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COURTESY DR. EDWARD C. JONES LÓPEZ

Cough aerosol analysis topped smear microscopy in flagging patients likely to transmit TB, reported Dr. Edward C. Jones López.

Most-infectious TB identified by aerosols

BY TARA HAELLE
IMNG Medical News

A new, effective method of assessing tuberculosis infectiousness involves directly measuring aerosols from the coughs of pulmonary TB patients, according to a study published in the American Journal of Respiratory and Critical Care Medicine.

An analysis of cough aerosols, when available, more accurately predicted transmission than did the traditional method of sputum smear microscopy or culture, reported Dr. Edward C. Jones López of Boston Medical Center and his associates (Am. J. Respir. Crit. Care Med. 2013 Jan. 10 [doi: 10.1164/rccm.201208-1422OC]).

The current standard test for a TB patient's infectiousness involves acid-fast bacilli (AFB) smear microscopy to determine the concentration of *Mycobacterium tuberculosis* in the patient's sputum. Yet, it's been long documented in research that TB transmission to patient contacts varies considerably, even among patients with a sputum AFB-positive smear.

Therefore, the researchers analyzed the number of *M. tuberculosis* colony-forming units (CFUs) in TB patients' aerosols to see whether the CFU number better predicted

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Smoking rate soars among mentally ill, CDC report says

Cessation tools work but are underused.

BY ELIZABETH MECHCATIE
IMNG Medical News

The rate of cigarette smoking among mentally ill adults is 70% higher than among adults without a mental illness and is particularly high in certain groups, including young adults, according to a report by the Centers for Disease Control and Prevention and the Substance Abuse and Mental Health Services Administration.

The estimates are based on data from SAMHSA's 2009-2011 National Survey on Drug Use and Health, which calculated the rates of cigarette smoking among people aged 18 years and older in the United States who reported having "any mental illness," defined as "a diagnosable mental, behavioral, or emotional disorder, excluding developmental and substance use disorders" in the past year.

During this period, 36.1% of adults with a mental illness were current smokers, compared with 21.4% of adults with no mental illness. Those with a mental illness who smoked were heavier smokers, smoking an average of 331 cigarettes a month, compared with 310 a month among adult

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INSIDE

Trials affirm 2 extended post-VTE drugs

BY MARY ANN MOON
IMNG Medical News

Two oral anticoagulants, apixaban and dabigatran, were found to be effective for the extended treatment of venous thromboembolism in three industry-sponsored randomized clinical trials reported in the New England Journal of Medicine.

Both medications also reduced the risk of bleeding complications, the investigators said.

In the first trial, two doses of apixaban were compared against placebo in 2,486 patients with venous thromboembolism who had finished 6-12 months of standard anticoagulation therapy and whose physicians were uncertain whether to stop or continue anticoagulation treatment,

See **Extended treatment** • *page 6*

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SARS echoes seen in new respiratory coronavirus

BY MITCHEL L. ZOLER
IMNG Medical News

VIENNA – The short-lived, worldwide epidemic of severe acute respiratory syndrome that began its streak across the globe 10 years ago, starting in February 2003, has been echoed over the past 8 months by what is so far a much more limited number of cases of a new, mysterious respiratory virus closely related to the SARS pathogen.

Mostly known so far as the "novel coronavirus" (NCoV), the new agent is very similar to the severe acute respiratory syndrome (SARS)–associated coronavirus, and by late February the new virus had been identified in 13 patients worldwide – in Saudi Arabia, Jordan, the United Kingdom, and Qatar – causing seven deaths and severe illness in 5 of the other 6 patients.

Since the World Health Organization (WHO) and other epidemiology groups first became aware of the NCoV last September, and as the number of identified cases has inched up, researchers have scrambled to gather information about the novel virus and heighten surveillance for new cases. SARS left a legacy of just over 8,000 probable cases in 29 countries, including 29 probable U.S. cases, with an overall fatality rate of 10. After bursting on the scene in early 2003, SARS quickly flamed out, with the last handful of clinical cases ever seen identified in China in early 2004

"It's likely we will see more" of the NCoV. "We'll need to cast a wide net since we now know there are a dozen cases and different clinical presentations," Dr. Larry Madoff said at the International Meeting on Emerging Diseases and Surveillance. Although almost every patient with confirmed NCoV infection has had severe illness, one U.K. patient who acquired the infection from another household member had a mild, flu-like illness. The milder case "calls into question the [WHO] established case definition for this illness," said Dr. Madoff, director of epidemiology and immunization at the Massachusetts Department of Public Health in Boston.

"Based on published evidence, there is close relatedness between the novel coronavirus and the SARS virus, but SARS uses a receptor that is deep in the respiratory tract. The novel virus uses a different receptor. It's not clear whether the novel virus can infect mucosa or the upper respiratory tract, but if it could it might be more transmissible," U.S. epidemiologist Jonathan Epstein, D.V.M., said in an interview.

A report from a team of Swiss researchers reported that the NCoV (which the Swiss researchers call human coronavirus [HCoV]-EMC) grew very efficiently in vitro on human bronchial epithelial cells, and that interferon treatment cut replication of the virus in these cells (mBio 2013;4:e00611-2).

The episodes of human infection by the NCoV so far that seem to be geographically disparate also have a precedent with SARS.

The pattern of cases "suggests that the source of the infection is common or widespread," Dr. Epstein said. "It's a challenge to identify common environmental features in the case histories of the infected patients. But with SARS there were multiple spill-over events in different regions of southeast China" when the SARS virus moved from civets into people.

"Genetic studies on this NCoV place it related to coronaviruses found in bats. But how did the jump from bats to humans occur? Is there an intermediate host animal?," Dr. Marjorie R. Pollack, a consultant medical epidemiologist based in New York, wrote in a recent comment on the new coronavirus (ProMed Mail, 2013;Archive Number: 20130221.1554109).

According to recent guidance from the WHO, member states should "continue their surveillance for severe acute respiratory infections and to carefully review any unusual patterns. Testing for the NCoV should be considered in patients with unexplained pneumonias or in patients with unexplained severe, progressive or complicated respiratory illness not responding to treatment, particularly in persons traveling from or resident in areas of the world known to be affected."

Dr. Madoff, Dr. Epstein, and Dr. Pollack reported having no disclosures.

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

CMS finalizes rules on physician-industry payments

BY MARY ELLEN SCHNEIDER
IMNG Medical News

Federal health officials have finally released the details on how online public reporting of industry payments to physicians will work.

Under the final rule released by the Centers for Medicare and Medicaid Services (CMS), drug, device, and medical supply manufacturers who participate in Medicare, Medicaid, or the Children's Health Insurance Program will be required to submit annual reports to the federal government on any payments of $10 or more that they made to physicians and teaching hospitals. They also will be required to report on all payments if the payments and transfers of value to a single physician reach $100 in aggregate value for a year.

Manufacturers and group purchasing organizations (GPOs) must also report on physician ownership and investment interests each year. CMS will post the information on a public website. The requirements are mandated under the Affordable Care Act.

Manufacturers and GPOs have until Aug. 1 to begin collecting data. They must submit their reports on payments made in 2013 by March 31, 2014. CMS will post the data online by Sept. 30, 2014.

The final rule contains plenty of exceptions, however. For instance, reporting is not required for gifts between individuals with an existing personal relationship. Other exclusions include small payments of less than $10, educational materials that directly benefit patients or are intended for patient use, discounts for rebates for drugs and devices, in-kind items for charity care, and samples.

Indirect payments made to speakers at accredited or certified continuing medical education events also do not need to be reported as long as the manufacturer doesn't suggest speakers.

The final rule also clarifies that companies sponsoring large-scale conferences do not need to track and report on small gifts and food items worth less than $10 such as pens and bottles of water. These items also won't count toward the minimum yearly reporting threshold of $100, according to CMS.

"I think this will make life easier, because it will contribute toward a more relaxed atmosphere at meetings so that attendees won't have to worry every time they pick up a bottle of water or a granola bar," said Dr. Daniel Carlat, project director for the Pew Prescription Project, which works for greater transparency in physician-industry relationships.

Although the data collection and reporting requirements are on the drug and device industry, physicians are responsible for reviewing their information before publication. Physicians will have 45 days to review the reports and another 15 days to work with manufacturers to correct any disputed reports. After that, if disputes remain, the information will be posted publicly but will include a disclaimer that it is disputed, according to the rule.

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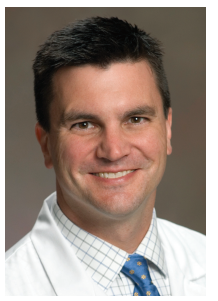
COMMENTARY: Why should doctors die differently?

BY MICHAEL J. PISTORIA, D.O.

My attention was drawn to a newspaper article pointing out that doctors die differently from their patients. As it turns out, we often do not request complicated treatment and life-sustaining therapies. The article referred to a 2012 piece in the Wall Street Journal by Dr. Ken Murray, who discussed evidence supporting the different decisions physicians reach about end-of-life care.

He had quoted a 2003 article by Dr. Joseph J. Gallo and his associates, who surveyed participants in the Johns Hopkins Precursors Study, which covered physicians graduating from Hopkins between 1948 and 1964. The researchers obtained responses from nearly 800 physicians about their end-of-life decisions. Compared with 20% of the general public, 64% of physician respondents had created an advanced directive. Nearly 90% of the physicians did not want CPR if they were in a chronic coma. This contrasts with 25% of the public not desiring "heroic measures." Clearly, physicians were outlining the care that they did and did not want to receive.



DR. PISTORIA

Dr. Murray also mentioned a 1996 study that examined how CPR was portrayed on television and the potential impact it might have on patients' decision making. In that paper, CPR was successful in 75% of the TV cases, with 67% of patients ultimately being discharged from the hospital (N. Engl. J. Med. 1996;334:1578-82).

Compare this with what we know: CPR rarely works. A 2010 study that evaluated the impact of 95,000 cases of CPR in Japan demonstrated that clearly. Only 8% of patients who had received CPR survived for more than 1 month. Of those who survived, 3% were able to lead "normal" lives.

We are able to make objective assessments of the likelihood of success of various therapies in our patients, but patients do not fully understand the risks and benefits of their therapy. Once the big picture is made clear to them, they often opt for more conservative therapy aimed at improving quality of life.

We have an obligation to our patients to share with them the reality of the care they receive. We need to understand what is important to them. Do they want to exhaust every medical option? Do they value comfort and quality time above all else? We need to ask these questions.

Previously, I wrote about my former colleague Darlene. Had I not known she did not desire continued therapy, she would have received several days of great care in the ICU – but would have died nonetheless.

If dying in comfort and advanced directives are good enough for us, they should be good enough for our patients.

Dr. Pistoria is affiliated with Coordinated Health in Bethlehem, Pa.

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Trials affirm 2 drugs for post VTE

Extended treatment *from page 1*

said Dr. Giancarlo Agnelli and his associates in the Apixaban After the Initial Management of Pulmonary Embolism and DVT With First-Line Therapy–Extended Treatment (AMPLIFY-EXT) study.

AMPLIFY, a 3-year look at Apixaban

Apixaban is an oral factor Xa inhibitor that is administered in fixed doses and doesn't require laboratory monitoring. The 5-mg (treatment) dose of apixaban has proved effective at preventing stroke in patients with atrial fibrillation, and the 2.5-mg (maintenance) dose has proved effective for thromboprophylaxis after major orthopedic surgery, said Dr. Agnelli of the department of internal and cardiovascular medicine-stroke unit at the University of Perugia (Italy) and his colleagues.

The study subjects were enrolled over a 3-year period at 328 medical centers in 28 countries. They were randomly assigned in double-blind fashion to receive the 2.5-mg dose (840 subjects), the 5-mg dose (813 subjects), or a matching placebo (829 subjects) twice daily for 1 year.

The primary efficacy outcome measure was a composite of symptomatic recurrent VTE or death from any cause. This occurred in 3.8% of the maintenance-dose group and 4.2% of the treatment-dose group, both significantly lower rates than in the placebo group (11.6%). Thus, both doses of apixaban significantly decreased the incidence of recurrent VTE, Dr. Agnelli and his associates said (N. Engl. J. Med. 2013 Feb. 21 [doi10.1056/NEJMoa1207541]).

The primary safety outcome measure was major bleeding, which occurred in 0.2% of the maintenance-dose group and 0.1% of the treatment-dose group, compared with 0.5% of the placebo group. Thus, both doses of apixaban were comparable to placebo in rates of major bleeding.

Clinically relevant nonmajor bleeding occurred in 3.0% of subjects taking 2.5 mg of apixaban and 4.2% of those taking 5 mg of apixaban, which were significantly higher than the 2.3% rate in subjects taking placebo.

The number of patients who would need to be treated with apixaban to prevent a single episode of recurrent VTE was 14. In contrast, the number who would need to be treated to cause an episode of major or clinically relevant nonmajor bleeding was 200, the investigators noted.

"For patients with venous thromboembolism for whom there is uncertainty about the benefits and risks of continued therapy, the results of this study provide a rationale for continuing anticoagulation therapy for an additional 12 months," they said.

"It should be noted, however, that only 15% of the patients in this study were older than 75 years of age, and few had a body weight below 60 kg or moderate or severe renal impairment. Consequently, more data are needed to better determine the benefit-to-risk profile of apixaban with respect to bleeding in such patients," the researchers said.

Dabigatran in long-term RE-MEDY and RE-SONATE studies

In a separate report, Dr. Sam Schulman and his associates in the RE-MEDY and RE-SONATE studies examined the direct thrombin inhibitor dabigatran as a long-term anticoagulation treatment. These trials were extensions of two previous studies of short-term anticoagulation after venous thromboembolism (N. Engl. J. Med. 2013 Feb. 21[doi:10.1056/NEJMoa1113697]).

In RE-MEDY, 2,866 VTE patients who had completed at least 3 months of anticoagulation therapy and were considered to be at increased risk for recurrence were randomly assigned to receive either fixed-dose dabigatran twice daily (1,430 subjects) or warfarin (1,426 subjects) for up to 36 months. They were followed at 265 medical centers in 33 countries, said Dr. Schulman of McMaster University Thrombosis and Atherosclerosis Research Institute, Hamilton, Ont., and his colleagues.

The RE-SONATE trial, in contrast, involved 1,343 VTE patients who had completed at least 3 months of anticoagulation therapy but were *not* considered to be at increased risk of recurrence, so it was ethical to assess the effect of dabigatran vs. placebo in these patients. The subjects were randomly assigned to receive either fixed-dose dabigatran (681 patients) or a matching placebo (662 patients) and were followed at 147 medical centers in 21 countries.

In both RE-SONATE and RE-MEDY, the primary efficacy outcome measure was recurrent symptomatic VTE or VTE-related death.

In RE-MEDY, this outcome occurred in 1.8% of the dabigatran group and 1.3% of the warfarin group, thus meeting the criteria for noninferiority to warfarin in preventing recurrent or fatal VTE.

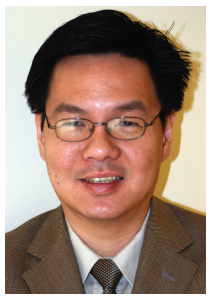
In RE-SONATE, this outcome occurred in 0.4% of the dabigatran group, compared with 5.6% of the placebo group, so the drug was significantly more effective than placebo at preventing recurrent or fatal VTE.

Dabigatran was associated with markedly fewer major bleeding events (0.9% vs. 1.8%) and clinically relevant bleeding events (5.6% vs. 10.2%) than was warfarin. However, the drug was associated with more major or clinically relevant bleeding events than was placebo (5.3% vs 1.8%).

In addition, there was a higher rate of acute coronary events with dabigatran (0.9%) than with warfarin (0.2%), although the number of affected patients was small. A recent meta-analysis of seven noninferiority trials also showed a significantly higher risk of MI or acute coronary syndromes with dabigatran than with the comparators. "Whether dabigatran increases the risk of MI is therefore still unclear," Dr. Schulman and his associates said.

AMPLIFY-EXT was funded by Bristol-Myers Squibb (BMS) and Pfizer; Dr. Agnelli reported ties to Bayer, Boehringer Ingelheim (BI), Daiichi Sankyo, BMS, and Sanofi-Aventis, and his associates reported ties to numerous industry sources. RE-MEDY and RE-SONATE were funded by BI; Dr. Schulman and his associates reported ties to numerous industry sources.

VIEW ON THE NEWS



Dr. Jun Chiong, FCCP, comments: Extending anticoagulation is really both a medical and social burden as patients have to frequently go to the laboratory and there may be days that anticoagulation may not be adequate only to be discovered days or weeks later during the next monitoring. Having effective alternatives that have better pharmacokinetic profiles is a plus. Further studies for subjects 75 and older are important to determine the bleeding and MI risk.

Dr. Chiong disclosed that he has received honoraria from Boehringer Ingelheim, maker of Pradaxa.

THE EHR REPORT: A tale of two EHRs: surviving a system switch

BY CHRIS NOTTE, M.D., & NEIL SKOLNIK, M.D.

We frequently receive comments that question our optimism about the benefits of electronic health records. The truth is that we continue to believe that electronic records will lead to better access to information, improved communication, and higher-quality patient care. We also agree that there are many problems with current EHRs and the physicians who use them encounter many challenges. Chris had one such experience recently that offered a heavy dose of reality and frustration. This occurred during the transition from one EHR to another, and we felt it would be worthwhile to share the story here.

The best of times...

In January 2012, Chris's practice was acquired by a regional health system in southeastern Pennsylvania. This certainly presented an amazing opportunity for growth, as the hospital's excellent reputation and expanding network would allow for better access and opportunities for both patients and providers. One such opportunity was the chance to adopt the system's enterprise-wide EHR. This was truly exciting to everyone in the practice, as the EHR software was the foundation of a successful health information exchange. Also, Neil, having been employed by the same system for years, was already using the EHR and felt that it was a system of quality and value. At first, Chris was really looking forward to the switch.

But there was a large elephant in the room: the practice's existing EHR.

For several years prior to the acquisition, the practice had been successfully using an excellent but different EHR. Also a high-quality and highly regarded product, this software had met the practice's needs and everyone in the practice become comfortable – and "meaningful" – users of the system. No one really understood what it would be like to learn a completely new EHR. The physicians, including Chris, thought that since they were already using an electronic record, it was unlikely that their workflow would need to change at all. Wasn't this just like buying a new car? Sure, some of the knobs and buttons would look different, but we all know how to drive. This should be a snap, right?

Unfortunately, the practice quickly learned that EHRs and automobiles have very little in common.

DR. SKOLNIK AND DR. NOTTE

The worst of times ...

We have specifically chosen not to mention either EHR company by name because both offer excellent products and meet their customers' needs; to continue the automotive analogy, we would be happy to own either as our "set of wheels." But no two EHRs are ever alike, and physicians who make the switch are often shocked by some of the differences.

For example, each EHR uses different terms to describe similar tasks. While the concepts might be easy to grasp, without a firm grip on this eu-phemistic language, it can be difficult to navigate the system. What one system might call a "task," another might call an "action." You could be searching for a "planned package" but should be searching for an "order set." And typically, none of the buttons or symbols look the same.

For physicians and staff in Chris's practice, the change in "language" represented a steep learning curve, and learning curves translate to loss of productivity. The "muscle memory" that staff had developed over years of using the complex software was not easily reprogrammed.

In addition, there was the issue of data migration. How could we take years of structured demographic data, progress notes, scanned documents, medications, allergies, lab results, and other information and move them into the new system? While technically possible, this is a costly and time-consuming undertaking, and requires the full cooperation of both EHR providers to successfully accomplish it. We were lucky to have the financial backing and influence of a large health system to see this through to completion; independent practices might not be as fortunate. Overall, the process went as planned, but it remains difficult to locate certain information when it's needed because each EHR has its own areas in which data elements are held.

Great support is key

Throughout the ordeal of changing our EHR, there was one factor that kept the process on-track: excellent support. Because of the resources provided by the health system, the practice did not need to rely on the expensive and sometimes less-than-responsive vendor to accomplish the transition. There was an entire team of individuals on- and off-site, dedicated to seeing us successfully transition from one EHR to the other. Even as the EHR "champion, Chris found his optimism tested, and now, almost a year after the transition, he is just starting to regain his prior efficiency.

Lessons learned

There were three important lessons learned from this experience that are relevant to practices planning to switch EHR systems:

First, make sure that you are picking the right EHR to which to transition, as changing will be a daunting task and added to the cost of the new software will be a cost in lost productivity. Second, make sure all members of the practice have as complete an understanding as possible about what to anticipate and expect the significant changes in the way things are recorded, stored, and processed. And third, since "no practice is an island," carefully plan and clarify who will be your main sources of support when the inevitable frustrations – which you could not anticipate – develop.

Dr. Skolnik is associate director of the family medicine residency program at Abington (Pa.) Memorial Hospital and aprofessor at Temple University, Philadelphia. He is editor in chief of a software company that creates medical handheld references. Dr. Notte practices family medicine and health care informatics at Abington Memorial. They are partners in EHR Practice Consultants. Contact them at info@ehrpc.com.

Time-dependent analysis questions vent bundles

BY DENISE NAPOLI
IMNG Medical News

When analyzed as a dynamic factor over time, use of the ventilator bundle was not associated with the prevention of ventilator-associated pneumonia in a study of over 600 patients.

The finding raises doubts about the widespread use of the bundle among intensive care units and calls into question efforts to make ventilator-associated pneumonias a "never event," said lead author Dr. Martin A Croce and his associates.

"While quality improvement initiatives are extremely important in the care of critically ill and injured patients, any potential penalty for institutions that actively participate in such initiatives is unwarranted," they wrote.

Their study, appearing in the February issue of the Journal of Trauma and Acute Care Surgery, involved 630 patients at six level 1 trauma centers over a 16-month period (J. Trauma Acute Care Surg. 2013;74:354-62).

All trauma patients who were admitted to an intensive care unit and received mechanical ventilation for at least 48 hours were eligible for study inclusion (90% with blunt trauma). They were followed daily in the ICU until the development of ventilator-associated pneumonia (VAP), ICU discharge, or death.

Dr. Croce, chief of the trauma division at the University of Tennessee Health Science Center, Memphis, and colleagues assessed compliance among these patients with the Institute for Healthcare Improvement (IHI) ventilator bundle, which is a set of core measures to be assessed daily and designed to improve the outcomes of mechanical ventilation.

The four core measures assessed in this study were presence of stress ulcer prophylaxis, deep vein thrombosis prophylaxis, elevation of the head of the bed, and a daily sedation vacation with assessment of weaning.

"Oral chlorhexidine was not part of the bundle since it was added by the IHI after the study protocol was already approved," the authors wrote.

Overall, 36% of patients developed VAP (96% diagnosed with bronchoalveolar lavage), and the overall mortality was 15%.

Sixteen patients were censored from the final analysis since they developed VAP late – that is, after 16 days in the study – and the authors assumed that the efficacy of the ventilator bundle would be greatest early in an ICU stay. In the end, a total of 210 patients were available for analysis.

The investigators then looked at the impact of the ventilator bundle on VAP in two ways: by individual patient and by patient-days.

To assess individual patient compliance, the authors summed each patient's bundle compliance score and then divided by the number of patients.

"Although this method is commonly used to calculate compliance, this method may not accurately measure bundle or component compliance because patients with either short or long stays are weighted equally," Dr. Croce and his associates said.

"Thus, equal weight is given to less severely injured patients with perfect or near-perfect compliance as is given to more severely injured patients with contraindications to some bundle components," they added.

Indeed, in this analysis, overall patient compliance with the bundle was significantly linked to a decrease in VAP. "To avoid this bias toward short stays, compliance was also calculated by patient-days," they noted. In this method, they counted each day's compliance as a unique event.

"Bundle compliance is a dynamic, time-dependent process during which an individual patient's status may change from noncompliant to compliant … depending on the patient's condition," Dr. Croce and his associates wrote. For example, DVT prophylaxis may be held in advance of surgery and restarted again later.

'Bundle compliance is a dynamic, time-dependent process ...'

DR. CROCE

In this analysis, ventilator bundle compliance was associated with neither the development nor the prevention of VAP, with a hazard ratio for bundle compliance of 1.26 (95% confidence interval, 0.845-1.877).

In fact, in this analysis, the only variable associated with VAP was male sex (hazard ratio, 1.75; 95% CI, 1.233-2.483). "It is important that [the Centers for Medicare and Medicaid Services] and third-party payers realize that in trauma patients, VAP is closely associated with uncontrollable risk factors such as sex and injury severity and its prevention is not associated with the four components of the IHI ventilator bundle," they said.

Dr. Croce and his coinvestigators stated that the study was funded by the National Trauma Institute and the U.S. Army. They disclosed no relevant conflicts of interest.

VIEW ON THE NEWS

Dr. Steven Q. Simpson, FCCP, comments: The reported prevalence of VAP in this study of 34% is far higher than in any study I have read previously, which would seem, on the face of it, to support the authors' contention. However, review of the paper reveals that overall bundle compliance in the study was only 48.9%. One could reliably predict that any therapy or preventive measure that is used only half the time would be unlikely to have any consistent positive or negative effect. The concept of bundle use relies on full compliance with all elements of the bundle, but that was not how they were used here.

Rather than demonstrating that the VAP bundle doesn't work, this study shows that some centers have difficulty using it and suggests that the intervention fails to work when it is not used as a bundle.

Hydroxyethyl starch riskier in acute fluid resuscitation

BY MARY ANN MOON
IMNG Medical News

Hydroxyethyl starch, a synthetic colloid used worldwide for acute fluid resuscitation in critically ill patients, appears to significantly raise the risks of mortality and severe renal injury, compared with other resuscitation solutions, according to a systematic review and meta-analysis published in JAMA.

The use of hydroxyethyl starch and other colloidal starch solutions has increased "despite their higher cost relative to crystalloid solutions, lack of evidence of their clinical superiority, and pervasive safety concerns," said Dr. Ryan Zarychanski of the section of critical care and the section of hematology and medical oncology, University of Manitoba, Winnipeg, and his associates (JAMA 2013;309:678-88).

Nonetheless, "over the years, hydroxyethyl starch products have appeared in several resuscitation guidelines, including those of the U.S. Hospital Consortium, and have often been advocated as the cornerstone of resuscitation therapy," the researchers noted.

Many of the data supporting the use of hydroxyethyl starch were recently retracted from the literature, however, after an investigation found that leading scientist Dr. Joachim Boldt had used unethical research practices and had fabricated data in at least 88 studies.

"All major systematic reviews and clinical guidelines are now being revised to account for the retracted data and permit sensitivity analyses on the remaining publications by Boldt et al.," Dr. Zarychanski and his colleagues said.

They performed a rigorous systematic review of randomized controlled trials comparing hydroxyethyl starch against crystalloid, albumin, or gelatin IV fluids for acute fluid resuscitation in critically ill adults. The study subjects were treated in emergency or intensive care settings during 1982-2012.

The meta-analysis covered 38 trials, including 7 studies by Dr. Boldt that had not been retracted because they had been published before 1999, the cutoff date for the misconduct investigation.

A total of 35 studies involving 10,880 patients contributed mortality data to the meta-analysis. The overall mortality risk was significantly higher for patients randomly assigned to receive hydroxyethyl starch than for those assigned to other solutions (relative risk, 1.07).

Continued on page 14

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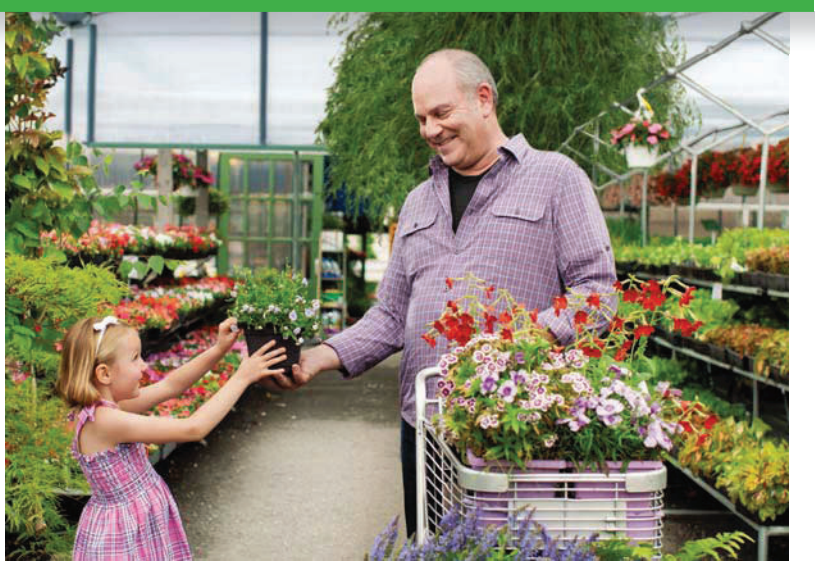
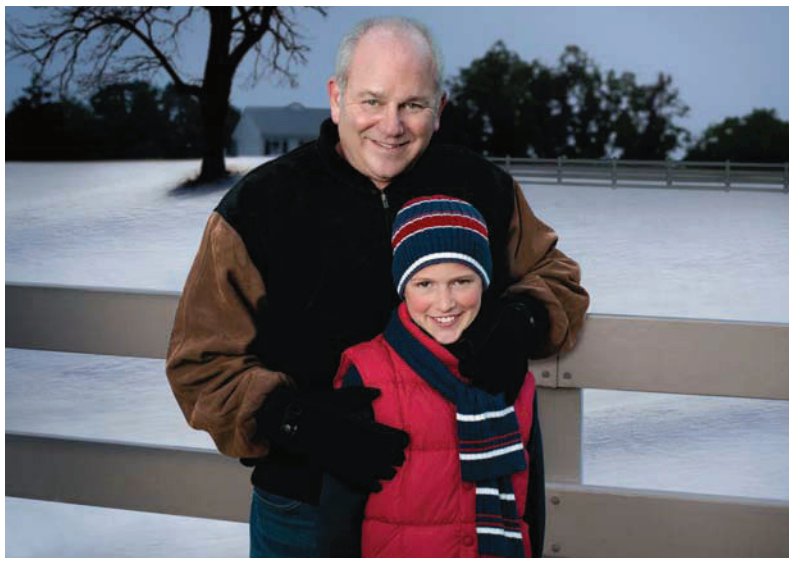
TUDORZA™ can help





IMPORTANT SAFETY INFORMATION

- TUDORZA PRESSAIR is not indicated for the initial treatment of acute episodes of bronchospasm (ie, rescue therapy).
- Inhaled medicines, including TUDORZA, may cause paradoxical bronchospasm. In addition, immediate hypersensitivity reactions may occur after administration of TUDORZA. If either of these occurs, treatment with TUDORZA should be stopped and other treatments considered.
- TUDORZA should be used with caution in patients with narrow-angle glaucoma or urinary retention. Instruct patients to consult a physician immediately should any signs or symptoms of narrow-angle glaucoma or prostatic hyperplasia or bladder-neck obstruction develop.

Introducing TUDORZA™ PRESSAIR™
A new long-acting anticholinergic treatment

For the long-term maintenance treatment of bronchospasm in patients with COPD

TUDORZA provides statistically significant improvements in bronchodilation that are consistent over time[1]

- Statistically significant improvements in morning predose lung function (forced expiratory volume in one second [FEV_1]) at 12 weeks (primary endpoint) or 24 weeks vs placebo[1-3]
- Mean peak improvements in FEV_1 relative to baseline observed after the first dose on day 1 were similar at 12 weeks[1]
- No overall differences in efficacy or safety were observed between older (≥70 years) and younger (<70 years) adult patients in 3 placebo-controlled studies[1]
- Common side effects occurred at rates of <7%[1]
  - The most common side effects (≥3% incidence and greater than placebo) were headache (6.6% vs 5.0%), nasopharyngitis (5.5% vs 3.9%), and cough (3.0% vs 2.2%), for TUDORZA vs placebo, respectively[1]
  - The incidence of common anticholinergic side effects was <1%, including dry mouth (0.8% vs 0.6%), constipation (0.0% vs 0.9%), tachycardia (0.3% vs 0.0%), and urinary retention (0.2% vs 0.0%), for TUDORZA vs placebo, respectively[2]
- Preloaded, multiple-dose inhaler with dose indicator and colored control window that confirms correct inhalation[1]
  - For a complete description of how to use the TUDORZA PRESSAIR inhaler, see the step-by-step Instructions for Use within the full Prescribing Information, available at www.TUDORZA.com
- The recommended dose is one oral inhalation of 400 mcg, twice daily[1]

IMPORTANT SAFETY INFORMATION

- Patients with a history of hypersensitivity reactions to atropine should be closely monitored for similar hypersensitivity reactions to TUDORZA. Use with caution in patients with severe hypersensitivity to milk proteins.
- The most common adverse reactions (≥3% incidence and greater than placebo) were headache, nasopharyngitis, and cough.

Please see Brief Summary of full Prescribing Information at the end of this ad.

New

Tudorza™ Pressair™

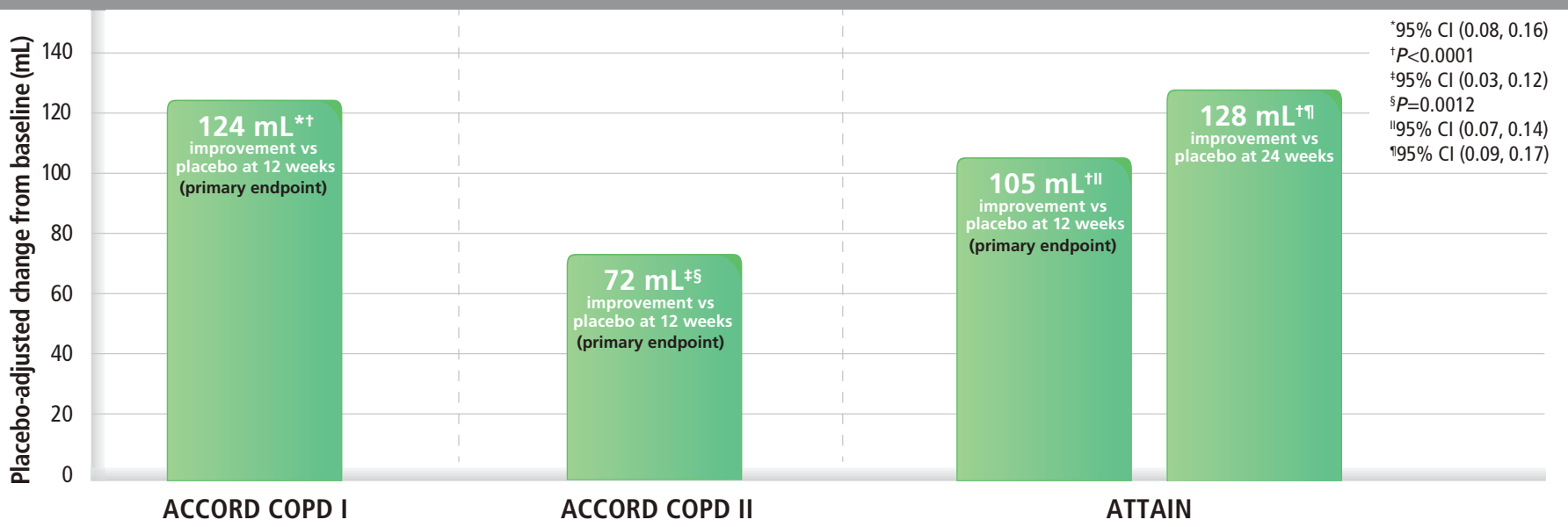
(aclidinium bromide inhalation powder)

400 mcg

In placebo-controlled studies

TUDORZA provided statistically significant improvements in morning trough (predose) lung function at 12 or 24 weeks

Morning trough (predose) FEV_1 treatment difference vs placebo at 12 or 24 weeks across 3 studies[2,3]



Please see study descriptions below, including results for individual treatment arms.

The primary endpoint for all 3 studies was the change from baseline in morning trough (predose) FEV_1 at 12 weeks. Morning trough (predose) FEV_1 was defined as FEV_1 measured 12 hours after the previous evening dose of TUDORZA. A secondary endpoint of change from baseline in morning trough (predose) FEV_1 at 24 weeks was measured in the ATTAIN study.[1-3]

Study design for ACCORD COPD I: A randomized, double-blind, 12-week study in patients with moderate to severe COPD (N=375; n=190 [TUDORZA] and n=185 [placebo]) that assessed the bronchodilator efficacy and safety of inhaled TUDORZA. Mean patient age was 65 years; 52.1% male, 94.7% Caucasian. Rescue medication, corticosteroids, methylxanthines (theophylline), and oxygen therapy were allowed as concomitant treatments. Major relevant medication classes not allowed included long-acting beta agonists, short-acting muscarinic antagonists, long-acting muscarinic antagonists, and long-acting beta agonist/inhaled corticosteroid combinations.[1-3]

Mean baseline values for morning trough (predose) FEV_1 were 1.33 L for the TUDORZA study group and 1.38 L for the placebo study group. The change from baseline in morning trough (predose) FEV_1 at 12 weeks was 99 mL for the TUDORZA study group and -25 mL for the placebo study group.[1-3]

Study design for ACCORD COPD II: A randomized, double-blind, 12-week study in patients with moderate to severe COPD (N=359; n=177 [TUDORZA] and n=182 [placebo]) that assessed the bronchodilator efficacy and safety of inhaled TUDORZA. Mean patient age was 62.5 years; 52.6% male, 91.4% Caucasian. Rescue medication, corticosteroids, methylxanthines (theophylline), and oxygen therapy were allowed as concomitant treatments. Major relevant medication classes not allowed included long-acting beta agonists, short-acting muscarinic antagonists, long-acting muscarinic antagonists, and long-acting beta agonist/inhaled corticosteroid combinations.[1,2]

Mean baseline values for morning trough (predose) FEV_1 were 1.25 L for the TUDORZA study group and 1.46 L for the placebo study group. The change from baseline in morning trough (predose) FEV_1 at 12 weeks was 64 mL for the TUDORZA study group and -8 mL for the placebo study group.[1,2]

Study design for ATTAIN: A randomized, double-blind, 24-week study in patients with moderate to severe COPD (N=542; n=269 [TUDORZA] and n=273 [placebo]) that assessed the long-term bronchodilator efficacy and safety of inhaled TUDORZA. Mean patient age was 62.5 years; 68.5% male, 95.4% Caucasian. Rescue medication, corticosteroids, methylxanthines (theophylline), and oxygen therapy were allowed as concomitant treatments. Major relevant medication classes not allowed included long-acting beta agonists, short-acting muscarinic antagonists, long-acting muscarinic antagonists, and long-acting beta agonist/inhaled corticosteroid combinations.[1,2]

Mean baseline values for morning trough (predose) FEV_1 were 1.51 L for the TUDORZA study group and 1.50 L for the placebo study group. The change from baseline in morning trough (predose) FEV_1 at 12 and 24 weeks was 58 mL and 55 mL, respectively, for the TUDORZA study group and -47 mL and -73 mL, respectively, for the placebo study group.[1,2]

Peak lung function in all 3 studies

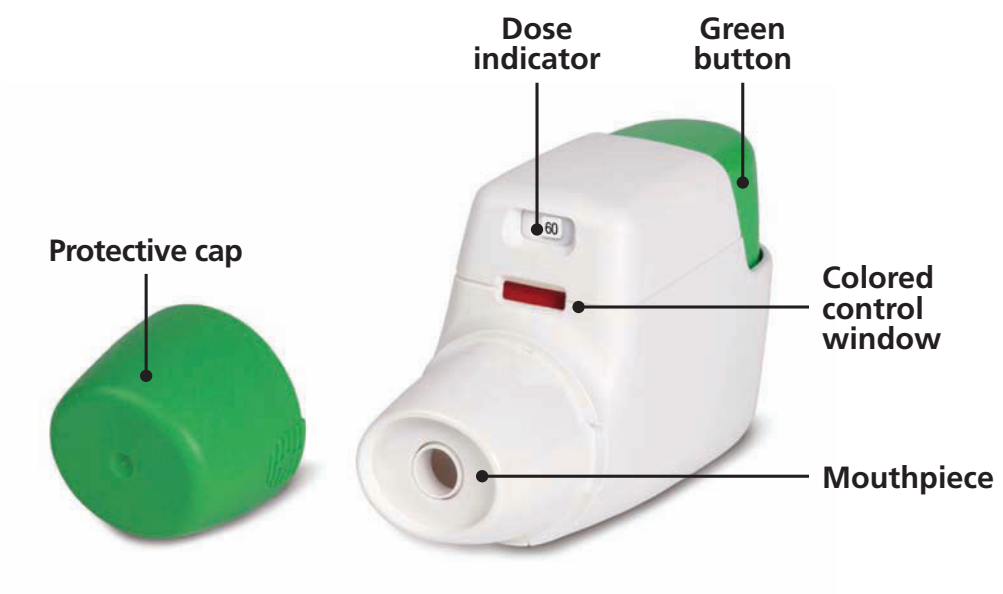
Mean peak improvements in FEV_1 relative to baseline observed after the first dose on day 1 were similar at 12 weeks[1]

IMPORTANT SAFETY INFORMATION

- TUDORZA PRESSAIR is not indicated for the initial treatment of acute episodes of bronchospasm (ie, rescue therapy).
- Inhaled medicines, including TUDORZA, may cause paradoxical bronchospasm. In addition, immediate hypersensitivity reactions may occur after administration of TUDORZA. If either of these occurs, treatment with TUDORZA should be stopped and other treatments considered.
- TUDORZA should be used with caution in patients with narrow-angle glaucoma or urinary retention. Instruct patients to consult a physician immediately should any signs or symptoms of narrow-angle glaucoma or prostatic hyperplasia or bladder-neck obstruction develop.

The new PRESSAIR™ inhaler

TUDORZA is administered using a preloaded, multiple-dose, dry-powder inhaler[1]



- **Preloaded** with 60 doses for 1 month of treatment[1]
- **Colored control window**—provides confirmation of successful inhalation[1]
  - Turns from red to green when the dose is ready, and from green to red when the patient has inhaled the full dose of medication correctly
- A **"click"** sounds during inhalation when the patient is using the inhaler correctly[1]
  - Patients should keep breathing in after the "click" to be sure they get the full dose
- **Dose indicator**—shows patients approximately how many doses remain in the inhaler[1]
  - Number of doses counts down in intervals of 10 (60, 50, 40, 30, 20, 10, 0) with use
- Taking a dose from the PRESSAIR inhaler requires patients to press and release the green button, and then inhale[1]
  - For a complete description of how to use the TUDORZA PRESSAIR inhaler, see the step-by-step Instructions for Use within the full Prescribing Information, available at www.TUDORZA.com

IMPORTANT SAFETY INFORMATION

- Patients with a history of hypersensitivity reactions to atropine should be closely monitored for similar hypersensitivity reactions to TUDORZA. Use with caution in patients with severe hypersensitivity to milk proteins.
- The most common adverse reactions (≥3% incidence and greater than placebo) were headache, nasopharyngitis, and cough.

Please see Brief Summary of full Prescribing Information at the end of this ad.

References: 1. TUDORZA PRESSAIR (aclidinium bromide inhalation powder) Prescribing Information. Forest Pharmaceuticals, Inc. St. Louis, MO. **2.** Data on file. Forest Laboratories, Inc. **3.** Kerwin EM, D'Urzo AD, Gelb AF, et al, on behalf of the ACCORD I study investigators. Efficacy and safety of a 12-week treatment with twice-daily aclidinium bromide in COPD patients (ACCORD COPD I). *COPD.* 2012;9:90-101.

New

Tudorza™ Pressair™

(aclidinium bromide inhalation powder)

400 mcg

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

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Continued from page 8

When the data from the 7 Dr. Boldt studies were excluded from the meta-analysis, the pooled results from the remaining 28 trials (10,290 patients) showed an even stronger increase in mortality risk (RR, 1.09).

The seven Boldt trials were then excluded from all further analyses.

Ten trials reported on the rate of renal replacement therapy in 9,258 patients. The use of hydroxyethyl starch was associated with a significantly greater risk of renal injury (RR, 1.32), compared with other resuscitation fluids.

The incidence of acute renal failure was reported in five trials involving 8,725 patients. Again, the incidence of this adverse effect was significantly greater in patients randomly assigned to receive hydroxyethyl starch than in those receiving other fluids (RR, 1.27).

Several sensitivity and subgroup analyses all supported the findings from the main analysis. The results indicate that "clinical use of hydroxyethyl starch for acute volume resuscitation is not warranted due to serious safety concerns," Dr. Zarychanski and his associates said.

Although hydroxyethyl starch solutions are effective volume expanders, their effects are not confined to the circulatory system, the investigators explained. The solutions also are deposited in the endothelial cells, kidneys, liver, muscle, skin, and spleen.

"Proponents of starch solutions have argued increased safety with each newly marketed product, but evidence from randomized trials [does] not support these claims," the study authors said.

In addition, their meta-analysis demonstrated that the publication of inaccurate or fraudulent data "can influence how the global medical community interprets a given body of literature, and how exclusion of questionable studies can shift the balance of evidence toward benefit or harm."

Dr. Zarychanski reported no relevant financial disclosures; an associate reported ties to Bristol-Myers Squibb and Abbott Laboratories.

VIEW ON THE NEWS

Dr. Lary Robinson, FCCP, comments: Numerous favorable clinical studies on the use of hydroxyethyl starch (hetastarch) were published starting in the 1990s by Boldt and associates in Germany but were subsequently found to be unethical and had fabricated data.

Dr. Ryan Zarychanski and associates published a rigorous meta-analysis of 38 randomized trials employing hydroxyethyl starch for fluid resuscitation compared with other solutions in critically ill adults from 1982 to 2012. When seven flawed studies of Dr. Boldt's were excluded from analysis, hetastarch patients had a significantly greater risk of renal injury/failure and need for renal replacement therapy, as well as a significantly higher mortality rate. The take-home message from this exhaustive analysis was that "clinical use of hydroxyethyl starch for acute volume resuscitation is not warranted due to serious safety concerns."

Smoking high among mentally ill

CDC *from page 1*

smokers who do not have a mental illness.

Wide variations were found in the proportion of people with a mental illness who smoked across states, ranging from a low of 18.2% in Utah to almost 50% in West Virginia. In addition to younger adults, the gap in smoking rates was particularly stark among certain populations, including American Indians and Alaska natives (54.7% of those with a mental illness smoked vs. 30.5% of those who did not have a mental illness) and people living below the poverty line (48% vs. 33%).

Rates were also higher among people with a mental illness who had lower levels of education (47% among those with less than a high school education and 40.2% of those with a high school education, vs. 19% of college grads).

During a telebriefing held to announce the results, CDC director Dr. Thomas Frieden emphasized that although adults with mental illness smoke more and are less likely to quit, smoking cessation programs work but are underused in this population, and more efforts should be directed toward helping adults with mental illness quit successfully.

"People with mental illness who smoke want to and can quit, and more needs to be done to provide them with the resources and services to help them quit successfully," including making mental health facilities tobacco- and smoke-free, he said at the telebriefing, which was sponsored by the CDC.

The CDC report is available at cdc.gov/vitalsigns/SmokingAndMentalIllness/.

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VIEW ON THE NEWS

Dr. Burt Lesnick, FCCP, comments: Most smokers begin their habit before age 21, thus it starts as a pediatric disease. Since onset of depression is frequent during the teen years, specific attention focused on this subset may be an effective strategy for reducing the rate of tobacco dependence.

Aerosol test flagged most-infectious TB patients

TB *from page 1*

new infection in contacts than did an AFB-positive smear. The study group included 96 adult TB patients with sputum AFB-positive culture and their 442 household contacts from May 2009 to January 2011.

The TB patients attended the Mulago Hospital National Tuberculosis and Leprosy Programme in Kampala, Uganda, and lived with at least three household contacts. All had an initial AFB of at least 1+ plus *M. tuberculosis* culture growth and had received fewer than 6 days of antituberculous treatment or no treatment.

VIEW ON THE NEWS

Dr. Vera DePalo, FCCP, comments: With communicable diseases, the clinician is always concerned with the patient's likelihood of infecting others. The ability to assess for "infectious potential" would be a significant tool from both a public health perspective and from a resource utilization perspective.

A total of 45% of patients (43) produced culturable *M. tuberculosis* in aerosols during the two 5-minute coughing periods of sample collection. The 26% of total study group patients who produced high aerosols (at least 10 CFUs) were more likely to transmit an infection to their contacts than the 19% with low aerosols (1-9 CFUs) or the 55% of aerosol-negative cases. Ten was selected as a CFU cut-off, based on an associated increase in tuberculin skin test (TST) conversion risk at this number.

While 69% of the contacts of high aerosol patients were "at-risk" of TST conversion, 25% of contacts of low aerosol patients and 30% of contacts of aerosol-negative patients were at risk of TST conversation.

New infections were diagnosed through a positive TST or interferon-gamma release assay (IGRA), with retests 6 weeks later for contacts who tested negative at baseline for both TST and IGRA.

TST conversion risk in low aerosol and aerosol-negative patient contacts was similar (odds ratio, 0.77). However, the risk in contacts of high aerosol patients was over five times greater than in contacts of low aerosol patients (OR, 5.18) before adjustment. An adjusted analysis yielded a similar odds ratio (OR, 4.81).

Meanwhile, "the same analysis using sputum AFB smear grade to classify exposure groups did not show a clear or consistent risk stratification," the authors wrote. Therefore, high-aerosol TB patients more accurately predicted new TB infections, based on risk of TST conversion.

"In addition to providing a more precise marker of source infectiousness, cough aerosols may help determine the individual risk of *M. tuberculosis* infection after exposure, which can be variable and is poorly understood," the authors wrote. Yet they acknowledge the limitation that cough aerosols' predictive value over time is unknown.

They noted three primary implications of their findings, first of which is a "new framework for rational and cost-effective infection control decisions" since the common wisdom that all sputum AFB- positive patients are equally infectious is no longer necessarily the case. They also noted that Latent Tuberculosis Infection treatment programs may be improved through more efficient selection of TB contacts with TB exposure.

This study was supported by the University of Medicine and Dentistry of New Jersey Foundation, the Division of Infectious Diseases at New Jersey Medical School, the section of infectious diseases at Boston Medical Center, and support to Dr. Matthew Fox from the National Institute of Allergy and Infectious Diseases.

Meta-analysis bolsters TB assay's strength

BY ELIZABETH MECHCATIE
IMNG Medical News

The sensitivity and specificity of a diagnostic test that rapidly detects tuberculosis support its use as an initial diagnostic test in adults suspected of having TB, including multidrug-resistant or HIV-associated disease, based on a meta-analysis, researchers say.

In addition, the meta-analysis results suggest that the test, the Xpert assay, "may also be valuable as an add-on test following a negative smear microscopy result in patients suspected of having TB," said Karen Steingart, of the University of Washington School of Public Health, Seattle, and her associates. The study was published in the Cochrane Database of Systematic Reviews (DOI:10.1002/14651858.CD009593.pub2.)

Xpert, made by Cepheid is an automated polymerase chain reaction test that detects *Mycobacterium tuberculosis* complex and rifampin resistance within 2 hours using a sputum sample, used outside of a reference lab "with minimal hands-on technical time," as opposed to conventional sputum smear microscopy, which is cheaper, but requires a microscope in a lab and does not detect drug resistance.

In 2010, Xpert was endorsed by the World Health Organization for use as the initial diagnostic test on people suspected of having MDR-TB or HIV-associated TB.

The study reviewed 18 studies of over 7,500 adults, mostly in low- and middle-income countries, with a high burden of TB, which evaluated the assay as an initial test used as a replacement for microscopy, and as an add-on test when a microscopy smear was negative, in adults suspected of having pulmonary TB, or multidrug-resistant TB, with or without HIV infection. The main results of the test are:

- A "modest" sensitivity of 88% and a "high" specificity of 98% for detecting TB when used as an initial test.
- Sensitivity of 67% and specificity of 98% as an add-on follow-up test to detect TB, after a negative smear microscopy.
- Sensitivity of 80% for detecting TB in people with HIV, 89% in people without HIV.
- Sensitivity of 94% and specificity of 98% for detecting rifampin resistance when used as a replacement for culture based-drug susceptibility testing.

The rate of indeterminate results was a "very low" 1%, they said.

One study author disclosed having published on the Xpert test. Others reported having no relevant financial conflicts.

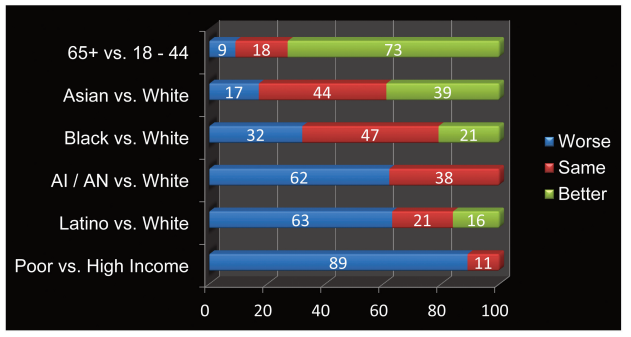
FROM THE PRESIDENT Diversity, health equity, and social justice

BY DR. DARCY D. MARCINIUK, FCCP; DR. MARILYN G. FOREMAN, FCCP; DR. C. SOLA OLOPADE, MPH, FCCP;

Despite significant expenditures and major technological advancements in medical care, the problems of health and health-care disparities persist. The 2002 Institute of Medicine report, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*[1] codified the issue, garnered attention, and galvanized individuals to action, but significant measurable progress remains to be made. In 2011, the US Department of Health and Human Services (HHS) and others[2] stated that life expectancy in the US increased, but health disparities persist. HHS estimated that disparities have increased for 13% of the Healthy 2010 Objectives,[3] and remained unchanged for 80% of the objectives. HHS Assistant Secretary for Health Howard K. Koh, MD, MPH, offered the following explanation: "But to reduce disparities and achieve true sustainable change in public health, we need to create a 'health in all policies' approach that reaches people where they live, work, play, and pray."

As pulmonary, critical care, and sleep medicine practitioners, our priorities should result in meaningful reduction in respiratory health disparities, such as lung cancer, pneumococcal vaccination rates, asthma, and active tobacco smoking.[4-7] Unfortunately, there has been a 12% increase in the prevalence of asthma since 2001,[8] and the death rate for adult African Americans with asthma is approximately three times greater than for whites and eight times greater for children.[9] Socioeconomic status, measured by education, has also been associated with FEV_1, in which high school completion was associated with increased FEV_1, an effect more pronounced in whites than African Americans.[10] Health disparities ultimately result in added health costs, lost work productivity, and premature death. It is estimated that 30% of direct medical costs for African Americans, Latinos, and Asian Americans is due to health inequities and that the economy loses an estimated $309 billion per year due to the direct and indirect costs of disparities.[11] Pending changes in health insurance coverage, disparities exist in access to medical care (Fig 1). With an increasing wealth gap and increasing diversity in the population, these disparities may continue to increase.

Figure 1. Disparities in Access to Care (%)



Focus on Health Disparities – Key Facts
Kaiser Family Foundation

Initiatives from community-based organizations or in medical education that increase awareness of disparities and teach cultural competence are integral parts of the solution to reduce disparities. However, these efforts have been criticized for lacking rigorous empirical methods to gauge effectiveness.[12-15] Nivet[16] suggests three concrete priorities in regard to diversity work: to measure progress and attain accountability on diversity efforts; to make apparent the overlap between diversity and excellence in patient care, research, and medical education; and not to lose sight of the social justice rationale at the heart of these efforts but to further support investment in diversity and inclusion with evidence of their value to organizational performance

Between 1978 and 2008, 75% of all medical school graduates were white with African Americans, American Indians/Alaska natives, and Latinos comprising 12.3% of the physician workforce (Fig 2). Approximately 3% of pulmonary trainees were African American in 2009 (Fig 3). [17]

In 2011, the percentages of Latino and African American trainees remained stagnant and continued to be low (Fig. 4).[18] Benefits to workforce diversification include better access for minority patients, improved patient satisfaction, strengthened cultural competence and sensitivity among other health professionals, and overall improved academic performance for students of the health professions. It is also apparent that increased opportunities for mentoring to facilitate professional advancement are also needed in these settings.

The American College of Chest Physicians recognizes these issues and challenges and has solidified the commitment to reduction in respiratory health disparities and increasing diversity in the pulmonary, critical care, and sleep workforce by elevating its College-wide efforts. The Diversity Committee, reporting directly to the President and the Board of Regents, is composed of four subcommittees: (1) Communication and Outreach; (2) Membership Development; (3) Underrepresented Minority Scholar Award; and (4) Professional Advancement/Development. Individuals who were previously active in the Cultural Diversity in Medicine NetWork may continue to volunteer their ideas and efforts through participation in Communication and Outreach Subcommittee, which is currently headed by Dr. Ahmed J. Khan, FCCP. The leadership of the Diversity Committee advises the ACCP Board of Regents and College leadership on issues of concern to underrepresented clinicians and investigators and spearheads programs and activities addressing various issues affecting researchers who are underrepresented, respiratory disorders in underrepresented populations, and other relevant topics. We strive to inculcate a culture across the College that instills, celebrates, and leverages diversity within the ACCP in a sustained fashion rather than functioning in isolation.

To date, the Diversity Committee has also been successful in the creation of two awards: the ACCP Diversity Committee Young

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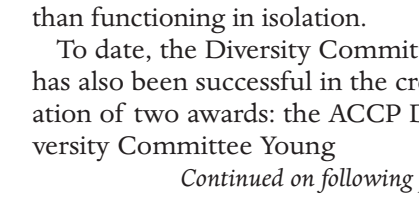
Figure 2.

Diversity in the Physician Workforce, 2008



Association of Amer Med Colleges (AAMC) 2010
AA = African American
AI / AN = American Indian or Alaska native
Source: AAMC Data warehouse: Minority Physician Database, AMA_Masterfile as of 11/30/2009.

Continued from previous page

Investigator Faculty Scholar in Pulmonary, Cardiovascular, Critical Care, or Sleep Research Grant and the Diversity Scholar in Pulmonary, Cardiovascular, and Sleep Research Award. Other goals include collaboration with outside organizations to develop quantifiable programs, projects, and platforms to promote diversity, health equity, and reduction in health disparities. This is consistent with the mission of the ACCP, increasing involvement of global members addressing global health disparities and developing metrics to gauge and track success.

The Diversity Committee requires the input, assistance, and support from the entire ACCP membership in order to translate commitment to action and to ignite meaningful change. Members and ACCP NetWorks should propose and undertake diversity projects and address diversity issues in their CHEST educational offerings and activities. The scope of diversity has broadened and is now more inclusive. Diversity needs to be seen and accepted as a moral imperative to increase access to care, reduce health disparities, shape a more inclusive biomedical clinical research agenda, and enhance cultural competence. Diversity and inclusiveness lead to institutional excellence, defined as the degree to which an organization achieves its stated mission and goals divided by the amount of resources to reach these goals.[16] With the full support of the membership and moving far beyond "feel good" diversity initiatives and political correctness, the Diversity Committee and the ACCP will achieve a self-sustaining College-wide culture that effectively promotes diversity in the workforce, enhances care for our constituents, and results in measurable effectiveness for all.

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Professional Advancement/Development: TBA

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Figure 3. Total Fellows – Race/Ethnicity Pulmonary/CCM/Sleep (%)

Data from 2009						
	White	Latino	AA	Asian	AI / AN	Total
Pulm/CC	694 (53.3)	135 (10.4)	36 (3.0)	433 (33.3)	4 (0.31)	1302
Pulm	22 (28.2)	8 (10.3)	5 (6.4)	43 (55.1)	0	78
CCM	64 (41.3)	16 (10.3)	9 (5.8)	65 (41.9)	1 (0.7)	155
Sleep	35 (36.8)	3 (3.2)	2 (2.1)	55 (57.9)	0	95
Total	815 (50)	162 (9.9)	52 (3.0)	596 (36.6)	5 (0.31)	1630
*Other/unknown and Native Hawaiian/Pacific Islander are not shown						

Adapted from Brotherton and Etzel.[17]

Figure 4. Total Fellows – Race/Ethnicity Pulmonary/CCM/Sleep (%)

Data from 2011						
	White	Latino	AA	Asian	AI / AN	Total
Pulm/CC	808 (55.4)	144 (9.9)	38 (2.6)	466 (31.9)	3 (0.2)	1459
Pulm	22 (28.0)	7 (9.0)	5 (6.0)	45 (57.0)	0	79
CCM	87 (45.0)	20 (10.4)	12 (6.2)	74 (38.3)	0	193
Sleep	55 (46.0)	9 (8.0)	4 (3.0)	51 (43.0)	0	119
Total	972 (53)	180 (10)	59 (3.2)	636 (34)	3 (0.2)	1850
*Other/unknown and Native Hawaiian/Pacific Islander are not included						

Adapted from Brotherton and Etzel.[18]

New grants support diversity and partnerships

Applications are now being accepted by The CHEST Foundation for more than $500,000 in research and community service grants. This year, two new grants reinforce the ACCP's commitment to promoting diversity, fostering health equity, and joining with partner organizations to support lung-health research.

The ACCP Diversity Committee Young Investigator Faculty Scholar in Pulmonary, Cardiovascular, Critical Care, or Sleep Research Grant is a 1-year, $25,000 grant designed to encourage outstanding underrepresented young investigators in their careers in pulmonary, cardiovascular, critical care, or sleep research, with the focus on community-based scholarly work that promotes health equity and addresses health disparity at the local or global level.

'When it comes to funding, even from large established funding sources, minority researchers are disproportionately underrepresented.'

The new grant stems from an initiative spearheaded by ACCP Past President Dr. David Gutterman, FCCP, to make diversity and inclusiveness a crucial part of the ACCP. That commitment also included the formation of the ACCP Diversity Committee and changes to the ACCP vision statement that emphasize the organization's global reach and commitment to creating health equity. The new vision statement, adopted in 2011, reads: "As the global leader in providing education in cardiopulmonary, critical care, and sleep medicine, the ACCP will promote diversity to optimize health, advance patient care, and support research while fostering health equity."

Dr. C. Sola Olopade, MPH, FCCP, Professor of Medicine and Clinical Director of the Global Health Initiative at the University of Chicago, is Vice-Chair of the Diversity Committee and was instrumental in development of the new grant. "Access to grant support is crucial for young minority physicians and researchers," he says.

"When it comes to funding, even from large established funding sources, minority researchers are disproportionately underrepresented. According to a study published in the journal *Science* in 2011, black applicants are 10 percentage points less likely to be awarded funding. Financial support early on provides an important head start."

Dr. Olopade recalls his own struggles as a young academic just out of fellowship training, when he says he had "ideas, but no money, and no mentor to show me how to navigate academic medicine." He sees the new grant as an important mechanism for providing needed support and mentoring to young underrepresented investigators and for creating ongoing minority engagement with the ACCP.

The Pulmonary Fibrosis Foundation and The CHEST Foundation

Clinical Research Grant in Pulmonary Fibrosis is a 1-year, $30,000 grant that supports a clinical or translational research project that would contribute to effective treatments or a cure for pulmonary fibrosis.

"Idiopathic pulmonary fibrosis is a disease with no FDA-approved therapy and no known cure. Funding for IPF research is critical," says Dolly Kervitsky, RCP, CCRC, Vice President for Patient Relations and Medical Affairs at the Pulmonary Fibrosis Foundation and an affiliate ACCP member.

"We are thrilled to be working with The CHEST Foundation to offer this grant, which we hope will ultimately make a difference in quality of life for patients with IPF," she says. "The Pulmonary Fibrosis Foundation is committed to substantially increasing funding for research through partnership grants like this.

Applicants for both new grants must be ACCP members who have completed at least 2 years of a pulmonary or critical care fellowship and are within 7 years of completing training.

Applications for these and other CHEST Foundation grants and awards are due May 1, 2013. For a complete list of available grants and awards or to apply, go to onebreath.org.

THE CHEST FOUNDATION®

The CHEST Foundation 2013 Grants and Awards include:

GlaxoSmithKline Distinguished Scholar in Respiratory Health (3 years, $150,000)
Alpha-1 Foundation and The CHEST Foundation Clinical Research Grant in COPD and Alpha-1 Antitrypsin (AAT) Deficiency (1 year, $25,000)
The CHEST Foundation and the Respiratory Health Association of Metropolitan Chicago Clinical Research Grant in Women's Lung Health (1 year, $10,000)
The Sheila J. Goodnight, MD, FCCP Clinical Research Grant in Women's Lung Health (1 year, $10,000)
OneBreath® Clinical Research Grant in Lung Cancer (2 years, $100,000)
The CHEST Foundation Clinical Research Grant in Pulmonary Arterial Hypertension (1 year, $50,000)
Roger C. Bone Advances in End-of-Life Care Award (1 year, $10,000)
McCaffree OneBreath® Community Service Grants (ranging from $5,000 to $15,000)

Applications for all CHEST Foundation grants and awards are due May 1, 2013. View criteria and apply at onebreath.org.

CHEST 2013: Act now ... opportunities abound

Call for Abstracts and Case Reports

Submission deadline: April 1

Submit an abstract of your original investigative work or a case report for presentation at the meeting. Categories are available for health professionals at all stages of their careers, including students and residents. Both domestic and international submissions are invited, and submission is free.

Consider these opportunities:

- Call for Abstracts (all attendees)
- Call for Clinical Case Puzzlers (all attendees)
- Call for Global Case Reports (Canadian and international attendees)
- Call for Affiliate Case Reports (ACCP affiliate members)
- Call for Medical Student/Resident Case Reports (medical students and residents)

All accepted abstracts and case reports (not puzzlers) will appear online in a *CHEST* Journal supplement. Accepted abstracts, affiliate case reports, and medical student/resident case reports will be eligible for cash prizes from The CHEST Foundation, while accepted global case reports will be eligible for recognition awards.

Learn more and submit at chestmeeting.chestnet.org.

The CHEST Foundation 2013 Grants and Awards Program

Application deadline: May 1

Each year, The CHEST Foundation offers more than $500,000 in grants for clinical and translational research, leadership, and volunteer community service. This year, grants are offered in:

- Respiratory health
- Lung cancer
- Pulmonary arterial hypertension
- COPD and alpha-1 antitrypsin deficiency
- End-of-life care
- Women's lung health
- Pulmonary fibrosis
- Community service

New this year is the ACCP Diversity Committee Young Investigator Faculty Scholar Grant, supporting underrepresented young researchers, and the Pulmonary Fibrosis Foundation and The CHEST Foundation Clinical Research Grant in Pulmonary Fibrosis.

Since The Foundation's inception in 1996, it has awarded more than $9 million to promote cutting-edge research and improve lung health around the world. CHEST Foundation grants support ACCP members early in their careers, Distinguished Scholars, leaders in end of life/palliative care, and humanitarians involved in pro bono work in 50 countries throughout the world and the United States.

CHEST 2013

October 26 - 31
Chicago, Illinois

Learn more and apply at OneBreath.org.

Play CHEST Challenge

Game ends: May 31

ACCP affiliate members, play CHEST Challenge to test your knowledge of pulmonary, critical care, and sleep medicine while competing for prizes:

- FREE trip to a 2013 ACCP board review course
- FREE trip to CHEST 2013
- Cash prizes

Play by taking an online test. All players will be scored, and the nine top-scoring programs from the online competition will be invited to the play-off rounds. These teams will compete in live Jeopardy game-show-style play-off rounds August 27, during the ACCP board review courses. All play-off contestants will receive:

- Airfare and registration to a 2013 ACCP board review course in San Antonio, Texas
- Complimentary hotel accommodations

The three top-scoring programs from the play-off rounds will compete in the CHEST Challenge Championship at CHEST 2013. All championship players will receive:

- Airfare and registration to CHEST 2013 in Chicago, Illinois
- Complimentary hotel accommodations
- Cash prizes

Game on! Take the online test at chestchallenge.org.

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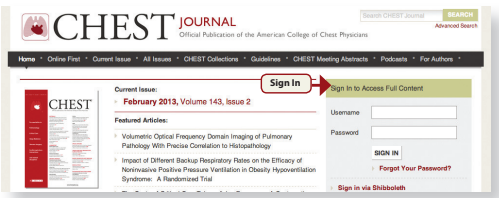

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3. **After landing on the page for the alert type, click "Get Email Alerts."**

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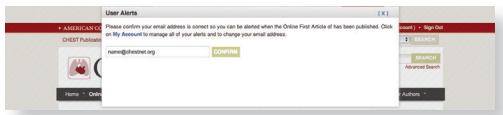


AMERICAN COLLEGE OF CHEST PHYSICIANS

CHEST 2013

October 26 - 31
Chicago, Illinois

Game On!

ACCP affiliate members, play CHEST Challenge to test your knowledge of pulmonary, critical care, and sleep medicine while competing for prizes:

- **FREE** trip to a 2013 ACCP board review course
- **FREE** trip to CHEST 2013
- Cash prizes

Online Contest: Through May 31

Play begins with an online test. The nine top-scoring programs will be invited to the play-off rounds.

CHEST Challenge Play-offs: August 27

The nine winning teams will go head-to-head in live Jeopardy game-show-style play-off rounds during the ACCP board review courses. All play-off contestants will receive:

- Airfare and registration to a 2013 ACCP board review course in San Antonio, Texas
- Complimentary hotel

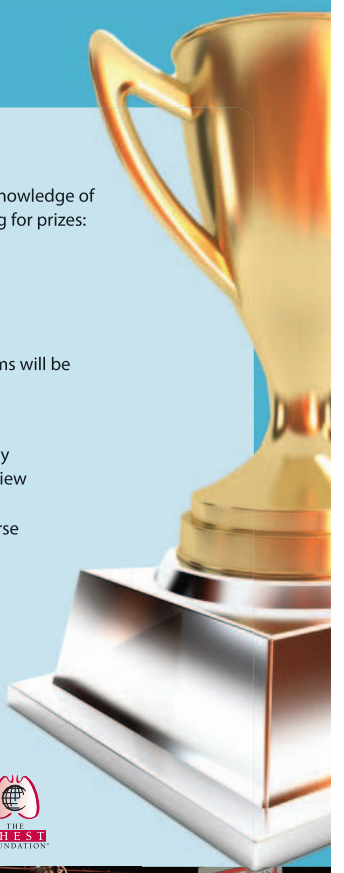
CHEST Challenge Championship: TBD

The three top-scoring programs will compete in the CHEST Challenge Championship at CHEST 2013. All championship players will receive:

- Airfare and registration to CHEST 2013 in Chicago, Illinois
- Complimentary hotel
- Cash prizes

Game On...Play Now!
chestchallenge.org

AMERICAN COLLEGE OF CHEST PHYSICIANS
THE CHEST FOUNDATION



NETWORKS: Research, critical care, disaster response, and more

Clinical Research

Interested in clinical research?

If so, please join our Clinical Research NetWork via the e-Community so we can build on our interests for personal development as members of the ACCP and support its mission "to promote the prevention, diagnosis, and treatment of chest diseases through education, communication, and research."

Last year, Dr. Marya Zilberberg and I wrote in *CHEST Physician* about our NetWork's evolution and new name (previously, Members in Industry). Our steering committee includes members in clinical research in practice, academia, industry, and education across a range of areas within pulmonary, critical care, and sleep medicine.

CHEST 2012 Clinical Research NetWork Highlights and open session included discussions about the placebo effect, nonfinancial conflicts of interest, and the future of peer-reviewed publication. There are projects and programs that we plan to develop as a NetWork if we have adequate participation, engagement, and support.

We have reached out to the ACCP community through our personal networks within the College, the e-Community, the NetWork Open House, and our NetWork open session. We heard through our outreach that there are many of you who participate in or would like to learn more about clinical research through the College, and we invite you to post your thoughts on the e-Community website (ecommunity.chestnet.org), to come to our NetWork session and NetWork Highlights at CHEST 2013, or to reach out directly to our Vice-Chair, Dr. Rebecca Persinger, to me, or to any of our steering committee members.

Dr. Roslyn F. Schneider, FCCP
Chair
Dr. Rebecca Persinger, FCCP
Vice-Chair

Critical Care Medicine

Fourth Eli Lilly and Company Distinguished Scholar in Critical Care Medicine

Dr. Marin Kollef, FCCP, a Critical Care NetWork member, was chosen by The CHEST Foundation as the Fourth Eli Lilly and Company Distinguished Scholar in Critical Care Medicine. Dr. Kollef serves as Professor of Medicine, Division of Pulmonary and Critical Care, Washington University School of Medicine, St. Louis, Missouri. He is also Director of Critical Care Research at Barnes-Jewish Hospital in St. Louis. The overall goal of Dr. Kollef's project is to develop a system to improve the care of patients at risk for clinical deterioration on the general hospital wards through the use of an automated early warning system (EWS) that identifies patients at risk and further develops and tests a low-cost portable

wireless pulse oximeter, providing real-time event detection in high-risk patients. His award-winning project is titled: *Preventing the Need for Intensive Care and Improving Outcomes of Hospitalized Patients Outside the Intensive Care Units Using an Evidence-Based Early-Warning System.* The study will begin in February 2013 using a randomization format, whereby patients having an EWS alert will be randomized to be seen by the rapid response team (RRT) vs usual care. An automated text message will be generated for patients assigned to the intervention group. The EWS text message will be sent real time to the on-call RRT pager. The RRT member will go into the flagged patient's room within 10 to 15 minutes of receiving the message and will perform a clinical assessment and order interventions as deemed clinically necessary. The goal of Dr. Kollef's study is to reduce ICU transfers and mortality for the alerted patients by early, appropriate intervention.

Dr. Steven Simpson, FCCP
Chair

Disaster Response

Protecting emergency responders and health-care workers by using personal protective equipment

Respirators protect the user in two basic ways. The first is by the removal of contaminants from the air. Respirators of this type include particulate respirators, which filter out airborne particles, and "gas masks," which filter out chemicals and gases. Other respirators protect by supplying clean respirable air from another source. Respirators that fall into this category include airline respirators, which use compressed air from a remote source; and self-contained breathing apparatus (SCBA), which include their own air supply.

Ninety-five percent is the minimal level of filtration that is approved.

- N95 – Filters at least 95% of airborne particles, not resistant to oil
- N99 – Filters at least 99% of airborne particles, not resistant to oil
- N100 – Filters at least 99.97% of airborne particles

Personal protective equipment refers to various barriers and respirators used to protect the mucus membranes, skin, airways, and clothing from contact with infectious agents.[1]

Respiratory protection (N95 and higher) is intended to prevent diseases that can be acquired through the airborne route. Examples of diseases requiring airborne precautions are persons with TB, measles, smallpox, and hemorrhagic fever viruses (NIOSH Guidance for the Selection and Use of Personal Protective Equipment (PPE) in Healthcare Settings).

The selection of facial PPE is determined by the isolation precautions required by the patient and the nature of the patient contact. Masks should fully cover the nose and mouth and prevent fluid penetration.

The respirators used in health care (N95, N99, N100) are particulate respirators that have a filtering capability exceeding particles that are less than 5 microns.

Prior to using a respirator, a person is required to be medically evaluated to determine that it is safe for him or her to wear a respirator, to fit test for the appropriate respirator size and type, and to train on how and when to use a respirator.[2, 3]

Surgical masks should not be confused with particulate respirators, which are recommended for protection from small particles in airborne isolation.

Alan Roth, MS
Steering Committee Member

References:

1. Hess DR, MacIntyre NR, Mishoe SC, Galvin, WF, Adams, AB . *Respiratory Care.* Sudbury, MA: Jones and Bartlett Learning; 2012.
2. Centers for Disease Control and Prevention (CDC). www.cdc.gov/niosh/topics/respirators. Accessed Feb. 26, 2013.
3. National Institute for Occupational Safety and Health (NIOSH). (2009). *Guidance for the Selection and Use of Personal Protective Equipment (PPE) in Healthcare Settings.* www.cdc.gov/niosh/contact/. Accessed Feb. 27, 2013.

Women's Health

COPD branches out

Long thought to be a disease of elderly men, COPD is increasingly becoming recognized as a significant cause of morbidity and mortality among women. While the prevalence of moderate COPD among men has decreased since the 1980s, among women, it has continued to steadily increase. In 2000, the number of women dying of COPD surpassed the number of men dying of COPD (*MMWR*. 2002;51[SS06]:1). Despite this, women are less likely to be diagnosed with COPD than men due to decreased awareness among physicians (Chapman et al. *Chest*. 2001;119[6]:1691).

COPD among women appears to be a much different disease entity than COPD in men. There are data to suggest that women may be more susceptible to the effects of cigarette smoke. There are significant differences in the rate of lung function decline among women and men, as well as differences in the rate of improvement in lung function with smoking cessation (Prescott et al. *Eur Respir J*. 1997;10[4]:822). Gender differences exist in the symptoms and quality of life of patients with COPD. Women are more likely to report dyspnea and less likely to report sputum production than men. Women report more severe dyspnea at a younger age and with less smoking exposure than male smokers (De Torres et al. *Chest*. 2005;128[4]:2012). Women with COPD exhibit higher levels of anxiety and depression than men (DiMarco et al. *Respir Med*. 2006;100[10]:1767). Pathologically, women are more likely to manifest a chronic bronchitis phenotype than emphysema. These differences suggest that women may respond to standard therapeutic options differently than men. However, most of the major trials are underpowered to detect the impact of treatment based on gender.

It is time to recognize that COPD is an increasing health burden among women. Measures to educate physicians and patients about this and to promote early diagnosis among women are sorely needed. In addition, research specifically addressing the biology and therapeutic options

Continued on page 27

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.

Take a look! New chestnet.org is live!

The new chestnet.org website launched in February and offers more of the information you want, when you want it, using the Internet device you choose. New features:

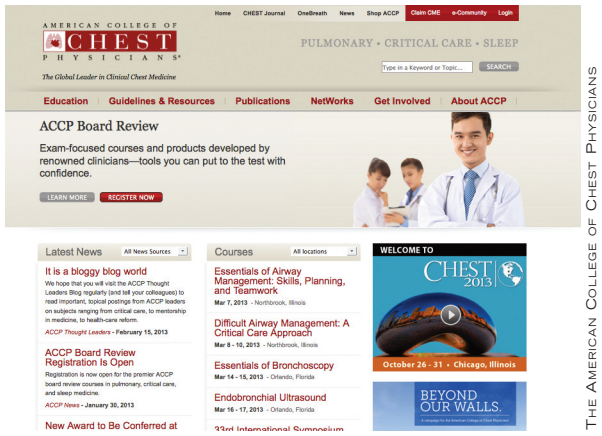
- An easy-to-navigate home page with menus for and links to important information and multimedia resources.
- A robust search function, including results from both chestnet.org and the *CHEST* Journal sites.
- Options to filter content and search results by specialty areas of interest.
- Ongoing access to clinically relevant resources.
- Easy access to the latest clinical news, ACCP blogs, and Twitter feed.
- A mobile-friendly version, accessible from any smartphone browser.

The new chestnet.org.is the culmination of extensive discovery, planning, preparation, and implementation following the drafting of the ACCP information and technology plan. The plan provided the strategic unpinning for designing and implementing a site that delivers technology solutions relevant to health-care professionals now and into the future. It is an essential connection to information you need, whenever and wherever you want it.

Five goals

Five overarching strategic principles that guided the creation of the new website include the following:

- Expansion of clinically relevant, up-to-date education resources, including interactive content and increased use of multimedia.



- Creation of a navigation system that facilitates content discovery based on need/interest and a robust search function that includes results from both chestnet.org and the *CHEST* Journal site.
- Implementation of tools to promote online networking and collaboration, such as the e-Community.
- Creation of a modern site that is easy to use and adaptable to mobile platforms.
- Implementation of a user dashboard, so users can chose content based on needs and interests.

We encourage you to test drive the new site and become familiar with the new features that support the ACCP technology strategy.

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Table 1: Number of Patients Experiencing Adverse Events from Two 12-Week, Double-Blind, Placebo Controlled Clinical Trials

	BROVANA 15 mcg twice daily		Placebo	
	n	(%)	n	(%)
Total Patients	288	(100)	293	(100)
Pain	23	(8)	16	(5)
Chest Pain	16	(6)	13	(4)
Back Pain	16	(6)	6	(2)
Diarrhea	16	(6)	13	(4)
Sinusitis	13	(5)	11	(4)
Leg Cramps	12	(4)	6	(2)
Dyspnea	11	(4)	7	(2)
Rash	11	(4)	5	(2)
Flu Syndrome	10	(3)	4	(1)
Peripheral Edema	8	(3)	7	(2)
Lung Disorder*	7	(2)	2	(1)

*Reported terms coded to "Lung Disorder" were predominantly pulmonary or chest congestion.

Adverse events occurring in patients treated with BROVANA 15 mcg twice daily with a frequency of <2%, but greater than placebo were as follows:

Body as a Whole: abscess, allergic reaction, digitalis intoxication, fever, hernia, injection site pain, neck rigidity, neoplasm, pelvic pain, retroperitoneal hemorrhage

Cardiovascular: arteriosclerosis, atrial flutter, AV block, congestive heart failure, heart block, myocardial infarct, QT interval prolonged, supraventricular tachycardia, inverted T-wave

Digestive: constipation, gastritis, melena, oral moniliasis, periodontal abscess, rectal hemorrhage

Metabolic and Nutritional Disorders: dehydration, edema, glucose tolerance decreased, gout, hyperglycemia, hyperlipemia, hypoglycemia, hypokalemia

Musculoskeletal: arthralgia, arthritis, bone disorder, rheumatoid arthritis, tendinous contracture

Nervous: agitation, cerebral infarct, circumoral paresthesia, hypokinesia, paralysis, somnolence, tremor

Respiratory: carcinoma of the lung, respiratory disorder, voice alteration

Skin and Appendages: dry skin, herpes simplex, herpes zoster, skin discoloration, skin hypertrophy

Special Senses: abnormal vision, glaucoma

Urogenital: breast neoplasm, calcium crystalluria, cystitis, glycosuria, hematuria, kidney calculus, nocturia, PSA increase, pyuria, urinary tract disorder, urine abnormality.

Overall, the frequency of all cardiovascular adverse events for BROVANA in the two placebo controlled trials was low and comparable to placebo (6.9% in BROVANA 15 mcg twice daily and 13.3% in the placebo group). There were no frequently occurring specific cardiovascular adverse events for BROVANA (frequency ≥1% and greater than placebo). The rate of COPD exacerbations was also comparable between the BROVANA 15 mcg twice daily and placebo groups, 12.2% and 15.1%, respectively.

Other adverse reactions which may occur with selective $beta_2$-adrenoceptor agonists such as BROVANA include: angina, hypertension or hypotension, tachycardia, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, muscle cramps, nausea, dizziness, fatigue, malaise, hypokalemia, hyperglycemia, metabolic acidosis and insomnia.

Drug Abuse and Dependence

There were no reported cases of abuse or evidence of drug dependence with the use of BROVANA in the clinical trials.

OVERDOSAGE

The expected signs and symptoms associated with overdosage of BROVANA (arformoterol tartrate) Inhalation Solution are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the signs and symptoms listed under **ADVERSE REACTIONS**, e.g., angina, hypertension or hypotension, tachycardia, with rates up to 200 bpm, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, muscle cramps, nausea, dizziness, fatigue, malaise, hypokalemia, hyperglycemia, metabolic acidosis and insomnia. As with all inhaled sympathomimetic medications, cardiac arrest and even death may be associated with an overdose of BROVANA.

Treatment of overdosage consists of discontinuation of BROVANA together with institution of appropriate symptomatic and/or supportive therapy. The judicious use of a cardioselective beta-receptor blocker may be considered bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of BROVANA. Cardiac monitoring is recommended in cases of overdosage.

Clinical signs in dogs included flushing of the body surface and facial area, reddening of the ears and gums, tremor, and increased heart rate. A death was reported in dogs after a single oral dose of 5 mg/kg (approximately 4500 times the maximum recommended daily inhalation dose in adults on a mg/m^2 basis). Death occurred for a rat that received arformoterol at a single inhalation dose of 1600 mcg/kg (approximately 430 times the maximum recommended daily inhalation dose in adults on a mg/m^2 basis).

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SLEEP STRATEGIES: Alcohol and sleep – a badly mixed cocktail

Alcohol is one of the most commonly abused substances worldwide. In Canada, the annual volume of alcohol consumption has increased over the last decade as has the prevalence of high-risk drinking. Abuse is also very common in the United States, with a prevalence of about 14%. This excessive consumption has a very significant impact on the health-care system and society, including increases in violent crime, accident rates, pharmaceutical expenses, and hospitalizations (Laramee et al. *Alcohol*. Jan 2013, e-pub ahead of print).

Sleep disturbance as a risk factor for alcohol intake

Alcohol is often used by the general population as self-medication to treat sleeplessness due to its sedating effect. An international survey found that almost one quarter of the general population complained of not sleeping well with about 31% reporting insomnia; these subjects were also more likely to report alcohol use (Soldatos et al. *Sleep Med*. 2005;6[1]:5). Epidemiologic studies have confirmed that adults with insomnia have a much higher risk of developing alcohol abuse compared with adults without insomnia, even in absence of associated psychiatric disorders. Shift workers with sleep problems, especially those who work predominantly at night, are more likely to use alcohol as a sleep aid and to have heavy alcohol consumption compared with day-workers without sleep problems (Morikawa et al. *Alcohol*. Nov 2012, e-pub ahead of print).

Sleep curtailment, defined as less than 7 to 8 hours of sleep, is becoming increasingly prevalent in modern society. Adults reporting less than 6 hours per night were found to have increased alcohol intake compared with longer sleepers, more so if they also demonstrated a high degree of disinhibited eating behaviors (Chaput et al. *Appetite*. 2012;59[3]:650); short sleepers were also more likely to binge drink.

Effects of acute alcohol intake on sleep

As patients afflicted with insomnia will report, a lack of good quality sleep can have a major impact on quality of life, leading some to turn to alcohol as treatment. Unfortunately, despite its initial sedative effect, alcohol can lead to significant sleep disruption. The effect of alcohol use prior to bedtime was studied in healthy subjects (Feige et al. *Alcohol Clin Exp Res*. 2006;30[9]:1527); at the level of "social drinking," there was no significant impact on sleep architecture or subjective complaints. As the dose of alcohol increased, a hypnotic-like effect was noted, leading to shortened sleep latency, reduced number of awakenings after sleep onset, increased delta sleep, and decreased REM density; this effect was more pronounced during the first part of the night due to the fairly rapid metabolism of ethanol. During the latter half of the night, more disrupted sleep was noted along with rebound REM sleep, which may account for an increased frequency of nightmares in some patients as their sleep fragmentation awakens them from their dreams.

Given the described association between sleep and memory consolidation, it is not surprising that acute alcohol intake can affect memory. Heavy social drinking just before bedtime can impair recall the following morning, despite the absence of detectable alcohol in the blood at that time. Studies have also demonstrated that more modest levels of alcohol ingestion before bed impair subsequent memory for recently learned procedural and cognitive tasks in alcohol-naïve subjects, compared with the use of alcohol in the afternoon (Smith et al. *Sleep*. 2003; 26:185).

Some reviews suggest an association between acute alcohol use and the incidence of parasomnias; given the known association between parasomnias and other agents that bind to the same $GABA_A$ receptors as alcohol (such as zolpidem and zaleplon), it seems reasonable to conclude that alcohol would also induce nocturnal behaviors. However, few case reports linking the two have been published. Because parasomnias are usually diagnosed clinically, it is also possible that reports of alcohol-induced sleepwalking might actually represent episodes of nocturnal wanderings during intoxicated awakenings.

Acute alcohol intake can decrease the dilating force of the pharyngeal muscles, leading to upper airway narrowing and can also alter chemosensitivity to carbon dioxide and oxygen tensions. Strangely, alcohol intake has not been shown to induce snoring among nonsnorers in published studies, though acute nocturnal intake can worsen the incidence and intensity of snoring among chronic snorers. Large quantities of alcohol have also been shown to exacerbate sleep-disordered breathing, especially in men. However, even moderate amounts of alcohol intake can worsen obstructive physiologic function and oxygenation indices among patients with mild-to-moderate obstructive sleep apnea (Izumi et al. *Environ Health Prev Med*. 2005;10[1]:16).

Effects of chronic alcohol intake on sleep

Sleep problems are more common among long-term alcohol abusers than in the general population. Many studies have shown that alcohol intake prolongs sleep latency in patients who chronically use alcohol, compared with nonalcoholic healthy subjects. These findings may suggest that alcoholic subjects have developed a tolerance to its sedative effects. Chronic alcoholics who are actively abusing have been reported to demonstrate decreased total sleep time, increased delta sleep, and an increased REM sleep latency with decreased REM sleep. However, these effects may not persist, with at least one review suggesting that prolonged continuous drinking can lead to reduced delta sleep, possibly related to drug tolerance (Landholt et al. *CNS Drugs*. 2001;15[5]:413). Most chronic alcoholics have a higher rate of dissatisfaction with their sleep compared with the general population and will report insomnia if they stop drinking.

Effects of alcohol withdrawal on sleep

Chronic alcohol users have significant problems with their sleep during detoxification; the withdrawal syndrome manifests as hyperactivity, a lowered seizure threshold, and worsening sleep disruption, usually starting within 2 days after the last drink. During this subacute withdrawal period, some alcoholics have marked difficulty with sleep-onset insomnia, a subsequent decrease in total sleep time, and a higher REM density during the first REM period compared with healthy control subjects, at the expense of decreased slow wave sleep (Gillin et al. *Biol Psych*. 1990;27[5]:477). The prevalence of insomnia can be as high as 58% in chronic alcoholics during the first week of acute alcohol withdrawal. Untreated alcoholics can progress from withdrawal into delirium tremens, characterized by increased adrenergic activity, delirium, agitation, and hallucinations. The sleep of these patients is very disturbed with polysomnographic features of wakefulness alternating with REM sleep without atonia mixed into light sleep (which has been called stage 1-REM); slow wave sleep tends to be absent during this period (Lugaresi et al. *Sleep Med*. 2011;12[suppl 2]: S3). The hallucinations commonly reported during alcohol withdrawal and delirium tremens may represent an intrusion of REM sleep into wakefulness, similar to what is seen in narcoleptics.

Sleep in alcoholics during protracted abstinence from alcohol

After 1-2 months of sobriety, the sleep of alcoholics is characterized by an increased sleep latency and increases in stage 1, 2, and REM sleep with continued impairment in slow wave sleep, although the intrusion of REM features into wakefulness usually resolves. Sleep continuity continues to be affected with significant increases in the number of nocturnal awakenings and decreased sleep efficiency. Although these polysomnographic abnormalities can attenuate over time, a persistence of fragmented sleep with decreased deep sleep and increased REM sleep has been reported even years after abstinence

Continued on following page

This Month in *CHEST*: Editor's Picks

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

Response of Chronic Cough to Acid-Suppressive Therapy in Patients With Gastroesophageal Reflux Disease. *By Dr. P. J. Kahrilas et al.*

Reduction of Peripherally Inserted Central Catheter-Associated DVT. *By Dr. R. S. Evans et al.*

Impact of the Administration of Probiotics on Mortality in Critically Ill Adult Patients: A Meta-analysis of Randomized Controlled Trials. *By Dr. D. Barraud et al.*

What Do You Mean, a Spot? A Qualitative Analysis of Patients' Reactions to Discussions With Their Physicians About Pulmonary Nodules. *By Dr. R. S. Wiener et al.*

TOPICS IN PRACTICE MANAGEMENT

Integrating Advanced Practice Providers Into Medical Critical Care Teams. *By Ms. C. McCarthy et al.*

Critical Care in the Surgical Global Period. *By Ms. J. R. Painter.*

Continued from previous page

(Drummond et al. *Alcohol Clin Exp Res*. 1998;22[8]:1796). Such persistent disturbances may predict the risk of relapse to alcoholism by impeding normalization of quality of life among quitters; patients with subjective sleep complaints have been shown to resume drinking at significantly higher rates. Optimization of sleep latency and sleep quality using pharmacologic agents may forestall relapse; gabapentin is one promising therapeutic agent to treat insomnia in these patients since it inhibits the release of excitatory neurotransmitters and can promote sleep. Furthermore, gabapentin is not metabolized by the liver and has no known abuse potential, in contrast to benzodiazepines and other drugs used as hypnotics; patients treated with gabapentin have shown subjective improvement in their sleep quality and may be more likely to remain abstinent (Mason et al. *Addict Biol*. 2009;14:73), though more studies are needed to evaluate this drug in preventing relapse.

Cognitive-behavioral therapy for insomnia in abstinent alcohol-dependent patients has shown subjective improvement in sleep efficiency compared with placebo (Arnedt et al. *Behav Res Ther*. 2011;49[4]:227). Despite the improvements in sleep quality, cognitive-behavioral therapy had no significant impact on the rate of relapse to alcohol.

Summary

Alcohol has a deleterious effect on sleep, which can be long lasting, even after protracted periods of sobriety. Continued abstinence from alcohol can improve but may not normalize sleep. Early diagnosis and treatment of sleep disorders, especially insomnia, should be prioritized, as it may prevent the development of alcoholism in healthy subjects and prevent relapse among previously alcohol-dependent patients.

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New Haven, Connecticut

Clinical documentation changes

BY RHONDA BUCKHOLTZ, CPC, CPMA, CPC-I, CGSC, COBGC, CPEDC, CENTC
AAPC Vice President of ICD-10 Education and Training

As we move toward the "go-live" date for ICD-10-CM of Oct. 1, 2014, you will hear the term CDI more frequently. Clinical documentation improvement (CDI) will be vital to every practice.

Following are a few examples of where changes may need to be made in documentation to follow the increased specificity of ICD-10-CM code assignment.

Most codes for diabetes are considered combination codes in ICD-10-CM. These codes require specific elements in the documentation to assign a code in ICD-10-CM.

Sleep apnea documentation requirements for ICD-10-CM include the following: type of sleep apnea, underlying conditions, and complication or manifestation.

Example: **C47.33** Obstructive sleep apnea (adult) (pediatric)

Neoplasm documentation requirements require specificity in both the site and laterality components. Documentation for neoplasms must include the type (malignant [primary, secondary, cancer in situ]; benign; uncertain; or unspecified behavior); location(s) (site-specific); if malignant [any secondary sites should also be determined]; and laterality (in some cases).

Example: Malignant neoplasm of the lung has 15 choices and requires specification of the site of the neoplasm on the lung and laterality. In addition, a code for exposure or tobacco use is required, if known.

Example: **C34.11** Malignant neoplasm of upper lobe, right bronchus or lung and **Z87.891** History of tobacco use.

Asthma codes in ICD-10-CM have been expanded to include the following concepts: severity of disease (mild intermittent, mild persistent, moderate persistent, and severe persistent); acute exacerbation; status asthmaticus; and other types (exercise-induced, cough variant, other).

Example: **J45.41** Moderate persistent asthma with (acute) exacerbation.

As you can see from examples above, the documentation requirements for ICD-10-CM will vary from ICD-9-CM documentation requirements in many cases. Working with your providers on clinical documentation improvement for ICD-10-CM through readiness assessments and education will help ease the transition. Knowledge of the coding guidelines and preparation will be essential.

Continued from page 21

for women with COPD should be undertaken.

Dr. Suryakanta Velamuri, FCCP
Steering Committee Member

Transplant

Lobar lung transplantation: expanding the donor pool for recipients with small chest cavities

Lung transplantation is an excellent option for many patients suffering from end-stage lung disease. Unfortunately, the persistent shortage of acceptable donor organs often leads to prolonged wait-times, gradual clinical deterioration, and ultimately death for many patients waiting on the transplant list. In the current era of the Lung Allocation Score (LAS), which does not consider donor and recipient size matching, many patients are at risk for death due to the unavailability of a suitably sized donor, especially for those patients with restrictive lung disease, leading to small chest cavities.

Historically, the only option for patients with small chest cavities awaiting lung transplantation was either use of a pediatric donor or extensive nonanatomic lung volume reduction of a larger allograft. The scarcity of pediatric donors makes this an unreliable option, especially for those with rapidly deteriorating illness. The use of extensive nonanatomic lung volume reduction of a larger allograft has been used but the long-term impact of extensive nonanatomic reduction is unknown. Also, some allografts remain too large despite aggressive nonanatomic volume reduction leading to chronic atelectasis, infection, and compromised lung function.

Lobar lung transplantation holds promise as a technique to expand the donor pool and to help alleviate the limitations currently experienced due to size mismatch in patients with small chest cavities. The procedure involves anatomic resection of the upper or lower lobe from each side and transplantation of the remaining, now downsized, allograft. Data recently presented by Dr. Norihisa Shigemura from the University of Pittsburgh Medical Center at The Society of Thoracic Surgeons Annual Meeting in January 2013 summarized the largest US experience with lobar lung transplant documenting 88% 90-day and 76% 1-year survival in a group of patients with a mean LAS of 85. Posttransplant lung function testing demonstrated a peak FEV_1 of 85% and a peak FVC of 73% at 24 month follow-up. As noted by the fact that all patients were either receiving >15 L of high flow oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) prior to lobar lung transplant, this procedure was offered only to those in the extremely advanced stages of disease.

Other studies, largely from Europe and Australia, have also described similar results. Further studies will be required to better understand the full impact of lobar transplantation on long-term functional outcomes before this option should be extended to patients at lesser stages of illness.

Additional reading:

Inci et al. *Eur J Cardiothorac Surg*. 2012 Oct 22. [Epub ahead of print]
Marasco et al. *Ann Thorac Surg*. 2012;93(6):1836.
Shigemura et al. *J Heart Lung Transplant*. 2009;28(2):130.

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