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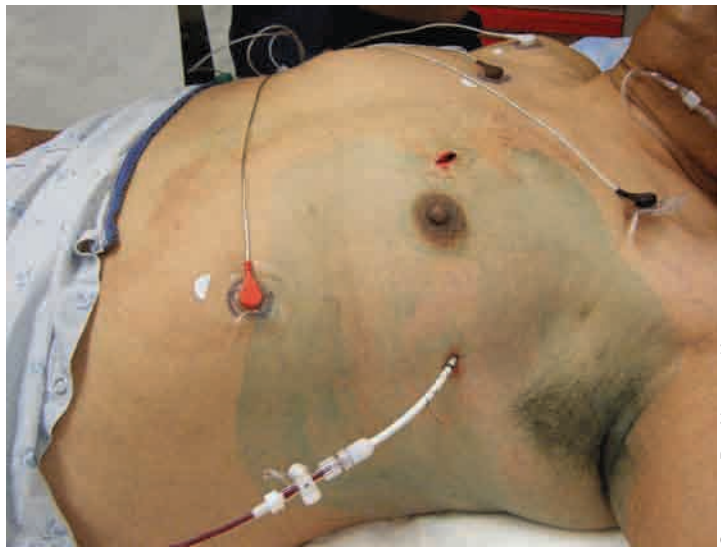

COURTESY DR. NARONG KULVATUNYOU

For traumatic pneumothorax, pigtail catheter yielded less site pain than did chest tubes. However, occlusion can be a concern.

Pigtails win pain game versus chest tubes

BY PATRICE WENDLING
IMNG Medical News

SCOTTSDALE, ARIZ. – In patients with traumatic pneumothorax, smaller really is better, a study suggests.

The prospective, randomized study found that 14-French pigtail catheters function as well as do traditional, large-bore 28-French chest tubes, and result in significantly less tube-site pain.

The average numerical rating tube-site pain score was 3.2 with the pigtail catheter vs. 7.7 with the chest tube on the day of insertion, 1.9 vs. 6.2 on day 1, and 2.1 vs. 5.5 on day 2.

Chest wall pain was similar between the two groups at all three time points (6.1 vs. 6.0; 5.5 vs. 5.9; and 4.2 vs. 5.9, as was intravenous pain medication use on day 1 (mean 10.3 U vs. 15.4 U) and day 2 (5.0 U vs. 8.6 U). One unit equaled 1 mg morphine, 25 mcg fentanyl, or 0.1 mg hydromorphone HCl (Dilaudid).

It stands to reason that the pigtail catheters are less painful because they're soft, have a coiled tip, and are inserted with a less-invasive percutaneous technique, whereas traditional, large-bore chest tubes are straight and stiff, and are typically placed via a cutdown technique, Dr. Narong Kulvatunyou said at

See **Drainage** • *page 6*

VAP prevention may not lie in gastric volume monitoring

Unchecked patients met nutrition goals.

BY MARY ANN MOON
IMNG Medical News

Among critically ill adults requiring mechanical ventilation and receiving early enteral nutrition, it may not be necessary to routinely monitor residual gastric volume as a means of averting vomiting and thus preventing aspiration and the development of ventilator-associated pneumonia, according to a recent report in JAMA.

In a multicenter randomized trial involving 449 such patients, forgoing routine monitoring of residual gastric volume was found "noninferior" at preventing ventilator-associated pneumonia to the standard practice of performing this monitoring every 6 hours. Moreover, patients who were not monitored actually were more likely to achieve their nutritional targets, while showing equivalent mortality, infection rates, lengths of hospital stay, lengths of ICU stay, and organ failure scores, said Dr. Jean Reignier of Centre Hospitalier Departemental de la Vendee, La Roche-sur Yon (France), and his associates.

"Residual gastric volume monitoring leads to unnecessary interruption of enteral

See **VAP** • *page 11*

Smoking's death grip squeezes all

BY MICHELE G. SULLIVAN
IMNG Medical News

Women smokers have caught up with men in the rate and reasons for their demise, researchers report in the New England Journal of Medicine.

Two large population-based studies have come to the same conclusion: Smokers are almost certainly going to die years and years sooner than nonsmokers, according to one team of investigators.

"This analysis showed that a person who had never smoked was about twice as likely as a current smoker to reach 80 years of age," Dr. Prabhat Jha and his associates reported.

"Among current smokers, survival was shorter by about 11 years for women

See **Risks** • *page 15*

INSIDE

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Infection control: Trust protocols, but verify compliance

BY NEIL OSTERWEIL
IMNG Medical News

SAN JUAN, P.R. – A healthy percentage of the morbidity, mortality, and costs associated with infections acquired in intensive care units are preventable by just following the rules, investigators said at the annual Congress of the Society of Critical Care Medicine.

Interventions such as strict hand hygiene, meticulous attention to preinsertion disinfection of the patient's skin, and the use of sterile dressings and drapes can dramatically reduce the incidence of catheter-related bloodstream infections (CRBSIs). Ventilator-associated pneumonia (VAP) can be prevented with precautions to avoid aspiration, reduction of upper airway colonization, and attention to sterilization of ventilatory equipment, said Dr. Alfred F. Connors Jr., senior associate dean of Case Western Reserve University, Cleveland.

"These are two areas where we are at a really important turning point, where we can really make a difference and change the incidence of these infections in our patients," he said.

VITALS

Major finding: A comprehensive hospital-wide infection reduction program resulted in an 18% decrease in antibiotic days and 32% reductions in both ventilator-associated pneumonia and catheter-related bloodstream infections.

Data source: A literature review and retrospective study of 415 ICUs in 250 hospitals.

Disclosures: Dr. Connors reported having no financial disclosures.

The key to making it all work is ensuring that staff adhere to best practices, said investigators from Sutter General Hospital in Sacramento. They reported that a physician-led multidisciplinary team charged with monitoring adherence to VAP prevention guidelines reduced the incidence of ventilator-associated infections from 17 out of 3,173 ventilator-days in 2004, to 2 in 12,694 ventilator-days from 2008 to 2011, a statistically significant reduction.

Protocols yes, compliance maybe

Dr. Connors noted that in a cross-sectional survey of 415 ICUs in 250 hospitals with a mean of 2.7 VAP infections per 1,000 ventilator-days, 68% of hospitals had a VAP bundle policy in place, but only 45% monitored compliance, and only 18% reported high compliance with the policy (Int. J. Qual. Health Care 2011;23:538-44).

"Unless you have a policy, you're monitoring it, and you're demonstrating high compliance, you won't show any effect on your ventilator-associated pneumonia rate. There's no magic to this. You can't just say 'Okay, we've got a policy, please follow it,' and expect ventilator-associated pneumonia rates to drop; we have to intervene actively to get high compliance, and that's easier said than done," he said.

At MetroHealth system in Cleveland, where Dr. Connors is chief medical officer, instituting and enforcing a stepped-up hand-hygiene program, isolation procedures, enhanced environmental cleaning, antibiotic stewardship, and implementation of evidence-based protocols for prevention of VAP, CRBSIs, and catheter-associated urinary tract infections resulted in an 18% decrease in antibiotic days of therapy from 2009 through the third quarter of 2012, and 32% decreases in both VAP and CRBSIs from 2010 to 2012.

'You can't just say "Okay, we've got a policy, please follow it," and expect [VAP] rates to drop.'

DR. CONNORS

More importantly, Dr. Connors said, such efforts save both lives and costs. He pointed to a 2011 study of national data on hospital-associated infections, which found that with proper infection control procedures, an estimated 44,762 to 164,127 central line–associated bloodstream infection cases could be prevented, translating into 5,520-20,239 lives saved, and an estimated 95,078-137,613 preventable VAP cases, equivalent to 13,667-19,782 lives saved (Infect. Control Hosp. Epidemiol. 2011;32:101-14).

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IN THIS ISSUE

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Tracheostomy collar yields faster ventilation weaning

BY NEIL OSTERWEIL
IMNG Medical News

SAN JUAN, P.R. – Patients on prolonged ventilation who had previously failed a 5-day breathing challenge were weaned more rapidly off ventilators when a tracheostomy collar rather than pressure support was used, Dr. Amal Jubran said at the annual congress of the Society of Critical Care Medicine.

Among 312 patients on prolonged ventilation (more than 21 days) transferred to a long-term acute care hospital, the median weaning time with unassisted breathing through tracheostomy collars was 4 days shorter than when pressure support was used as the weaning method, reported Dr. Jubran of the division of pulmonary and critical care medicine at the Edward Hines Jr. VA Hospital in Hines, Ill.

Outcomes of patients who require prolonged ventilation at a long-term care facility were improved.

DR. JUBRAN

'Observing a patient breathing through a tracheostomy collar provides the clinician with a clear view of the patient's respiratory capabilities.'

"The method of ventilator weaning significantly improves the outcome of patients who require prolonged ventilation … at a long-term care facility," she said.

The study findings were published simultaneously online in JAMA. There, the authors suggested that the more rapid weaning achieved with the use of the tracheostomy collar could be because the collar allows clinicians to directly observe whether patients are capable of breathing spontaneously (JAMA 2013 [doi:10.1001/jama.2013.159]).

"During a tracheostomy collar challenge, the amount of respiratory effort is determined solely by the patient. As such, observing a patient breathing through a tracheostomy collar provides the clinician with a clear view of the patient's respiratory capabilities. In contrast, a clinician's ability to judge weanability during pressure support is clouded because the patient is receiving ventilator assistance," the investigators wrote.

Clinicians may be more willing to wean patients who do better than expected on a trachesotomy challenge than they would patients who are on only low levels of pressure support, the authors suggested.

Weaning failures randomized

They based their conclusions on a decade-long randomized trial of patients with tracheotomies on prolonged ventilation who were

Continued on following page

Continued from previous page

transferred to a single center for weaning.

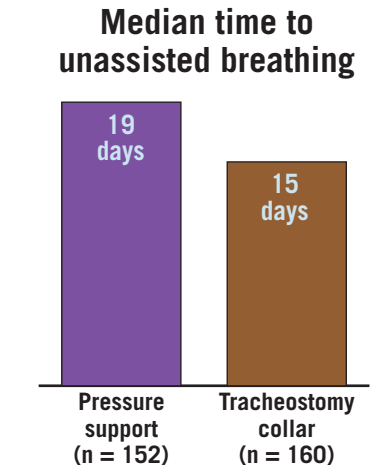
A total of 500 patients had a 5-day screening process during which they were given humidified oxygen through a tracheostomy collar and observed for signs of respiratory distress. Patients with no signs of distress during the challenge were considered to be weaned from ventilation and were excluded from the study, and the remaining 316 were randomly assigned to weaning with either a tracheostomy collar or pressure support.

Patients in each study arm were stratified into one of four underlying disease categories, and to either early- or late-failure groups, based on the time it took for the breathing trial to fail (0 to less than 12 hours for early failures, 12-120 hours for late failures).

Ultimately, a total of 312 patients were included in the analysis.

Of the 160 patients in the tracheostomy collar group, 15 were deemed to be unweanable, 15 withdrew for various reasons, 16 died, and 10 were transferred to an acute care hospital. Of the remaining 104 patients in this arm, 85 (53.1% of the total group) were successfully weaned.

Of the 152 patients in the pressure support group, 21 were judged to be unweanable, 12 withdrew, 7 were transferred to an acute care hospital, and 22 died. Of the remaining 90 patients, 68 (45% of the total) were successfully weaned.



Note: 45% of patients on pressure support and 53.1% of those using the collar were successfully weaned.
Source: Dr. Jubran

IMNG Medical Media

The median weaning time for patients on the collar was 15 (interquartile range [IQR], 8-25 days), compared with 19 days (IQR, 12-31 days) for patients on pressure support. (See graph.)

In an analysis adjusted for baseline clinical covariates, the hazard ratio (HR) favoring tracheostomy collar weaning was 1.43. Among patients in the late-failure subgroup, tracheostomy offered significantly more rapid weaning than did pressure support (HR, 3.33). There was no significant difference between the methods in time to weaning among patients who were deemed to be early screening failures, however. There were also no significant differences between weaning protocols in either 6- or 12-month mortality rates.

Dr. Jubran and colleagues acknowledged that their study was limited by the inability to fully mask treatment type from investigators (although investigators analyzing the data were blinded to protocol assignment), and by the use of single-center data, potentially limiting generalizability.

The study was supported by funding from the National Institute of Nursing Research. Dr. Jubran reported having no relevant financial disclosures.

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High-frequency oscillatory ventilation may worsen ARDS

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

High-frequency oscillatory ventilation doesn't improve and may actually worsen moderate to severe acute respiratory distress syndrome in adults, compared with standard ventilation, according to two reports.

In two large, separate, randomized controlled trials comparing the two ventilation strategies, 1-month mortality in critically ill adults with ARDS who received high-frequency oscillatory ventilation (HFOV) was either higher or not significantly different from that in patients who received standard low tidal volume and high positive end–expiratory pressure ventilation.

There is doubt about HFOV, even in light of life-threatening refractory hypoxemia.

DR. FERGUSON

In one study, which was terminated early because of the large discrepancy in short-term mortality, HFOV also was associated with higher mean airway pressures and significantly greater need for sedatives, neuromuscular blockers, and vasoactive drugs.

Both trials call into question the current widespread use of HFOV early in the course of ARDS when patients don't show an adequate response to conventional mechanical ventilation, the two research groups noted.

HFOV, which delivers very small tidal volumes at very high rates, is thought to minimize the lung damage done by ventilation's repeated forced opening and collapsing of lung structures. Many clinicians now use it earlier in the course of ARDS, even though there are other approaches for improving oxygenation, based solely on the results of animal studies and small trials that used outdated ventilation methods as a control. The commercial availability of HFOV equipment has accelerated this trend.

In the absence of good evidence of HFOV's effectiveness, experts in Canada and the United Kingdom called for rigorous randomized controlled trials.

Dr. Niall D. Ferguson and his associates in the Oscillation for Acute Respiratory Distress Syndrome Treated Early (OSCILLATE) trial compared the two strategies in patients aged 16-85 years who had moderate to severe ARDS and were treated at 39 intensive care units in Canada, Saudi Arabia, the United States, Chile, and India.

The OSCILLATE steering committee terminated the trial early, after only 548 subjects had been randomized, because three consecutive interim analyses showed that 1-month mortality was consistently higher with HFOV. "The effect size was sufficiently large that we concluded that even if early HFOV did not increase mortality, it would be very unlikely to decrease mortality," wrote Dr. Ferguson of the division of critical care medicine and the departments of medicine and physiology, University of Toronto, and his colleagues.

At that time, 1-month mortality was 47% for HFOV (129 of 275 patients), compared with 35% (96 of 273 patients) in the control group (N. Engl. J. Med. 2013 Jan. 23 [doi:10.1056/NEJMoa1215554]).

This result remained robust in three further analyses of the data that controlled for numerous variables. It also persisted in several subgroup analyses, regardless of the subjects' baseline severity of hypoxemia, the subjects' body mass index, the use or nonuse of vasopressors, or the level of experience with ventilation at each medical center.

In addition, the use of vasopressors, which had been equivalent between the two study groups at baseline at approximately 63%, increased in the HFOV group to 73% within 4 hours of beginning the procedure and to 78% the next day. In contrast, vasopressors were used in only 62% and 58%, respectively, in the control group.

The use of neuromuscular blockers followed the same pattern, increasing in the HFOV group from 27% at baseline to 46% at 4 hours and 46% at 24 hours but remaining more steady in the control group at 29%, 31%, and 26%, respectively, they reported.

Cumulatively, vasoactive agents were used in 91% and neuromuscular blockers in 83% of the HFOV group, compared with 84% and 68%, respectively, in the control group. Vasoactive agents were required for an average of 2 days longer in the HFOV group, and neuromuscular blockers were required for an average of 1 day longer, compared with the control group.

Sedatives and opioids (primarily midazolam and fentanyl) were given for the same duration to the two study groups, but doses were higher in the HFOV group.

"Our results raise serious concerns about the early use of HFOV for the management of ARDS in adults. The results of this study increase the uncertainty about possible benefits of HFOV even when applied in patients with life-threatening refractory hypoxemia," Dr. Ferguson and his associates said.

In the Oscillation in ARDS (OSCAR) study, commissioned by the U.K. National Institute for Health Research, two ventilation techniques were compared in 795 patients in general ICUs at 12 university hospitals, 4 university-affiliated hospitals, and 13 district general hospitals in England, Wales, and Scotland.

As this was a pragmatic study meant to reflect real-world practice, HFOV was compared against whatever conventional ventilation was used in local practice, and the ICUs were "encouraged" to use the recommended combinations of positive end-expiratory pressure and fraction of inspired oxygen values. Consequently, management of the control group varied greatly from one ICU to the next, according to the researchers, led by Dr. Duncan Young of John Radcliffe Hospital and the University of Oxford, both in Oxford.

The primary outcome, 30-day all-cause mortality, occurred in 41.7% of the HFOV group (166 of 398 patients) and in 41.1% of the control group (163 of 397 patients), a nonsignificant difference. These rates remained largely unchanged in further analyses that adjusted for several variables, Dr. Young and his colleagues said (N. Engl. J. Med. 2013 Jan. 23 [doi:10.1056/NEJMoa1215716]).

The duration of ICU stay was 17.6 days with HFOV and 16.1 days with conventional ventilation, and the duration of hospital stay was 33.1 days and 33.9 days, respectively.

"Since data collection is ongoing, we cannot yet report the longer-term outcomes (including survival and health-related quality of life)," they added.

In conclusion, "we were unable to find any benefit or harm from the use of HFOV in adult patients with ARDS. We recommend that this mode of ventilation not be used for routine care," Dr. Young and his associates said.

CareFusion provided the SensorMedics HFO ventilator and technical support for the OSCILLATE trial but had no role in study design, data collection or analysis, or manuscript preparation. Inspiration Healthcare supplied the ventilators for the OSCAR study but had no role in the study design, data acquisition or analysis, or manuscript preparation.

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VITALS

Major finding: 1-month mortality was significantly higher with HFOV (47%) than with control ventilation (35%) in the OSCILLATE study; no significant difference was seen between groups in the OSCAR study (41.7% vs 41.1%).

Data source: Two randomized controlled trials comparing HFOV against either low tidal volume, high positive end–expiratory pressure ventilation or conventional ventilation among 548 ARDS patients in Canada, Saudi Arabia, the United States, Chile, and India and among 795 ARDS patients in England, Wales, and Scotland.

Disclosures: The OSCILLATE study was supported by the Canadian Institutes of Health Research, the King Abdullah International Medical Research Center, and Fonds de Recherche de Quebec. Dr. Ferguson's associates reported ties to numerous industry sources. The OSCAR study was supported by the National Institute for Health Research Health Technology Assessment Programme. Dr. Young and his associates reported no relevant financial conflicts of interest.

COMMENTARY

Dr. Steven Q. Simpson, FCCP, comments: As intensivists, we perhaps epitomize the very human desire to not just stand there, but to do something. HFOV and, for that matter, other complex mechanical ventilation techniques, are so tempting to use when our ARDS patients are failing to show improvement with more conventional mechanical ventilation. However, these two well-designed studies demonstrate that any salutary effects attributed to HFOV are illusory. It is time to move on.

Less pain with pigtail catheters

Drainage *from page 1*

the annual meeting of the Eastern Association for the Surgery of Trauma.

A recent prospective observational study found no difference in tube-site pain with large (36- to 40-French) versus small (28- to 32-French) chest tubes inserted for chest trauma (J. Trauma Acute Care Surg. 2012;72:422-7), but the analysis still compared two large bores and both used the cutdown technique, he observed.

Based on their early experience in trauma patients, Dr. Kulvatunyou and colleagues at the University of Arizona, Tucson, reported that 11% of pigtail catheters failed vs. 4% of chest tubes (J. Trauma 2011;71:1104-7).

VITALS

Major finding: The average tube-site pain score was 3.2 with the pigtail catheter vs. 7.7 with the chest tube on the day of insertion, 1.9 vs. 6.2 on day 1, and 2.1 vs. 5.5 on day 2.

Data source: A prospective, randomized trial of 40 patients with traumatic pneumothorax.

Disclosures: Dr. Kulvatunyou, his coauthors, and Dr. King reported no relevant financial disclosures.

The 2-year review did not assess tube-site pain, prompting the current prospective study involving 40 patients with traumatic pneumothorax evenly randomized to a 14F pigtail catheter placed at the bedside with a modified Seldinger technique or a 28F chest tube placed via a cutdown technique. The tubes were left on suction for 24 hours.

Patients were excluded if they required emergency pigtail or chest tube placement or were unable to respond to the nurse-led pain assessment.

Demographics in groups were similar in average Injury Severity Score (14.5 vs. 12.2), abbreviated chest injury score (3 vs. 3), blunt trauma injury (85% vs. 80%), rib fractures (both 1.5), and pulmonary contusion (both 25%). Patients' mean age was 46 years; 80% were male.

Contrary to expectations, tube-site pain was similar whether the pigtail catheter was placed anteriorly between the second and third rib (n = 9) or laterally (n = 11) between the fourth and fifth rib, Dr. Kulvatunyou said.

Failure rate, defined as unresolved or recurrent pneumothorax requiring a second tube, was 5% in the pigtail group and 10% in the chest tube group ($P = .55$). Secondary endpoints included insertion-related complications (10% for both groups), median number of tube days (2 for both), and median hospital stay (4 days for both).

Invited discussant Dr. David King, a trauma and acute care surgeon at Massachusetts General Hospital, Boston, questioned whether patients were receiving oral pain medications, as this could impact the results, and how the team mitigated a potential Hawthorne effect and observer bias.

"I know you said that the nurses who were getting the pain scores were blinded, but it's pretty difficult to blind someone to the difference between a garden hose and a straw coming out of their chest wall," he said.

Dr. Kulvatunyou acknowledged that 10 out of 10 patients would prefer a smaller tube if asked, but that patients were asked only whether they would be willing to receive a "different tube that works pretty well," with no mention of tube size. As for the nurses, he said the tubes were typically under dressings and that some nurses may not have noticed the difference – a remark that was not well received based on comments after the session.

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COMMENTARY

Dr. Lary Robinson, FCCP, comments: In a small prospective trial investigators concluded that a 14F pigtail catheter could be used effectively with a traumatic pneumothorax. However, the role of a small pigtail catheter in a traumatic hemo- or hemopneumothorax is undefined.

As a thoracic surgeon frequently involved in chest tube drainage from various causes, I have found pigtail catheters to commonly occlude if draining blood or thicker pleural fluids, requiring placement of a larger chest tube. I would be quite skeptical of the utility of using a pigtail catheter in this setting, and reluctant to employ the smaller pigtail in the emergency department for the initial and the usual longer-term pleural drainage needed in a traumatic hemothorax.

NEWS FROM THE FDA

Panel gives thumbs down for inhaled mannitol for cystic fibrosis

Uncertainty over safety and efficacy data, particularly in children, moved the Pulmonary-Allergy Drugs Advisory Committee to unanimously recommend against approval of a dry powder formulation of mannitol for treating cystic fibrosis.

At a Jan. 30 meeting, the committee voted 14-0 against Food and Drug Administration approval of the product for the management of cystic fibrosis in patients aged 6 years and older. The proposed dose is 400 mg twice a day, administered via a breath-actuated dry powder inhaler over about 5 minutes, using 10 40-mg capsules for the total dose.

Mannitol "hydrates the lung surface, leading to improved airway clearance," according to the Australian manufacturer, Pharmaxis. Dry powder mannitol (DPM) is approved for people aged 6 years and older in Australia and for adults in the European Union.

"I wish I could have voted yes, because I think there is a place for a drug like this, but I think that further studies are necessary," said one of the panelists, Dr. Mary Cataletto, a pediatric pulmonologist and professor of clinical pediatrics at the State University of New York at Stony Brook. Dr. Jeffrey Wagener, professor of pediatrics at the University of Colorado, Aurora, said he may have voted in favor of approval if the indication had been limited to adults. "But there was no evidence DPM was effective in children, he said.The safety issue that was a main focus of discussion was the higher rate of hemoptysis associated with treatment, particularly among those under age 18. In the two phase III studies presented by Pharmaxis, the rate of hemoptysis (reported as an adverse event, not associated with an exacerbation), was almost 11% in adults on DPM, compared with about 8% of controls. But in those aged 6-17 years, the rate was almost 8% among those on DPM, compared with almost 2% among controls.

FDA reviewers raised statistical issues regarding the data, and questioned whether the results provided an accurate estimate of the treatment's effects.

If approved, Pharmaxis plans to market DPM as Bronchitol.

Olodaterol once-daily beta-agonist for COPD earns committee support

Olodaterol, an inhaled long-acting beta$_2$-adrenergic agonist, is an effective bronchodilator and should be approved for the treatment of chronic obstructive pulmonary disease, based on clinical trials in more than 3,000 patients with moderate to very severe COPD, the majority of an advisory panel agreed.

The Pulmonary-Allergy Drugs Advisory Committee voted 15-1 on Jan. 29, with 1 abstention, to recommend approval of olodaterol for the long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with COPD including chronic bronchitis and/or emphysema – the indication proposed by the manufacturer, Boehringer Ingelheim. Olodaterol is formulated in an inhalation spray solution, administered once a day via a metered-dose inhaler (the Respimat device), at a dose of 5 mcg (two actuations of 2.5 mcg each).

The panelists voting in favor of approval agreed that clinical trial results showed that the drug had a bronchodilator effect comparable to other established bronchodilators, in a real-world setting where patients were on background medications, and at a dosing regimen that was similar to other treatments.

In separate votes on safety and efficacy, the panel also voted 15-1, with 1 abstention, that the data provided "substantial evidence" that the drug was effective; and 15-1, with 1 abstention, that the safety profile was adequate for the proposed indication and was comparable to that of other LABAs. But the panel recommended postmarketing surveillance of safety, including malignancies, and safety in black patients, who made up less than 5% of the enrolled patients in the studies.

In the studies, there were more neoplasms among those treated with olodaterol, but the increase was not statistically significant and did not reach the level of a safety signal, according to the company. But several panelists said that they were struck by the four diagnoses of small-cell lung cancers in patients on the 10-mcg daily dose that was also tested in the studies. While this was not a reason to recommend against approval, they said that malignancies – lung cancers in particular – in treated patients should be closely monitored after approval.

If approved, olodaterol will be marketed as Striverdi Respimat. It has already been approved in more than 60 countries.

Zolpidem drugs get lower recommended dosage

The agency announced new, lower dosing requirements for certain sleep drugs that contain zolpidem, including Ambien, Ambien CR, Edluar, and ZolpiMist. Ambien and Ambien CR are also available as generics. The move comes on the heels of new data from driving simulation and laboratory studies showing that zolpidem blood levels in some individuals may be high enough the morning after use to impair activities that require alertness, including driving.

"After analyzing these new data, we felt it necessary to add new drug safety information to the labeling, including lowering of the recommended dose," Dr. Ellis Unger, director of the Office of Drug Evaluation in the FDA's Center for Drug Evaluation and Research, said during a teleconference. " We urge health care professionals to caution all patients who use these products about the risks of next morning impairment for activities that require complete mental alertness."

For women, the FDA now recommends that the dose of zolpidem should be lowered from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for extended-release products.

"We have learned rather recently that women appear to be more susceptible to the risk of next morning impairment, because they eliminate zolpidem more slowly from their bodies than men," Dr. Unger said, noting that reasons for this association remain unclear.

For men, the FDA advises health care professionals to consider these same lower doses (5 mg for immediate-release products and 6.25 mg for extended-release products).

More details about the development can be found in a Drug Safety Communication that was issued concomitantly.

Dr. Unger also explained that next-morning impairment is not limited to sleep drugs that contain zolpidem.

–Elizabeth Mechatie and Doug Brunk

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EHR REPORT: Clinical decision support in search of a smarter EHR

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

We have written routinely about the positive impact of implementing an electronic health record, citing potential improvements in areas such as charge capture, data sharing, and population management. In an attempt to be balanced, we've also discussed the financial implications and the risks of decreased productivity and provider frustration, among others. One area

DR. SKOLNIK AND DR. NOTTE

that we have not focused on – but which has been attracting increasingly more attention – is that of the advantages and limitations of Clinical Decision Support Systems.

CDSSs are tools that add evidence-based clinical intelligence to patient care, providing assistance to the provider as he or she treats patients and makes decisions about their management. A simple example of this would be an alert, reminding a physician to provide an immunization to age-appropriate patients while seeing them in the office. Some EHRs ship with this capability, while others completely lack real-decision support. Most commonly, however, an EHR will have the capability to provide support but rely heavily on end-user customization prior to implementation. Many of us are beginning to ask how using a clinical decision support system will ultimately affect patient outcomes.

The promise and liability of clinical intelligence

There is no question that the medical community has accepted the concept of guideline-based workflows and the importance of evidence-based medicine at the point of care. More recently, though, several studies have begun to look at how CDSS tools that are packaged into EHRs have affected care delivery. Surprisingly, the results are inconsistent; while many studies have demonstrated the benefits of decision support, others have not shown impressive changes in patient outcomes.

Findings from a review of 100 studies comparing the outcomes in care provided with and without a CDSS showed that 64% of the studies demonstrated improvements in practitioner performance when using a Clinical Decision Support System. While the specific systems varied in type and purpose, improvements in performance were "associated with CDSSs that automatically prompted users," compared with those "requiring users to activate the system," (JAMA 2005;293:1223-38).

Similar results were seen in a multidisciplinary randomized trial pin which investigators analyzed data from 21 centers and demonstrated

that "computerized decision support increased concordance with guideline-recommended therapeutic decisions" for numerous treatment options and "reduced cases of both overtreatment and undertreatment" (BMJ 2009;338:b1440 [doi:10.1136/bmj.b1440]).

But not all of the studies have been so optimistic. Findings from a more recent study showed that there is little benefit to having a CDSS in place. Using survey data collected from more than 250,000 ambulatory patient visits, they discovered that only 1 of 20 quality indicators proved better in the group of patients treated using EHRs with a CDSS in place, compared with those treated without decision support. The investigators offered little explanation for these unexpected results, but they did theorize that the value of current support systems may be minimal in the absence of standardization and better quality control (Arch. Intern. Med. 2011;171:897-903).

Searching for help

To meet certification for meaningful use, electronic records are required to have some minimal CDSS functionality available from Day 1. With most products, the depth and breadth of this built-in support is sorely lacking. For practitioners who simply view the EHR as a more complicated way of documenting progress notes and phone calls, this might not seem like a big deal. After all, the world of paper offered no clinical intelligence to speak of. But for others hoping to realize the true promises of health information technology, high-quality decision support may be essential.

The usefulness of clinical decision support systems is typically limited by the EHR itself, so it's critical to investigate CDSS capability early. We would encourage everyone to request a demonstration of what – if any – decision support is present in the EHRs they are considering, and ask a lot of questions about how the information is accessed and kept current. Does the product have a standard toolset based on outdated practice suggestions or is it updated as new guidelines are published? Is the information customizable to meet the needs of the implementation, or is it a "one-size-fits-all" solution? Finally, does the provider need to go searching for the support, or is the software smart enough to offer support in the form of an "alert" or "pop-up"?

A tale of art and science

When chess champion Gary Kasparov defeated IBM's Deep Blue Supercomputer back in 1996, people around the globe shared in a warm feeling of vindication. In the same way, it is possible to find the data questioning the value of CDSSs oddly reassuring. But the irony of history reminds us not to get comfortable in our assertions; just 1 year later, Deep Blue returned to defeat Kasparov in a devastating rematch. We suggest viewing this irony as instructive; if one accepts – as we do unequivocally – the value of evidence-based medicine, one must also accept that the right decision support delivered in a timely fashion will ultimately lead to better care and improved clinical outcomes.

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Early-a.m. team evaluations slash ventilator time, VAP

BY NEIL OSTERWEIL
IMNG Medical News

SAN JUAN, P.R. – To extubate or to keep the patient on a ventilator? That is the question which, when answered by a respiratory therapy team before the next morning's rounds began, halved the rate of ventilator-associated pneumonias and significantly decreased the time patients spent on ventilators in a surgical critical care unit, investigators reported at the annual congress of the Society of Critical Care Medicine.

Previously, spontaneous breathing tests had occurred either during or after morning rounds, with extubations being left until sometime later in the day. Under the new protocol, however, respiratory therapists assigned exclusively to the surgical CCU conducted rounds three times daily, consulted with nurses and physicians, and performed spontaneous breathing tests as recommended under joint 2001 guidelines. Thus armed with the information, the multiprofessional team could make the final decision to extubate, and the extubation itself could occur at morning rounds, getting patients off the ventilator that much sooner, said Dr. Vijay Jayaraman, a resident in surgery at the Christiana Care Health System in Wilmington, Del.

VITALS

Major finding: Ventilator-associated pneumonia event rates dropped from 10.8 to 5.3/1,000 ventilator-days when evaluations for extubation were performed before morning rounds.

Data source: A prospective study of 399 patients treated in a 28-bed CCU in Delaware; a retrospective study of records on 2,240 patients treated in five CCUs in New York hospitals

Disclosures: Both studies were internally funded; no relevant financial disclosures were reported.

Under the new protocol, Dr. Jayaraman and his colleagues saw the rate of ventilator-associated pneumonia (VAP) events decline from 10.8/1,000 ventilator-days before the protocol was implemented, to 5.3/1,000 afterward. The mean time to start a spontaneous breathing trial dropped from 2.67 to 1.77 days, and the time to extubation was shortened by a full day, 4.47 to 3.43 days. There was no difference in days spent in the CCU post extubation, days spent on the patient floor after the CCU stay, or hospital length of stay, Dr. Jayaraman reported.

"This was established in an ICU that was already fully functioning with an active care team. It just required some reorganization, and the most important thing is that the respiratory therapist can be empowered to help us and actively drive the spontaneous breathing test and extubation process," he commented.

Dr. Juliana Barr, who moderated the session at which Dr, Jayaraman presented his study, commented that although other groups have published ventilator-weaning protocols incorporating respiratory therapists, she was not aware of any studies that had previously shown a reduction in VAP rates. Dr. Barr is the acting medical director of critical care at the VA Palo Alto (Calif.) Health Care System.

The respiratory team uses predetermined criteria in a coordinated process consisting of awakening patients, performing the spontaneous breathing test, and, whenever possible, making the decision to extubate either before or during rounds.

The authors prospectively collected data on 180 patients admitted to their 28-bed level 1 surgical CCU from July through December 2010, before the protocol was implemented, and in 219 patients admitted over the same months in 2011, after the protocol had been in place for 6 months.

Extubate when the time is right

In a separate study, investigators from Montefiore Medical Center and other New York City institutions looked at whether outcomes following extubations in the CCU differed according to the time of day.

They retrospectively studied records of 2,240 patients on mechanical ventilation in one of five CCUs, and found that there were no significant differences in either 24-hour or 72-hour reintubation rates or in morality between patients extubated during daytime hours or at night.

"Our data provides evidence that nighttime extubation is itself not associated with elevated risk of reintubation or mortality. Patients should be extubated when weaning parameters are met, irrespective of time of day, with appropriate staffing and resources," Dr. Bryan R. Tischenkel said in a poster presentation. Dr. Tischenkel is an anesthesia resident at New York Presbyterian Hospital.

Gastric monitoring: Skip it?

VAP *from page 1*

nutrition delivery with subsequent inadequate feeding, and should be removed from the standard care of critically ill patients receiving invasive mechanical ventilation and early enteral nutrition," the investigators said.

It is thought that higher gastric volume causes intolerance of enteral feeding, with its attendant gastroesophageal reflux and vomiting. Monitoring of residual gastric volume involves periodically aspirating the stomach through the nasogastric tube with a 50-mL syringe. If the volume exceeds a cutoff – usually 250 mL – enteral nutrition is stopped or decreased to minimize the risk of vomiting, aspiration, and subsequent development of ventilator-associated pneumonia.

DR. REIGNIER

However, it has never been definitively established that increased gastric volume does lead to vomiting (or exactly what the cutoff amount should be), that this vomiting does lead to ventilator-associated pneumonia, or that the monitoring procedure actually reduces the risk of pneumonia. And monitoring has been linked to decreased calorie delivery and its associated morbidity.

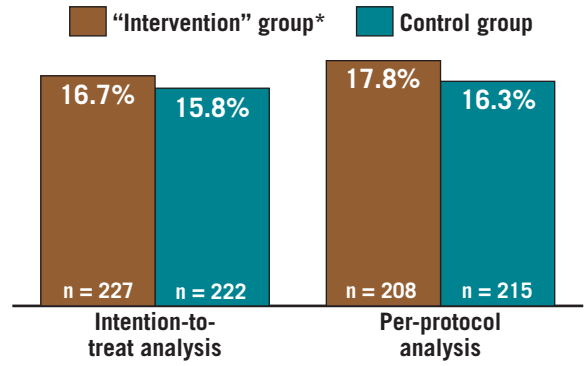
Dr. Reignier and his colleagues found in a preliminary study at a single ICU that forgoing the monitoring procedure did not raise the rate of ventilator-associated pneumonia. They then performed this noninferiority study to test the theory that residual gastric volume monitoring may not be necessary for this purpose.

Adult patients who were expected to require more than 48 hours of mechanical ventilation at nine ICUs were enrolled over a 1-year period. Three of the ICUs were medical and six were medical-surgical. Three were in university hospitals and six were in general hospitals affiliated with a university.

The study subjects were randomly assigned to receive either standard care, which included monitoring of residual gastric volume every 6 hours, or the "intervention" of no monitoring.

The primary outcome was the rate of ventilator-associated pneumonia. In the intention-to-treat analysis, this rate was 15.8% in the control group (222 patients) and 16.7% in the "intervention" group (227 patients), a nonsignificant difference. In the per-protocol analysis, this rate was 16.3% in the control group (215 patients) and 17.8% in the intervention group (208 patients), also a nonsignificant difference.

Rate of ventilator-associated pneumonia



*Intervention involved *not* performing standard residual gastric volume monitoring.
Source: JAMA 2013;309:249-56

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Thus, forgoing routine monitoring of residual gastric volume was noninferior to performing such monitoring at preventing this form of pneumonia, the researchers said (JAMA 2013;309:249-56).

In further analyses, the cumulative incidences of ventilator-associated pneumonia also were not significantly different between the two study groups. Microbiologic testing showed that the organisms causing pneumonia were the same between the two groups, as were the proportions of infections caused by *Staphylococcus aureus*, *Streptococcus* species, *Enterobacteriaceae*, and *Pseudomonadaceae*.

The two study groups also did not differ in short- or long-term mortality; rates of other ICU-acquired infections; scores on measures of organ failure; or the duration of ventilation, ICU stay, or hospital stay.

It was interesting that the proportion of patients who vomited was significantly higher in the unmonitored than in the monitored group, and that the number of vomiting episodes also was significantly higher in the unmonitored group, yet the rate of pneumonia was not significantly different, Dr. Reignier and his associates noted.

Despite higher rates of vomiting, more patients in the unmonitored group achieved their calorie targets on enteral nutrition.

The investigators proposed several explanations for their findings.

In several previous studies, residual gastric volumes did not correlate with vomiting or aspiration rates. Volumes lower than 250 mL did not correlate with decreased complications, and values as high as 500 mL did not correlate with increased rates of pneumonia.

Second, the measurement of residual gastric volume has never been standardized or validated. And the accuracy of gastric aspiration through the nasogastric tube may vary according to tube position, tube diameter, the number of tube openings in the stomach, the level of aspiration in the stomach, and the clinician's experience, the investigators said.

Third, and perhaps most important, many studies have challenged the role of gastric aspiration in the development of ventilator-associated pneumonia. The oral cavity, not the stomach, may be the significant reservoir of pathogens that cause this form of pneumonia, they said.

Eliminating the routine monitoring of residual gastric volume would be advantageous in that it would significantly reduce the workload of nurses and other clinicians, allowing them to focus on other interventions that have proved their value, Dr. Reignier and his colleagues added.

The study was sponsored by Centre Hospitalier Departmental de la Vendee. No financial conflicts of interest were reported.

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COMMENTARY

Dr. Steven Q. Simpson, FCCP, comments: The results of this study suggest that routine monitoring of gastric secretions is less important than one might think. However, the strikingly high rate of VAP in both groups raises some doubt about the general applicability of the findings, especially in an era when we have little tolerance for VAP at all, and when our methods of monitoring are on the verge of a game changing shift.

ED ventilation habits can lead to ALI

BY NEIL OSTERWEIL
IMNG Medical News

SAN JUAN, P.R. – The incidence of acute lung injury in patients started on mechanical ventilation in the emergency department could be reduced if ED staff paid a little more attention to ventilator settings and patient monitoring, said investigators at a poster session of the meeting annual congress of the Society of Critical Care Medicine.

A retrospective study of 251 mechanically ventilated patients with severe sepsis found that tidal volumes delivered to patients were highly variable, and the high tidal volumes and other preventable causes of acute lung injury (ALI) were common in the treatment of intubated patients in the ED, reported Dr. Brian M. Fuller of the departments of emergency medicine and anesthesiology – critical care at Washington University in St. Louis, Missouri, and his colleagues.

Pulmonary specialists can intervene by recommending that respiratory therapists lower tidal volumes delivered to acceptable rates, monitor plateau pressures more frequently, and inform physicians if the plateau pressures are too high. said Dr. Rahul Nanchal of the department of medicine at the Medical College of Wisconsin, Waukesha, who comoderated the session.

Researchers defined lung-protective ventilation as tidal volume less than 8 mL/kg of ideal body weight (IBW).

They found that the median tidal volume was 8.8 mL/kg per IBW (range 7.8-10.0). Inspiratory plateau pressures were recorded for only 76 (30.3%) of patients. In 236 patients (94%), the first tidal volume delivered was the highest, and non–lung-protective ventilation was used for a median of 230 minutes (range 0 to 354.0).

Patients were exposed to a fraction of inspired oxygen of 100%, for a median of 251 (range 148-373) minutes. In addition, 60 patients (24.8%) were exposed to the same tidal volume for more than 24 hours.

They noted that acute lung injury occurs in about 8.8%, and progression to acute injury occurs in more than one-fourth of patients (27.5%) early after admission, at a mean of 2.1 days.

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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.

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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.

ACS weighs in on CT screens for lung cancer

Costs, access to quality centers, contribute to guidance on low-dose tests for high-risk patients

BY MARY JO M. DALES
IMNG Medical News

Low-dose CT scans were endorsed for lung cancer screening in select high-risk individuals in guidelines from the American Cancer Society.

"Clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about lung cancer screening with patients aged 55 years to 74 years who have at least a 30–pack-year smoking history, currently smoke, or have quit within the past 15 years, and who are in relatively good health," wrote Dr. Richard Wender and the members of the guidelines committee in an article published online in CA: A Cancer Journal for Clinicians (doi:10.3322/caac.21172).

The recommendations are centered on the eligibility criteria used in the NLST (National Lung Screening Trial). Because of the uncertainty regarding the balance of benefits and harms, low-dose CT screening is not recommended for individuals at younger or older ages, with less lifetime exposure to tobacco smoke, and with sufficiently severe lung damage to require oxygen. The guideline writers acknowledge that clinicians will need to rely on their best judgment in cases when risk seems to approximate or exceed the NLST eligibility criteria in one category but not in another.

Since few government or private insurance programs provide coverage for the initial low-dose CT for lung cancer screening, "clinicians who decide to offer screening bear the responsibility of helping patients determine if they will have to pay for the initial test themselves and to help the patient know how much they will have to pay," according to the guideline writers. "In light of the firm evidence that screening high-risk individuals can substantially reduce death rates from lung cancer, both private and public health care insurers should expand coverage to include the cost of annual (low-dose CT) screening for lung cancer in appropriate high-risk individuals."

The "meaningful use" criteria for electronic health records under the recent HITECH (Health Information Technology for Economic and Clinical Health) Act are likely to improve identification of patients eligible for this screening as clinicians are required to determine the smoking status of more than 50% of their patients who are aged 13 years or older and to track the percentage of patients aged 10 years and older who are current smokers, according to Dr. Wender, chair of the department of family and community medicine, Jefferson Medical College, Philadelphia, and the other guideline writers.

While low-dose CT screening has been shown to substantially reduce the risk of dying of lung cancer, the technology will not detect all lung cancers or all lung cancers in early enough stages to avoid death from lung cancer. Further, a false-positive finding runs the risk of prompting an invasive procedure for incidental findings. The guidelines also warn that current smokers should not view screening as a substitute for smoking cessation. Counseling is recommended for current smokers, and all patients eligible for annual screening should make the decision only if they are willing to accept the risks and costs of annual screening until they reach age 74 years.

The guidelines also note that chest x-rays should not be used for lung cancer screening.

Wherever possible, screening should be performed as part of an organized program at an institution with expertise in low-dose CT screening and a multidisciplinary team skilled in the evaluation, diagnosis, and treatment of abnormal lung lesions. When those options are not available but patients strongly wish to be screened, they should be referred to a center that performs high volume of lung CT scans, diagnostic tests, and lung cancer surgeries. Otherwise, "the risks of cancer screening may be substantially higher than the observed risks associated with screening in the NLST, and screening is not recommended."

Multiple members of the guideline committee had financial disclosures related to drug manufacturers. The single committee member with ties to a device manufacturer declared his work was not directly related to the article.

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Smoking data fuel prevention fire

Risks *from page 1*

and by about 12 years for men, as compared with participants who had never smoked."

The report wasn't all bad news, however. Kicking the habit at any time added years of life, said Dr. Jha of the Center for Global Health Research, Toronto, and his coauthors.

The investigators examined smoking and smoking cessation among 113,752 women and 88,496 men who participated in the U.S. National Health Interview Survey from 1997 to 2004. These data were then correlated to information in the National Death Index up until the end of 2006 (N. Engl. J. Med. 2013:368:341-50).

The investigators then calculated the probability of survival in each group from 25 to 79 years of age. The mean follow-up was 7 years, with 10,743 deaths occurring in that age range.

This finding is new and confirms the prediction that, 'women who smoke like men die like men.'

DR. THUN

After adjustment for education, alcohol use, and adiposity, men and women who smoked were three times more likely to have died than nonsmokers. The estimated probability of survival to the age of 80 years was 38% among women smokers but 70% for those who had never smoked. For male smokers, the probability of survival to age 80 was 26%, compared with 61% for those who had never smoked.

Both women and men who smoked were significantly more likely than nonsmokers to die in all of the smoking-related conditions examined:

- Lung cancer (hazard ratios of 18 and 15 for women and men, respectively).
- Other cancers (HR, 2 and 2).
- All cancers (HR, 3 and 4).
- Ischemic heart disease (HR, 3.5 and 3).
- Stroke (HR, 3 and 2).
- Other vascular disease (HR, 3 and 2).
- Respiratory disease (HR, 8.5 and 9).
- Other unspecified causes (HR, 2 and 2).
- All medical disorders (HR, 3 and 3).
- Accidents (HR, 4 and 2).

"At 25-79 years of age, about 62% of all deaths among female smokers and 60% of all deaths among male smokers would have been avoided if the rates of death from diseases among smokers had been the same as the rates among those who had never smoked," the authors noted.

Quitting smoking, on the other hand, conferred significant survival benefits, no matter when it occurred (see graphic).

Smokers who quit at age 25-34 years had similar survival to that of never-smokers. "Smokers who had quit by about 39 years of age still had a 20% excess risk as compared with those who had never smoked. Although this hazard is substantial, it is much smaller than the 200% excess risk among those who continued to smoke."

"Even cessation at the age of 45 to 54 years reduced the excess risk of death by about two-thirds," according to Dr. Jha and his coauthors.

While the study concluded that quitting at any age is a good idea, it shouldn't be construed as a license to smoke longer. "That is not to say, however, that it is safe to smoke until 40 years of age and then stop, for the remaining excess risk of about 20% is substantial; it means that about one in six of these former smokers who dies before the age of 80 years would not have died."

Death risk identical for women

A second study found, for the first time, that women smokers are dying just as quickly – and from the same conditions – as men who smoke.

"The relative risks of death from lung cancer, chronic obstructive pulmonary disease, ischemic heart disease, any type of stroke, and all causes are now nearly identical for female and male smokers," Dr. Michael Thun and his colleagues wrote (N. Engl. J. Med. 2013:368:351-64). "This finding is new and confirms the prediction that, in relative terms, 'women who smoke like men die like men.' "

Dr. Thun, an epidemiologist with the American Cancer Society, and his colleagues drew their three study cohorts from seven national studies and databases. The entire study group comprised 1.32 million women and 899,000 men. Two of the cohorts were considered historical, covering 1959-1988; five were considered contemporary, covering 2000-2010. The participants' ages by the end of each group's follow-up period ranged from 50 years to more than 80 years.

For never-smokers, the analysis showed a general overall improvement in mortality between the historical and contemporary cohorts. But smokers did not enjoy this benefit. Between the historical and contemporary cohorts, all-cause mortality was 50% higher in smokers than in nonsmokers.

Again, women were particularly at risk, the investigators noted. "In contrast, there was no temporal decrease in the all-cause death rate among women who were current smokers and there was a 23.6% decrease among men who were current smokers. … The risk of death from lung cancer among male smokers appears to have stabilized since the 1980s, whereas it continues to increase among female smokers."

Dr. Thun and his associates also found the threefold increase in the risk of death between smokers and never-smokers. Their data determined that at least two-thirds of these deaths were directly associated with smoking, including ischemic heart disease, all other heart disease, stroke, and lung cancer.

A comparison of nonsmokers and smokers within all the time cohorts showed that the highest risks of death for most disorders occurred from 1982 to 1988. Since then, the mortality risks have declined and stabilized but still remain elevated compared with never-smokers. The lung cancer mortality risks were strikingly evident, the authors said: a relative risk of 25 for both men and women.

In contrast to the stabilized rates of other diseases, the mortality risk of chronic obstructive pulmonary disease has continued to increase in smokers. The biggest jump affected smokers older than 55 years and occurred after the 1980s period. The overall COPD mortality risk in the 2000-2010 cohort was more than double that of the 1980s (relative risk 10 vs. 25.6). The risks were similar for women (RR, 10.3-22.3) and men (RR, 12.5-27.3).

The increase is somewhat of a mystery, the authors said. It can't be explained by aging, smoking duration, or the improved ability to diagnose COPD. Instead, the finding may be related to changes in the way cigarettes are manufactured.

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COMMENTARY

Dr. Vera DePalo, FCCP, comments: The studies referenced underscore the toll that smoking takes overall on the life of a smoker and emphasizes that women are just a likely as men to suffer the negative consequences of smoking. This information helps give doctors, both primary care physicians and specialists, an added tool for smoking cessation advocacy with patients, in easily understandable terms.

Individuals who have shortness of breath are often able to understand the link between their smoking and their lung dysfunction. Smokers of shorter duration, before noticeable dysfunction occurs, are sometimes more difficult to convince of the negatives of smoking. Framing the conversation in terms of years of life lost, and the potential for regaining some of those years with smoking cessation, may tip the balance in favor of quitting.

FROM THE EVP/CEO: 2012–An ACCP Whirlwind

By any reasonable assessment, the year just past was a whirlwind for the American College of Chest Physicians. So much has happened–and so many more good things are coming–that it's almost an impossible task to tell you all about it in the space of this column.

To begin with, we just broke ground on a state-of-the art learning center for ACCP that will be the premier educational facility in the nation for chest medicine, providing our members with unlimited opportunities to learn more about the profession and, in turn, pass that knowledge on to patients. Our numbers continue to grow, as we start 2013 with 18,522 members, exceeding the goal we set at this time last year.

The planning is underway for our CHEST World Congress 2014 to meet in Madrid, Spain, a gathering that will significantly expand ACCP's global work and outreach by providing simulation-based education to a large and diverse medical community.

All of this was accomplished even as we met–and surpassed–our major goals for 2012. We're very proud of the accomplishments and what they mean for the future. The following is a brief overview of our key priorities.

Maintaining and diversifying our successful programs

Advancing our mission of delivering innovative, high-quality education, we are proud to be the global leader in clinical chest medicine and to have achieved our 6-year reaccreditation, with commendation, from ACCME, a coveted honor that underscores the importance we place on education.

BY PAUL A. MARKOWSKI, CAE

More than 4,000 physicians and other health-care providers attended our successful CHEST 2012 annual meeting. At this world-class educational event, they received state-of-the-art learning opportunities in pulmonary, critical care, and sleep medicine by way of a multitude of instructional formats. These included simulation, case- and problem-based learning, small-group discussions, self-study, and others. We conducted more than 40 education programs delivered across the country and expanded our international outreach through programs in India, Saudi Arabia, Israel, and South America.

We launched new products to deliver our education in innovative formats, such as new apps and two evidence-based guidelines on nonsteroidal immunosuppressive drugs and antithrombotic therapy and prevention of thrombosis (journal.publications.chestnet.org/ss/guidelines.aspx). In addition, we expanded publication of our premier *CHEST* journal in Asia and to India, thus broadening our international reach.

Strong finances

We met our operating budget in 2012, particularly expanding in business development. By raising revenues beyond expectations, we earned Board approval of the formation of a for-profit, wholly owned subsidiary. We diversified our revenue sources with new partnership opportunities, demonstrated by two prime examples: our Centers of Excellence presentations and exhibit area at CHEST 2012, showcasing unique programs and practices advancing outcomes; and our ACCP PREP (Professional Representatives Education Program) offerings that have two large programs already on the books for this year.

As I travel domestically and internationally for the ACCP, I am met with requests for details about our work and our innovative processes. It is a reminder of how sharply our educational tools differentiate us from any other member society.

You can't find a better example than our new building, where we'll provide more of the hands-on training and simulation initiatives for which we've been recognized. Our focus on continuing medical education forms the basis of who we are, and our ACCME honor demonstrates that we are heading in the right direction, giving health-care providers advanced, hands-on learning for medical teams to provide the highest quality care for their patients.

We are well on our way to being the global leader in providing education in cardiopulmonary, critical care, and sleep medicine. It's a profound and challenging pleasure to be the EVP of the ACCP and to be part of a group whose incredible efforts impact so many patients worldwide.

NETWORKS: Clinical Research, Critical Care

Clinical Research

Interested in Clinical Research?

If so, please join our Clinical Research NetWork via the e-Community so that we can build on our interests for personal development as members of the ACCP and to 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 (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
NetWork Chair
Dr. Rebecca Persinger, FCCP
NetWork 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 developing and testing of 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 format, whereby patients having an EWS alert will be randomized to be seen by the rapid response team (RRT) vs usual care. A 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 perform a clinical assessment and order interventions as clinically necessary. The study's goal is to reduce ICU transfers and mortality for the alerted patients by early, appropriate intervention.

Dr. Steven Simpson, FCCP
NetWork Chair

2012 McCaffree Humanitarian Awards

The 2012 CHEST Foundation Humanitarian Award winners represent ACCP's global reach: From the Midwest to Sub-Saharan Africa, from Texas to China, the winners, like many ACCP members, donate their time and talent to help those in need.

Gregory Erhabor, MBBS, FCCP, Obafemi Awolowo Univ., Ile-Ife, Nigeria
Mastering Your Asthma: Asthma Among Rural Communities in Ile-Ife, Nigeria

For 15 years, Dr. Erhabor and the Asthma and Chest Care Foundation have been educating people in rural Nigeria about self-care for asthma, which previously had been considered a death sentence. This grant allows Dr. Erhabor to expand his work by purchasing peak flow meters, translating education pamphlets into local languages, and obtaining basic medications for the very poor.

American College of Chest Physicians

Humanitarian Award Winner Gregory Erhabor, MBBS, FCCP, presents a peak flow meter to an asthma patient in Nigeria.

Renli Qiao, MD, FCCP, Univ. of Southern California
The Training Program for Village Doctors in Rural Southern China

In rural China, according to Dr. Qiao's China California Heart Watch program, medical care is close to primitive, preventive medicine is nonexistent, and hypertension is not considered a "disease" because patients don't feel sick. This grant helps further the organization's work teaching village doctors to recognize and treat hypertension in rural areas, where 95% of hypertension is currently undiagnosed.

Samuel Joseph, DO, FCCP, Spokane Respiratory Consultants
Healing Hearts Northwest Rwanda Cardiac Surgery Mission

Healing Hearts Northwest, based in Spokane, Washington, provides heart surgery in Rwanda for patients with cardiac disease who can't afford to travel abroad for care and offers hands-on training for Rwandan medical staff. The organization is using this grant to provide INR coagulation monitors and supplies to patients following cardiac surgery.

Michael Shea, MD, FCCP, Univ. of Michigan Health System
Shelter Association of Washtenaw County, Ann Arbor, Michigan

In Ann Arbor, the Shelter Association is the primary provider of temporary shelter and supportive services for homeless men and women. This grant supports the Shelter Association Health Clinic, where Dr. Shea volunteers his time as an attending physician in providing free medical care, connecting people to ongoing health coverage, and helping to break the cycle of poverty and homelessness.

The Ambassadors for OneBreath® Humanitarian Award
De De Gardner, MSHP, RRT; and Diane Rhodes, RRT, Univ. of Texas Health Science Center at San Antonio
2+2 Asthma Education Crew—Asthma Education in the Elementary School Environment

This project brings a fun, interactive asthma education curriculum to several San Antonio, Texas, schools where there is a high prevalence of asthma and corresponding absenteeism. After a pilot at one school last year, students missed fewer days of school and improved their academic standing.

The D. Robert McCaffree, MD, Master FCCP Humanitarian Awards are given to nonprofit and nongovernmental organizations where ACCP members volunteer their time and medical expertise, both domestically and internationally.

For information, please visit onebreath.org.

The ACCP to Collaborate at HIMSS13

New Orleans welcomes the 2013 HIMSS Annual Conference and Exhibition, March 3-7, 2013, at the Ernest N. Morial Convention Center. More than 36,000 health-care industry professionals are expected to attend to discuss health information technology issues and review innovative solutions designed to transform health care.

The ACCP is proud to support this annual event that helps HIT professionals make the right decisions for their organizations.

Conference education sessions include symposia on ICD-10, clinical/business intelligence, health information exchanges, clinical engineering, meaningful use, informatics, physicians' IT, RFID, and RTLS in health care, plus peer-reviewed sessions, including workshops and roundtables.

President Bill Clinton leads a keynote roster that also includes James Carville, political consultant; and Karl Rove, media contributor and former deputy chief of staff. The Meaningful Use Experience is designed to help providers find EHR solutions that are certified for acute or ambulatory facilities.

Visit HIMSS13 at www.himssconference.org.

ACCP AROUND THE GLOBE: Ultrasound Course in India

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

As a global professional organization, the ACCP is committed to developing and conducting innovative educational activities for clinicians around the world. From December 12-14, 2012, US faculty conducted ACCP's first hands-on course in pulmonary and critical care ultrasonography outside of the United States. In collaboration with All India Institute of Medical Sciences (AIIMS), a prestigious public hospital and medical school in New Delhi, established by an act of the Indian Parliament, US and Indian faculty used the ACCP curriculum to conduct the ACCP 3-day "Ultrasonography: Essentials in Critical Care" course (aiimspulmocrit.com/workshop.html). This program is designed to give participants practical skills that can be used immediately, and 80 physicians from around India were trained intensively in acquiring and interpreting ultrasound images of the lungs, pleura, blood vessels, abdomen, and heart. A postcourse assessment confirmed the impact of the program in improving knowledge and hands-on skill. The US ACCP faculty was especially impressed by how rapidly and thoroughly the participants acquired these skills.

American College of Chest Physicians

Indian physicians gather with instructor Dr. Paul H. Mayo, FCCP, to learn new skills related to acquisition and interpretation of images.

Following the ultrasound course, ACCP faculty participated in the AIIMS 2-day PULMOCRIT-2012, a conference devoted to education in pulmonary, critical care, and sleep medicine (aiimspulmocrit.com/workshop.html). Chaired by Dr. Randeep Guleria, FCCP, head of AIIMS' Department of Pulmonary and Sleep Medicine, with Dr. G. K. Khilnani, FCCP (Co-Chair) and Dr. Anant Mohan, FCCP (Organizing Secretary), this meeting covered the range of clinical topics in the three specialty areas. Hundreds of participants from around India attended this event, with plans to offer similar programs annually.

The first ACCP ultrasonography program outside of the United States, the AIIMS course demonstrated that ACCP hands-on courses can be as successful abroad as at home. This activity served the ACCP educational mission well.The College leadership and faculty look forward to offering more programs around the world.

Centers of Excellence at CHEST 2012 – Wrap-up

In the Centers of Excellence at CHEST 2012, 11 specially selected hospitals, non-hospital-based medical practices, and companies featured their programs and practices that improve health-care outcomes. The participants showcased outstanding characteristics and special practices that make their programs exceptional.

Center for Asbestos Related Disease

Libby, Montana
www.libbyasbestos.org
Response to a Public Health Emergency Through Patient Care and Clinical Research

In Libby, Montana, this Center (CARD) has emerged as a national center of excellence in addressing health-care issues associated with Libby amphibole asbestos. The CARD is a nonprofit 501(c) 3 devoted to health care, outreach, and research to benefit all people impacted by exposure to Libby amphibole asbestos.Through the clinic, CARD fulfills its primary mission of providing specialty health care for the varied diseases associated with Libby amphibole asbestos and collaborates with many clinical and basic science researchers acting as the gateway to the affected population by facilitating ethical representative research activities with the Libby cohort.

Children's Hospital of Atlanta: The Children's Asthma Center

Atlanta, Georgia
www.choa.org/Childrens-Hospital-Services/Pulmonology/Asthma-Program_
Merging Subspecialty Care With Community Outreach

The Center is a cooperative effort to provide subspecialty care for high-risk children with asthma. The majority of patients served by this Center are African-American and Hispanic children living in the inner city and funded through public payers such as Medicaid. The Center is unique in the collaboration between academic medicine, private practitioners, and a not-for-profit hospital-based infrastructure. Attendees received copies of all patient education materials, written descriptions of the Center infrastructure, including job descriptions and guidelines for establishing an asthma center in their own communities, and an outline of our community outreach efforts and guidelines for working effectively with community-based organizations in individual communities.

Georgia Pediatric Pulmonology Associates, PC

Atlanta, Georgia
www.gppa.net_
Georgia Pediatric Pulmonology Associates High Risk Asthma Program

This program was designed to help identify, monitor, and treat those children with high-risk asthma. Goals include providing our patients and their families with the medical care, education, and support, which will help keep their asthma under control and improve their overall quality of life. By identifying these patients, we are able to: maintain regular contact with families; provide consistent and regular follow-up at least every 1 to 3 months; provide medical and nutritional education to families specific to the needs of a child with high risk asthma; and routinely screen for associated conditions known to impact asthma control.

Johns Hopkins University Interventional Pulmonology

Baltimore, Maryland
www.hopkinsmedicine.org/ip_
Johns Hopkins University Interventional Pulmonology

An interactive, evidence-based informational session provides institutions and centers with guidance toward building an interventional pulmonary program highlighting our pleural disease service and percutaneous tracheostomy service resulting in increased safety, increased procedural volumes, and improved outcomes. Research information regarding ongoing Johns Hopkins research projects, as well as multicentered interventional pulmonary research efforts, was highlighted. Our physicians were available for consultations regarding specific issues that individual programs may experience.

Klingensmith HealthCare

Ford City, Pennsylvania
www.Klingshc.com_
Transition of Care Home Care Program for COPD/CHF/Pneumonia Patients

This is a respiratory-focused home health program that augments nursing and OT/PT services with respiratory therapists to reduce 30-day readmissions by 75%. The DASH program combines risk assessment, performance improvement, and metric-based reports into a patient management toolset to provide continuity of care from acute care to the home. The program has been integrated into hospital order sets and discharge processes, as well as LTAC/SNF facilities to improve transitions throughout the care network. Outcomes have been able to reduce 30-day readmits from 24% to less than 6%, improve ADL capabilities, and lower dyspnea scores while quantifying best practice scores and skill attainment.

Lahey Clinic

Burlington, Massachusetts
Rescue Lung Rescue Life: Early Lung Cancer Screening With Low Dose Contrast Chest CT Scan

Lung cancer remains the leading cause of cancer-related deaths in men and women. Lahey Clinic has taken a leading role in offering free, low dose chest CT scan screening as part of our multidisciplinary RESCUE LUNG RESCUE LIFE movement in patients identified as being moderate to high risk for lung cancer based on the NSLT and NCCN lung cancer screening guidelines. Presented—a PowerPoint presentation, educational CDs, Web-based education, and a panel presentation on the elements of how our program has been initiated, how to navigate patients to maximize screening, community education, and how other institutions may also start their own programs. Also described was our LUNG RADS radiographic correlations defining low, intermediate, and high risk radiographic characteristics, in addition to guidance for primary care physicians to ensure proper referral and follow-up after the initial screening chest CT scan is performed.

OSF Saint Francis Medical Center

Peoria, Illinois
www.osfsaintfrancis.org_
Comprehensive Lung Care for Pulmonary Nodules

From diagnosis to treatment, this Center offers total comprehensive lung care for patients with pulmonary nodules and specializes in the multidisciplinary treatment of lung cancer. Highlighted was our patient care process from presentation to treatment plan. This includes our CT lung screening, lung nodule clinic, interventional pulmonary lab, and comprehensive lung cancer clinic. By sharing our processes, we were able to demonstrate the patient care continuum, highlighting the importance of how one influences the necessity and productivity of another.

Pulmonary Thromboendarterectomy Program at UCSD

La Jolla, California
www.heartcenter.ucsd.edu/pte_
Evaluation and Management of Patients With Chronic Thromboembolic Pulmonary Hypertension

This program at UCSD consists of a team of physicians, nurses, and technicians committed to providing the most advanced care to patients with chronic thromboembolic pulmonary hypertension. The approach to evaluation, the thromboendarterectomy procedure, and postoperative care plans was highlighted in this presentation. The unique requirements of a referral practice and the attention to patient and family needs throughout this process was reviewed.

San Antonio Military Medical Center (SAMMC)

Fort Sam Houston, Texas
Standardized Evaluation of Post-Deployment Dyspnea

The post-deployment dyspnea clinic (PDDC) at SAMMC serves as the primary clinical site for numerous research protocols investigating the respiratory health of military personnel that include "Study of Active Duty Military for Pulmonary Disease Related to Environmental Dust Exposure (STAMPEDE)" and a clinical registry for post-deployment respiratory disease. The expertise provided includes a clinical algorithm for evaluation of military personnel for dyspnea and specific guidelines to diagnose exercise-induced bronchospasm, vocal cord dysfunction, and other disorders unique to a highly fit population.

University of Virginia Medical Center

Charlottesville, Virginia
Joint Commission Certified COPD Disease Specific Center

A work process to establish Joint Commission certification was presented. Defining outcomes measures and subsequent follow-up of these outcomes; initiating institute-wide clinical practice guidelines; and building a multidisciplinary team to care for patients with COPD was covered.

Continued on following page

CHEST Foundation Opens 2013 Applications for Grants

Each year, The CHEST Foundation offers more than $500,000 in grants for clinical and translational research, leadership, and volunteer community service. In 2013, 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, and community service. New this year is the ACCP Diversity Committee Young Investigator Faculty Scholar Grant, designed to support underrepresented young researchers; and the Pulmonary Fibrosis Foundation and The CHEST Foundation Clinical Research Grant in Pulmonary Fibrosis.

Grant applications and complete criteria can be accessed through The CHEST Foundation's website, onebreath.org. The application deadline for all grants is May 1, 2013.

GlaxoSmithKline Distinguished Scholar in Respiratory Health

The Distinguished Scholar in Respiratory Health grant supports a clinical educational project designed to improve patient care and is intended for the investigation of issues that are not easily supported through traditional sources. Funding is $150,000 over the course of 3 years. Applicants must be Fellows of the American College of CHEST Physicians (FCCP).

Alpha-1 Foundation and The CHEST Foundation Clinical Research Grant in COPD and Alpha-1 Antitrypsin (AAT) Deficiency

This 1-year, $25,000 grant supports research focused on COPD and AAT deficiency. While research projects primarily in usual COPD (not associated with AAT deficiency) are allowed, those with a focus on AAT deficiency are encouraged. Applicants must be in an ACGME fellowship program and within 5 years of completion.

The CHEST Foundation and the Respiratory Health Association of Metropolitan Chicago Clinical Research Grant in Women's Lung Health and **The Sheila J. Goodnight, MD, FCCP, Clinical Research Grant in Women's Lung Health**

Two, 1-year, $10,000 grants support clinical research related to women's lung health. Topics may include research on gender differences in lung diseases, such as COPD and lung cancer. Applicants must be ACCP members.

OneBreath® Clinical Research Grant in Lung Cancer

This 2-year, $100,000 grant ($50,000 annually) supports a clinical/translational research project that could lead to improved treatment and/or cure of lung cancer. Applicants must be ACCP members who have completed at least 2 years of a pulmonary or critical care fellowship or a thoracic surgery residency and are within 7 years of completing training.

The CHEST Foundation Clinical Research Grant in Pulmonary Arterial Hypertension

Established through a grant from Actelion Pharmaceuticals, US, Inc., this 1-year, $50,000 grant supports a clinical/translational research project that contributes to the understanding of the pathophysiology or treatment of pulmonary arterial hypertension (PAH). Applicants 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.

American College of Chest Physicians

(L-R) Dr. Stephanie Levine, FCCP, CHEST Foundation Chair, presents the "2012 CHEST Foundation Clinical Research Award in PAH" to Dr. Corey Ventetuolo.

ACCP Diversity Committee Young Investigator Faculty Scholar in Pulmonary, Cardiovascular, Critical Care, or Sleep Research Grant

This 1-year, $25,000 grant is designed to encourage outstanding underrepresented young investigators in their careers in pulmonary, cardiovascular, critical care, or sleep research, with the focus on promoting equity and reducing disparity within a global setting. The grant supports clinical/translational research in pulmonary, cardiovascular, critical care, or sleep medicine. Applicants 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.

The Pulmonary Fibrosis Foundation and The CHEST Foundation Clinical Research Grant in Pulmonary Fibrosis

A new $30,000, 1-year grant supports a clinical/translational research project that could contribute to effective treatments or a cure for pulmonary fibrosis.

Applicants 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.

Roger C. Bone Advances in End-of-Life Care Award

This 1-year, $10,000 award supports leadership in end-of-life care that stresses the importance of communication, compassion, and effective listening. The award is given for leadership—on the international, national, or local level—and does not fund research or provide seed money for new end-of life or palliative care programs or projects. Applicants must be ACCP members who hold the degree of MD, DO, MBBCh, PharmD, PhD, or the equivalent.

McCaffree OneBreath® Community Service Grants

The Foundation offers several community service grants, from $5,000 to $15,000, to support the volunteer efforts of those ACCP members who donate time and medical service to improve the health of people in communities throughout the world. Funds are granted to the nonprofit or nongovernmental organizations for which ACCP members give pro bono service.

Continued from previous page

Yale Lung Screening and Nodule Program (Yale Lung SCAN)

New Haven, Connecticut

www.medicine.yale.edu/cancer/patient/programs/thoracic/specialties/screening_

Understanding Risk and Managing Fears to Rationally Implement Lung Cancer Screening Into Clinical Practice

Yale Lung SCAN is a comprehensive, multidisciplinary organized program that delivers a personalized evidence-based approach to lung cancer screening to individuals at risk. Lung screening is a process, not just a scan. Implementation is complicated by patients' prominent fears, poor understanding of actual cancer risk, and consequences of screening. Our program integrates risk assessment, personalized counseling through a decision support tool, risk modification, a structured approach, and several research initiatives. The activity showcases these various components and how they are integrated into practice. Yale Lung SCAN is part of the Yale Thoracic Oncology Program.

This Month in *CHEST*: Editor's Picks

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

▶ Baseline and Follow-up 6-Min Walk Distance and Brain Natriuretic Peptide Predict 2-Year Mortality in Pulmonary Arterial Hypertension. *By Dr. J. S. Fritz et al.*

▶ Characteristics of Infectious Diseases in Hospitalized Patients During the Early Phase After the 2011 Great East Japan Earthquake: Pneumonia as a Significant Reason for Hospital Care. *By Dr. T. Aoyagi et al.*

▶ Perception by Family Members and ICU Staff of the Quality of Dying and Death in the ICU: A Prospective Multicenter Study in The Netherlands. *By Dr. R. T. Gerritsen et al.*

CRITICAL CARE COMMENTARY: New Strategies in Management of Critical Illness Myopathy and Polyneuropathy

Critical illness myopathy (CIM) and polyneuropathy (CIP) results from complications of severe illness affecting the motor and sensory axons, leading to symmetric flaccid weakness, sensory deficits, and loss of deep tendon reflex. CIM/CIP manifest as axonal neuropathy demonstrated by flaccid muscle groups (proximal and distal); decreased response to pain, temperature, and vibration; and it can progress to axonal denervation and muscle damage. CIM/CIP can involve the limbs, diaphragm, and intercostal muscles but rarely the facial muscles. The incidence of CIM/CIP depends on several factors (duration of illness, exposure risk factors, diagnostic criteria, and others) (Stevens et al. Intensive Care Med. 2007;33[11]:1876) but increases with age and severity of disease. Reported incidence may range from 25% to 60% in critically ill patients ventilated for 5 to 7 days in the ICU (De Jonghe et al. *JAMA*. 2002;288[22]:2859); 70% in patients with SIRS/sepsis; and may be as high as 100% when complicated by multiorgan failure (Tennila et al. *Intensive Care Med*. 2000;26[9]:1360).

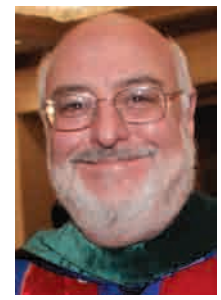
CIM/CIP may be on the rise and sometimes initially recognized when weaning from mechanical ventilation is difficult, thus frequently leading to reintubation (Stevens et al. *Crit Care Med*. 2009;37:299). A high index of suspicion is needed in order to make an early diagnosis, which can be confirmed by the use of electrophysiologic studies and, ultimately but rarely, a muscle biopsy can be done when other myopathic processes are suspected.

CIM/CIP is a known independent predictor of prolonged weaning, mortality, and increased ICU stay, and its prolonged effects may last up to 5 years. It is reversible in most cases but may be irreversible, leading to permanent paralysis (Fletcher et al. *Crit Care Med*. 2003;31[4]:1012); (Garnacho-Montero et al. *Crit Care Med*. 2005;33[2]:349).

Risk Factors

CIM/CIP and its long lasting consequences may be prevented by modifying known risk factors and avoiding medications that may result in the illness Garnacho-Montero et al. *Intensive Care Med*. 2001;27[8]:1288). Several risk factors have been identified, among which are sepsis and use of medications (neuromuscular blocking agents [NMBA], corticosteroids, aminoglycosides, vasopressors, and catecholamine support). Other independent risk factors include female sex, severity of illness,

BY DR. OLUFEMI LAWAL



BY DR. PETER SPIRO, FCCP

duration of organ dysfunction, renal failure, renal replacement therapy, hyperosmolality, parenteral nutrition, low serum albumin level, duration of ICU stay, and central neurologic failure. Recently, hyperglycemia has been implicated, and glycemic control has been shown to be beneficial. The data on corticosteroids as a risk factor for CIM/CIP remain controversial, with a number of studies identifying use of corticosteroids as a risk factor and some unable to verify corticosteroids as a sole cause of CIM/CIP. Other studies show the combination of corticosteroids and NMBAs may have an additive effect that leads to CIM/CIP (Hermans et al. *Cochrane Database SysRev.* 2009:CD006832).

Given the increasing incidence, morbidity, mortality, and rising cost of health care associated with CIM/CIP, especially in the elderly population, it is important to ensure risk factor modification and offer timely treatment when the condition is suspected. Several studies recommend the use of several modalities; however, a multidisciplinary approach remains the best way to manage CIM/CIP.

Management

Essential areas in management include avoiding or limiting use of the medications that may predispose to CIM/CIP, modifying known risk factors, and use of supportive therapy. Most authors also agree to discontinue or, if impossible, reduce the dose of medications that may contribute to CIM/CIP. These modalities may prevent or shorten the duration of CIM/CIP (Lacomis et al. *Muscle Nerve*. 2000;23:1785).

In addition, it is essential to aggressively manage underlying critical illness, like sepsis, hypotension, and hypoxemia. Other essential areas of caring for the critically ill include the appropriate use of DVT prophylaxis and decubitus ulcer prevention.

The best specific therapy for CIM/CIP remains insulin therapy for tight glucose management. Two large randomized studies have shown the mortality benefit of intensive insulin therapy in the ICU. A mortality reduction from 8.0% to 4.6% ($P < .04$) was noted in the surgical ICU in a study published by Van den Berghe and colleagues (*N Engl J Med*. 2006;354[5]:449). Afterwards, Hermans et al (*Am J Respir Crit Care Med*. 2007;175[5]:480) published a prospective study (subanalysis) that showed reduction in incidence of CIM/CIP from 49% to 25% in the SICU ($P < .0001$) and from 51% to 39% in the MICU ($P = .02$). Incidence of prolonged mechanical ventilation (mechanical ventilation for at least 2 weeks) was reduced from 42% to 32% in the SICU ($P = .04$) and from 47% to 35% in the MICU ($P = .01$). The efficacy of intensive insulin therapy has been attributed to its antiinflammatory properties, improvement of lipid profile, and its endothelium protection properties in critically ill patients (Wittet al. *Chest*. 1991;99[1]:176). Although the Hermans et al study showed a decrease in incidence of CIM/CIP, there was no significant decrease noted in duration of ICU stay or mortality. There is also a risk of hypoglycemia associated with intensive insulin therapy, and measures must be taken to prevent it.

'Recently, hyperglycemia has been implicated, and glycemic control has been shown to be beneficial. The data on corticosteroids as a risk factor for CIM/CIP remain controversial ...'

Despite the beneficial effect of corticosteroids in specific diseases, for example, septic shock, MODS, and ARDS, its use may be a risk factor for CIM/CIMP. While some studies did not show corticosteroids as a significant causative factor (De letter et al. *Crit Care Med*. 2001;29[12]:2281), other studies implicated corticosteroids as a cause of CIM/CIP but neither of these studies observed the effect of glucose control or treated hyperglycemia, a now known treatment of CIM/CIP. A prospective trial by Hermans and colleagues, however, suggested a preventive role of corticosteroids in this disease. Its risk and use in CIP/CIM remains controversial and would require further studies for clarification.

Most authors agree that rehabilitation and physiotherapy is beneficial in treating CIM/CIP. Rehabilitation ranges from maintaining functional range of motion to ensuring independence. There is some evidence to support the use of IV immunoglobulin, but randomized studies will be needed in this area (Mohr et al. *Intensive Care Med*. 1997;23[11]:1144). The use of testosterone derivatives, growth hormone, nutritional supplements, and antioxidant therapy has not been shown to be useful and may be harmful in CIM/CIP (Van den Berghe et al. *N Engl J Med*. 2006;354[5]:449; Pichard et al. *Crit Care Med*. 1996;24[3]:403; Mohr et al. *Intensive Care Med*. 1997;23[11]:1144; Waldhausen et al. *Intensive Care Med*. 1997;23[8]:922).

Conclusion

In conclusion, CIM/CIP is a potentially preventable disease with significant morbidity and mortality. Although further studies are needed to certify the role of intensive glucose control and corticosteroids in management of this disease, a higher index of suspicion and a multidisciplinary approach may be the most effective way to reduce the burden of this disease.

Dr. Olufemi Lawal
Fellow, Pulmonary/Critical Care Medicine
Harlem Hospital Center, Columbia University;
and
Dr. Peter Spiro, FCCP
Chief, Pulmonary/Critical Care Medicine
Elmhurst Hospital
Professor of Medicine
Mount Sinai School of Medicine
New York, NY

With COPD

Limited lung function makes breathing more difficult

INDICATIONS AND USAGE

TUDORZA™ PRESSAIR™ (aclidinium bromide inhalation powder) is an anticholinergic indicated for the long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

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

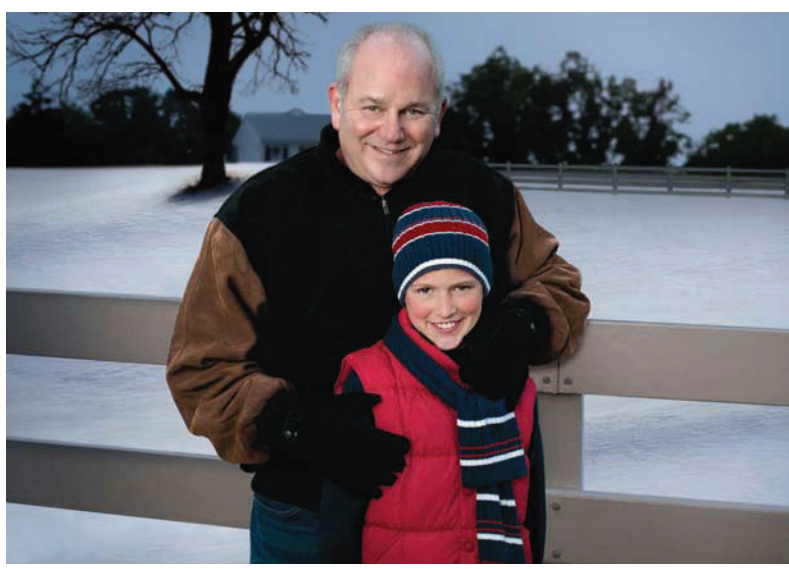
New

Tudorza™ Pressair™

(aclidinium bromide inhalation powder)

400 mcg

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™

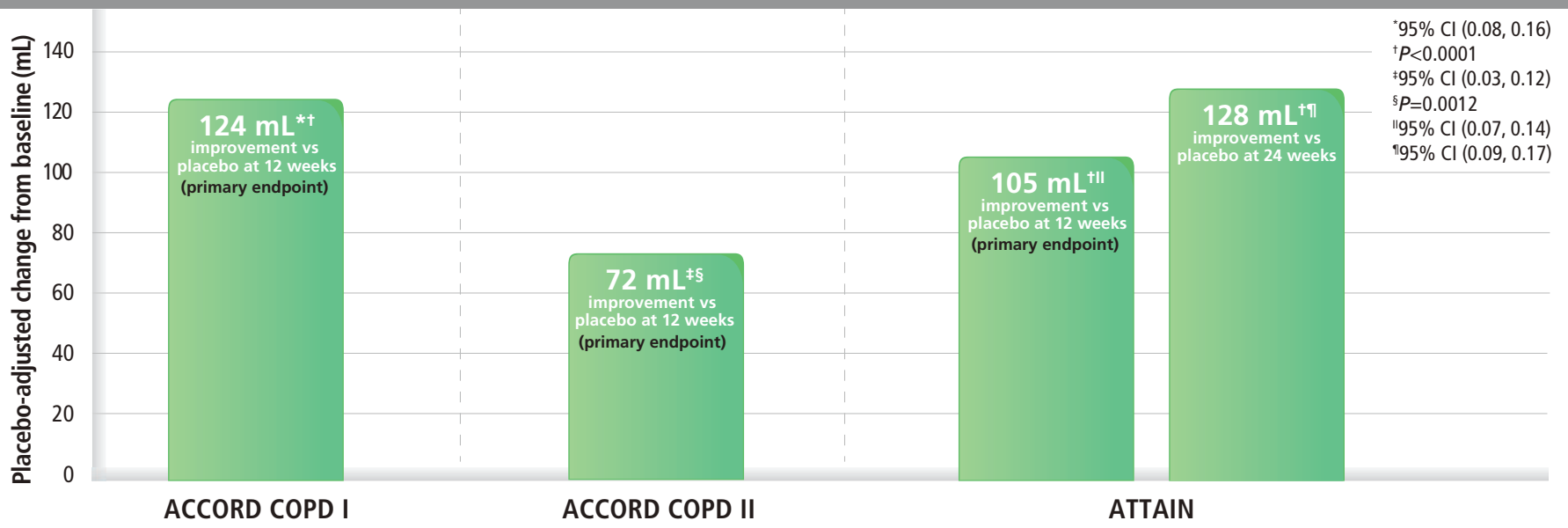
(aclidinium bromide inhalation powder)

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

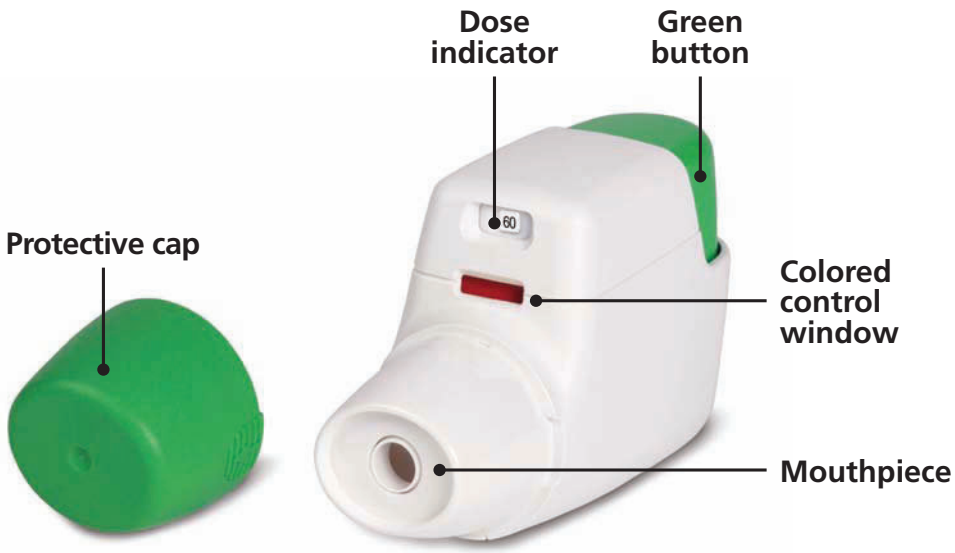
Mean peak improvements in FEV_1 relative to baseline observed after the first dose on day 1 were similar at 12 weeks[1]

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

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PULMONARY PERSPECTIVES: Reflections on Hurricane Sandy–Bellevue Hospital 3 Months Later

On October 29, 2012, Hurricane Sandy devastated New York City (NYC) and the surrounding region. High winds and rain were accompanied by a record-breaking nearly 14-foot storm surge that inundated parts of lower Manhattan, including New York University School of Medicine's (NYU) three main teaching hospitals. By the time the storm passed, all three hospitals had been evacuated and would be closed for weeks to months. Bellevue Hospital, the main teaching site for NYU School of Medicine, and the nation's oldest public hospital had continuously served the people of New York City since its establishment in 1736. It had never before been closed.

BY DR. LAURA EVANS, FCCP

Even before Sandy made landfall near NYC and brought with it that storm surge, the effects on Bellevue and other NYU-affiliated hospitals were apparent. The Manhattan Veterans Affairs (VA) Hospital preemptively evacuated 2 days before the storm, while staff at NYU Langone Medical Center (NYULMC) and Bellevue Hospital Center prepared to shelter in place. The day before the storm, the ICUs at Bellevue were busy, both with usual patient care activities, as well as storm preparation. We asked staff scheduled to work during the period of the storm to arrive well before their scheduled shifts, as much as 24 hours ahead of time in cases where staff was dependent on public transportation and to be prepared to stay well after their shift was completed. We made preparations to keep staff fed and entertained during the days ahead: we stocked up on food from local grocery stores and brought in DVDs from home. As preparations continued, to make sure that we always had a very accurate knowledge of the clinical status of each patient and their particular care needs, we conducted rounds approximately every few hours beginning the day before the storm.

When the storm arrived, bringing with it extensive flooding, Bellevue Hospital went on back-up power. That same night, when the fuel pumps to the backup generators failed, we thought it was only a matter of an hour or two before we were plunged into darkness. A spontaneous effort of hundreds of staff members throughout the hospital who passed fuel up 13 flights of stairs to refuel the emergency generators, kept the emergency lights

Continued on following page

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on, and the ventilators and other equipment in the ICU running. Even with this heroic effort, due to damage to a multitude of hospital systems, Bellevue could not continue operations and had to evacuate more than 700 patients from a 25-story building without any working elevators. During the storm and subsequent evacuation, staff in the ICUs worked tirelessly. Our nurses and respiratory therapists alternated caring for patients and trying to rest in 12-hour shifts, as many of their scheduled replacements could not arrive from other areas of New York City and the surrounding region. The ICU residents and fellows did the same. Pharmacists hand delivered all necessary medications throughout the hospital. My colleagues and I in ICU leadership tried to rest when we could, but many of us worked nearly 96 hours straight with minimal rest. Fortunately, all patients were evacuated safely to other facilities in the region without any storm-related deaths or serious adverse events. Even despite operating at near capacity, facilities throughout the region welcomed our patients, sometimes opening additional wards in order to accommodate the increase in patient volume.

Many people recognize that effective teamwork is central to providing high quality critical care. Everyday, the staff of the Bellevue ICUs exemplifies outstanding teamwork under normal circumstances; we are a cohesive unit. I had little idea that our whole team could step it up to another level entirely during the storm and evacuation. Everyone was focused on

COURTESY NISHAY CHITKARA, MD

the difficult tasks at hand, keeping our patients safe, and continuing to provide outstanding care, even though these same staff members were, at times, unable to contact their own families to know that they were safe. Even when travel to and from the hospital became possible again, many staff members chose to stay to continue to care for their patients. I was so proud to be a part of this amazing team. When I walked out of the hospital 3 days after the storm, I had no idea how hard the disruption of our team would be with Bellevue closed for repairs.

After the evacuation was complete, hospital leadership was better able to assess the extent of the damage to Bellevue. I, and many other ICU staff members, expected the hospital to be closed for a week or two for repairs. I don't think any of us expected in early November that Bellevue would resume full operations in February 2013. Our tight-knit ICU team was dispersed over much of New York City for the following 3 months. Our nurses, physician assistants, respiratory therapists, pharmacists, and clerical staff were deployed to nine other public hospitals throughout New York City. Some were deployed to other ICUs, others were deployed to areas outside of critical care, such as outpatient clinics. All were separated from their usual colleagues and teammates. The director of critical care nursing and the head nurse in the Bellevue Medical ICU each received dozens of text messages each day in the early days after the evacuation from team members trying to stay in touch. Our residents and fellows were assigned to newly created disaster relief rotations at hospitals and clinics across the city where they learned to work with different teams in different systems. Frequent communication among our team members, which had previously been almost taken for granted, required active effort with the displacement.Although the evacuation of Bellevue hospital was unprecedented and received much attention, I think the hospital closure and months that followed the evacuation were even harder on the ICU staff. Bellevue is a safety net hospital and plays a crucial role in the health care of some of the most vulnerable residents of New York; we in the ICU are part of that and feel that mission acutely. Our roles as ICU team members at Bellevue are fulfilling and give us a sense of purpose—we lean on one another and support one another. We are good at our jobs and our patients need us. With the displacement subsequent to the evacuation and many of our staff in new roles for that 3-month period, we had to find new purpose in that and support from new colleagues, while continuing to support one another after a traumatic event. While the hospital was closed for repairs and changes were made to the infrastructure to harden the facility against damage from future storms, our ICU staff showed the same resiliency and adaptability handling the postevacuation displacement. Our patients and our team returned to Bellevue in February. I like to think our ICU team is even stronger for the experiences we had with Hurricane Sandy.

Dr. Laura Evans, MSc, FCCP
Assistant Professor NYU School of Medicine
Medical Director of Critical Care, Bellevue Hospital Center
New York, NY

EDITOR'S COMMENT

Diverging a bit from a usual Pulmonary Perspectives, this account of the events surrounding the devastation brought by Hurricane Sandy on one of New York City's premier medical centers is both fascinating and inspiring.

The absolute power of the storm—with the rapidity of its onset and the enormity of its damage (estimated at $1 billion for NYU alone—are almost impossible to grasp unless you experienced it firsthand.The rescue of hundreds of critically ill patients from Langone Medical Center and Bellevue Hospital without a single death or adverse event was nothing short of a miracle, carried out by hundreds of dedicated health-care professionals, city workers, and hospital administrators working toward a common goal.

These efforts serve to illustrate the level of dedication and selflessness of all those involved and remind us of the reason we choose this profession: to heal the sick and to aid and comfort those in need.

Sometimes, it's not pretty or based on guidelines or even based on scientific method, and it may even bend some rules and ruffle some feathers, but it is knowing that we made a difference in someone's life that serves as the ultimate reward.

Dr. Loren J. Harris, FCCP
Section Editor, Pulmonary Perspectives

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