exacerbations; those with grade B disease are similar to those with grade A, except they have more symptoms (in this study, the grade B patients had no exacerbations).

Those who have grade C disease experience minimal symptoms, severe airflow limitation, and/or two or more exacerbations each year; those with grade D disease are similar to those with grade C disease, except they have more symptoms.

"One thing we were actually really surprised to find is that the group of A and C with minimal symptoms may be a lot more similar than we think, whereas D and B with the severe symptoms – even though they have significant differences in exacerbations and/or airflow limitation, may be very similar," she said.

Indeed, no differences on the various measures used in this study were seen between the A and C patients, and between the B and D patients. But when the A and C patients were combined and compared with the combined group of B and D patients, significant differences emerged for every measure.

"Again, the big difference is symptoms; A and C have minimal symptoms and B and D have severe symptoms," Dr. Adams said.

As it turned out, grades A and C patients had significantly higher CRQ scores (higher scores are better) than did grades B and D patients (mean of 105 and 98 for A and C vs. 80 and 84 for B and D, respectively). Grades A and C also had statistically and clinically significantly greater 6-minute walk test distances, Dr. Adams noted.

On a physical function measure of steps walked in a day, the A and C patients averaged 7,900, and the B and D patients averaged only 4,800, she added.

That's 3,900 fewer steps despite inclusion of B-group patient (10% of the total study population) in the B/D combined group, Dr. Adams noted.

"Again … grade B had relatively normal lung function and no exacerbations, but yet they're severely dyspneic," she noted.

As for depression, the history was similar across all grades, although more grade B and D patients than A and C patients had PHQ-9 scores of 10 or greater, which indicates significant depression. On linear regression, an mMRC dyspnea scale score of 2 or higher was associated with a significant increase in depression (odds ratio, 2.8).

"So the bottom line to this is grades A and C have similar levels of depression, quality of life, physical function, and physical activity despite significant differences in FEV_1 percent predicted and and/or the number of exacerbations, Dr. Adams said, explaining that it appears that the perception of dyspnea is the main factor associated with these outcomes.

"And, in fact, those who report severe dyspnea may be even more limited than those with frequent exacerbations," she said.

What are the clinical implications of the findings?

"We ask our patients, 'How are you doing? How is your shortness of breath?' but actually getting an assessment and also trying to really address the dyspnea in addition to the exacerbations is going to be really key in this population," Dr. Adams concluded. ■

COPD Severity Criteria

Grade	Patient Description
A	Mild disease severity, airflow limitation, and few exacerbations.
B	Similar to grade A, but with more symptoms.
C	Minimal symptoms, severe airflow limitation, and/or two or more exacerbations each year.
D	Similar to grade C, but with more symptoms.

Source: Global Initiative for Chronic Obstructive Lung Disease

IMNG Medical Media

VITALS

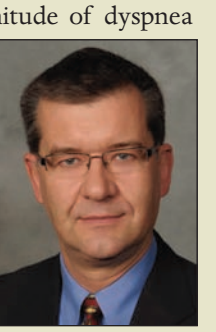
Major Finding: The patients with more perceived dyspnea had poorer outcomes on measures of quality of life, functional status, and depression.

Data Source: Results were taken from a cross-sectional study of 158 patients from the CASCADE trial.

Disclosures: Dr. Adams disclosed that she has received grant money for research from the Chest Foundation, the NIH, the Veterans Affairs Cooperative Studies Program, Bayer, Boehringer Ingelheim, Centocor, GlaxoSmithKline, Novartis, Pfizer, and Schering-Plough. She also has received honoraria for speaking from ABCam, Altana, AstraZeneca, Aventis, Bayer, Boehringer Ingelheim, GSK, Novartis Pharmaceuticals, AG, Mycomed, Pfizer, and Schering-Plough.

COMMENTARY

Dr. Darcy D. Marciniuk, FCCP, comments: The magnitude of dyspnea symptoms that were experienced by COPD patients correlated with reduced activity (assessed by the 6MWT) and increased depression (assessed by the PHQ-9 depression scale).



Although it may be a misnomer to state that patients with reductions in lung function of up 50% have 'relatively normal lung function' (GOLD A and B), it has become clear that impaired lung function by itself does not completely describe the patient experience in COPD. The results of this study highlight the importance of a multi-modality assessment of COPD patients and the varying clinical phenotypes in this very complex disease.

Stereotactic Radiation Boosts Lung Cancer Survival

BY NEIL OSTERWEIL
IMNG Medical News

BOSTON – Delivering stereotactic body radiation for early-stage, inoperable non–small cell lung cancer doubled overall survival rates achieved in historical series with conventional radiation, investigators reported at the annual meeting of the American Society for Radiation Oncology.

The 3-year overall survival rate reached 59.9% for 100 patients whose stage IA non–small cell lung cancer (NSCLC) was treated with stereotactic body radiation therapy (SBRT), said Dr. Yasushi Nagata. He compared results of the nonrandomized phase II trial with 31%-39% in historical series with conventional radiation.

Stereotactic body radiation should replace conventional radiotherapy for early inoperable lung cancer.

DR. NAGATA

The 5-year overall survival rate was 40.8%, compared with 13%-22.2% historically, added Dr. Nagata from Hiroshima University, Japan.

He described SBRT as well tolerated with only mild toxicities, making it a suitable alternative to other therapies, particularly in older patients. "Patients with early inoperable lung cancer should consider this treatment," Dr. Nagata advised in a briefing.

The investigators concluded that the treatment should be the new standard, replacing conventional radiotherapy in this population.

Similar in concept to stereotactic radiosurgery with a cyberknife, SBRT is a technique for precise high-dose targeting of tissues from multiple angles and planes, allowing delivery of much larger doses by fraction than conformal 3-dimensional or intensity-modulated radiation therapy. With SBRT, radiation therapy sessions can often be compressed into as little as 4-6 fractions delivered over 2 to 2.5 weeks, compared with 8 to 9 weeks of daily fractions for other techniques.

The phase II Japanese Clinical Oncology Group trial, JCOG-0403, is said to be the first to evaluate SBRT in both operable and nonoperable NSCLC. At the 2010 ASTRO annual meeting, the investigators reported 3-year survival rates for 64 patients with surgically resectable NSCLC: overall survival was 76%; progression-free survival, 54.5%; local progression-free survival, 68.5%; and event-free survival, 51.4%.

In the current study, 77 men and 27 women with a median age of 78 years (range 59-90 years) were enrolled; four patients were later excluded from the study, three because they developed a second primary cancer within 5 years of registration, and one was "unexpectedly" treated with SBRT and chemotherapy.

The median tumor size was 21 mm (range 9-30 mm). Fifty patients had adenocarcinomas, 40 had squamous cell carcinomas, and 14 had other tumor histologies. All patients had histologically or cytologically proven NSCLC, clinical T1N0M0 disease, and were determined by thoracic surgeons to be inoperable.

All patients completed the treatment protocol, consisting of a dose of 48 Gy at the isocenter divided into 4 fractions over 4-8 days.

The progression-free survival rate at 3 years was 49.8%; the local progression-free survival rate was 52.8%, and event-free survival, 46.8%.

Grade 3 adverse events include dyspnea in 10 patients, hypoxia in 8, pneumonitis in 7, chest pain in 2 and cough in 1. There was one case each of grade 4 dyspnea and hypoxia, but no treatment-related deaths. ■

VITALS

Major Finding: The 3-year overall survival rate for 100 patients with stage IA NSCLC treated with stereotactic body radiation therapy was 59.9%, compared with 31%-39% for conventional radiation.

Data Source: This was a nonrandomized phase II trial.

Disclosures: The study was supported by Japan's Ministry of Health. Dr. Nagata and Dr. Chang disclosed no relevant conflicts of interest.

New SARS-Like Virus Seen in Pneumonia Patient

BY HEIDI SPLETE
IMNG Medical News

A novel coronavirus has been identified in a 60-year-old man with acute pneumonia who died of progressive respiratory and renal failure 11 days after hospital admission, according to a report in the New England Journal of Medicine.

The virus, known as HCoV-EMC, is a previously unknown betacoronavirus species. The closest known relatives are two bat coronaviruses: HKU4 and HKU5.

"The clinical picture was remarkably similar to that of the severe acute respiratory distress syndrome [SARS] outbreak in 2003 and reminds us that animal coronaviruses can cause severe disease in humans," said lead author Dr. Ali Moh Zaki of the Dr. Soliman Fakeeh Hospital in Jeddah, Saudi Arabia, and his colleagues.

The patient was a 60-year-old Saudi man who first presented with a 7-day history of fever, cough, expectoration, and shortness of breath, the researchers said (N. Engl. J. Med. 2012 [doi:10.1056/NEJMoa211721]). He had no history of heart or kidney disease, did not smoke, and took no medications chronically.

The researchers tested a sputum sample when the patient was admitted to the hospital, and the results suggested that the virus was replicating. Tests of infected cell cultures with indirect immunofluorescence assays were negative for likely viruses including influenza A and B, respiratory syncytial virus, adenovirus, and parainfluenza viruses types 1-3. But serum samples collected at 10 and 11 days after the patient was hospitalized "reacted strongly when dilutions of 1:20 were tested on immunofluorescence assay specific for IgG antibodies," the researchers noted. By contrast, 2,400 control samples from other patients at the same hospital between 2010 and 2012 were negative, suggesting that the patient had developed antibodies to a previously unknown virus.

Genetic sequencing of the new virus linked it to a *Betacoronavirus* genus and set it apart from known human coronaviruses, which belong to the *Alphacoronavirus* genus, the researchers explained.

At the time of hospital admission, the patient's body mass index was 35 kg/m^2, his blood pressure was 140/80 mm Hg, his pulse was 117 beats per minute, and his temperature was 38.3 C. The patient was initially treated with oseltamivir, levofloxacin, piperacillin-tazobactam, and micafungin; meropenem was started on day 4.

"No symptoms were observed in the hospital among doctors and nurses caring for the patient, which suggests that the

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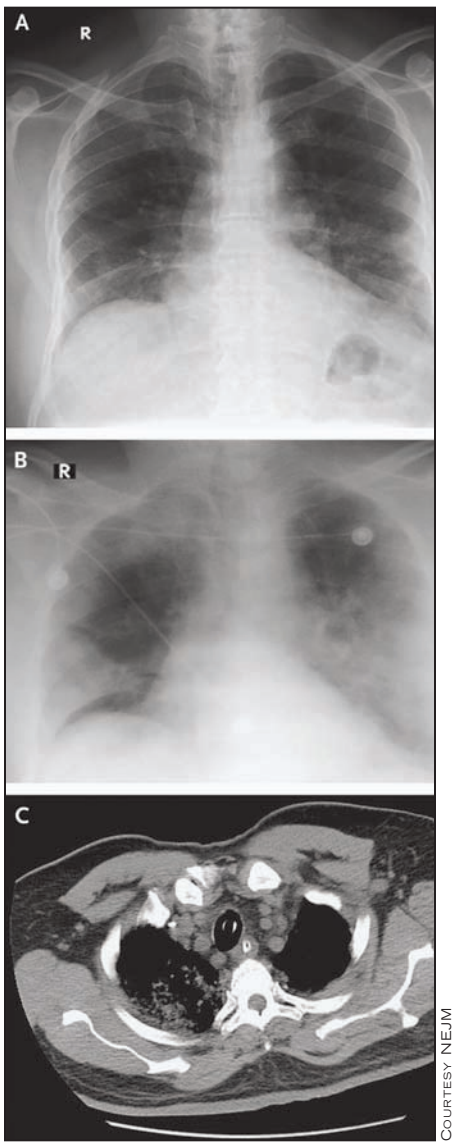


COURTESY NEJM

Chest radiographs show the pulmonary involvement at admission (top) and 2 days later (middle). A CT scan taken on day 4 shows extensive involvement.

Continued from previous page

disease did not spread readily," the researchers said. However, the more thorough epidemiologic investigations can be conducted with the completion of the genomic sequencing of HCoV-EMC and the development of virus-specific rapid diagnostic tests, they added.

The Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota reported on the gene sequencing and testing methods used to identify the virus, and on the status of a second infected patient – a 49-year-old man from Qatar – who presented with similar symptoms and was last reported to be in stable condition.

"Although HCoV-EMC does not have many of the worrisome characteristics of SARS-CoV, we should take notice of the valuable lessons learned during the 2003 SARS outbreak with respect to outbreak investigations and management," the researchers said.

The study was supported in part by the European Commission Seventh Framework Program for Research and Technology Development Project EMPERIE.

Lead author Dr. Zaki had no financial conflicts to disclose. Several of the study coauthors have financial interest in Viroclinics Biosciences B.V. through a holding company administered by Erasmus Medical Center in Rotterdam, the Netherlands. Viroclinics and Erasmus Medical Center have jointly filed a patent on the new virus genome. ■

COMMENTARY

Dr. Marcos I. Restrepo, FCCP, comments: Clinicians, laboratory specialists, and epidemiologists should remain vigilant for unusual, atypical, and aggressive presentations of common conditions. It is our responsibility to alert the appropriate agencies to timely assess the risk of emergent pathogens that may have important implications in developing outbreaks and cause significant morbidity, mortality, and cost.

IGRA Tests Top Skin Pricks for TB Screening

SAN FRANCISCO – Interferon-gamma release assay tests appear to be better than tuberculin skin tests for picking up latent TB in solid organ transplant candidates, according to Dr. Shimon Kusne.

It's not just because of IGRA's well-known benefits; as a blood test, results are known after one visit so patients don't need to return for skin spots to be read, and there are no false positives in patients vaccinated against TB or exposed to environmental strains of mycobacterium.

Instead, IGRA tests simply seem to be better at picking up latent TB, Dr. Kusne, professor of medicine in the division of infectious diseases at the Mayo Clinic Hospital in Phoenix, said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

He and his colleagues gave 179 kidney, liver, or heart transplant candidates TB skin prick tests and two IGRA tests, the QuantiFERON-TB Gold In-Tube test (QFT-GIT) and the T-Spot test.

QFT-GIT was 2.74 times more likely to be positive than tuberculin purified protein derivative skin tests and T-Spots were 3.10 times more likely to be positive. The findings were statistically significant.

IGRA tests appear to be a fine-toothed comb; positive tests might turn negative the second time around in a small minority of patients. What that means, exactly, still needs to be worked out (Chest 2012;142:55-62). For now, the Centers for Disease Control and Prevention is okay with hospitals checking for latent TB with either IGRA or skin tests in most cases, he said.

Even so, the Mayo Clinic has moved away from skin tests in transplant candidates. "I think mainly it's because CDC has said it's okay to use either and because many [patients] come to get their [skin test] and then disappear," Dr. Kusne said.

"But cost is always a consideration, too. It's very cheap" to do a skin test, he said at the meeting, sponsored by the American Society for Microbiology.

Dr. Kusne said he had no relevant financial disclosures.

–By M. Alexamder Otto

Riociguat Promising for PAH

PAH • *from page 1*

cally significant reduction of 432 ng/L in the serum biomarker, he said.

The findings suggest that riociguat – the first of the new sGC-stimulator class of drugs – represents a new treatment option for patients with PAH.

Riociguat has a dual mode of action, as it synergizes with endogenous nitric oxide and directly stimulates sGC independent of nitric oxide availability. Therefore, it may restore the NO-sGC-cGMP pathway, Dr. Ghofrani explained.

ROBUST IMPROVEMENTS WERE SEEN ON SEVERAL SECONDARY END POINTS, INCLUDING PULMONARY VASCULAR RESISTANCE.

"I think it is well appreciated that, despite the major achievement over the past 2 decades in the field of the treatment of PAH, there is still a high mortality in this devastating progressive disease, which welcomes this representative of a new class of drug to the therapeutic armamentarium of this very special disease form," he said, noting that study of riociguat is ongoing.

Patients who participated in the multicenter, multinational PATENT-1 study (Pulmonary Arterial Hypertension sGC-Stimulator Trial) were adults aged 18-80 years (with an average of about 50 years), including both treatment naive patients and patients pretreated with endothelin receptor antagonists or prostanoids. They were randomized to receive placebo or treatment with riociguat at a starting dose of 1 mg three times daily titrated over 8 weeks in 0.5-mg increments up to 2.5 mg three times daily.

The completion rate among participants was high, at about 93% for the treatment group and 88% for the placebo group, with 90% in the treatment group achieving the maximum dose, which reflected the tolerability of the drug, Dr. Ghofrani said.

The drug was also safe, with only 1.2% of patients experiencing an adverse event, although it is important to note that the observation period was relatively short, he added.

The 10 most frequently reported treatment-emergent adverse events occurring more often in the treatment group were headache, dyspepsia, peripheral edema, nausea, dizziness, diarrhea, nasopharyngitis, dyspnea, cough, and vomiting, explained Dr. Ghofrani.

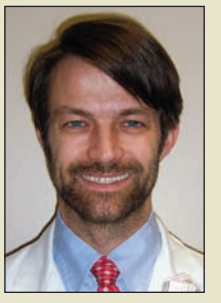
When combined with phase II study data, PATENT-1 now has 5 years of follow-up, and it appears that the treatment effect is preserved for up to 12 months. Those who completed phase III had the option of continuing in an open-label phase, and results from that study are expected to be reported next year.

Additionally, riociguat was found in the phase III CHEST-1 study to improve 6-minute walk distance in patients with inoperable chronic thromboembolic pulmonary hypertension. Thus, riociguat appears to be the first-ever drug to demonstrate robust efficacy in two distinct pulmonary hypertension groups, Dr. Ghofrani said.

The PATENT and CHEST studies are supported by Bayer, the maker of riociguat.

Dr. Ghofrani disclosed that he has received sponsored grants over the past 3 years from the German Research Foundation, Excellence Cluster Cardiopulmonary Research, and the Germany Ministry for Education and Research. He has also received industry-sponsored grants over the last 3 years from Bayer HealthCare AG, Aires, Encysive/Pfizer, and Novartis, and has received payment for consulting and serving on speaker bureaus and/or advisory committees for Bayer HealthCare AG, Actelion, Encysive, Pfizer, Ergonex, Novartis, and Glaxo-SmithKline. ■

COMMENTARY



Dr. Joseph Barney, FCCP, comments: I think the developments with riociguat as a first-in-class drug with early evidence of clinical effectiveness in treating CTEPH and improving dyspnea are very significant for the community of specialists who treat or diagnose pulmonary hypertension. While excitement must be married to caution in this early development, one could imagine that further investigation into treatment of pulmonary hypertension in the myriad of diseases that lead to it could mean improvement in quality of life and more breath for those patients. Here we see not only improved clinical data but also biological improvements in biomarkers associated with right heart strain and poor hemodynamics and a very reasonable side effect profile. All reasons for excitement on this molecule advancing to larger trials and hopefully a clinical indication for treatment.

CHEST-1 Study: Riociguat Shows Efficacy in CTEPH

BY SHARON WORCESTER
IMNG Medical News

ATLANTA – Riociguat, a novel first-in-class soluble guanylate cyclase stimulator, significantly improved 6-minute walk distance in patients with inoperable chronic thromboembolic pulmonary hypertension in the randomized, placebo-controlled phase III CHEST-1 study.

The overall 46-m improvement in 6-minute walk distance at 16 weeks in the study population was largely attributable to improvements in the 173 patients randomized to receive riociguat treatment, as opposed to fleeting improvements in 88 patients who received placebo, Dr. Hossein A. Ghofrani reported at the annual meeting of the American College of Chest Physicians.

The improvement in the treatment group was progressive and had not reached a plateau at 16 weeks after treatment initiation. Meanwhile, an initial improvement in the placebo group was followed by a constant decline in the placebo group, said Dr. Ghofrani, who is with University Hospital Giessen and Marburg in Germany.

Treatment with riociguat also was associated with consistent, significant improvements in a number of secondary end points, including change in pulmonary vascular resistance (PVR), change in World Health Organization functional class, time to clinical worsening, change in Borg dyspnea score, and quality of life assessments, he said.

Hemodynamics were robustly improved, he added, noting that treatment was associated with a 32% reduction in PVR, which translated into a highly significant 246-dyne reduction.

Patients enrolled in the multicenter CHEST-1 study – the largest placebo-controlled study to date of chronic thromboembolic pulmonary hypertension (CTEPH), for which there are currently no approved medical treatments – were aged 18-80 years with either inoperable disease or persistent or recurrent pulmonary hypertension after pulmonary endarterectomy. They had a mean PVR of greater than 480 dyn.s/cm^5.

VITALS

Major Finding: An overall 46-m improvement in 6-minute walk distance at 16 weeks in the study population was largely attributable to improvements in the 173 patients randomized to receive riociguat treatment, as opposed to fleeting improvements in 88 patients who received placebo.

Data Source: Data are from the randomized, controlled, phase III CHEST-1 study.

Disclosures: The PATENT and CHEST studies are supported by Bayer, the maker of riociguat. Dr. Ghofrani disclosed that he has received grants from the German Research Foundation, Excellence Cluster Cardiopulmonary Research, and German Ministry for Education and Research; and from Bayer HealthCare, Aires, and other companies. He also has received payment for consulting and serving on speakers bureaus or advisory committees of several pharmaceutical companies.

Treatment with riociguat was initiated at an oral dose of 1 mg three times daily titrated up to a maximum of 2.5 mg three times daily as tolerated according to systolic blood pressure; 90% achieved the highest dose, attesting to the tolerability of the drug, Dr. Ghofrani said.

In fact, the adverse event rate was very low, and side effects were similar to those seen in the PATENT-1 study of riociguat for pulmonary arterial hypertension (PAH), which also was reported at the meeting.

These included headache, dizziness, peripheral edema (which occurred more often in the placebo group), cough, dyspnea, nasopharyngitis, nausea, diarrhea, and vomiting.

The findings are encouraging given the lack of medical treatments for CETPH patients who either are ineligible for surgical treatment or have persistent pulmonary hypertension after surgery, Dr. Ghofrani said at the meeting.

The study of riociguat for CETPH is ongoing. CHEST-1 completers were allowed to enroll in a long-term extension study (CHEST-2), and results of that study will be reported next year, Dr. Ghofrani said.

As for how it is that a single molecule appears to have efficacy for two distinct pulmonary hypertension subgroups (PAH and CETPH), which are believed to have differing pathophysiological mechanisms, he explained that the disease might have some "common denominators."

"After a certain level of severity, they have a lot of commonalities, and the progressive component, for instance for pulmonary vascular remodeling beyond a certain point of no return, becomes very much alike in the different disease entities. The lack of the endogenous [nitric oxide] signaling pathway has been proven for many of these diseases. … I think there may be a common denominator for the disease, even if the underlying pathophysiology may be different," he explained.

This is not to say riociguat is a "magic bullet" for all pulmonary hypertension subgroups, he added.

The drug's efficacy "has to be proven in each single indication with a proper randomized controlled trial," he said.

In addition to the PATENT-1 and CHEST-1 studies showing efficacy in PAH and CETPH, respectively, studies of other pulmonary hypertension disease subgroups are underway, including one involving patients with left heart systolic disorders and PAH; phase II data from that study will be presented at an upcoming meeting of the American Heart Association, he said. ■

COPD Tool Rings True on Community Hospital Level

BY SHARON WORCESTER
IMNG Medical News

ATLANTA – The BAP-65 score – a clinical scale developed to predict the need for mechanical ventilation and inpatient mortality in acute exacerbation of chronic obstructive pulmonary disorder – was nearly as strong a predictor of mortality in a single community hospital–based study as in the much larger original multicenter score validation study.

The score, which is calculated by giving one point each for elevated blood urea nitrogen (BUN) of more than 25 mg/dL; altered mental status; pulse more than 109 beats/min; and age over 65, also predicted the need for mechanical ventilation in this study, but not as precisely as in the original study, Dr. Rameet Thapa reported at the annual meeting of the American College of Chest Physicians.

In the first validation study of nearly 35,000 patients admitted for acute exacerbation of COPD, mortality increased with increasing BAP-65 score, ranging from less than 1% in those with a score of 0, to more than 25% in those meeting all BAP-65 criteria. Similarly, mechanical ventilation was needed in about 2% of those with a score of 0 and in 55% of those with the highest score (Chest 2011;140:1177-83).

'THE BAP-65 SCORE IS VERY SIMPLE AND USEFUL IN INITIAL TRIAGE ASSESSMENT, AND IT GIVES A GENERAL IDEA ABOUT MORTALITY IN PATIENTS.'

The area under the receiver operating curve (AUROC) for mortality and/or the need for mechanical ventilation in that study was 0.79.

In the current study, a review of 1,984 patients with acute exacerbation of COPD who were discharged over a period of 6 years from Greater Baltimore Medical Center, the mortality rate was 1.4% for those with lower scores, and 12.2% for those with higher scores; the AUROC was 0.69 for mortality, 0.62 for predicting the need for mechanical ventilation, and 0.65 for the combined outcome, he said. Dr. Thapa is a third-year resident at the center.

The AUROC for mortality was similar to that in the initial study, but the AUROC for predicting the need for mechanical ventilation was lower than the 0.77 for that measure in the initial study. The combined AUROC for both mechanical ventilation and mortality was also lower than the 0.79 for that measure in the initial study, he said.

Patients in the study were mean age 74.5 years and had been admitted to either an intensive care unit or a medical floor at the hospital between October 2005 and September 2011 with an acute exacerbation of COPD diagnosis. Less than a third (29%) were men. Other than the single-center design and smaller sample size, this study differs from the first in that many patients were discharged to hospice care closely affiliated with the hospital, and outcomes in these patients were included in the analysis.

Hospice referral is an increasingly common practice and one that is therefore important to consider in this context, Dr. Thapa noted.

Although the results of this community hospital setting were not as striking as those in the larger study, they nonetheless suggest that BAP-65 would be of value for risk stratification and appropriate allocation of resources for patients with acute exacerbation of COPD if it were incorporated into clinical practice, he said."We still think the BAP-65 score is very simple and useful in initial triage assessment, and it gives a general idea about mortality in patients," he concluded. ■

VITALS

Major Finding: The mortality rate was 1.4% for those with lower scores, and 12.2% for those with higher scores. The AUROC was 0.69 for mortality, 0.62 for predicting the need for mechanical ventilation, and 0.65 for the combined outcome.

Data Source: This was a retrospective analysis of patient data.

Disclosures: Dr. Thapa reported having no disclosures.

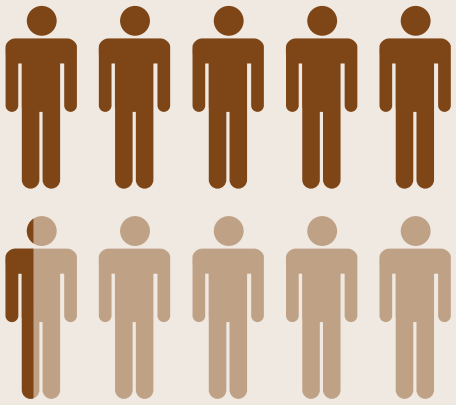
THORACIC ONCOLOGY UPDATE:

Molecular Biomarker Testing Is Essential for Non-Small Cell Lung Cancer Patients

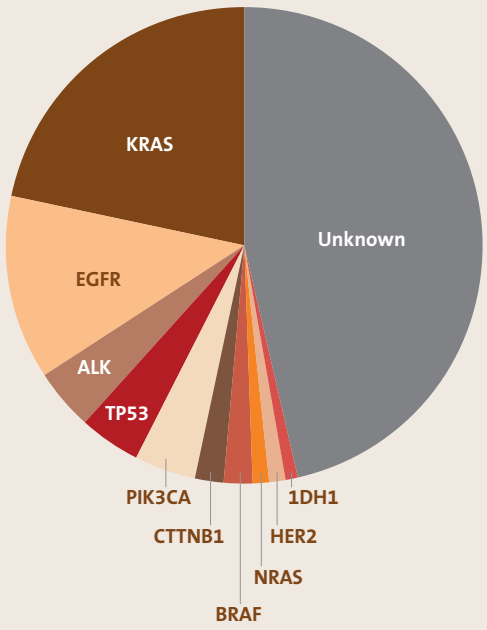
During the past decade the identification of molecular biomarkers for clinically relevant mutations or other genetic abnormalities in non-small cell lung cancer (NSCLC) has improved the understanding of lung cancer pathogenesis, and of the proliferation and survival of cancer cells.[1] This significant development is setting the stage for a paradigm shift toward the adoption of treatments directed to the particular genetic makeup of the tumor.[1,2]

Over 50% of NSCLC Cases Are Linked to Known Molecular Biomarkers

According to recent studies, more than 50% of NSCLC cases are linked to one of at least 10 currently known biomarkers for NSCLC — and many of these patients may test positive for mutations or other genetic abnormalities that are "drivers" for their cancers and are treatable with approved biomarker-driven therapies or investigational agents in clinical trials.[2,3]



At Least 10 Known Molecular Biomarkers in NSCLC[3]



Now that more than half of NSCLC cases can be linked to one or more of these biomarkers, it is possible to subdivide the histological subtypes of NSCLC — adenocarcinoma, squamous cell carcinoma, and large cell carcinoma — into clinically relevant molecular subsets.[1]

These molecular subsets show the considerable heterogeneity of non-small cell tumors and suggest why patients with similar clinical stage and tumor histology can have dramatically different clinical outcomes.[4]

Indeed, biomarkers may give clinicians an indication of the patient's prognosis (outcome independent of treatment), as well as the treatment sensitivity/resistance of the tumor to specific agents.[4,5]

Moreover, as genomic and mutational research continues, more biomarkers will inevitably be discovered, so that the proportion of NSCLC cases with unknown drivers will continue its decline. The ultimate goal of this approach to treatment is to identify every driver mutation for non-small cell lung cancer, and design a corresponding treatment for each of these oncogenes.[1,2,4]

New Diagnostic Paradigm: Histology + Molecular Profile

Recently it has been proposed that lung cancer treatment be based on the histology of the tumor. But there is a growing consensus that molecular profiling — testing the tumor at biopsy for all appropriate biomarkers — should be part of the clinician's standard approach to pathologic evaluation.[1,2] And this is supported by the National Comprehensive Cancer Network (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for all non-squamous non-small cell lung cancer (NSCLC) histologies, which state[5]:

> **"Determination of the specific molecular abnormalities of the tumor is critical for predicting sensitivity or resistance to a growing number of targeted therapies."**
>
> *– NCCN Guidelines® Version 3.2012, for Non-Small Cell Lung Cancer* [5]

The NCCN® recommends EGFR and ALK testing for all advanced non-squamous NSCLC, in order to guide treatment decisions.[5] Multiplex molecular profiling assays may make the prospective genotyping of tumors possible, to aid clinical decision making and management.[1]

For patients whose tumors test positive for a biomarker that is treatable with approved or investigational agents, the benefits of testing are self-evident.[1,5,6]

But in the future, molecular profiling will help an increasing proportion of patients with NSCLC because the additional information it reveals about their tumor has the potential to guide clinical management.[2,7]

Molecular Profiling Is Key in NSCLC

The discovery of biomarkers has demonstrated the molecular complexity of NSCLC, and it highlights the need to move toward molecularly based classification and treatment of these tumors.[1,4] But only if patients are tested is it possible for them to potentially benefit from these developments.

As additional mutations are discovered through efforts such as the National Cancer Institute's Lung Cancer Mutation Consortium (LCMC) and the Cancer Genome Atlas — and as new agents are developed to address these abnormalities — the hope for the over 215,000 people diagnosed with lung cancer each year is that these advances will lead to more treatment options.[1,8-10] In the words of Dr. David Gandara, Director of Thoracic Oncology at UC Davis Comprehensive Cancer Center, "Our goal is to learn the 'molecular fingerprint' of each person's lung cancer, and to personalize their therapy based on this information. The discoveries that could make this possible are being made at a rapid pace."

CURBSIDE CONSULT

David R. Gandara, MD
Director, Thoracic Oncology Program, UC Davis Comprehensive Cancer Center

What is the most significant development you've seen in the treatment of lung cancer today?

DG Knowing what is driving the cancer! We have recently been using histology to treat cancer based on the appearance of the cells. But cells that look identical under the microscope can have dramatically different clinical outcomes because of what is driving them at the molecular level. And *that* is leading us to molecularly based treatment options.

Can many NSCLC patients benefit from this testing? Who should be tested?

DG When you consider both approved and investigational agents, yes, a considerable proportion of NSCLC patients can receive therapy based on molecular testing. But at present I believe that all patients with NSCLC of the adenocarcinoma subtype should be tested.

That seems like a lot of testing. Wouldn't that require a re-biopsy for many patients?

DG These tests do require adequate tumor tissue. Some patients will need to be re-biopsied — some for lack of sample tissue, but also to look for changes that have occurred over time and as a result of therapy. Other patients may not have to be re-biopsied. To do the testing that reveals the "molecular fingerprint" of each person's lung cancer, we have to get sufficient tumor tissue at biopsy.

Visit www.lungcancerprofiles.com for the patient perspective on molecular profiling.

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Printed in USA/September 2012 CRI433117-04

Lung-Volume Reduction Coils Boost Walk Distance

Positive safety profile seen in minimally invasive option for severe emphysema patients.

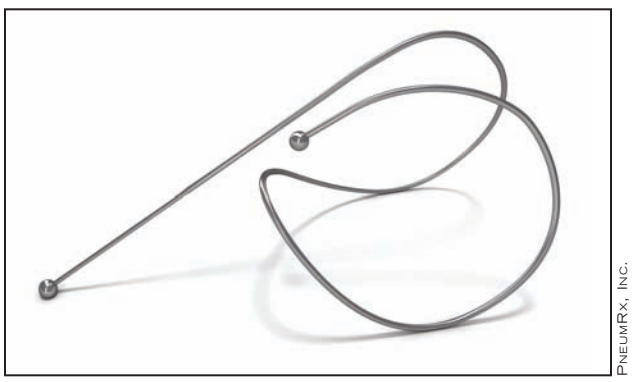
BY SHARON WORCESTER
IMNG Medical News

ATLANTA – The implantation of nitinol coils that grab and compress diseased lung tissue, thereby allowing for better functioning of healthy tissue, significantly improved quality of life, exercise capacity, and pulmonary lung function in a randomized controlled trial of patients with severe emphysema and hyperinflation.

Specifically, use of the investigational, self-actuating implantable devices in the RESET (Randomized Controlled Trial of RePneu Endobronchial Coils for the Treatment of Severe Emphysema With Hyperinflation) study was associated with a significantly improved mean St. George's Respiratory Questionnaire score at 90 days after the final treatment in 23 patients who received active treatment, compared with 24 controls who received best medical care.

After adjustment for baseline variables, the between-group difference in the scores was 8.35 points in favor of the treatment group, Dr. Zaid Zoumot reported at the annual meeting of the American College of Chest Physicians.

The lung-volume reduction coils also were associated with significant improvements in mean 6-minute walk distance (mean between-group difference of 63.5 m in favor of the treatment group) and forced expiratory volume in 1 second (FEV_1, mean between-group difference of 12% in favor of the treatment group), said Dr. Zoumot of Royal Brompton and Harefield Hospital Trust, London. The between-group difference in change in mean residual volume did not reach statistical significance, despite a 0.64-L reduction in the treatment group compared with the control group, he noted.



PNEUMRX, INC.

The RePneu coil was associated with a significantly improved mean St. George's Respiratory Questionnaire score at 90 days.

RESET participants were adults with severe emphysema and hyperinflation with significant dyspnea and gas trapping who were screened at three participating centers in the United Kingdom.

Those randomized to the treatment group initially underwent implantation of the coils in one lung, with treatment of the contralateral lung after 1 month if appropriate.

Treatment was generally safe and well tolerated; three patients in the treatment group had pneumothoraces, which were picked up on chest x-ray routinely performed 1 hour following the procedure and treated successfully, Dr. Zoumot said.

No differences in adverse effects occurred between the groups after the first month of follow-up, including in exacerbations of chronic obstructive pulmonary disorder, he added.

"The safety profile was definitely acceptable, and in fact, the procedures were a lot safer than other endobronchial lung-volume reduction devices at this same stage of development, and certainly a lot safer than lung-volume reduction surgery, which has a quite high morbidity and mortality rate," he said.

The findings are encouraging given the limited therapeutic options for patients with severe emphysema with gas trapping and hyperinflation – particularly those with heterogeneous disease, he said.

Drug therapy is typically of little benefit in these patients, and although lung-volume reduction surgery and endobronchial valve treatment can be helpful in some patients, their use is precluded in many patients, including those with heterogeneous disease in the absence of collateral ventilation, he explained.

The RePneu lung-volume reduction coils, however, provide a minimally invasive mechanical approach to lung-volume reduction that is effective in both homogeneous and heterogeneous emphysema, with benefits unaffected by collateral ventilation, he said. The coils, which are made entirely of nitinol – a highly biocompatible "shape memory" material used in numerous implantable devices – are deployed to the lung bronchoscopically using a proprietary delivery system. Initially, the coils are encased in a sheath to allow delivery in a straight configuration, but once they are in place, they return to their original coil configuration, gathering and compressing the diseased tissue as they recoil.

The goal is to implant 10 coils per lobe in a fanlike distribution, Dr. Zoumot said at the meeting. The procedure, which took about 45 minutes on average in this study, is typically performed under conscious sedation, he added.

Patients in the current study will be followed until 12 months after their final treatment, with results reported at both 6 and 12 months. A larger, multicenter randomized controlled trial with longer follow-up is also set to begin recruiting, Dr. Zoumot said. ■

VITALS

Major Finding: Implantation LVRC was associated with a mean between-group difference of 63.5 m in 6-minute walk distance and a mean between-group difference of 12% in FEV_1 in favor of the treatment group.

Data Source: This was a randomized controlled trial (RESET) of 23 patients who received active treatment and 24 controls who received best medical care.

Disclosures: This study was funded by PneumRx, the maker of the RePneu coils, and the study sites. Dr. Zoumot reported receiving grant funding and payment for travel expenses from PneumRx.

FDA: Bleeding Risk Similar With Dabigatran, Warfarin

BY ELIZABETH MECHCATIE
IMNG Medical News

The Food and Drug Administration is satisfied that dabigatran's bleeding risk is no greater than that of warfarin and will not change the drug's label.

The rates of gastrointestinal and intracranial bleeding among patients who have been prescribed the anticoagulant dabigatran "do not appear to be higher" than the rates among patients who have been prescribed warfarin, according to an analysis of insurance claims and administrative data conducted by the agency.

The results of this analysis, conducted in response to postmarketing reports of bleeding among people treated with dabigatran, are "consistent with observations" in the RE-LY trial, the study of 18,000 patients that was the basis of the approval of the anticoagulant for reducing the risk of stroke and blood clots in patients with nonvalvular atrial fibrillation (AF), the FDA said in a MedWatch safety alert. In the RE-LY study, the rates of serious bleeding was similar among those treated with dabigatran and those with warfarin (N. Engl. J. Med. 2009;361:1139-51).

The agency is evaluating different sources of data in its review of this safety issue, which is ongoing. Dabigatran, an orally administered direct thrombin inhibitor, was approved in October 2010 for reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation and is marketed as Pradaxa by Boehringer Ingelheim.

The FDA's analysis found that the rates of bleeding were actually higher among those on warfarin, although the statement does not point this out.

The FDA analyzed data from a database of nearly 100 million patients and determined that the combined incidence of intracranial and gastrointestinal hemorrhages per 100,000 days at risk was 1.8-2.6 times higher for new users of warfarin than for new users of dabigatran. When they analyzed the two events separately, they found that the incidence rate of gastrointestinal hemorrhage events per 100,000 days at risk was 1.6-2.2 times higher for new users of warfarin than for new users of dabigatran. The incidence rate of intracranial hemorrhage events per 100,000 days at risk was 2.1-3.0 times higher for new users of warfarin than for those on dabigatran.

CLINICIANS ARE ADVISED TO EVALUATE A PATIENT'S RENAL FUNCTION BEFORE PRESCRIBING DABIGATRAN, WHICH IS ELIMINATED BY THE KIDNEYS.

These estimates do not account for age, medical conditions, or other differences between the patients on warfarin and dabigatran that could affect bleeding outcomes, according to the FDA.

In addition, although a "large" number of reports of bleeding in treated patients were submitted to the FDA's Adverse Events Reporting System (FAERS) after dabigatran was approved, the agency believes that a "simple comparison" between the number of postmarketing bleeding events associated with dabigatran and warfarin is "misleading" because it is likely that bleeding events associated with warfarin are under reported. This is because the drug has been available for so long and bleeding is a well-recognized consequence of warfarin treatment, the agency noted.

At this time, the FDA is not changing any recommendations on the dabigatran label and is continuing to monitor postmarketing reports of bleeding in patients on dabigatran "for evidence of inappropriate dosing, use of interacting drugs, and other clinical factors that might lead to a bleeding event," according to the statement. The recommendations in the statement include advice to clinicians that they evaluate a patient's renal function before prescribing dabigatran, which is eliminated by the kidneys, and the dosing regimens for patients with severe renal impairment and those with a creatinine clearance above 30 mL/min. ■

The Medwatch safety alert, released Nov. 2, is available at fda.gov via http://tinyurl.com/bleedsFDA. Adverse events associated with dabigatran should be reported to the FDA at (800) 332-0178 or www.fda.gov/medwatch.

Surgical Risk Tool Useful Amid Limited Resources

Simple model can open door to analysis and quality improvement programs in smaller settings.

BY ELIZABETH MECHCATIE
IMNG Medical News

A risk-adjusted tool based on three preoperative variables from the National Surgical Quality Improvement Program had a high rate of efficacy in predicting inpatient mortality, which suggests it may be useful in resource-limited settings such as small rural hospitals or low- and middle-income countries.

"By offering a simplified risk-adjustment tool, we can compare surgical outcomes among hospitals on a global scale, regardless of the spectrum of surgical procedures offered or hospital resources," Jamie E. Anderson and associates in the department of surgery, University of California, San Diego, wrote in Archives of Surgery.

"Although participation in programs such as the NSQIP offers administrative support and comparison of outcomes among participating hospitals, the low-cost options reported can expand the number of hospitals that participate in risk-adjustment outcomes analysis and quality improvement programs," they added.

The American College of Surgeons' NSQIP risk-adjusted tool uses more than 130 variables plus a 30-day patient follow-up, and thus is not affordable for use in settings where resources are limited, including small, rural hospitals, the authors pointed out (Arch. Surg. 2012;147:798-803).

Using data from more than 600,000 patients in the 2005-2009 NSQIP database, they developed different models to predict inpatient mortality and validated the models based on data on 239 patients from a 110-bed hospital in California with a level IV trauma center. They calculated that the "area under the receiver operator characteristic curve (AUROC)" for each model as a measure of how well the model separated the two groups of interest (survivors vs. nonsurvivors) with a value of 1.0 (or 100%) would mean that the model was able to completely separate the two groups.

The model using three preoperative NSQIP variables – age, American Society of Anesthesiologists (ASA) physical status classification, and functional status – had AUROC values that were more than 0.90, or more than 90%, which was similar to the value achieved for the model that used four or six variables. The model that used 66 variables was about the same as the value achieved with the model that used 4 variables (about 91%).

Considering that an AUROC value of 0.5 indicates that the model cannot distinguish between two groups any better than chance and that an AUROC value of 1.0 indicates that the model completely discriminates between the two groups, the authors said that an AUROC value of greater than 90% is substantial. Therefore, based on their results, "3 or 4 variables may be sufficient for adequate risk adjustment to measure surgical outcomes," they added.

"Future risk-adjustment tools [should] be based on 6 or fewer variables to allow for surgical outcomes to be measured and compared within and among hospitals in resource-limited settings," they concluded.

The authors had no disclosures. ■

VITALS

Major Finding: A risk-adjusted tool using three preoperative variables from the National Surgical Quality Improvement Program (NSQIP) database was more than 90% effective at predicting inpatient mortality – an efficacy rate comparable with that of tools using many more variables.

Data Source: The study entailed developing the tool with a different number of variables from the NSQIP database between 2005 and 2009 to predict inpatient mortality and validating the tool using patient data from a 110-bed community hospital in California.

Disclosures: The authors reported having no conflicts.

COMMENTARY

Dr. Lary Robinson, FCCP, comments: The National Surgical Quality Improvement Program (NSQIP) was developed in the 1990's at the Veterans Administration hospitals and this program led to decreased surgical mortality and morbidity as well as increased patient satisfaction and decreased length of stays. The American College of Surgeons expanded the NSQIP to hundreds of participating hospitals and it has shown consistent benefits in reducing surgical complications, mortality, and costs.In an important study, Anderson and associates at the University of California, San Diego, carefully analyzed the NSQIP database for 2005-2009 and developed a simpler, risk-assessment tool, which they validated in small 110-bed hospital. They found that using just 3 variables (age, functional status, and ASA score) was nearly as predictive of surgical outcome as the 130-variable NSQIP tool.

They correctly concluded that this simpler tool would be much more widely applicable to limited-resource, smaller hospitals inside and outside of the United States, who want to improve surgical quality but cannot afford the more expensive NSQIP program."

Sternal SSIs Plummet With Preop Decolonization

BY DOUG BRUNK
IMNG Medical News

SAN DIEGO – Conducting preoperative nasal screening and decolonization of *Staphylococcus aureus* in patients undergoing cardiothoracic surgery led to a significant reduction in the rate of all sternal surgical site infections, including those attributable to S. *aureus*, results from a large single-center study showed.

"*Staphylococcus aureus* sternal surgical site infections [SSIs] are associated with significant morbidity and mortality," lead researcher Jennifer Madigan said in an interview following her presentation at IDWeek 2012, the combined annual meetings of the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the HIV Medicine Association, and the Pediatric Infectious Diseases Society. "Multiple studies in the past have shown that screening and decolonization of *S. aureus* carriers are associated with a reduction in sternal SSIs."

Sternal SSIs attributable to *S. aureus* dropped by 82% and *S. aureus* mediastinitis cases, by 87%, researcher Jennifer Madigan reported.

One recent intervention that identified *S. aureus* nasal carriers concluded that *S. aureus* SSIs can be reduced by rapid screening and decolonization of nares on hospital admission (N. Engl. J. Med. 2010;362:9-17), she reported.

"This study used [polymerase chain reaction testing] for identification of *S. aureus* nasal carriers, followed by treatment with mupirocin nasal ointment and chlorhexidine soap," said Ms. Madigan, an practicioner in the department of infection prevention and control at St. John Hospital and Medical Center, Detroit.

"The results showed more than a 50% reduction in *S. aureus* infections."

Ms. Madigan and her associates compared the SSI rates 57 months before and 24 months after initiation of an *S. aureus* decolonization program for cardiothoracic surgery patients.

For this program *S. aureus* nasal carriers were decolonized with mupirocin nasal ointment daily for 5 days and were asked to bathe with chlorhexidine gluconate rinse for 5 days immediately before surgery.

The researchers reported results from 580 patients who were screened from April 2010 through March 2012.

Of these patients, 118 (20%) tested positive for *S. aureus* colonization, including 34 (6%) who tested positive for methicillin-resistant *S. aureus*.

After the *S. aureus* decolonization program was initiated, the rate of postoperative sternal SSIs following coronary artery bypass grafting (CABG) decreased by 65% (from 76 infections per 1,416 cases before screening to 8 infections per 427 cases after screening; $P = .0019$), with a 75% drop in the number of mediastinitis cases (from 39 infections per 1,416 cases before screening to 3 infections per 427 cases after screening; $P = .0106$).

The researchers also found that sternal SSIs attributable to *S. aureus* dropped by 82% (from 39 infections per 1,416 cases before screening to 2 infections per 427 cases after screening; $P = .0044$), with *S. aureus* mediastinitis dropping by 87% (from 21 infections per 1,416 cases before screening to 1 infection per 427 cases after screening; $P = .0337$).

"We encourage hospitals that perform CABG surgeries to incorporate this [decolonization program] into their process," Ms. Madigan said.

"The program is associated with significant reductions in infection, morbidity, and mortality. It provides a great tool to reduce the risk of patient harm. In addition, this may have a positive financial impact on hospitals as mediastinitis is no longer a reimbursable condition." ■

VITALS

Major Finding: Following initiation of a preoperative *S. aureus* decolonization program, the rate of postoperative sternal SSIs following coronary artery bypass grafting dropped by 65%, and the rate of mediastinitis cases dropped by 75%.

Data Source: A single-center study of 580 cardiothoracic surgery patients who were screened from April 2010 through March 2012.

Disclosures: The researchers reported having no relevant financial conflicts.

For twice-daily maintenance treatment of COPD

With **the right fit**, they may get back into **daily living**

Not an actual patient.

The BROVANA® (arformoterol tartrate) basics

Nebulized long-acting beta$_2$-agonist

BROVANA (arformoterol tartrate) should not be used with other medications containing long-acting beta$_2$-agonists.

12-hour bronchodilation, few daily troughs[1]

While some tolerance to the bronchodilator effect was observed after 6 weeks of dosing (at the end of the dosing interval), it was not accompanied by other clinical manifestations of tolerance.[1,2]

Requires low peak inspiratory flow rate

As with other inhaled beta$_2$-agonists, BROVANA can produce paradoxical bronchospasm that may be life-threatening.

Minimal coordination or dexterity required

Covered under Medicare Part B*

To learn more, please visit us at www.brovana.com/CP

*No guarantee of coverage.

INDICATION

BROVANA is indicated for the long term, twice daily (morning and evening) maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. BROVANA is for use by nebulization only.

IMPORTANT SAFETY INFORMATION

WARNING: ASTHMA-RELATED DEATH

Long-acting beta$_2$-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 beta$_2$-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 arformoterol, the active ingredient in BROVANA (see WARNINGS). The safety and efficacy of BROVANA in patients with asthma have not been established. All LABA, including BROVANA, are contraindicated in patients with asthma without use of a long-term asthma control medication (see CONTRAINDICATIONS).

Please see the Brief Summary of Prescribing Information on the following pages for additional Important Safety Information.

Please visit **www.brovana.com** for full Prescribing Information.

References: 1. Baumgartner RA, Hanania NA, Calhoun WJ, Sahn SA, Sciarappa K, Hanrahan JP. Nebulized arformoterol in patients with COPD: a 12-week, multicenter, randomized, double-blind, double-dummy, placebo- and active-controlled trial. *Clin Ther*. 2007;29(2):261-278. **2.** BROVANA [prescribing information]. Marlborough, MA: Sunovion Pharmaceuticals Inc; 2012.

Twice-Daily
Brovana® 15 mcg
(arformoterol tartrate) Inhalation Solution

Get them back into daily living

BROVANA® (arformoterol tartrate) Inhalation Solution 15 mcg*/2 mL

*potency expressed as arformoterol

FOR ORAL INHALATION ONLY

BRIEF SUMMARY

WARNING: ASTHMA RELATED DEATH

Long-acting beta$_2$-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 beta$_2$-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 arformoterol, the active ingredient in BROVANA (see WARNINGS). The safety and efficacy of BROVANA in patients with asthma have not been established. All LABA, including BROVANA, are contraindicated in patients with asthma without use of a long-term asthma control medication (see CONTRAINDICATIONS).

INDICATIONS AND USAGE

BROVANA (arformoterol tartrate) Inhalation Solution is indicated for the long-term, twice daily (morning and evening) maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. BROVANA is for use by nebulization only.

CONTRAINDICATIONS

BROVANA (arformoterol tartrate) Inhalation Solution is contraindicated in patients with a history of hypersensitivity to arformoterol, racemic formoterol or to any other components of this product.

All LABA, including BROVANA, are contraindicated in patients with asthma without use of a long-term asthma control medication. (see **WARNINGS**).

WARNINGS

- **ASTHMA RELATED DEATH**
  Long-acting beta$_2$-adrenergic agonists may increase the risk of asthma-related death. The safety and efficacy of BROVANA in patients with asthma have not been established. All LABA, including BROVANA, are contraindicated in patients with asthma without use of a long-term asthma control medication (see CONTRAINDICATIONS).
  - A 28-week, placebo-controlled US study comparing the safety of salmeterol with placebo, each added to usual asthma therapy, showed an increase in asthma-related deaths in patients receiving salmeterol (13/13, 176 in patients treated with salmeterol vs. 3/13, 179 in patients treated with placebo; RR 4.37, 95% CI 1.25, 15.34). The increased risk of asthma-related death may represent a class effect of the long-acting beta$_2$-adrenergic agonists, including BROVANA. No study adequate to determine whether the rate of asthma related death is increased in patients treated with BROVANA has been conducted.
  - Clinical studies with racemic formoterol (Foradil® Aerolizer™) suggested a higher incidence of serious asthma exacerbations in patients who received racemic formoterol than in those who received placebo. The sizes of these studies were not adequate to precisely quantify the differences in serious asthma exacerbation rates between treatment groups.
- **The studies described above enrolled patients with asthma. Data are not available to determine whether the rate of death in patients with COPD is increased by long-acting beta$_2$-adrenergic agonists.**
- **BROVANA is indicated for the long term, twice daily (morning and evening) maintenance treatment for bronchoconstriction in chronic obstructive pulmonary disease (COPD), and is not indicated for the treatment of acute episodes of bronchospasm, i.e., rescue therapy.**
- **BROVANA should not be initiated in patients with acutely deteriorating COPD, which may be a life-threatening condition. The use of BROVANA in this setting is inappropriate.**
- **BROVANA should not be used in children as the safety and efficacy of BROVANA have not been established in pediatric patients.**
- **BROVANA should not be used in conjunction with other inhaled, long-acting beta$_2$-agonists. BROVANA should not be used with other medications containing long-acting beta$_2$-agonists.**
- **When beginning treatment with BROVANA, patients who have been taking inhaled, short-acting beta$_2$-agonists on a regular basis (e.g., four times a day) should be instructed to discontinue the regular use of these drugs and use them only for symptomatic relief of acute respiratory symptoms.**
- **See PRECAUTIONS and Information for Patients.**

Paradoxical Bronchospasm

As with other inhaled beta$_2$-agonists, BROVANA can produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, BROVANA should be discontinued immediately and alternative therapy instituted.

Deterioration of Disease

COPD may deteriorate acutely over a period of hours or chronically over several days or longer. If BROVANA no longer controls the symptoms of bronchoconstriction, or the patient's inhaled, short-acting beta$_2$-agonist becomes less effective or the patient needs more inhalation of short-acting beta$_2$-agonist than usual, these may be markers of deterioration of disease. In this setting, a re-evaluation of the patient and the COPD treatment regimen should be undertaken at once. Increasing the daily dosage of BROVANA beyond the recommended 15 mcg twice daily dose is not appropriate in this situation.

Cardiovascular Effects

BROVANA, like other beta$_2$-agonists, can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms. Although such effects are uncommon after administration of BROVANA at the recommended dose, if they occur, the drug may need to be discontinued. In addition, beta-agonists have been reported to produce ECG changes, such as flattening of the T wave, prolongation of the QT_c interval, and ST segment depression. The clinical significance of these findings is unknown. BROVANA, as with other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension (see **PRECAUTIONS, General**).

Immediate Hypersensitivity Reactions

Immediate hypersensitivity reactions may occur after administration of BROVANA as demonstrated by cases of anaphylactic reaction, urticaria, angioedema, rash and bronchospasm.

Do Not Exceed Recommended Dose

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. As with other inhaled beta$_2$-adrenergic drugs, BROVANA should not be used more often, at higher doses than recommended, or with other long-acting beta-agonists.

PRECAUTIONS

General

BROVANA (arformoterol tartrate) Inhalation Solution should not be used to treat acute symptoms of COPD. BROVANA has not been studied in the relief of acute symptoms and extra doses should not be used for that purpose. When prescribing BROVANA, the physician should also provide the patient with an inhaled, short-acting beta$_2$-agonist for treatment of COPD symptoms that occur acutely, despite regular twice-daily (morning and evening) use of BROVANA. Patients should also be cautioned that increasing inhaled beta$_2$-agonist use is a signal of deteriorating disease for which prompt medical attention is indicated (see **Information for Patients**).

BROVANA, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension; in patients with convulsive disorders or thyrotoxicosis; and in patients who are unusually responsive to sympathomimetic amines. Clinically significant changes in systolic and/or diastolic blood pressure, pulse rate and electrocardiograms have been seen infrequently in individual patients in controlled clinical studies with arformoterol tartrate. Doses of the related beta$_2$-agonist albuterol, when administered intravenously, have been reported to aggravate preexisting diabetes mellitus and ketoacidosis.

Beta-agonist medications may produce significant hypokalemia in some patients, possibly though intracellular shunting, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation.

Clinically significant changes in blood glucose and/or serum potassium were infrequent during clinical studies with long-term administration of BROVANA at the recommended dose.

Information for Patients

Patients should be instructed to read the accompanying Medication Guide with each new prescription and refill. Patients should be given the following information:

1. Patients should be informed that long-acting beta$_2$-adrenergic agonists, such as BROVANA, increase the risk of asthma-related death. All LABA, including BROVANA, are contraindicated in patients with asthma without use of a long-term asthma control medication (see **CONTRAINDICATIONS**).
2. BROVANA is not indicated to relieve acute respiratory symptoms and extra doses should not be used for that purpose. Acute symptoms should be treated with an inhaled, short-acting, beta$_2$-agonist (the health-care provider should prescribe the patient with such medication and instruct the patient in how it should be used). Patients should be instructed to seek medical attention if their symptoms worsen, if BROVANA treatment becomes less effective, or if they need more inhalations of a short-acting beta$_2$-agonist than usual. Patients should not inhale more than one dose at any one time. The daily dosage of BROVANA should not exceed one ready-to-use vial (15 mcg) by inhalation twice daily (30 mcg total daily dose).
3. Patients should be informed that treatment with beta$_2$-agonists may lead to adverse events which include palpitations, chest pain, rapid heart rate, tremor, or nervousness.
4. Patients should be instructed to use BROVANA by nebulizer only and not to inject or swallow this inhalation solution.
5. Patients should protect BROVANA ready-to-use vials from light and excessive heat. The protective foil pouches should be stored under refrigeration between 2ºC and 8ºC (36º–46ºF). They should not be used after the expiration date stamped on the container. After opening the pouch, unused ready-to-use vials should be returned to, and stored in, the pouch. An opened ready-to-use vial should be used right away. Discard any ready-to-use vial if the solution is not colorless.
6. The drug compatibility (physical and chemical), efficacy and safety of BROVANA when mixed with other drugs in a nebulizer have not been established.
7. Women should be advised to contact their physician if they become pregnant or if they are nursing.
8. It is important that patients understand how to use BROVANA appropriately and how it should be used in relation to other medications to treat COPD they are taking.

Drug Interactions

If additional adrenergic drugs are to be administered by any route, they should be used with caution because the pharmacologically predictable sympathetic effects of BROVANA may be potentiated.

When paroxetine, a potent inhibitor of CYP2D6, was co-administered with BROVANA at steady-state, exposure to either drug was not altered. Dosage adjustments of BROVANA are not necessary when the drug is given concomitantly with potent CYP2D6 inhibitors.

Concomitant treatment with methylxanthines (aminophylline, theophylline), steroids, or diuretics may potentiate any hypokalemic effect of adrenergic agonists.

The ECG changes and/or hypokalemia that may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded. Although the clinical significance of these effects is not known, caution is advised in the co-administration of beta-agonists with non-potassium sparing diuretics.

BROVANA, as with other beta$_2$-agonists, should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QT_c interval because the action of adrenergic agonists on the cardiovascular system may be potentiated by these agents. Drugs that are known to prolong the QT_c interval have an increased risk of ventricular arrhythmias. The concurrent use of intravenously or orally administered methylxanthines (e.g., aminophylline, theophylline) by patients receiving BROVANA has not been completely evaluated. In two combined 12-week placebo controlled trials that included BROVANA doses of 15 mcg twice daily, 25 mcg twice daily, and 50 mcg once daily, 54 of 873 BROVANA-treated subjects received concomitant theophylline at study entry. In a 12-month controlled trial that included a 50 mcg once daily BROVANA dose, 30 of the 528 BROVANA-treated subjects received concomitant theophylline at study entry. In these trials, heart rate and systolic blood pressure were approximately 2-3 bpm and 6-8 mm Hg higher, respectively, in subjects on concomitant theophylline compared with the overall population.

Beta-adrenergic receptor antagonists (beta-blockers) and BROVANA may interfere with the effect of each other when administered concurrently. Beta-blockers not only block the therapeutic effects of beta-agonists, but may produce severe bronchospasm in COPD patients. Therefore, patients with COPD should not normally be treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-blockers in patients with COPD. In this setting, cardioselective beta-blockers could be considered, although they should be administered with caution.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies were conducted in mice using oral administration and rats using inhalation administration to evaluate the carcinogenic potential of arformoterol.

In a 24-month carcinogenicity study in CD-1 mice, arformoterol caused a dose-related increase in the incidence of uterine and cervical endometrial stromal polyps and stromal cell sarcoma in female mice at oral doses of 1 mg/kg and above (AUC exposure approximately 70 times adult exposure at the maximum recommended daily inhalation dose).

In a 24-month carcinogenicity study in Sprague-Dawley rats, arformoterol caused a statistically significant increase in the incidence of thyroid gland c-cell adenoma and carcinoma in female rats at an inhalation dose of 200 mcg/kg (AUC exposure approximately 130 times adult exposure at the maximum recommended daily inhalation dose). There were no tumor findings with an inhalation dose of 40 mcg/kg (AUC exposure approximately 55 times adult exposure at the maximum recommended daily inhalation dose).

Arformoterol was not mutagenic or clastogenic in the following tests: mutagenicity tests in bacteria, chromosome aberration analyses in mammalian cells, and micronucleus test in mice.

Arformoterol had no effects on fertility and reproductive performance in rats at oral doses up to 10 mg/kg (approximately 2700 times the maximum recommended daily inhalation dose in adults on a mg/m^2 basis).

Pregnancy: Teratogenic Effects

Pregnancy Category C

Arformoterol has been shown to be teratogenic in rats based upon findings of omphalocele (umbilical hernia), a malformation, at oral doses of 1 mg/kg and above (AUC exposure approximately 370 times adult exposure at the maximum recommended daily inhalation dose). Increased pup loss at birth and during lactation and decreased pup weights were observed in rats at oral doses of 5 mg/kg and above (AUC exposure approximately 1100 times adult exposure at the maximum recommended daily inhalation dose). Delays in development were evident with an oral dose of 10 mg/kg (AUC exposure approximately 2400 times adult exposure at the maximum recommended daily inhalation dose).

Arformoterol has been shown to be teratogenic in rabbits based upon findings of malpositioned right kidney, a malformation, at oral doses of 20 mg/kg and above (AUC exposure approximately 8400 times adult exposure at the maximum recommended daily inhalation dose). Malformations including brachydactyly, bulbous aorta, and liver cysts were observed at doses of 40 mg/kg and above (approximately 22,000 times the maximum recommended daily inhalation dose in adults on a mg/m^2 basis).

There are no adequate and well-controlled studies in pregnant women. BROVANA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Use in Labor and Delivery

There are no human studies that have investigated the effects of BROVANA on preterm labor or labor at term. Because beta-agonists may potentially interfere with uterine contractility, BROVANA should be used during labor and delivery only if the potential benefit justifies the potential risk.

Nursing Mothers

In reproductive studies in rats, arformoterol was excreted in the milk. It is not known whether arformoterol is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when BROVANA is administered to a nursing woman.

Pediatric

BROVANA is approved for use in the long term maintenance treatment of bronchoconstriction associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema. This disease does not occur in children. The safety and effectiveness of BROVANA in pediatric patients have not been established.

Geriatric

Of the 873 patients who received BROVANA in two placebo-controlled clinical studies in adults with COPD, 391 (45%) were 65 years of age or older while 96 (11%) were 75 years of age or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Among subjects age 65 years and older, 129 (33%) received BROVANA at the recommended dose of 15 mcg twice daily, while the remainder received higher doses. ECG alerts for ventricular ectopy in patients 65 to ≤75 years of age were comparable among patients receiving 15 mcg twice daily, 25 mcg twice daily, and placebo (3.9%, 5.2%, and 7.1%, respectively).

A higher frequency (12.4%) was observed when BROVANA was dosed at 50 mcg once daily. The clinical significance of this finding is not known. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Experience in Adult Patients with COPD

Of the 1,456 COPD patients in the two 12-week, placebo-controlled trials, 288 were treated with BROVANA (arformoterol tartrate) Inhalation Solution 15 mcg twice daily and 293 were treated with placebo. Doses of 25 mcg twice daily and 50 mcg once daily were also evaluated. The numbers and percent of patients who reported adverse events were comparable in the 15 mcg twice daily and placebo groups.

The following table shows adverse events where the frequency was greater than or equal to 2% in the BROVANA 15 mcg twice daily group and where the rates of adverse events in the BROVANA 15 mcg twice daily group exceeded placebo. Ten adverse events demonstrated a dose relationship: asthenia, fever, bronchitis, COPD, headache, vomiting, hyperkalemia, leukocytosis, nervousness, and tremor.

COMMENTARY

Surgical Intensivists: Their Patients' Keepers

"Is he dying?" Reluctantly, we turned away from the patient in the ICU bed in front of us to gaze at the face of one of his daughters, who stared back intently. For 2 weeks, our team had been caring for her father in the surgical ICU. After having undergone a massive liver resection for cholangiocarcinoma, he had since suffered many complications and was now anuric and encephalopathic. Without hemodialysis, he would further deteriorate and likely die.

It was clear that the patient's two daughters were growing frustrated and angry. When the future had seemed much rosier, their father and his surgeon had made decisions involving goals of care, but now the patient was in no frame of mind to contribute to such a discussion.

Regrettably, this is a scenario that the surgical intensivist frequently encounters. Surgeons and their teams frequently make early morning rounds before families arrive at the hospital, and then are unavailable because they are operating. Thus, the SICU team members who see the patients in consultation and rounds later in the day become the names and faces familiar to the family. And this often leaves intensivists in the uncomfortable position of answering families' and patients' questions after an unexpected or poor outcome has occurred.

When we did not respond, the daughter commented, "I think we should stop; this isn't what my dad would want."

CAROLYN PINKERTON, M.D.,

KAREN BRASEL, M.D., MPH, FACS

When confronted with such a situation, what is the role of the intensivist? Although the primary team is not always available for these seemingly impromptu discussions, to bypass them completely in the communication process is both unprofessional and counterproductive. In addition, the family may not want to break the bond or covenant with the primary surgeon; deviating from the agreed-upon preoperative goals may leave the family feeling that they have let the surgeon down by "giving up."

This scenario may help explain why these conversations often occur first with the SICU team, even as the primary surgical team continues to have daily conversations with the family. On the other hand, as intensivists, we are the trustees of our ICU patients and families, sharing a bond with them simply by virtue of the fact that we are present. To ignore this and not advocate for our patients, taking the stance of "We are only consultants," betrays their trust. But how can we achieve this goal while keeping all parties invested yet still satisfied with our care?

Rather than seeing this situation as a pitfall, perhaps we should view it as an opportunity. In a climate in which health care costs are being scrutinized by a federal microscope and medical malpractice suits seem entrenched in our culture, an opportunity to have good communication while upholding those ethical ideals of autonomy, beneficence, and justice is a true gift.

In the case of this patient, all that was needed was a phone call to the patient's surgical attending, to candidly communicate the necessity of his presence for a meeting with the family. The attending, unaware of the family's feelings, was thankful for the call. Fortunately, the meeting resulted in an appreciative family and a patient who was transferred to the palliative care floor where he subsequently lived out his days in comfort and dignity.

The key to our success was not waiting until it was too late to begin these conversations. By anticipating the need for a plan in a proactive way, intensivists can serve not only their patients but also their surgical colleagues, making things easier when eventually the time for action arrives.

To borrow from a Biblical proverb, intensivists are their patients' keepers, not just their consultants. By the same token, we are the keepers of our surgical colleagues, leaving them to operate on others with the knowledge and confidence that their ICU patients are safe in our hands. ■

DR. PINKERTON *and* DR. BRASEL *are with the department of surgery, division of trauma/critical care, at the Medical College of Wisconsin in Milwaukee.*

Update Ahead for Surviving Sepsis Guidelines

Revisers say dopamine gets the boot, fluid choice is in flux, first-hour antibiotics are key.

BY BRUCE JANCIN
IMNG Medical News

DENVER – Look for some big changes ahead in the forthcoming update of the Surviving Sepsis Campaign international guidelines.

In the 4 years since the last version of the guidelines came out, major studies have been released that resolved hot debates regarding sepsis management and in some cases overturned established dogma. At the annual American College of Emergency Physicians (ACEP) meeting, emergency physicians deeply involved in crafting the Surviving Sepsis Campaign 2012 guidelines provided a preview of what's to come.

Among the areas that will see key new recommendations are antibiotic therapy, fluid resuscitation, vasopressors, and lactate monitoring.

'At this time, we're thinking stay away from low-molecular-weight starches for resuscitation.'

DR. OSBORN

► **Antibiotics ASAP.** The critical importance of getting empiric antibiotics on board within 6 hours after recognizing that a patient has sepsis has been effectively hammered home over the years. But how fast is fast enough? Several recent small studies have reached conflicting conclusions. Now, however, an 800-lb gorilla of a study has provided a definitive answer.

This study, now in press, involved 14,895 patients enrolled in the Surviving Sepsis Campaign's worldwide database. All had severe sepsis or septic shock, and all received antibiotics within the first 6 hours, explained Dr. Tiffany M. Osborn, a coauthor of the study and of the forthcoming guidelines.

"This was a big question for us. The results strengthen the importance of getting antibiotics started as soon as possible – within the first hour if possible. We found there's about a 4% increase in mortality for every hour delay. And it's cumulative: it's 4% after the first hour, 8% after the second, 12% after the third, and so on," according to Dr. Osborn of Washington University at St. Louis.

A similar time-dependent increase in mortality was observed in patients with severe sepsis as well as in those in septic shock, she added.

► **Fluid resuscitation.** The initial fluid of choice for resuscitation in severe sepsis and septic shock remains crystalloids, as before. That's a grade 1A recommendation. What's brand new is a recommendation to consider adding albumin in the initial fluid resuscitation (grade 2B). This guidance was heavily influenced by a meta-analysis of 17 studies involving close to 2,000 patients that demonstrated a significant protective effect for the use of albumin as an initial resuscitation fluid (Crit. Care Med. 2011;39:386-91).

At this late date, Dr. Osborn said, the guideline panel is strongly leaning toward a recommendation against the use of low-molecular-weight colloids or starches such as hydroxyethyl starch 130/0.42. That would be ground shaking, as synthetic colloids or starches, particularly those of low molecular weight, are a very popular resuscitation fluid both in the United States and abroad. However, recent studies implicate these fluids in increased risks of 90-day mortality and renal failure, compared with the use of Ringer's lactate.

"Having said this, there are two other trials currently pending. Any month now the results will come out, and we'll see where we are at that point. But at this time, we're thinking stay away from low-molecular-weight starches for resuscitation," Dr. Osborn said.

One of the main reasons the Surviving Sepsis Campaign 2012 guidelines won't actually be published before January 2013 is the guideline panel's eagerness to see the results of those two studies, she added.

► **Vasopressor therapy.** The initial target remains, as before, a mean arterial pressure of at least 65 mm Hg. But while the 2008 guidelines recommended either norepinephrine or dopamine as the first-choice vasopressor to correct hypotension in patients not sufficiently responsive to fluid resuscitation, the new guidelines will state that norepinephrine is the preferred agent (grade 1B). That's a major change. Dopamine has been essentially kicked to the curb in response to multiple studies in the last 4 years implicating it in an increased incidence of arrhythmias and, in some studies, higher mortality.

'By far and away, I'm going to choose norepinephrine as the initial vasopressor agent.'

DR. WINTERS

The final nail in dopamine's coffin for use in patients with severe sepsis or septic shock was a recent meta-analysis involving five observational and six interventional studies totaling nearly 2,800 patients (Crit. Care Med. 2012;40:725-30).

"Dopamine has actually fallen by the wayside. By far and away, I'm going to choose norepinephrine as the initial vasopressor agent," declared Dr. Michael E. Winters of the University of Maryland, Baltimore.

The new guidelines will suggest that

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Fluid: "We want to give patients what they need but not more," Dr. Tiffany M. Osborn said.

be reserved for highly selected patients: those at very low arrhythmia risk and with a low cardiac output and/or low heart rate (grade 2C), he noted.

Another change in the new guidelines will be a recommendation that epinephrine be added when an additional agent is needed in order to maintain adequate blood pressure (grade 2B).

► **Don't overdo the fluids.** "We want to give patients what they need but not more," Dr. Osborn explained. The 2012 guidelines will recommend that physicians use some sort of fluid challenge test while administering fluid boluses. The goal is to keep giving fluid only so long as hemodynamic improvement is seen in response. This can be achieved in a variety of ways, including monitoring change in pulse pressure, stroke volume variation, heart rate, or arterial pressure.

► **Lactate clearance.** Serum lactate is recognized as an indicator of global organ hypoperfusion and shock. But incorporating lactate clearance as one of the goals of early sepsis therapy has been "a very hot topic," Dr. Winters observed.

Improved clarity was provided by a prospective 556-patient quality improvement study by investigators in the Asian Network to Regulate Sepsis Care. Patients who got the primary severe sepsis management bundle of care as recommended in the 2008 Surviving Sepsis Campaign guidelines had an unadjusted mortality of 43.6%. This bundle includes early antibiotic administration, hemodynamic monitoring and support, and achievement of a central venous oxygen saturation level greater than 70% by 6 hours. However, patients who got the bundle plus lactate clearance had a 20.5% mortality rate (Crit. Care 2011;15:R229 [doi:10.1186/cc10469]).

The importance of lactate clearance was further underscored by the findings in the GENESIS Project (Generalized Early Sepsis Intervention Strategies). This quality improvement initiative, conducted at five U.S. community hospitals and six tertiary centers, showed a 42.8% mortality in 1,554 historical controls treated for sepsis before implementation of the Surviving Sepsis Campaign resuscitation bundle. In another 4,801 patients who got the bundle, mortality was significantly lower at 28.8%. And, in those who received the bundle plus lactate clearance, mortality further fell to about 22% (J. Intensive Care Med. 2012 [doi:10.1177/0885066612453025]).

Thus, the coming Surviving Sepsis Campaign 2012 guidelines will suggest that in patients with elevated lactate levels as a marker of hypoperfusion, resuscitation should be targeted at normalizing lactate as rapidly as possible (grade 2C). Having said that, however, a normal lactate doesn't indicate absence of shock. Other factors, such as the patient's central venous oxygen saturation level, need to be considered as well, the physicians emphasized.

The Surviving Sepsis Campaign guidelines are sponsored by 27 medical organizations. Among them are the Society of Critical Care Medicine, ACEP, the Society of Hospital Medicine, the American College of Chest Physicians, the American Thoracic Society, the Infectious Diseases Society of America, the Surgical Infection Society, the Pediatric Acute Lung Injury and Sepsis Investigators, and a host of international groups.

Dr. Osborn and Dr. Winter reported having no financial conflicts. ■

COMMENTARY

Dr. Vera De Palo, FCCP, comments: Evidence has shown us that implementing the right care at the right time can alter outcome in severe sepsis and septic shock. When knowledge base builds because of additional study results, it is important to reexamine previously disseminated guidelines and update them with the strategies supported by the most recent, best evidence. As these advances are more broadly included in protocols for the treatment of the patient with severe sepsis and septic shock, it is hoped that the survival rates from these life-threatening entities will further improve.

Carotid Intima Media Is Thicker in Young Smokers

The Swiss study is the first to show the impact of smoking on the arterial walls of adolescents.

BY NASEEM S. MILLER
IMNG Medical News

MUNICH – Smoking in young people can induce structural changes to the arterial wall and possibly lead to the development of atherosclerosis before adulthood, according to a Swiss study.

Ultrasound analysis of the common carotid artery of adolescents who actively smoked showed that their intima media was as much as 0.03 mm thicker than those of youth who didn't smoke, researchers reported at the annual congress of the European Society of Cardiology.

While the preliminary findings may not dissuade adolescents from smoking, they highlight the need for prevention efforts, such as implementing smoking bans in cities and states, said study investigator Dr. Julia Dratva, a research fellow at the Swiss Tropical and Public Health Institute, Basel.

Previous studies have established the negative health effects of tobacco exposure in adolescents, but the Swiss study is one of the first to show the impact of smoking on the arterial walls of young people.

"What the study does is make it clear that the vascular wall starts falling into pieces," in youth who smoke, session moderator Dr. Joep Perk said in an interview. "So you are starting on a path that your vascular wall is going to be eventually plugged," added Dr. Perk, professor of health sciences at Linnaeus University, Sweden.

Researchers recruited 279 subjects in the Swiss Study on Air Pollution and Lung and Heart Disease in Adults (SAPALDIA) Youth Study. Study participants were between ages 9 and 20. Their clinical examination included anthropometry, blood pressure measurement, ultrasound assessment of the carotid artery intima-media thickness, and blood tests for cardiovascular biomarkers.

Many of the study participants had cardiovascular disease risk factors that are known to continue into adulthood and are associated with increased atherosclerotic risk, the authors reported. Thirteen percent of the youth were overweight, 3% had elevated cholesterol, 5% had a hemoglobin A_{1c} level higher than 5.7%, and blood pressure was elevated in 7%.

Ten percent of the participants reported weekly smoking (at least one cigarette per week), and 14% reported smoking monthly. Very few reported daily smoking habits, said Dr. Dratva. Mean smoking duration was 2.3 years in ever-smokers. Exposure to passive smoke up to 10 years of age was reported by 31% and current parental smoking by 25%.

Results showed that smoking duration was positively associated with common carotid intima media thickness (0.014-mm increase/year). The carotid intima media was significantly thicker in youth who smoked weekly (0.03 mm) compared with those who didn't smoke.

The results remained consistent after adjustment for parental smoking. ■

VITALS

Major Finding: Common carotid intima-media thickness in adolescents who actively smoked was as much as 0.03 mm greater than in youth who didn't smoke.

Data Source: The SAPALDIA Youth Study is a nested study of 279 subjects between the ages of 9 and 20 years.

Disclosures: Dr. Dratva reported no financial conflicts.

VIEW VIDEO ONLINE

To view a video of Dr. Perk discussing his research, scan this QR code.

Most Readmissions Stem From Initial Surgeries

BY HEIDI SPLETE
IMNG Medical News

CHICAGO – A majority of unplanned 30-day readmissions of general surgery patients to a pediatric hospital resulted from the initial surgery or procedure for which the child was hospitalized, according to data on more than 300 patients.

Hospital readmission within 30 days has become an important quality measure, but data on the frequency and epidemiology of pediatric surgery readmissions are limited, said Dr. Andre Marshall of Vanderbilt University, Nashville, Tenn.

"In order to decrease readmissions, pediatric surgeons must know where to focus efforts," he said at the annual clinical congress of the American College of Surgeons.

To determine the proportion of readmissions associated with each surgical service, Dr. Marshall and his colleagues reviewed data from 12,438 surgical admissions at a single center between January 2007 and December 2010. Data were taken from the Pediatric Health Information System database and electronic medical records.

A 30-day readmission was defined as any readmission within 30 days of an index hospitalization.

Surgical services included general surgery, thoracic surgery, neurosurgery, cardiac surgery, orthopedics, otolaryngology, urologic surgery, ophthalmology, plastic surgery, and kidney and liver transplants.

In all, 1,178 patients were readmitted during the study period, for a readmission rate of 10%. Of these, 318 (27%) were general surgery readmissions. The next highest readmission rates by specialty were neurosurgery (26%), cardiac surgery (18%), and orthopedics (10%). The average age of the readmitted patients was 3 years, and 58% were male.

Of the 318 general surgery readmissions, 295 were unplanned, Dr. Marshall said. Of these, 174 (59%) were related to the index surgery or procedure, and 121 (41%) were related to a new illness, new trauma, or other reason not related to the initial procedure.

Among general surgery patients, infection complications were the most common reason for 30-day readmission (38%), followed by gastrointestinal issues (28%), respiratory complications (9%), planned readmissions (7%), and postoperative pain (5%).

The most common preoperative diagnoses associated with 30-day readmission were acute appendicitis (18%), congenital malformations (17%), and gastroesophageal reflux disease (14%).

"Improving processes to anticipate which patients and diagnoses are at the greatest risk of 30-day readmission will potentially allow for early interventions by providers," Dr. Marshall said.

Early intervention will allow clinicians to implement strategies to help reduce overall readmission rates and improve the quality of patient care, he added. ■

VITALS

Major Finding: More than half (59%) of 30-day readmissions for pediatric general surgery patients were related to their initial surgeries or procedures.

Data Source: The data come from 12,438 surgical admissions at a single center between January 2007 and December 2010.

Disclosures: Dr. Marshall said he had no relevant financial conflicts to disclose.

Sleep Loss Spurred Insulin Resistance in Fat Cells

BY MARY ANN MOON
IMNG Medical News

Sleep deprivation caused a 30% decline in the insulin sensitivity of fat cells of healthy, lean young adults, according to a study in Annals of Internal Medicine.

Restricting sleep for 4 nights markedly impaired the phosphorylation of Akt within the adipocytes in subcutaneous fat, which is a crucial early step in the pathway that mediates most of insulin's metabolic action. "This finding identifies for the first time a molecular mechanism that may be involved in the reduction in total-body insulin sensitivity consistently observed in multiple laboratory studies of partial sleep deprivation in healthy adults," said Josiane L. Broussard, Ph.D., and her associates at the University of Chicago.

Moreover, "our finding of marked alterations in adipocyte function after experimental sleep restriction challenges the widely held belief that the primary function of sleep is the restoration of central nervous system function and suggests that sleep may play an equally important role in peripheral energy metabolism," they noted.

Insufficient sleep is known to raise the risk of metabolic disturbances, particularly insulin resistance, obesity, and type 2 diabetes. But "to our knowledge, no studies to date have linked sleep restriction to alterations in molecular metabolic pathways in any peripheral human tissue." Dr. Broussard and her colleagues examined whether experimental sleep restriction would reduce insulin sensitivity in subcutaneous fat, "a peripheral tissue that is a key site of insulin action and plays a pivotal role in energy metabolism as well as in the communication of energy balance to the brain."

Six men and one woman aged 18-30 years (mean age 23.7 years) who were healthy and lean were selected from the community as study subjects. All reported routine sleep times of 7.5-8.5 hours/night. All underwent overnight polysomnography to ensure they had no sleep disorders, standard glucose tolerance testing to rule out any occult disorders of insulin metabolism, and standard laboratory tests to rule out any other problem that could affect either sleep or metabolism.

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A recent study showed that sleep deprivation caused a 30% decline in the insulin sensitivity of fat cells and a 16% decline in total-body insulin sensitivity.

These subjects were then assessed under two experimental sleep conditions in randomized order: after 4 consecutive nights of 8.5 hours of normal sleep and after 4 consecutive nights of 4.5 hours of restricted sleep. The subjects lived as sedentary inpatients during these experiments, with strictly controlled diets that were identical under the two sleep conditions.

At the conclusion of the sleep periods, abdominal subcutaneous fat tissue was sampled for in vitro measurement of phosphorylated Akt in response to increasing doses of insulin. Total body insulin sensitivity also was assessed using frequently sampled intravenous glucose tolerance tests.

The study subjects averaged 8.78 hours of sleep per night under the normal sleep condition and 4.35 hours under the restricted sleep condition. The amount of REM sleep was reduced by 56.8% in the latter condition.

After normal sleep, insulin provocation caused dose-dependent increases in phosphorylated Akt, as expected. In dramatic contrast, sleep restriction consistently induced an approximately 30% reduction in phosphorylated Akt in response to insulin provocation.

In addition, total-body insulin sensitivity was reduced by 16% after partial sleep deprivation, compared with normal sleep.

The 30% decline "lies within the range of the difference in insulin sensitivity in adipocytes from obese vs. lean participants and from diabetic patients vs. nondiabetic participants" in previous studies. "Thus, the impairment of insulin signalling in adipocytes from persons who are chronically sleep-deprived or have sleep disorders is likely to have important metabolic consequences," Dr. Broussard and her associates wrote (Ann. Intern. Med. 2012;157:549-57).

"From a clinical standpoint, our study provides additional evidence that insufficient sleep may contribute to the development of or exacerbate metabolic disorders." But the findings also "shed novel light on the still-elusive function of sleep, traditionally conceptualized as necessary only for the brain, because they suggest that sleep plays an important role for the functional integrity of multiple peripheral cell types, as well as for whole-body energy homeostasis," they said.

Dr. Broussard and her colleagues make a valuable contribution to our understanding of how sleep deprivation may directly contribute to diabetes and obesity, wrote Dr. Francesco P. Cappuccio and Dr. Michelle A. Miller, Ph.D., of the University of Warwick, Coventry, England, in an accompanying editorial (Ann. Intern. Med. 2012;157:593-4).

Their findings also challenge "the traditional view that the primary purpose of sleep is confined to restorative effects on the CNS. [They] point to a much wider influence of sleep on bodily functions, including metabolism, adipose tissue, cardiovascular function, and possibly more," they said. The results also highlight the need to address factors that limit sleep duration, as a strategy to improve the overall health of individuals as well as of society, they added.

This study was limited in that it was performed at a single center, involved a very small sample size, and involved only one woman. "The findings will therefore need to be replicated in a larger and more diverse population," the researchers added.

In addition, future studies are needed "to determine whether optimizing sleep duration may delay the development or reduce the severity of metabolic alterations in persons who are at increased risk for diabetes."

They reported having no relevant conflicts of interest. ■

COMMENTARY

Dr. Paul A. Selecky, FCCP, comments: "The relationship between sleep deprivation and health, particularly obesity, has been known for some time. It is exciting from this study to begin to understand the potential pathophysiology of sleep deprivaton on metabolic function."

Sleep Strategies

Restless Legs Syndrome: More Difficult Than It Seems

Restless legs syndrome (RLS) is a common disorder characterized by a nearly overpowering urge to move the legs. This sensation is often accompanied by uncomfortable paresthesias, which are occasionally painful, worsened by rest and temporarily relieved by movement of the legs. The pathogenesis of RLS is incompletely understood, but it is clear that dopamine metabolism, brain iron stores, and genetic factors are involved. The great majority of RLS patients also demonstrate periodic limb movements of sleep (PLMS) on polysomnography, though this finding is also commonly found in patients without RLS symptoms. While this review will focus on the treatment of symptomatic RLS, it should be noted that there is an ongoing debate regarding the appropriateness of treatment of PLMS in the presence of symptoms other than RLS (such as fatigue); this syndrome is known as periodic limb movement disorder (PLMD).

Treatment of RLS

There are four agents approved by the US Food and Drug Administration for the treatment of RLS: ropinirole, pramipexole, gabapentin enacarbil, and, most recently, rotigotine; the first three agents are orally administered, while the latter is delivered via a cutaneous patch. In October 2012, the American Academy of Sleep Medicine published an updated series of practice parameters for the treatment of RLS and PLMD based upon a systematic review of the literature (Aurora et al. *Sleep.* 2012;35[8]:1039, and Aurora et al. *Sleep.* 2012;35[8]:1037). Pramipexole and ropinirole were recommended for treatment of RLS as a standard based on a high level of evidence and an assessment that the benefits clearly outweighed potential harms. Gabapentin enacarbil and rotigotine were recommended at the lower "guideline" level, despite high-level evidence, because there was felt to be uncertainty regarding the balance between benefit and harm. Other agents recommended at the guideline level included opioids and levodopa coadministered with a dopa decarboxylase inhibitor. Gabapentin, pregabalin, carbamazepine, and clonidine were recommended as a lower-level option because of only lesser supportive evidence. Note that the use of supplemental iron for RLS treatment, even in patients with low ferritin levels, has been based on very low quality evidence (Trotti et al. *Cochrane Database Syst. Rev.* 2012;16;5: CD007834). The systematic review identified insufficient data to support any recommendation related to the treatment of PLMS.

There is a widespread perception that dopamine agonist treatment of RLS is safe, well-tolerated, and effective. In clinical practice, these agents are often used empirically as a therapeutic trial in the presence of an uncertain diagnosis. However, recent studies suggest that this enthusiasm should be tempered with a reasonable degree of caution despite their role as preferred agents because of a number of potential complications of treatment.

Augmentation

Augmentation, a drug-related increase in RLS symptoms, occurs in the majority of patients receiving long-term treatment with dopaminergic medications. This phenomenon is manifested by an earlier onset of RLS symptoms in the afternoon and evening, more rapid onset of symptoms with rest, increased symptom severity, shorter duration of medication effects, and extension of involvement to other body parts. Allen and colleagues conducted a community-based survey of 266 patients and found that 20% reported strong evidence of augmentation (Allen et al. *Sleep Med.* 2011;12[5]:431). A far greater number (56%) demonstrated symptoms consistent with possible augmentation, with new cases occurring at a rate of 8% per year of therapy. The development of augmentation appears to be related to several factors: dose and half-life of medication used (with higher dosages of shorter-acting agents increasing risk), longer duration of treatment, lower serum ferritin level, and a family history of RLS.

In clinical practice, the response to the development of augmentation is often an expedient and progressive increase in dose and frequency of medication, which unfortunately increases the likelihood that the patient will experience subsequent further complications of treatment. Once high-dose therapy is in place, it is often not possible to discontinue the medication completely without development of a severe recurrence of RLS symptoms. It is possible that availability of longer-acting formulations of dopamine agonists will be helpful in minimizing the incidence of augmentation; for now, it seems prudent to avoid escalation of dosage through the use of lifestyle changes, correction of iron deficiency, and the addition of non-dopaminergic medications.

Impulse Control Disorders

Dopaminergic agents have been shown to induce impulse control disorders (ICDs) in some patients with Parkinson disease, but these side effects have been thought to be uncommon in patients with RLS. Recognized ICDs include pathologic gambling, hypersexuality, compulsive shopping, compulsive eating, compulsive medication use, and punding (complex, repetitive, stereotyped actions like sorting, purposeless manipulation of common objects, excessive grooming or cleaning, and hoarding). It is thought that these conditions are related to dysfunction of a central dopamine reward system. Cornelius and colleagues performed a case-control study of patients with RLS using a screening questionnaire followed by a confirmatory telephone interview (Cornelius et al. *Sleep.* 2010;33[1]:81). They reported a surprisingly high prevalence of compulsive shopping (9%), pathologic gambling (5%), compulsive eating (11%), hypersexuality (3%), and punding (7%), with an overall frequency of any ICD of 17%. The mean latency between onset of treatment and development of an ICD was 9.5 months. It may be possible to identify patients with an increased risk of development of dopaminergic medication-induced ICDs. Risk factors include higher dopamine agonist dosage, younger age of onset of RLS, female gender, a history of experimental drug use, and a family history of gambling disorders (Voon et al. *BMC Neurol.* 2011;11:117).

These behavior disorders may be devastating to the patient and his or her family. It is critically important for the clinician to actively screen for the development of such problems throughout the span of RLS treatment because, due to the nature of these disorders, the patient may not volunteer that they are occurring. Clinicians discovering these symptoms who are unaware that the patient is taking a dopaminergic medication or that ICDs are a relatively common complication of these agents may initiate treatment with an additional medication, such as an antidepressant, which may exacerbate expression of RLS, creating a vicious cycle of progressive problems.

Dopamine Agonist Withdrawal Syndrome

A syndrome of physical and psychological symptoms related to the withdrawal of dopamine agonists (DAWS) has been reported in patients with Parkinson disease (Rabinak and Nirenberg. *Arch Neurol.* 2010;67[1]:58). Because of the augmentation phenomenon discussed above, some patients with RLS are taking doses of dopaminergic medications equivalent to PD patients and are consequently at risk of DAWS. Symptoms are similar to those seen in other drug withdrawal syndromes and include anxiety, panic attacks, agoraphobia, depression, dysphoria, diaphoresis, fatigue, pain, orthostatic hypotension, and drug cravings. There is some evidence that DAWS occurs much more commonly in patients who are forced to discontinue treatment in response to the development of ICDs.

The recognition that dopaminergic medications can result in dramatic improvement in RLS symptoms has made it possible to avoid treatment of this common condition with controlled drugs (such as opioids and benzodiazepines) that have the potential for habituation and dependency. Unfortunately, it now appears that use of these "safer" medications is more problematic than was initially appreciated. Until new approaches to the management of this common and frustrating ailment are available, clinicians need to remain vigilant for the multiple side effects associated with the preferred treatments. ■

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This Month in *CHEST*: Editor's Picks

BY DR. RICHARD S. IRWIN, MASTER FCCP

▶ Executive Summary: Monitoring of Nonsteroidal Immunosuppressive Drugs in Patients With Lung Disease and Lung Transplant Recipients: ACCP Evidence-Based Clinical Practice Guidelines (Journal hard copy)
Complete Supplement available online only. http://journal.publications.chestnet.org

▶ Comparison of Indacaterol With Tiotropium or Twice-Daily Long-Acting Beta-Agonists for Stable COPD: A Systematic Review. *By Dr. G.J. Rodrigo and Dr. H. Neffen.*

▶ Asthma Action Plans and Patient Satisfaction Among Women With Asthma. *By Dr. M. R. Patel, et al.*

▶ Pulmonary Langerhans Cell Histiocytosis-Associated Pulmonary Hypertension: Clinical Characteristics and Impact of Pulmonary Arterial Hypertension Therapies. *By Dr. J. Le Pavec, et al.*

POINT/COUNTERPOINT EDITORIAL
Should All ICU Patients Receive Continuous Sedation?
Yes: Dr. J. P. Kress, FCCP
No: Dr. A. G. Vinayak

ACCP Around the Globe

BY DR. MARK J. ROSEN, FCCP
Director, Global Education and Strategic Development

CHEST 2011 in Honolulu signaled a commitment to expanding the College's educational activities around the world. At least 20% of our members, a third of attendees, and 40% of abstracts at CHEST 2011, and more than half of the articles in the *CHEST* journal come from outside the United States and Canada. Our clinical education is recognized as arguably the finest in the world, but most international clinicians rarely or never attend the CHEST meeting, and more are asking us to bring education to them. The Board of Regents resolved to build on our experience to fulfill the College's vision of being the global leader pulmonary, critical care, and sleep medicine education.

The plan of action involved some organizational changes that started a year ago. A new Global Education and Development Committee (GEDC) was established to set the course of ACCP's global activities by evaluating existing and new programs, to articulate specific strategic goals, and to work toward their implementation. Chaired by Dr. David Gutterman, FCCP, a Past President of the ACCP, leadership and members of the College with international expertise make up the group. In the last year, GEDC revised the criteria for endorsement and support of international programs, streamlined the application process, and brought sound educational methodology to our global educational activity.


ACCP

Dr. Sanjeev Mehta, FCCP, discussing challenging cases at the Indian physicians' ACCP symposium.

The Council of International Regents and Governors and a group of FCCP members from around the world saw similar structural improvements that are making the group more effective in advancing the College's educational mission. To that end, the membership categories and roles were restructured into the new Council of Global Governors, which met for the first time at CHEST 2012. Chaired by Dr. Panagiotis Behrakis, FCCP, from Greece, the Council is charged with promoting ACCP educational activities in collaboration with local and regional medical societies, hospitals, and industry. The nominations process was likewise revised to facilitate participation of current and future global ACCP leaders.

Among last year's global activities, ACCP faculty led the following:

India:
- ▶ Three offshore courses for Indian physicians on a variety of topics in pulmonary and critical care medicine
- ▶ Hands-on mechanical ventilation simulation activities (led by Dr. Suhail Raoof, FCCP, and Dr. Kalpalatha Guntupalli, FCCP)
- ▶ CHEST Challenge INDIA, an online competition modeled on the US project

Israel:
- ▶ ACCP meeting in collaboration with Israel Society of Pulmonology
- ▶ Hands-on bronchoscopy simulation course

Saudi Arabia:
- ▶ International Medical Center in Jeddah: Asthma and COPD for Primary Care and Pulmonary Physicians, with hands-on training in spirometry and metered-dose inhaler use

Peoples' Republic of China:
- ▶ ACCP programs in Beijing, Xi'an, and Shanghai

Greece:
- ▶ Hellenic Thoracic Society-ACCP Board Review Course

Perhaps the most important development of the last year is the start of planning for **CHEST WORLD CONGRESS 2014** in Madrid, March 21-24, 2014. In partnership with SEPAR, the Spanish Society of Pneumology and Thoracic Surgery, the ACCP will conduct a world-class program that will offer ACCP clinical education outside North America, with the same scope, faculty expertise, and innovation. ■

ACCOUNTABLE CARE ORGANIZATIONS

The Promise and Challenge of a New Model of Care

BY DR. ALAN M. FEIN, FCCP; AND DR. LAWRENCE SHULMAN

A high level of anxiety pervades the health-care community, including the ACCP membership. It is common knowledge that while we Americans have the best health-care technology, we also spend too much and get too little. Life expectancy and infant mortality lags behind much of the developed world despite America significantly outspending many other nations. There is strong evidence of uncoordinated and duplicative care that not only drives down quality but adds to cost.

What are the options to address these problems? Tucked within this drive for innovative health-care delivery is the presumption that our traditional volume-driven "fee for service" payment model contributes to a cycle of waste and, in some instances, fosters fraud and abuse. One proposed solution is the Accountable Care Organization. Mentioned only briefly in the Affordable Health Care law (Obamacare), it is still somewhat opaque and mysterious to most physicians and other providers.

So what is Accountable Care? From the government's perspective, this complex network of programs, dubbed the Accountable Care Organizations, seeks to improve quality and coordination of care though creating an "organization" "accountable" to a selected group of at least 5,000 Medicare recipients. There are many flavors to this delivery system, which all must have at their foundation sufficient primary care physicians with supporting specialists, hospitals, and home health-care providers to care for their assigned beneficiaries. They will be financially incentivized to coordinate care across the inpatient and outpatient continuum. It is hypothesized that they will improve outcomes with lower resource expenditure for elderly patients with multiple comorbid illnesses. Qualifying groups are incentivized to have in place communication systems usually in the form of electronic health records. The ACO also recognizes a commitment to apply evidence-based medicine. As outlined by Centers for Medicare and Medicaid Services (CMS), the unifying incentive is "shared" savings; providers working together to reduce costs below a baseline established over the previous 3-year period.

CMS estimates a savings approaching 1 billion dollars within the first 3 years. The government and the ACO will share in these savings once a threshold is reached (5%), providing a potential route away from the traditional fee-for- service, volume-driven model of reimbursement. There are two general models for the initial "pioneer" programs for the ACO. First is one in which the provider organizations share in the risk of their endeavor but may get potentially greater reimbursement. The other "no-risk" option allows for the organization to participate with no financial risk but with mitigated rewards.

Patients may be concerned that these ACOs represent a stealth form of reintroducing the health maintenance organizations of the 1990s. This model was unpopular primarily because it restricted care. Patients will not voluntarily opt into the ACO and will not share in the savings. Patients receive notification that they have been selected as a beneficiary of the ACO and are allowed to "opt out" of sharing their health-care data. If the patient does not opt out, the data sharing can begin 30 days after the notification. While the potential downsides include provider incentives to limit care as a means of reducing cost and improving "bottom lines," careful quality monitoring and guideline benchmarking along with the professionalism of the ACO are expected to restrain these tendencies. Unlike the HMO, ACO patients may seek care from any provider, including those outside the ACO network. While preserving choice, it nudges the ACO to provide a "better" product and experience, so the patients will voluntarily stay within their assigned network.

AS OUTLINED BY CMS, THE UNIFYING INCENTIVE OF ACOs IS 'SHARED' SAVINGS.

Physicians are also concerned. The business model of the ACO is untested, and high initial capital investments focused primarily on information technology and electronic medical records are likely to encourage greater consolidation of medical groups. These consolidations often are spearheaded by regional health-care systems fostering further concentration of medical care delivery, limiting choice and competition. In capital-starved rural and inner-city urban locations, establishing effective ACOs may be challenging. Fortunately, antitrust regulations were temporarily waived to permit the nurturing of the ACO concept. Where ACOs have been field tested, significant shared savings have often been difficult to achieve. Only 5% of the beneficiaries generate approximately half of the costs. It has been suggested that the heterogeneity of the ACO population limits the potential for targeting interventions to improve care of high resource-consuming patients, particularly reducing hospitalization. To reduce costs and enhance savings, pressures to limit referrals to specialists like pulmonologists and sleep specialists are likely to increase. Uniform schema for division of shared savings between primary and specialist physicians have yet to be devised.

One example of cost savings focuses on the reduction of hospitalizations. If one hospitalization is avoided for an ACO beneficiary, the yearly Medicare savings would far exceed the 5% minimum threshold. Additionally, the ACO is rewarded for timely follow-up with the patient's physician after discharge from the hospital. Many ACOs have begun to create urgent care centers that provide 24-hour "nonhospital" care as an alternative to the emergency department. The ACO model has targeted heart failure and COPD/asthma patients as two groups that are frequently admitted. Cardiologists and pulmonologists will be called upon to help keep these groups out of the hospital, potentially increasing the referral base to these specialists.

So, the ACO can be best be thought of as a clinical trial, testing the hypothesis that financial incentives for coordinated care will make health-care delivery more cost effective. Many believe this is a stepping-stone to a fully capitated system of reimbursement. Ideally, these incentives will tilt toward more preventive, less reactive care. This is a hypothesis that has yet to be proven on a grand scale. ■

Ambassadors for OneBreath® Welcomes New Chair

Like all pediatricians, Dr. Carla Marciniuk is well acquainted with the importance of lung health, as many of her young patients struggle with asthma and other respiratory problems. She brings that expertise and a passion for education to her role as incoming chair of the newly renamed Ambassadors for OneBreath® group.

DR. CARLA MARCINIUK

Carla describes herself as "a proud, busy mother who is devoted to my career and close to my family." In addition to her private practice in Saskatoon, the largest city in the Canadian province of Saskatchewan, she is on the faculty at the University of Saskatchewan, where she teaches undergraduate medical students and pediatrics residents. She is active in local and regional medical organizations and associations and is currently president of the Saskatchewan Pediatric Society.

Medicine seems to in the Marciniuk family's genes. Carla met her husband, Dr. Darcy Marciniuk, FCCP, new ACCP President, during their first year of medical school. Currently, their children, a 22-year-old-daughter and 19-year-old son, are both studying medicine.

The new Ambassadors for OneBreath name, which was adapted at CHEST 2011, reflects the group's alignment with goals of The CHEST Foundation's OneBreath initiative: to improve lung health by providing prevention resources, raising public awareness, and encouraging healthy behaviors. As the new chair, Carla hopes to strengthen the group's work in those areas. Specific goals include increasing membership both internationally and within the United States and fostering the involvement of high school and college-age student members. The Foundation is also in the process of creating an e-community for the group so that members can share thoughts and ideas online, between meetings and across continents.

Ambassadors for OneBreath include spouses, families, and friends of ACCP members who come together to promote lung health in local communities worldwide through networking, educational outreach, fundraising, and support of ACCP members' pro bono humanitarian work. For more information on the Ambassadors for OneBreath, contact Lee Ann Fulton at lfulton@chestnet.org. ■

Humanitarian Award Expands Asthma Education

This year's Ambassadors for OneBreath® Humanitarian Award will bring asthma education to several San Antonio schools, where there is a high prevalence of asthma and corresponding absenteeism. The fun, interactive curriculum, designed by a respiratory therapist at the University of Texas Health Science Center in San Antonio was piloted at one elementary school last year to great results – after going through the program, the students' absentee rates dropped and their academic standings improved. The Ambassadors for OneBreath grant will expand the program to include four additional elementary schools, reaching many more children.

Doctors Undertrained in Antismoking Efforts

BY FRANCES CORREA
IMNG Medical News

WASHINGTON – While doctors can serve a critical role in advocating for their patients to stop smoking, most aren't trained on how to do so, according this year's Tobacco Atlas, a report detailing tobacco's effects on health care and global economics.

The report, now in its fourth edition, was published by the World Lung Foundation and the American Cancer Society.

Dr. Judith L. Mackay, the Tobacco Atlas coauthor and a senior policy adviser to the World Health Organization, said smoking cessation training is missing from undergraduate and graduate medical schooling and, hence, from the exam room.

"[Doctors] might say to [their patients] 'Smoking is harmful' but there's a whole manner of tips and advice, groups that can be set up, [and] pharmaceutical agents that can be used, where countries can afford it. … But if you're not trained in knowing them and understanding them and how to use them, there's a massive gap between the needs of the patients and then the actual ability of the health profession to basically help them, Dr. Mackay said in an interview.

She added that physicians should also receive training in health advocacy.

"Doctors are not taught how to make a representation to a finance minister, to put the tax up. They're not taught how to run a press conference. They're not basically taught how to do interviews … and yet what can be more important than getting our health messages to the right people, whether they be government or whether they be the media."

Michael Eriksen, Sc.D., lead author of the report, also suggested that one of the easiest ways for physicians to address tobacco use is to treat it as a vital sign during physician encounters and monitor it accordingly.

The report defines five steps physicians should actively take with patients:

- ► Ask about tobacco use.
- ► Advise patients to quit and inform them on the health risks.
- ► Assess the patient's willingness to quit.
- ► Assist the patient in quitting through pharmacologic and counseling measures.
- ► Arrange for follow-up and monitor progress.

When considering effective measures to help patients quit, Dr. Eriksen advised that pharmacologic measures alone have only a 6% success rate, compared with 20% for patients who take medication and also attend antismoking groups and 10% for those who only attend a group.

Outside of clinical measures, however, Dr. Eriksen said physicians can be effective advocates for policy changes, such as clean indoor air laws, tobacco education in schools, and state-level tobacco tax increases. He added that patients with tobacco-related conditions often don't survive long enough to advocate on their own behalf.

"The chest physicians who deal with the devastation are powerful advocates for changing the status quo," said Dr. Eriksen, who serves as dean of the Institute of Public Health at Georgia State University, Atlanta. "If you're in a community where you do both [clinical monitoring and advocacy], that's really going to have a double-barreled impact on success rates and getting people to quit smoking." Dr. Eriksen is also former director of the Office on Smoking and Health and is currently a consultant at the Centers for Disease Control and Prevention.

As advocates for smoking cessation, physicians can also have a lasting affect on the healthcare system, according to Keith Hansen, the World Bank's director of human development in Latin America and the Caribbean.

"[Health care] puts tremendous strain on the state, which has to pay for expensive health services much earlier than it should if we prevent these [tobacco-related] illnesses. And, of course, it's a tremendous drain on the health system," Mr. Hansen said.

The report details that, in the United States, cigarette smoking was responsible for $193 billion in annual health-related losses, including $96 billion in direct medical costs, from 2000 to 2004. This represents nearly 5% of total health care expenditures from 2003 to 2008. ■

ONLINE EXTRAS

► Scan the QR code: The American College of Chest Physicians offers a free resource to help patients stop smoking. The ACCP Tobacco Dependence Treatment ToolKit is available at tobaccodependence.chestnet.org/.

MI Rate Declined After Smoke-Free Laws Enacted

BY MARY ANN MOON
IMNG Medical News

VITALS

Major Finding: The rate of incident MI dropped 34%, from 150.8/100,000 people to 100.7/100,000, after laws prohibiting smoking in public places and workplaces were enacted.

Data Source: An analysis of data in the Rochester Epidemiology Project concerning the incidence of MI and sudden cardiac death in Olmsted County, Minn., during the 18 months before and the 18 months after smoke-free legislation was enacted.

Disclosures: This study was supported by ClearWay Minnesota; the National Heart, Lung, and Blood Institute; and the National Institute on Aging. No financial conflicts of interest were reported.

The rate of myocardial infarction dropped by one-third after laws prohibiting smoking in public places and workplaces were enacted in Olmsted County, Minnesota, according to a report in Archives of Internal Medicine.

Although this epidemiologic study could not establish causality, no other interventions during the study period could plausibly explain this community-wide reduction in the MI rate. And the only major MI risk factor that declined concurrently was the prevalence of smoking; rates of hypertension and hypercholesterolemia remained steady, and rates of diabetes and obesity increased, said Dr. Richard D. Hurt of the Nicotine Dependence Center and the department of internal medicine at the Mayo Clinic in Rochester, Minn., and his associates.

"Secondhand smoke should be considered a major risk factor for MI, joining family history, hypertension, hyperlipidemia, diabetes mellitus, and low physical activity. Hence, all clinicians should ascertain secondhand smoke exposure and promote the elimination of secondhand smoke exposure as part of their lifestyle recommendations," they noted.

"All people should avoid secondhand smoke exposure as much as possible, and those with [coronary heart disease] should have no exposure to secondhand smoke," the investigators added.

Several studies have documented declines in hospital admissions for MI after implementation of smoke-free laws, and the Institute of Medicine has concluded that there is a causal relationship between smoking bans and reductions in acute coronary events. To more closely examine the magnitude of that risk reduction, Dr. Hurt and his colleagues analyzed data from the Rochester Epidemiology Project, in which all cases of MI and sudden cardiac death in a well-defined community were validated using rigorous epidemiologic criteria. This project "has a long track record (more than 50 years) of robust epidemiologic studies," they said.

In Olmsted County, restaurants were required to be smoke free as of Jan. 1, 2002; bars and workplaces were required to follow suit on Oct. 1, 2007. The researchers examined rates of MI and sudden cardiac death during the 18 months before and the 18 months following implementation of each ordinance.

During the entire study period, there were 717 incident MIs and 514 cases of sudden cardiac death.

The age- and sex-adjusted MI rate dropped from 150.8 per 100,000 before the laws were implemented to 100.7 per 100,000 afterward – a 34% decline, the investigators said (Arch. Intern. Med. 2012 [doi: 10.1001/2013.jamainternmed.46]).

Similarly, there was a 17% decline in the incidence of sudden cardiac death during this period, which indicates a trend but does not constitute a statistically significant reduction.

Smoke-free legislation is effective not only because it decreases nonsmokers' exposure to secondhand smoke but also because it reduces the intensity of smoking in smokers, increases quit rates, and reduces the rate of taking up smoking in the first place, Dr. Hurt and his associates said.

Other research has demonstrated that as little as 30 minutes of exposure to secondhand smoke causes an abrupt and dramatic decrease in coronary artery flow velocity reserve and vascular injury that inhibits endothelial function. Exposure also has been associated with low HDL cholesterol levels, increased markers of inflammation, increased serum levels of fibrinogen and homocysteine, decreased antioxidant levels, and increased insulin resistance, they wrote.

Taken together, these findings indicate that physicians should "become advocates for effective tobacco control policies, such as increased taxes, graphic labeling, smoke-free workplaces, and marketing and advertising restrictions," the researchers said.

One limitation of this study was that the population of Olmsted County is predominantly white. Further studies are needed "in communities of more diverse racial and ethnic composition," Dr. Hurt and his colleagues said. ■

COMMENTARY

Dr. Sara Kalkhoran and Dr. Pamela M. Ling comment: The evidence documenting positive health outcomes from smoking bans continues to grow, as more areas adopt smoke-free legislation.

Clinicians should now work on closing loopholes in existing smoke-free policies and expanding those policies to include bans in multiunit housing, motor vehicles, casinos, and outdoor locations. Studies have shown that smoking bans enacted in multiunit housing not only reduce exposure to second-hand smoke, but also increase quit attempts in persons more likely to smoke, such as those with low socioeconomic status.

DR. KALKHORAN *and* DR. LING *are with the University of California, San Francisco. These remarks were taken from their invited commentary accompanying Dr. Hurt's report (Arch. Intern. Med. 2012 [doi: 10.1001/2013.jamainternmed.269]). They reported no financial conflicts of interest.*

EHR REPORT

Patient Portals: Opening Our Charts to Patients

BY CHRISTOPHER NOTTE, M.D. AND NEIL SKOLNIK, M.D.

The old cliché "When it rains, it pours," is hardly more appropriate than in the world of health care. Every day, the industry changes, and we are forced to adapt to new regulations and expectations from the government, insurance companies, and patients that dramatically affect the way we practice.

Recently, the storms have been raging in the area of health IT. As an example, consider the initiative that began with a simple requirement for e-prescribing and then developed into a huge undertaking called "meaningful use."

It begs the question: Why is it that electronic health records, which were sold on the idea of making our lives easier, have only seemed to complicate things?

While there are certainly no easy answers, one thing is clear: Electronic records are here to stay, and they have had a significant impact on physician practice and patient care.

This month, we'll explore the idea of implementing a patient portal, that is, granting patients immediate access to their medical records through the Web. This has evoked a tremendous amount of anxiety among physicians – and while these concerns are significant, they have not slowed the adoption of the new technology.

Unsealing the Sacred Book

There are a number of issues raised anytime a practice or health system decides to install a patient portal.

First and foremost, physicians become quite concerned about what a patient will see in their personal records, and how this will affect the doctor-patient relationship. This is particularly salient in areas such as mental health, social history, and life-altering diagnoses. A care provider may document something in a problem list or differential diagnosis that the patient could find shocking or offensive. Issues such as "morbid obesity" or "bipolar disorder," while perfectly legitimate and accurate, can be viewed as judgmental and insulting. Other comments, such as "possible malignancy" or "suspicious for multiple sclerosis," could be devastating to a patient who has not had time to process them with his or her physician.

It is critical, therefore, that providers are aware of what parts of the record will be available to the patient, and how to document sensitive issues. Most Web portals allow for customization and limits to be placed on what a patient can access. While it is true that patients have a right to the entirety of their record, it is not necessary to provide them with information they have not requested.

We would argue that the standard should be to provide as much access as possible – a standard adopted by many major health systems across the country. The onus is then placed on the doctor to be prudent in how he or she documents in the record, with full knowledge that patients can and will be reviewing it.

Why More Is (Usually) Better

Many of the people we speak to ask us whether or not we believe that sharing health records with our patients is a good thing. Until recently, we had only our own opinion, and had limited to no data to back it up. This all changed this month with an article by Dr. Tom Delbanco entitled "Inviting Patients to Read Their Doctors' Notes: A Quasi-experimental Study and a Look Ahead" (Ann. Intern. Med. 2012;157:461-70).

In this study, more than 13,000 patients at multiple medical centers were given access to their physicians' notes to see how reviewing them affected "behaviors, benefits, and negative consequences." The results are quite interesting. Of the patients who reviewed their notes and answered follow-up surveys, 77%-87% felt more in control of their care, and 60%-78% reported better medication adherence. Only about a quarter of those surveyed had privacy concerns, and just 1%-8% reported that the notes caused "confusion, worry, or offense."

This study also examined physician behavior. Of the 105 primary care physicians

Continued on following page

ACP: Measures Needed for 'Low-Value' Services

BY JANE ANDERSON
IMNG Medical News

Performance measures targeting services that provide little value for patients can help control health care costs by changing physicians' behavior through feedback and financial incentives, according to a policy paper by the American College of Physicians published Oct. 30 in Annals of Internal Medicine.

Performance measurement data have been used to encourage physicians to provide more high-value services, such as immunizations and medications for chronic diseases. But measures for low-value services could be equally valuable.

"The first step in addressing the high cost of health care should be decreasing use of interventions that provide no or very little benefit and are of low value," the paper states. Diagnostic imaging for uncomplicated low back pain is an example of a low-value intervention, the paper noted, because evidence shows that use of routine x-ray or advanced imaging does not improve outcomes for patients.

Low-value services include those for which the harms likely exceed the benefits and those that may provide benefits, but for which the tradeoff between benefits and costs is undesirable. There's no "bright line" that defines the point where the tradeoff indicates a service isn't cost-effective, the authors wrote, adding that this will be "a societal decision that depends on how much money we are willing to spend on health care."

Measures that target low-value interventions will need to be applied at the level of the hospital or multispecialty group practice because many individual physicians won't see enough patients with the target conditions. "Primary care physicians and specialists are often involved in decision making, and both should be held accountable rather than just the person who ordered the test," the paper said.

The policy recommends that performance measures be based on high-quality evidence that assesses the benefits, risks, and costs of interventions. Performance measures for low-value services could be used for feedback and public reporting, and to provide financial incentives to change physician behavior, according to the ACP. ■

Continued from previous page

involved across three states, 3%-36% reported changing documentation content, and many reported taking more time to write their notes.

In the end, the authors report that "99% of patients wanted open notes to continue, and no doctor elected to stop." Clearly, the process seemed to be beneficial for both physician and patient, and the benefits outweighed the risks.

Managing Liabilities

As our last column showed ("How to Avoid EMR Legal Pitfalls," www.bit.ly/Ts8SaP), the use of electronic health records has unearthed new legal pitfalls, and the realities of a patient portal underscore this unfortunate fact. Patients – and their attorneys – can scrutinize their medical records, and any missed lab result or diagnostic error is available for anyone to see. It's a significant concern for many physicians, but so far history has shown the opposite to be true. As we noted above, when patients feel more ownership of their health care, they perceive they are being better cared for, and fewer important details get overlooked. Abnormal lab values that may slip by a physician in the deluge of the daily mail are easily caught by a patient who is anxiously anticipating them.

But what about patients who will trouble their doctor over less than concerning results? While the cost might be a panicked phone call from someone with a slightly elevated BUN or low MCH, the reward could be a providential request to reevaluate the results of a CT scan showing a mass the primary care physician somehow missed.

We are hopeful that in the end, EHR technology will fulfill its touted promises, and that the downpour of new challenges will actually make the landscape more fertile to the growth of better patient care. ■

DR. SKOLNIK *is associate director of the family medicine residency program at Abington (Pa.) Memorial Hospital and professor of family and community medicine at Temple University, Philadelphia. He is editor in chief of Redi-Reference, a software company that makes medical handheld references.* DR. NOTTE *practices family medicine and health care informatics for Abington Memorial Hospital. They are partners in EHR Practice Consultants. Contact them at info@ehrpc.com.*

COMMENTARY

Dr. Stuart M. Garay, FCCP, comments: Patient portals are the latest extension of electronic health records. The majority of major academic medical centers have instituted or are in the process of developing them for their patients. Like it or not, patients are demanding similar portals from their individual physicians.

While there are benefits as noted by the authors, there are also liabilities. Pandora's box has been opened! Take heed!

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IMNG MEDICAL MEDIA

Medical Use of Apps Grows

Concerns • *from page 1*

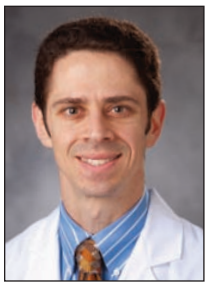
which mobile technology to regulate in a draft report in July 2012.

Even the basic functions of smartphones can be convenient in clinical practice, such as taking photos or videos and transmitting information by text or e-mail, but make sure you protect patient privacy and autonomy in ways that maintain trust and comply with HIPAA, Dr. Broder said.

The Duke University Health System has resolved any issues with HIPAA so that it's safe for physicians to transmit images and video as long as they're not sent outside the system. Talk to the HIPAA compliance officer at your medical center to establish the ground rules, he said. You can refresh your memory about which parts of data are considered by HIPAA to be protected information via a University of Miami site.

Dr. Broder reviewed some smartphone functions and apps that may be helpful and others that are not yet ready for medical prime time. Many are available for no cost or for a nominal fee. One study of health and fitness apps suggests that apps costing $0.99 or more tend to be higher quality and more trustworthy than less-expensive ones, he noted (J. Med. Internet Res. 2012;14:e72).

► **Sleep:** One of his residents swears by "smart alarm clock" apps that claim to use a smartphone's accelerometer to assess where you are in your sleep cycle (based on your movements in bed) to wake you at a time that will leave you feeling less fatigued. You may set for 6 a.m., but the alarm may wake you at 5:45 a.m. Apps like Sleep Cycle ($0.99) and Sleep as Android have some underlying sleep science behind them, but no independent studies have verified their claims.



Make sure that you protect patient privacy in ways that comply with HIPAA.

DR. BRODER

► **CPR:** The accelerometer also is used in the free app PocketCPR to give real-time feedback during CPR on the rate and depth of compression. Its has not been cleared by the FDA for use in humans, however, so the app warns that it's meant for practice only. One prospective, randomized trial in 1,586 cardiac arrests that happened outside of hospitals found that use by emergency services personnel did not significantly change the likelihood of return of spontaneous circulation or other outcomes (BMJ 2011;342:d512).

► **Chest:** If you're trying to teach students and residents about heart and lung sounds, or if you still get confused between mitral regurgitation and aortic stenosis, you might want to have a digital stethoscope app handy. These apps interpret heart and lung sounds heard typically through your smartphone's microphone, which may not be good enough for clinical use. The Thinklabs Stethoscope app at $70 is pricey, compared with others, but it records sounds directly via the smartphone or through an attached electronic stethoscope.

A case that turns an iPhone into an ECG device has been submitted to the FDA for approval. The AliveCor iPhone ECG is expected to sell for between $100 and $200, compared with the usual price tag of thousands of dollars for conventional ECG machines, according to PC Magazine.

One small prospective study of experimental software that programs an iPhone to detect atrial fibrillation by placing a patient's finger over the camera lens showed it was 98% sensitive and nearly 100% specific in detecting atrial fibrillation (IEEE Trans. Biomed. Eng. 2012 [doi:10.1109/TBME.2012.2208112]).

► **Translation:** When your hospital's interpreter isn't available, a free app

Continued on following page

Medical Images on Smartphones

Do:

► Obtain consent to acquire images or transmit them for the patient's medical benefit.

► Explain to the patient and get consent for any other intended use, such as education or publication.

► Tell the patient what you will do with images when their use is completed – delete them or upload them to the medical record.

► Confirm receipt if you send to other health care providers.

► Specify in your message what that provider should do with the image.

► Document in the patient's chart that consent was obtained, what was sent, who received it, and content of the images.

Don't:

► Obtain images covertly.

► Send to any unnecessary recipients.

► Show images to anyone for fun.

► Post to social media sites.

► Blog about "funny" patient encounters.

Source: Dr. Joshua S. Broder

Continued from previous page

like Google Translate is far, far from perfect, but can help. You can write or speak in one language and your device will write and say the message in a wide selection of languages. You'll need a wireless Internet connection for some translation apps.

► **Light:** You want to inspect a patient's sore throat, but the light in the exam room is broken. Use the flash on your smartphone camera, or use one of many free "flashlight" apps that turn the smartphone screen into a light source. Be sure to turn it off when you're done, though, or your battery will run down quickly.

► **Ultrasound:** The miniaturization of ultrasound devices continues, with systems such as the Mobisante MoblUS that attaches a probe to show images on your smartphone screen.

► **Decision support:** The PediStat app ($2.99 and up) makes it easy to determine the right pediatric drug dosing, among other features. The free Calculate (Medical Calculator) by QxMD app provides quick intuitive guides to common decision rules and can be customized by medical specialty.

► **Drugs:** Look up drug dosing, side effects, interactions and other information on free apps from Micromedex and others.

► **Photos/videos:** These apps are handy for documenting and sharing the appearance of a wound, a patient's range of motion, or performance on a neurologic exam. Anyone who thinks they see uvula deviation in the throat of a struggling 3-year-old can snap a photo or video for review with other health care providers, medical students, or parents and avoid having to repeat the exam. Images of a wound problem after surgery can be sent to the surgeon when he or she is out of town. (See the sidebar on Page 34 for Dos and Don'ts for using photos and videos.)

Once you've got an image or data you want to transmit, avoid texting as first-line means of communication because texts typically are not encrypted. Be careful when e-mailing to make sure it's going to the correct address and only that address. Use e-mail options such as "confirm delivery" or "request read receipt," and add a sentence to the e-mail saying, "Please delete once no longer necessary for patient care," he advised.

Always document in the patient's chart that you obtained patient consent and describe what was sent and who received it. Describe any images you send.

Don't leave images on your portable devices. They're easily lost, and most have inadequate encryption. Make images part of the medical record by uploading to the patient's record, printing and scanning, or describing them clearly in the medical record. Then delete them from your device.

Store images and data in "cloud" computing sites with caution, Dr. Broder said. Services such as Google Drive or Dropbox allow sharing of very large files but provide no assurances about the quality of encryption or security. Cloud sites may be best used for giving patients access to instructions, instructional videos, reference papers, anatomic diagrams, etc.

The FDA approved the free Centricity Radiology Mobile Access app, which lets you view CT and MRI images on your iPhone if the images are stored in a GE Centricity PACS (picture archiving and communication system) platform – which may include 20% of U.S. radiology images, according to the company.

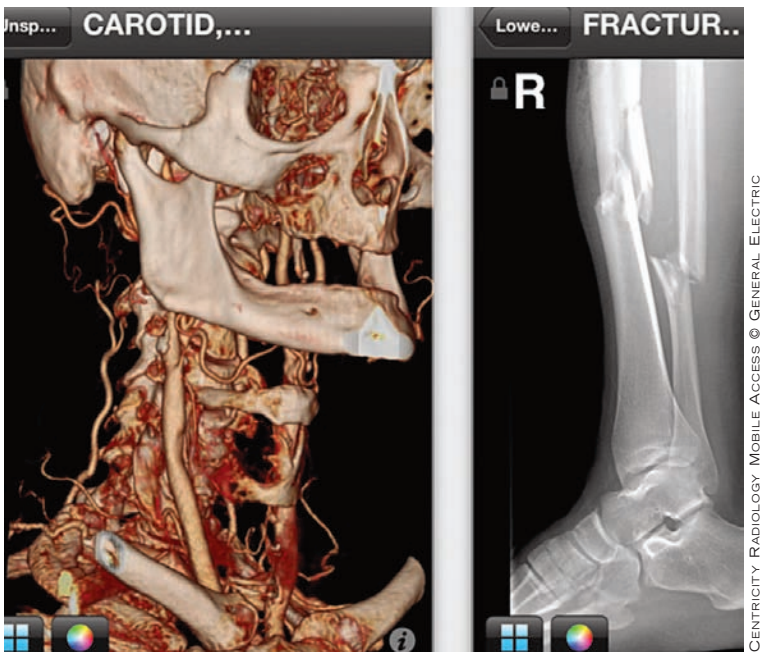
The free CloudOn app lets you use MS Office software (including Word, Excel, and Powerpoint) on an iPad.

Various screen replicators that allow you to remotely access your computer desktop from your mobile device (such as ones by Citrix, or Splashtop Remote Desktop) all have the same problem, Dr. Broder said – they're too clunky and not "touchscreen friendly."

And one final word on an underappreciated perk of medical apps on smartphones: When your medical director stops by, wanting to talk about your productivity, pull out your smartphone to show the data you've entered about patient encounters in your free iRVU app, which calculates total RVUs, charges, and average charge per encounter, among other features.

Apps on smartphones and tablets will become part of daily medical practice, Dr. Broder predicted, but physicians need to be conscious about their limitations and potential problems as well as their assets.

Dr. Broder disclosed that he owns stock in Apple. ■



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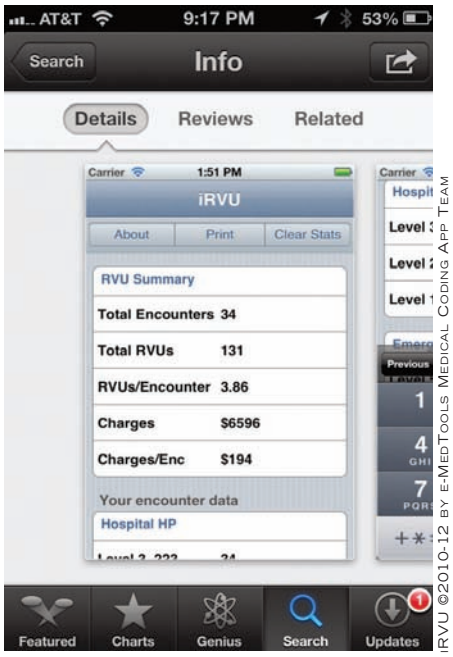

iRVU ©2010-12 BY E-MEDTOOLS MEDICAL CODING APP TEAM

Radiology and RVUs get their closeups: At left, the Centricity Radiology Mobile Access app is FDA approved for viewing CTs. The iRVU app uses patient-encounter data to calculate charges. Both are free.

VIEW VIDEO ONLINE

Apps are a good tool, but should be used with care, Dr. Broder says. Scan the code to watch an interview.

Text Messaging May Drown Out Pagers

BY NASEEM S. MILLER
IMNG Medical News

NEW ORLEANS – More physicians are using text messaging to communicate with each other and their teams in hospitals, a hint toward a shift from pagers, which have been a regular accessory to scrubs and white coats for the past 30 years.

The trend is driven by the surge in cell phone use and advances in technology, not to mention the new crop of tech-savvy interns and residents, according to the few studies that have focused on text messaging among health care professionals.

The studies are quick to point out one major caveat: Most text messages are not encrypted, and many hospitals and health systems have yet to implement policies and secure programs to protect the exchanged information.

"This is wake-up call," Dr. Stephanie Kuhlmann said at the annual meeting of the American Academy of Pediatrics. "Hospitals need to be aware of this trend and need to find a way to secure these text messages."

Dr. Kuhlmann, who is a pediatric hospitalist and assistant professor of pediatrics at the University of Kansas, Wichita, doesn't carry a pager. She receives pages on her cell phone. She uses text messaging with colleagues, residents, and other members of the hospital team, whether it's for administrative purposes, patient-care issues, or arranging a meetup.

Seeing the trend in her workplace, Dr. Kuhlmann and her colleagues decided to survey pediatric hospitalists about their use of text messaging.

The electronic survey revealed that although face-to-face and phone communication were the most common types of contact (92% each) among the 106 surveyed, nearly 60% of the respondents said they received work-related text messages and 12% said they sent more than 10 messages per shift.

The text messages were to or from other pediatric hospitalists 59% of the time, from fellows or residents 34% of the time, and from subspecialists and consulting physicians 25% of the time. Nearly half of the respondents said that they received text messages when they were not on call.

"It's a quick way to communicate or ask a quick question. You don't have to stay on hold on the phone," she said.

Meanwhile, 41% of the respondents said they were worried about violating the Health Insurance Portability and Accountability Act (HIPAA), highlighting a need for text messaging encryption, said Dr. Kuhlmann.

In another survey, conducted by the IT security company Imprivata, more than 60% of hospital IT executives said that they were very concerned about HIPAA compliance.

Roughly 72% of the 114 respondents said that they had policies in place to prevent personal health information from being included in text messages. Yet, some 60% said they didn't have a secure text messaging solution in place.

Almost two-thirds said that they believed pagers will be replaced by secure text messaging within 3 years. Imprivata is among a handful of companies to offer HIPAA-compliant or encrypted text messaging programs and software for hospitals and health care systems.

Dr. Kuhlmann said that she wasn't aware of any head-to-head comparisons for available encrypted texting programs.

She and her colleagues, who are conducting more studies on the subject, said that there's a need for more research on the accuracy and effectiveness of text message communication in hospitals and patient privacy issues. ■

VITALS

Major Finding: Nearly 60% of survey respondents said they received work-related text messages, and 12% said they sent more than 10 messages per shift.

Data Source: This was an electronic survey about text messaging among 106 pediatric hospitalists

Disclosures: Dr. Kulhmann said she had no relevant financial disclosures.

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