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CHEST® Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

ANDREW BOWSER/FRONTLINE MEDICAL NEWS

"Workplace violence is not just active shooter – it's ubiquitous, and we only know a little bit about it," noted Dr. Lewis J. Kaplan.

How to manage workplace violence

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – Active-shooter events and other episodes of workplace violence can be better managed with proper planning and training by hospitals and staff, Lewis J. Kaplan, MD, said in a late-breaking session at the Critical Care Congress.

"Workplace violence is not just active shooter – it's ubiquitous, and we only know a little bit about it," noted Dr. Kaplan, section chief, surgical critical care, Corporal Michael J. Crescenz VA Medical Center, Philadelphia. "The facility and everyone in the health care team have a role in being an active participant, rather than a passive one."

To actively prepare for premeditated events, clinicians should develop partnerships with local law enforcement officials and initiate active training that involves anyone who could come into contact with an active shooter, Dr. Kaplan recommended.

There are many steps that can be taken to protect the facility, including visitor screening and management, security that extends to the perimeter of the facility, building design that limits access to specific places in the facility, and deployment of firearm-detection canines, Dr. Kaplan said, during the session at the congress, sponsored by the Society of Critical Care Medicine.

WORKPLACE VIOLENCE // *continued on page 6*

Prehospital antibiotics improved sepsis care

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – Training EMS personnel in early recognition of sepsis improved some aspects of care within the acute care chain, but did not reduce mortality, according to results of a randomized trial.

Emergency medical service (EMS) personnel were able to recognize sepsis more quickly, obtain blood cultures, and give antibiotics after the training, reported investigator Prabath Nanayakkara, MD, PhD, FRCP, at the Society of Critical Care Medicine's Critical Care Congress.

However, the hypothesis that this training would lead to increased survival was not met, noted Dr. Nanayakkara, of the acute medicine section of the department of internal medicine at VU University Medical Center, Amsterdam.

At 28 days, 120 patients (8%) in the prehospital antibiotics group had died, compared with 93 patients (8%) in the usual care group (relative risk, 0.95; 95% confidence interval, 0.74-1.24), according to the study's results that were simultaneously published online in Lancet Respiratory

PREHOSPITAL ANTIBIOTICS // *continued on page 7*

INSIDE HIGHLIGHT

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Bringing respiratory care for asthma to Guyana

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Climate change is worsening allergies, expert says

BY THOMAS R. COLLINS
Frontline Medical News

ORLANDO – Climate change is not just eroding coastlines and threatening seaside cities and taking lives with increasingly powerful hurricanes, but appears to be contributing to increases in allergy and asthma, an expert told the audience at the joint congress of the American Academy of Allergy, Asthma, and Immunology and the World Asthma Organization.

Longer pollen seasons, allergens unleashed by felled trees and ripped-up plants, mold growth following floods, and irritants launched into the air by wildfires are some of the concerns that should be alarming physicians and policy makers, said Nelson A. Rosario, MD, PhD, professor of pediatrics at Federal University of Paraná (Brazil).

"This is related to disease," he said. "I'm trying to convince you that something is happening. This is not a matter of believe it or not."

And evidence suggests that his fellow allergists and their patients agree.

A 2015 international survey found that 80% of rhinitis patients blamed climate change for contributing to their symptoms.

GILITUKHA/THINKSTOCK

In a survey published in 2016, 63% of AAAAI members said that climate change was relevant to patient care either "a great deal" or in "a moderate amount." Only 11% said that climate change wasn't relevant at all. Asked how patients have been affected by climate change, about two-thirds said "increased care for allergic sensitization and symptoms on exposure to plants or mold."

Science supports these views, Dr. Rosario said.

A 2011 study of North American pollen seasons found that some cities had significant increases of 11-27 days, compared with 15 years before.

DR. ROSARIO

This year, a New England Journal of Medicine (2018 Mar 8;378[10]:881-3) article pointed out the respiratory dangers of increasing wildfires, noting the carbon dioxide, particulate matter, trace minerals, and thousands of other compounds that are unleashed.

"This is related to disease. ... This is not a matter of believe it or not," Dr. Rosario said.

And a 2017 review noted the impacts of the consequences of climate change, from increased allergies due to heavy precipitation events, asthma prompted by intense tropical cyclones, and allergic conditions caused by extremely high sea levels.

Dr. Rosario suggested that, rather than wait for official agencies to take action, physicians need to adapt and help their patients adapt. A team of doctors wrote in 2013 that while "improved governmental controls" could lead to cleaner air, they "meet strong opposition because of their effect on business and productivity." So, they said, the allergy community should adjust, by "anticipating the needs of patients and by adopting practices and research methods to meet changing environmental conditions."

Dr. Rosario urged physicians to think of the climate-change effects on allergy and asthma as a "collective action" problem, not an individual one.

"The consequences will come," he said. "There must be international cooperation."

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Jim Varney/Science Source

Workplace violence // continued from page 1

In all, Dr. Kaplan listed 19 steps that facilities could take to avert a planned attack, drawing in part on recommendations from the FBI publication, Workplace violence: Issues in response.

"This is a lot, and you don't need to do all of it," Dr. Kaplan said. "But you need to have an internally consistent plan for how you will do this at your facility, and it must involve everyone. They all need to be able to be part of your team."

Recent data on workplace violence

The latest data show that the great majority of workplace violence is perpetrated by individuals outside the organization. According to the International Association for Healthcare Security and Safety Foundation 2017 Healthcare Crime Survey, 89% of events involved a customer or patient of the workplace or employees.

In-hospital violence is prevalent, according to 2016 data from Occupational Safety and Health Administration that identified 24,000 workplace assaults in a 3-year span covering 2013-2015, including 33 homicides, 30 assaults, and 74 rapes.

Many in-hospital incidents are marked by failures in communication, patient observation, noncompliance with workplace violence policies or lack of such policies, and perhaps most importantly, an inadequate assessment for the violent potential of the perpetrator, according to Dr. Kaplan.

In a 2017 survey of 150 trauma nurses, 67% said they had been the victim of physical violence at work, though many did not report the incidents, Dr. Kaplan noted. Some reasons nurses gave for not reporting violence included the feeling that it was "just part of the job" in 27% of cases, and concerns about patient satisfaction scores in 10% of the cases.

Active-shooter events in the workplace are of particular concern, though they are relatively rare; one recent report identified 160 events that occurred during 2000-2013 in which 1,043 individuals were injured, according to Dr. Kaplan.

Other presentations in the late-breaking session covered issues related to disaster preparedness and the Charlie Gard case.

"We picked these three topics to be in a late-breaker session not only because of the recent events that had happened, but because they have a common thread – it's not a matter of if it will happen, but when will it happen, and are you ready and how do we prepare," said session chair Gloria M. Rodriguez Vega, MD.

"One of the things I learned as a fellow was that part of the success in critical care was attention to detail and layers of safety," said Dr. Rodriguez Vega, an intensivist in Bayamon, Puerto Rico. "I think you can apply that to all these situations."

Dr. Kaplan had no industry disclosures related to his presentation.

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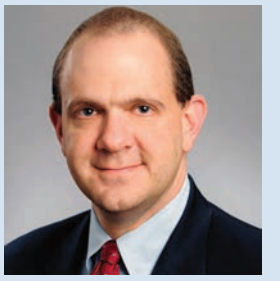

David A. Schulman, MD, FCCP, is Medical Editor in Chief of CHEST Physician.

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ICU corticosteroid insufficiency guidelines explained

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – When corticosteroids are used for septic shock, the dose should be low to moderate, the timing should be early, and the duration should be at least 3 days, said a speaker at the Critical Care Congress sponsored by the Society for Critical Care.

Dosing, timing, and duration are "three critical questions" critical care specialists face that are answered by the new critical illness–related corticosteroid insufficiency (CIRCI) guidelines, continued Stephen M. Pastores, MD, a cochair of the task force that developed guidelines for the diagnosis and management of CIRCI in critically ill patients.

The recently published guidelines come in two parts. The first takes into account the most current evidence on the use of corticosteroids in disorders that most clinicians associate with CIRCI, including sepsis/septic shock, acute respiratory distress syndrome, and major trauma (Crit Care Med. 2017 Dec;45[12]:2078-88). Part two of the guidelines, published separately, covers other syndromes, such as influenza, meningitis, burns, and other conditions that at least 80% of the task force members agreed were associated with CIRCI (Crit Care Med. 2018 Jan;46[1]:146-8).

During his presentation, Dr. Pastores limited his remarks to discussion of sepsis and septic shock with corticosteroids. He cautioned that, despite careful deliberations by the panel, the level of evidence behind some of the recommendations was "low to moderate and never high" and that not all task force members agreed with all recommendations.

"There were a lot of back and forth disagreements behind these recommendations," said Dr. Pastores, who is the director of the critical care medicine fellowship training and research programs at Memorial Sloan Kettering Cancer Center, New York. "We only required 80% of the panelists to agree that these were the recommendations and statements that we were going to go by."

The guidelines recommend against the use of corticosteroids in adult patients who have sepsis without shock, Dr. Pastores noted.

In contrast, the guidelines do suggest using corticosteroids for hospitalized adults patients with septic shock that is not responsive to fluid and moderate- to high-dose vasopressor therapy.

In an analysis of available data from randomized clinical trials including patients with septic shock, corticosteroids significantly reduced 28-day mortality when compared with placebo, Dr. Pastores said.

That survival benefit seems to be dependent on several factors: dose of the corticosteroids (hydrocortisone less than 400 mg/day), longer duration (at least 3 or more days), and severity of sepsis. "The more severe the sepsis, the more septic shock the patient was in, the more likely the corticosteroids were likely to help those patients," Dr. Pastores explained.

Accordingly, the guidelines further suggest using long-course, low-dose corticosteroid treatment, namely intravenous hydrocortisone at no more than 400 mg/day for at least 3 days.

The expert panel specifically recommended hydrocortisone as the corticosteroid of choice in this setting, according to Dr. Pastores. That recommendation was based in part on a recent systematic review and meta-analysis showing that hydrocortisone, given as a bolus or an infusion, was more likely than placebo or methylprednisolone to result in shock reversal.

Dr. Pastores reported disclosures related to Theravance Biopharma, Bayer HealthCare Pharmaceuticals, Spectral Diagnostics, and Asahi-Kasei.

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Prehospital antibiotics

// continued from page 1

Medicine.

The intervention group received antibiotics a median of 26 minutes prior to emergency department arrival. In the usual care group, median time to antibiotics after ED arrival was 70 minutes, versus 93 minutes prior to the sepsis recognition training ($P = .142$), the report further says.

"We do not advise prehospital antibiotics at the moment for patients with suspected sepsis," Dr. Nanayakkara said, during his presentation at the conference.

Other countries might see different results, he cautioned.

In the Netherlands, ambulances reach the emergency scene within 15 minutes 93% of the time, and the average time from dispatch call to ED arrival is 40 minutes, Dr. Nanayakkara noted in the report.

"In part, due to the relatively short response times in the Netherlands, we don't know if there are other countries with longer response times that would have other results, and whether they should use antibiotics in their ambulances," Dr. Nanayakkara said in his presentation.

The study was the first-ever prospective randomized, controlled open-label trial to compare early prehospital antibiotics with standard care.

Before the study was started, EMS personnel at 10 large regional ambulance services serving 34 secondary or tertiary hospitals were trained in recognizing sepsis, the report says.

A total of 2,672 patients with suspected sepsis were included in the intention-to-treat analysis, of whom 1,535 were randomized to receive prehospital antibiotics and 1,137 to usual EMS care, which consisted of fluid resuscitation and supplementary oxygen.

ANDREW D. BOWSER/FRONTLINE MEDICAL NEWS

"[We] don't know if there are other countries with longer response times that would have other results, and whether they should use antibiotics in their ambulances," Dr. Prabath Nanayakkara (left) noted.

The primary end point of the study was all-cause mortality at 28 days.

The negative mortality results of this trial are "not surprising," given that the trial's inclusion criteria allowed individuals with suspected infection but without organ dysfunction, said Jean-Louis Vincent, MD, PhD, of Erasmus Hospital, Brussels, in a related editorial appearing in the Lancet Respiratory Medicine (2018 Jan. doi: 10.1016/S2213-2600[17]30446-0).

Recent consensus definitions of sepsis recognize that sepsis is the association of an infection with some degree of organ dysfunction, according to Dr. Vincent.

"After this initial experience, I believe that a randomized, controlled trial could be done to assess the potential benefit of early antibiotic administration in the ambulance for patients with organ dysfunction associated with infection," Dr. Vincent wrote in his editorial.

Dr. Nanayakkara and his coauthors declared no competing interests related to their study.

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SOURCE: Alam N et al. Lancet Respir Med. 2018 Jan;6(1):40-50.

FDA proposes lower nicotine levels in cigarettes

BY GREGORY TWACHTMAN
Frontline Medical News

Nicotine levels in cigarettes could see a significant reduction under regulatory options being considered by the Food and Drug Administration.

Cigarettes "are the only legal consumer product that, when used as intended, will kill half all long-term users," FDA Commissioner Scott Gottlieb, MD, said in a statement announcing the effort.

The agency is seeking comment on a proposed regulation regarding "a potential maximum nicotine level that would be appropriate for the protection of public health, in light of scientific evidence about the addictive properties of nicotine in cigarettes." An advance notice of proposed rule making was posted online March 15 and published in the Federal Register on March 16.

The FDA also is seeking comments on a number of other areas to help inform potential regulatory action down the road, including whether a new standard for lower nicotine levels should be implemented at once or whether a phased-in approach should be taken; whether FDA should specify a method for manufacturers to use in order to detect nicotine levels in their products; and whether the proposed lower level is technically achievable.

The agency also is seeking comment on potential unintended effects of lowering the amount of nicotine in cigarettes, such as turning to other combustible tobacco products including cigars in conjunction with or as a replacement for cigarette use; increasing the number of cigarettes smoked; or seeking comparable nicotine from noncombustible tobacco sources.


RICKY_68FR/FOTOLIA

At this time, FDA is not suggesting what the target might be on a specific nicotine level. While the advanced notice asks specifically about the "merits of nicotine levels like 0.3, 0.4, and 0.5 mg nicotine/g of tobacco filler," it is not suggesting that this is the range being considered.

"Not to prejudge any possible proposed rule that we would do or any possible level, that is the purpose of an advanced proposed rule making, but we share all the science that we are aware of, and we characterize the studies that have been done to date in trying to find out what that right level is," Mitch Zeller, director of the FDA Center for Tobacco Products, said during a March 15 press call.

He said that the FDA aiming to make sure the level is low enough that it cannot be compensated for by smoking more or inhaling deeper and holding the breath in longer, much like how smokers compensated when they smoked "light" cigarettes in the unregulated market.

Mr. Zeller said that seeking comments on those levels is based on the scientific evidence that is laid out in the advanced notice, but it is not necessarily foreshadowing where the standard will be set.

Drastically reducing the amount of nicotine in cigarettes is expected to significantly lower not only the number of people addicted to cigarettes but also the negative health effects of nicotine addiction, FDA experts wrote in a perspective piece published March 15 in the New England Journal of Medicine (doi: 10.1065/NEJMsr1714617).

"Our findings show that reducing the nicotine level in cigarettes has the potential to substantially reduce the enormous burden of smoking-related death and disease," Benjamin J. Apelberg, PhD, director of the Division of Population Health Science, Office of Science, within the FDA Center for Tobacco Products, and his colleagues, wrote in the report.

Modeling for the implementation of a lower nicotine level policy suggests that smoking prevalence will decline from a median of 12.8% in baseline scenario to a median of 10.8% within a year of implementation, with the increase related to smoking cessation.

"We estimate that approximately 5 million additional smokers would quit smoking within a year after implementation of the hypothetical policy," Dr. Apelberg and his colleagues wrote. "By 2060, smoking prevalence drops from 7.9% in the baseline scenario to 1.4% in the policy scenario."

Their analysis is based on a nicotine level that is "so low that there would not be enough nicotine available in cigarette tobacco for smokers to sustain addiction," they noted.

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FDA wants data on flavored tobacco products

BY GREGORY TWACHTMAN
Frontline Medical News

The Food and Drug Administration is seeking data on the role that flavors, including menthol, in tobacco products play in the initiation, use, and cessation of tobacco products, with an emphasis on how flavoring impacts young people.

"In the spirit of our commitment to preventing kids from using tobacco, we are taking a closer look at flavors in tobacco products to better understand their level of impact on youth initiation," FDA Commissioner Scott Gottlieb, MD, said in statement. It is important "that we also explore how flavors, under a properly regulated framework that protects youth, may also be helping some currently addicted adult cigarette smokers switch to certain noncombustible forms of tobacco products."

The agency issued an advance notice of proposed rule making March 20 that seeks information on flavoring in tobacco products to inform future policy making.

"Youth consistently report product flavoring as a leading reason for using tobacco products," Dr. Gottlieb noted. "In fact, there is evidence indicating that youth tobacco users who reported their first tobacco was flavored had a higher prevalence of current tobacco product use, compared to youth whose product was not flavored."

The advance notice calls for information across a number of areas, including the role of flavors other than tobacco in tobacco products; flavors and initiation and patterns of tobacco product use, particularly among youths and young adults; and flavors and cessation, dual-use, and relapse among current and former tobacco product users.

It also is seeking comment on whether standards should be set on tobacco flavoring, including whether there should a prohibition or restriction on flavors and to which types of products these standards should apply. The notice specifically asks about menthol and its role in cigarette initiation and whether limitations on menthol could lead to use of other tobacco products.

"Because almost 90% of adult smokers started smoking by the age of 18, it's imperative we look at new ways we can ensure that kids don't progress from experimentation to regular use," Commissioner Gottlieb said.

The American Heart Association called the action "long overdue."

"We encourage the FDA to quickly move beyond information gathering and develop a strong flavoring product standard," CEO Nancy Brown said in a statement. "There is already clear evidence that flavored tobacco products, including menthol, harm the public health. To make it worse, fruit- and candy-flavored e-cigarettes, cigars, and other tobacco products are highly attractive to kids and make it more likely that they will take up this addiction."

The action comes less than a week after FDA published an advance notice seeking information comments on reducing nicotine levels in cigarettes to help combat nicotine addiction.

The advance notice was published in March in the Federal Register.

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Different OSA subtypes respond differently to therapy

BY MADHU RAJARAMAN
Frontline Medical News

Patients with obstructive sleep apnea can be grouped into distinct clinical subtypes that differ in response to positive airway pressure treatment, according to two studies published in the March issue of the journal Sleep.

In the first study, investigators evaluated whether patients in different clinical clusters responded differently to positive airway pressure (PAP) treatment. Authors identified 706 patients with moderate to severe obstructive sleep apnea (OSA) from the Icelandic Sleep Apnea Cohort. All patients completed a sleep study prior to starting PAP treatment, and completed questionnaires to assess symptoms. Patients were grouped into one of three clusters based on symptomatology: disturbed sleep, minimally symptomatic, or sleepy, wrote Grace W. Pien, MD, of the division of pulmonary and critical care medicine at Johns Hopkins University, Baltimore, and her coauthors.

PAP adherence was assessed using questionnaires and PAP device memory card data. At the 2-year follow-up, 457 (64.7%) patients reported PAP adherence. Objective adherence measures were available for 351 (76.8%) patients; for the remainder, PAP adherence was determined using self-reported data. Patients in the sleepy cluster were more likely than the other two subtypes to be PAP users at 70.0% usage, compared with 61.1% of those in the disturbed-sleep group and 60.0% in the minimally symptomatic group (P = .034), the authors said in Sleep.

Patients in the minimally symptomatic cluster reported symptoms at lower rates than patients in the other clusters at baseline, and they remained relatively asymptomatic at follow-up, the authors noted. By comparison, patients in the sleepy group reported the highest Epworth Sleepiness Scale scores at baseline (16.0 plus or minus 3.4), which fell by five points at follow-up (mean change, −5.3; 95% confidence interval, −5.8 to −4.8). Also, patients in the sleepy group reported higher rates of drowsy driving (37.8%) at baseline, which dropped to 8.1% at follow-up (odds ratio, 0.06; 95% CI, 0.03-0.14).

At baseline, the disturbed-sleep group reported mainly insomnia-related symptoms, including difficulty falling asleep (43.2%), waking often at night (90.8%), restless sleep (74.2%), and waking up early (62.3%). At follow-up, improvements in the frequency of insomnia-related symptoms ranged from 0.28 to 1.25 points, and Epworth Sleepiness Scale scores fell significantly (−2.06; 95% CI, −2.64 to −1.48). Reductions in the proportion of patients with insomnia symptoms ranged from 13.1% (OR, 0.35; 95% CI, 0.20-0.59) for difficulty falling asleep to 39.0% (OR, 0.08; 95% CI, 0.04-0.14) for restless sleep, the researchers noted.

The results "demonstrate that although symptoms improved overall among each of the three clinical phenotypes of moderate to severe OSA, patterns of treatment response … varied based on initial clinical presentation," the authors wrote. "Our findings underscore the need to consider initial OSA phenotype when designing future trials."

In the second study, also published in Sleep, investigators confirmed the three clinical OSA subtypes previously identified in the Icelandic Sleep Apnea Cohort. In analysis of an international sample, they also expanded these clusters to include two additional disease subtypes. One of these subtypes consisted of patients with symptoms dominated by indications of upper airway obstruction. The other new subtype, sleepiness dominant OSA, included patients who had excessive sleepiness but no symptoms of upper airway obstruction.

The study authors performed a cluster analysis using data from 972 patients from the Sleep Apnea Global Interdisciplinary Consortium with moderate to severe OSA, with 215 of these patients being from Iceland.

In total, 688 (70.8%) patients were diagnosed using laboratory-based polysomnography and 284 (29.2%) with home-based sleep studies. Patients completed questionnaires related to symptoms including sleepiness, insomnia, sleep disturbance, abnormal behaviors during sleep, upper airway symptoms, and other symptoms such as headaches and excessive sweating, wrote Brendan T. Keenan, of the University of Pennsylvania, Philadelphia, and his coauthors.

In the Icelandic group, results identified 72 (33.5%) patients in the disturbed-sleep cluster, 62 (28.8%) in the minimally symptomatic cluster, and 81 (37.7%) in the excessively sleepy cluster, similar to prior research. The three subtypes were found in the international sample of patients as well, with 150 (19.8%) in the disturbed-sleep cluster, 306 (40.4%) in the minimally symptomatic cluster, and 301 (39.8%) in the excessively sleepy cluster.

Both studies were funded by the National Institutes of Health.

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SOURCES: Pien GW et al. Sleep. 2018 Mar. doi: 10.1093/sleep/zsx201; Keenan BT et al. Sleep. 2018 Mar. doi: 10.1093/sleep/zsx214.

VIEW ON THE NEWS

Results underscore importance of personalized treatment

The results of these studies "advance the personalization of sleep apnea care by validating distinct symptom-based groups that generalize across nations and assessing how members of these clinical phenotypes respond to therapy," wrote Vishesh K. Kapur, MD, of the division of pulmonary, critical care and sleep medicine at the University of Washington, Seattle, in an editorial published in the March issue of Sleep (2018 Mar. doi: 10.1093/sleep/zsy042).

"Patients with OSA differ in their presenting symptoms," he said, and future studies should aim to "elucidate whether the proposed phenotypes will enable a more personalized paradigm of sleep apnea care that results in better tailored and more effective care."

Dr. Kapur did not report any relevant disclosures.

Effectiveness, adherence similar for nasal pillows and standard masks

BY MADHU RAJARAMAN
Frontline Medical News

Nasal pillows showed equal long-term efficacy as standard nasal masks and both tools were used equally in patients treated with continuous positive airway pressure therapy, according to results of a study.

In a retrospective observational study of 144 patients with obstructive sleep apnea, respiratory measures including apnea-hypopnea index (AHI), oxygen desaturation index, mean oxygen saturation, and Epworth Sleepiness scale scores did not differ between the two treatment groups at baseline and during a 12-month follow-up appointment. Treatment adherence was also similar between the two groups, reported Andrea Lanza of the Sleep Medicine Center at Niguarda Hospital in Milan and coauthors in Sleep Medicine.

Patients received continuous positive airway pressure (CPAP) treatment between May 2012 and September 2014, and were assigned to one of two groups based on their choice of treatment. Initially, 102 opted for nasal pillows (Group P), and 42 chose the standard nasal mask (Group N). Patients who either changed masks or add-

Continued on following page

graustufe/Thinkstock

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ed a new one during titration or follow-up were assigned to a third group, Group C.

AHI did not differ significantly between groups at baseline or follow-up. In Group P, mean AHI at titration was 1.2 events per hour, compared with 1.8 in Group N and 1.9 in Group C ($P = .109$). At follow-up, AHI was 0.7 in Group P, 1.1 in Group N, and 0.9 in Group C ($P = .172$). Oxygen desaturation index and oxygen saturation also remained similar between the groups at baseline and follow-up, the investigators reported.

Additionally, long-term adherence did not differ significantly between the groups, with mean daily CPAP usage of 5.5 hours per night in Group P, 5.3 in Group N, and 5.6 in Group C. Mean usage was less than 4 hours per night for 11.6% in group P, 18.5% in group N, and 13.9% in group C, the authors added.

The frequency of side effects occurring in patients in two of the groups were similar (49% in Group P, vs. 61% in Group N; $P = .212$), though the nature of the side effects differed. Nostril pain or burning was reported only by patients in the nasal pillows group, and skin breakdown was reported only in the nasal mask group.

Though nasal pillows have typically been reserved for patients who do not tolerate the standard mask, the results of this study suggest that "nasal pillows could be safely prescribed as first-line interfaces," the authors wrote. "They seem to be efficacious for CPAP titration and long-term treatment, ensuring a good rate of adherence."

All of the authors reported having no disclosures.

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SOURCE: Lanza A et al. Sleep Med. 2018 Jan;41:94-9.

VIEW ON THE NEWS

Retitration may be necessary with mask changes

These results add to the body of evidence about the efficacy of nasal pillows and nasal masks. Future research should address the need for retitration when changing mask type, said Matthew R. Ebben, PhD, associate clinical professor at Cornell University, New York, in an editorial published with the study in Sleep Medicine.

"Many working in the field of sleep medicine continue to be unaware that differences in efficacy exist between mask styles, particularly in cases of moderate to severe obstructive sleep apnea," he wrote.

"New clinical practice guidelines are needed to promote the necessity for PAP [positive airway pressure] retitration when changes in mask style are required," he added. "Ensuring that PAP therapy is as effective as possible will reduce the need for patients and clinicians to investigate other treatment options for obstructive sleep apnea, which may be both less effective and have an inferior side effect profile compared to PAP treatment."

Intermittent dosing cuts time to extubation for surgical patients

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – Intermittent administration of sedation and analgesia significantly reduced mechanical ventilation time among surgical patients requiring ventilation, according to a preliminary analysis of a randomized trial.

Additionally, the researchers found that much lower amounts of sedation and analgesia were given to patients who underwent intermittent dosing, compared with patients who received a continuous infusion.

Lead investigator Nicholas Sich, MD, presented these findings of the SATIRE trial (Sedation Administration Timing: Intermittent Dosing Reduces Times to Extubation), at the Critical Care Congress sponsored by the Society for Critical Care Medicine. Dr. Sich's study was a 2-year, single-blinded, randomized, controlled trial of surgical patients requiring ventilation.

Of the 95 patients in the trial, 39 were randomized to intermittent dosing and 56 to the control group of continuous infusion, with the drugs midazolam and fentanyl having been given to both groups.

Mean mechanical ventilation time was 65 hours in the intermittent-dosing arm versus 111 hours in the continuous-infusion arm (*P* less than .03), noted Dr. Sich, a fourth-year general surgery resident at Abington (Pa.) Memorial Hospital, during his presentation.

"This is a new way to use an old drug, and it really might be beneficial, and can even be used as first-line therapy and a way to keep patients awake and off the ventilator," said Dr. Sich.

Patients in the continuous-infusions arm of the trial received a mean of 73.1 mg of midazolam, compared with 18 mg for the intermittent-dosing arm, a difference that approached very closely to statistical significance (*P* = .06) and was thrown off in the latest iteration by an outlier, Dr. Sich explained. The relative difference between the mean fentanyl doses administered was even greater between the two groups, with 5,848 mcg given to patients in the control group, versus the 942 mcg given to participants in the intermittent-dosing group (*P* less than 0.01).

"This is a new way to use an old drug, and it really might be beneficial, and can even be used as first-line therapy and a way to keep patients awake and off the ventilator," said Dr. Sich, referring to the intermittent dosing. Continuous infusions leave patients oversedated and prolong ventilation time.

"What we propose, rather, is using a sliding-scale intermittent pain and sedation regimen," he said. "We believe that it won't compromise patient care and won't compromise patient comfort, and it will lead to shorter mechanical ventilation times for surgical patients than continuous infusions."

Dr. Sich also pointed out that there was no difference in time spent at target levels of sedation and analgesia between the two trial groups. Referring to this finding, he noted that "we wanted to make sure that in the intermittent arm we're giving them less drug, but we don't want them to be [less comfortable]."

One potential drawback to the intermittent-dosing approach is that it is more nursing intensive, according to Dr. Sich, since it is based on a nursing treatment protocol to give medications every hour.

Intermittent dosing is "more hands-on" than a typical continuous-infusion approach and so was more challenging for nurses who, per the treatment protocol, had to give medications every hour, he explained. However, "when they saw the data in the months and year as we've been going on, they're actually quite proud of our work and their work."

Gilman Baker Allen, MD, a pulmonologist and intensivist at the University of Vermont Medical Center, Burlington, said the study was "terrific work" and acknowledged the importance of gauging nurse satisfaction with the protocol.

"I think that when you feed this kind of data back to nursing staff, they may not be satisfied with the intensity of the work, but when they see the rewards at the end, it oftentimes is a very positive experience," said Dr. Allen, who moderated the session.

Dr. Sich and his colleagues had no financial disclosures or conflicts of interest related to the study.

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SOURCE: Sich N et al. CCC47, Abstract 18.

Haloperidol does not prevent delirium in ICU patients

BY M. ALEXANDER OTTO
Frontline Medical News

Prophylactic haloperidol did not prevent delirium or improve survival in a placebo-controlled trial of 1,789 critically ill adults at 21 ICUs in the Netherlands.

Haloperidol is used routinely in ICUs to both treat and prevent delirium, which strikes up to half of ICU patients and is associated with prolonged mechanical ventilation, longer ICU and hospital stays, and increased mortality. Results of past studies have been mixed, with some showing a benefit for haloperidol in the ICU and others not.

"These findings do not support the use of prophylactic haloperidol in critically ill adults," said the authors of a new study, led by Mark van den Boogaard, PhD, of Radboud University Medical Center, Nijmegen, the Netherlands (JAMA. 2018 Feb 20;319[7]:680-90).

The subjects were all expected to be in the ICU for at least 2 days, and were not delirious at baseline. The patients were randomly assigned to receive one of two treatments or a placebo three

Continued on following page

VIEW ON THE NEWS

Nondrug options may be the key

The study has demonstrated that, in critically ill patients currently receiving best-practice nonpharmacological interventions to prevent delirium, the addition of haloperidol does not improve survival nor reduce the incidence of delirium or the harms associated with delirium. The findings challenge the current model that the addition of psychoactive medication to patients who are already receiving multiple interventions may be beneficial. Prophylactic haloperidol is not the solution for the complex problem of delirium in critically ill patients. It may be that no single pharmacological intervention can provide a solution.

Future research is warranted into nonpharmacological interventions. They generally involve either doing less for patients (avoiding excessive sedation, benzodiazepines, nocturnal noise, and stimulation) or ensuring the continued provision of relatively simple therapies (mobilization, maintaining a day-night schedule, and noise reduction). Although some of these interventions may require planning and cooperation of a multidisciplinary team, a strength of ICU care in general, other interventions may be as simple as providing earplugs and eye patches to improve sleep.

Anthony Delaney, MD, PhD, is associate professor of intensive care medicine at the University of Sydney. Naomi Hammond, PhD, is a research fellow and senior lecturer at the University of New South Wales, Sydney. Edward Litton, MD, PhD, is an intensive care specialist in Perth, Australia. They made their comments in a JAMA editorial, and had no disclosures (JAMA. 2018 Feb 20;319[7]:659-60).

On-demand nebulization in ICU equivalent to standard

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – Among ICU patients receiving invasive ventilation, on-demand nebulization of acetylcysteine or salbutamol was noninferior to routine nebulization with both medications, according to the results of a randomized clinical trial presented by Frederique Paulus, RN, PhD.

ANDREW BOWSER/FRONTLINE MEDICAL NEWS

"On-demand nebulization was noninferior to routine nebulization, but routine nebulization is associated with more side effects," said Dr. Frederique Paulus.

In this study, adverse events such as tachyarrhythmia and agitation were less frequent with the on-demand approach, in which patients receive nebulization based on strict clinical indications, Dr. Paulus reported at the Critical Care Congress sponsored by the Society for Critical Care Medicine. The study was published simultaneously in JAMA.

"On-demand nebulization was noninferior to routine nebulization, but routine nebulization is associated with more side effects, so we think on-demand nebulization may be a reasonable alternative to routine nebulization," said Dr. Paulus of the department of intensive care at the Academic Medical Center, University of Amsterdam, during her presentation.

The on-demand approach may also be cost saving, she noted, citing an economic analysis underway that is not yet ready for publication.

"In our ICU, it will save us 350,000 Euros a year," she said. "In the Netherlands, 40,000 patients will be mechanically ventilated in a year, so it will save us millions in the Netherlands alone."

The study included adult ICU patients who were expected not to be extubated for at least 24 hours. Dr. Paulus presented the primary analysis of the study, which included data for 922 patients who were randomized either to the on-demand group (n = 455) or the routine nebulization group (n = 467) and completed follow-up.

Patients assigned to the on-demand group received acetylcysteine-containing solutions if they had thick or tenacious secretions, or salbutamol-containing solutions if wheezing was observed or suspected or when findings were suggestive of lower-airway obstruction, according to the paper, published in JAMA.

The primary outcome, number of ventilator-free days at day 28 of the study, was noninferior in the on-demand group versus the routine group, Dr. Paulus said.

The median number of ventilator-free days was 21 for the on-demand group and 20 for the routine group, said the paper.

The length of stay, mortality, and proportion of patients developing pulmonary complications did not differ between the two study arms, the investigators also reported in JAMA.

However, adverse events occurred in just 13.8% of the on-demand group, compared with 29.3% of the routine group (*P* less than .001), with the difference in adverse events mainly attributable to less tachyarrhythmia and agitation in the experimental group, according to the researchers.

Dr. Paulus and coauthors reported no conflicts of interest related to the study.

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SOURCE: van Meenen DMP et al. JAMA. 2018 Feb. doi: 10.1001/jama.2018.0949.

VIEW ON THE NEWS

Eric Gartman, MD, FCCP, comments: I would not say there is necessarily a standard way people do this, and practice patterns likely vary widely. There are some places where respiratory therapy has wide control of vented patients and often implements protocols, while at other places every vented patient has to have specific orders for things by the providers. I would find it very likely that more patients receive standing bronchodilator therapy than should (thus the reason for the study). Our practice pattern locally mirrors the idea of the study (where a patient's therapy is tailored to the reason for their intubation).

I would suspect local practice patterns with nebulized acytylcysteine to vary even more widely than bronchodilator administration strategies.

Continued from previous page

times daily, with 350 receiving 1 mg of haloperidol; 732 receiving 2 mg of haloperidol; and 707 receiving a 0.9% sodium chloride placebo. The 1-mg haloperidol arm was stopped early because of futility.

The ICUs also used nonpharmacologic interventions to prevent delirium, including early mobilization and noise reduction.

There was no statistically significant difference in survival at the primary endpoint of 28 days following entrance into the study. At that point, 83.3% of the patients who received 2-mg doses of haloperidol and 82.7% of the of the subjects who received the placebo were alive (absolute difference, 0.6%; 95% confidence interval, –3.4% to 4.6%).

Prophylactic haloperidol had no effect on reducing the incidence of delirium, which was diagnosed in 33.3% of haloperidol subjects and 33.0% of placebo patients. Likewise, there were no significant differences between the groups in the number of delirium-free and coma-free days, duration of mechanical ventilation, and ICU and hospital length of stay. The number of reported adverse events with treatment also did not differ significantly between the groups: 0.3% in the 2-mg haloperidol group versus 0.1% in the placebo arm.

The duration of prophylactic therapy was a median of 2 days, but a subgroup analysis in patients treated for more than 2 days also did not show any benefits with haloperidol.

DR. OUELLETTE

"The study population included severely ill ICU adults whose brains may have been too seriously affected for haloperidol to exert a prophylactic effect, since in non-ICU adults, prophylactic haloperidol may have beneficial effects. But the subgroup of patients with a low severity of illness score also demonstrated no beneficial effects," the investigators said.

Subjects were a mean of 66.6 years old; 61.4% were men. Most of the ICU admissions were urgent and for medical or surgical reasons.

"Delirium and other problems of cognition are important epi-phenomenon of critical illness. Not only do these conditions obstruct management and impair recovery, but they may have long term sequelae," noted Daniel Ouellette, MD, FCCP, of the Henry Ford Hospital in Detroit and member of *CHEST Physician*'s editorial advisory board, in an interview. "My hospital has developed protocols based on best evidence to provide pain relief and sedation to critically ill patients in order to avoid these problems. The use of haloperidol as a prophylactic agent for delirium is an intriguing idea; unfortunately early research does not show that it benefits patients."

He added, "When I was a resident in medicine in the ICU during the 1980s, I was taught that we should reduce ICU noise to allow for rest, orient our patients to a day/night cycle, and provide for early mobilization. Those teachings are still important!"

This study was supported by ZonMw, the Netherlands Organization for Health Research and Development. Dr. van den Boogaard had no disclosures. One author reported grants and consultant and speaker fees from Pfizer, Merck, Astellas, and Gilead, among others.

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SOURCE: van den Boogaard M et al. JAMA. 2018 Feb 20;319(7):680-90.

Increasing sepsis survivorship creates new challenges

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – An upward trend in sepsis survivorship drove increases in sepsis survivors at risk for readmission and returns of these patients to the hospital via the emergency department, results of a retrospective, single-center analysis suggest.

Andrew Bowser/Frontline Medical News

Dr. Mark E. Mikkelsen

The number of sepsis survivors at risk for hospital readmission rose substantially in recent years, according to the analysis of 17,256 adult medical and surgical admissions to University of Pennsylvania Health System hospitals between July 1, 2010, and June 30, 2015. The journal Critical Care Medicine published these results online as Mark E. Mikkelsen, MD, was presenting them at the Critical Care Congress sponsored by the Society for Critical Care Medicine.

While 30-day readmission rates declined modestly over the same time period, that decrease was offset by a rise in emergency department treat-and-release visits, explained Dr. Mikkelsen, who coauthored the study.

Over the time period that Dr. Mikkelsen and his colleagues analyzed, the proportion of sepsis hospitalizations more than doubled from 3.9% to 9.4%, while in-hospital mortality rates for sepsis hospitalizations fell from 24.1% to 14.8%. As a result, the proportion of discharged patients at risk for readmission increased from 2.7% to 7.8%, noted Dr. Mikkelsen, associate professor of medicine at the Hospital of the University of Pennsylvania, Philadelphia.

Thirty-day hospital readmission rates modestly declined from 26.4% to 23.1% over that time period, driven by reduced readmissions among survivors of nonsevere and non-pneumonia sepsis, Dr. Mikkelsen said. This decline in overall sepsis patient readmissions was offset by an increase in emergency department treat-and-release visits. Such visits rose from 2.8% in 2010 to a peak of 5.4% in 2014, Dr. Mikkelsen

explained. Generally, readmission rates for severe sepsis patients have not changed over time, he added.

"I anticipate that each and every hospital represented in this room will experience a similar phenomenon," he said. "Therefore, high-quality postdischarge care is in fact urgently needed," he added. "It is warranted that there is an international spotlight on sepsis beginning in the hospital but now continuing thereafter into the phase of life after sepsis."

These findings reflect "great sepsis survivorship" and suggest new challenges to address, said Timothy G. Buchman, MD, PhD, editor-in-chief of the Critical Care Medicine and past president of the Society for Critical Care Medicine.

"It's really extraordinary to see that the efforts that have been made by the Surviving Sepsis campaign have paid off," Dr. Buchman said in an interview. "Now we need to look much more carefully at both the readmission issues, as well as the consequences of long-term sepsis survivorship, not just on patients, but also on their families."

Dr. Mikkelsen and a study co-author received support for article research from the National Institutes of Health.

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SOURCE: Meyer N et al. Crit Care Med. 2018 Mar. doi: 10.1097/CCM.0000000000002872.

Corticosteroid combo cuts deaths in septic shock

BY IAN LACY
Frontline Medical News

Hydrocortisone in combination with fludrocortisone significantly reduced 90-day mortality in septic shock patients in a double-blind, randomized, controlled trial.

Prior to this study, two large trials had displayed that corticosteroids were beneficial in improving hemodynamic status and organ function, but little was known about corticosteroids' ability to increase survival in sepsis patients.

"[Corticosteroids] improve cardiovascular function by restoring effective blood volume through increased mineralocorticoid activity and by increasing systemic vascular resistance, an effect that is partly related to endothelial glucocorticoid receptors," wrote Djillali Annane,

MD, of the University of Paris and his colleagues in the New England Journal of Medicine. "This might explain why in our trial there was less need for vasopressors with hydrocortisone plus fludrocortisone than with placebo."

The study, named the Activated Protein C and Corticosteroids for Human Septic Shock (APROCCHSS) trial, was designed to assess the benefit/risk ratio of using activated protein C – drotrecogin alfa (activated) – and corticosteroids together or separately in septic shock patients. The original design of the study included Xigris (drotrecogin alfa) and was composed of four parallel groups, but Xigris was removed from the market in October of 2011, so the study continued with only two parallel groups.

"[Corticosteroids] improve cardiovascular function by restoring effective blood volume through increased mineralocorticoid activity and by increasing systemic vascular resistance, an effect that is partly related to endothelial glucocorticoid receptors."

A total of 1,241 patients experiencing chronic septic shock were recruited into the two double-blind, parallel groups, with patients in one group receiving hydrocortisone plus fludrocortisone and the other receiving placebos. The placebos used in this study were similar in appearance to the actual treatment drugs. The placebos for hydrocortisone and fludrocortisone were either parenteral mannitol (133.6 mg), disodium phosphate (8.73 mg), and sodium phosphate (0.92 mg) or tablets of microcrystalline cellulose (59.098 mg), respectively.

Hydrocortisone was given intravenously every 6 hours as a 50-mg intravenous bolus, and fludrocortisone was given once a day as a 50-mcg tablet through a nasogastric tube. Patients in ICUs who had septic shock for less than 24 hours were included in the study. Septic shock was identified by the presence of a clinically or microbiologically documented infection, a Sequential Organ Failure Assessment score of 3 or 4 for at least two organs and for at least 6 hours, and receipt of vasopressor therapy for at least 6 hours.

DIGITAL VISION/THINKSTOCK

After 90 days, 264 of 614 of the patients (43%) in the hydrocortisone/fludrocortisone group and almost half (49.1%) of 627 patients in the placebo group had died (P = .03). The relative risk of death was 0.88 (95% confidence interval, 0.78-0.99), which favored the hydrocortisone/fludrocortisone group. The researchers also observed that death was significantly lower in the hydrocortisone/fludrocortisone group, compared with the placebo group, at time of ICU discharge (35.4% vs. 41.0%, respectively; P = .04).

While mortality was reduced, patients still experienced adverse

Continued on following page

A 'silver bullet' for ventilator liberation?

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – Among medications to facilitate extubation, dexmedetomidine offers favorable attributes, but whether it's the best choice for patients who have difficulty being liberated from the ventilator remains to be proven, said Gilles L. Fraser, BS Pharm, PharmD.

The current CHEST/ATS guidelines on liberation from mechanical ventilation in critically ill adults strongly suggest extubation to noninvasive mechanical ventilation in high-risk patients (Chest. 2017 Jan;151[1]:160-5. doi: 10.1016/j.chest.2016.10.037). Guideline authors also suggested protocols attempting to minimize sedation for acutely hospitalized patients ventilated for more than 24 hours, based on some evidence showing a trend toward shorter ventilation time and ICU stay, as well as lower short-term mortality.

"Is dexmedetomidine the silver bullet to facilitate extubation? It's absolutely not clear," said Dr. Fraser, one of the coauthors of the guidelines, during his presentation at the Critical Care Congress sponsored by the Society for Critical Care Medicine.

"I'll leave you up to your own devices," he told attendees, at a session on conundrums in critical care that are not addressed in current guidelines. "We use it all the time, frankly, but I don't have any firm data to support that contention."

Despite best practices, extubation attempts are not always successful: "If you follow the rules of the road, success is going to occur about 85% of the time," said Dr. Fraser, who is a clinical pharmacist at Maine Medical Center, Portland, and professor of medicine at Tufts University, Boston. "That means that about 15% of our patients have difficulties in being liberated from the ventilator."

In terms of medications to facilitate ventilator liberation, benzodiazepines, dexmedetomidine, and propofol all have roles to play, according to Dr. Fraser. Clinicians have to consider agent-specific side effects, pharmacokinetics and dynamics, and "econotoxicity," or the cost of care, he added.

Although there are few comparative data available to guide choice of medication, Dr. Fraser and his colleagues have published a systematic review and meta-analysis of randomized trials of benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adult patients (Crit Care Med. 2013 Sep;41[9 Suppl 1]:S30-8. doi: 10.1097/CCM.0b013e3182a16898).

They found that dexmedetomidine- or propofol-based sedation regimens appeared to reduce mechanical ventilation duration and length of ICU stay versus benzodiazepine-based sedation, but they stated that larger controlled studies would be needed to further define outcomes in this setting.

More recently, other investigators reported an evaluation of 9,603 consecutive mechanical ventilation episodes (Chest. 2016 Jun;149[6]:1373-9. doi: 10.1378/chest.15-1389). In this large, real-world experience, propofol and dexmedetomidine were both associated with less time to extubation versus benzodiazepines, and dexmedetomidine was associated with less time to extubation versus propofol.

Relatively few patients (about 12%), however, received dexmedetomidine in that large series, and that was mostly in the setting of cardiac surgery, Dr. Fraser noted. Moreover, the investigators reported finding no differences between any two agents in hospital discharge or mortality hazard ratio.

"We're not suggesting the benzodiazepines as routine sedative agents in our patient populations," Dr. Fraser said in his presentation. "The primary reason is that they result in a longer time on the vent, typically between 1 and 2 days."

But this doesn't mean that the benzodiazepines are the "devil's handiwork," he added, noting that they may be useful in patients with anxiety related to ventilator weaning and those recovering from hemodynamic instability or at risk for GABA-agonist withdrawal.

Dexmedetomidine is opioid sparing and has a minimal effect on respiratory drive, among other advantages; however, some potential drawbacks include its hemodynamic effects and its cost, noted the speaker during his presentation at the conference.

Dr. Fraser said that his institution's daily acquisition cost for dexmedetomidine is $500, compared with $120 for propofol and $40 for benzodiazepines, but some pharmacoeconomic evaluations suggest use of dexmedetomidine may actually save between $3,000 and $9,000 per ICU admission. "At least in our place, one day in the ICU costs about $5,000, so that all makes sense … and I can argue fairly effectively that dexmedetomidine really isn't that expensive compared to midazolam," he said.

Dr. Fraser reported having no disclosures related to his presentation.

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events. 326 of 614 (53.1%) patients in the hydrocortisone/fludrocortisone group and 363 of 626 patients (58.0%) in the placebo group experienced at least one serious adverse event by day 180 ($P = 0.08$).

"Seven-day treatment with a 50-mg intravenous bolus of hydrocortisone every 6 hours and a daily dose of 50 mcg of oral fludrocortisone resulted in lower mortality at day 90 and at ICU and hospital discharge than placebo among adults with septic shock," concluded Dr. Annane and his coauthors.

The majority of researchers had no relevant financial disclosures to report, while some doctors received grants and personal fees unrelated to this study. This study was funded in part by public grants from the French Ministry of Health.

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SOURCE: Annana A et al. N Engl J Med. 2018 Feb 28. doi: 10.1056/NEJMoa1705716.

VIEW ON THE NEWS

Corticosteroids: What's their place in treating septic shock?

The results of the Activated Protein C and Corticosteroids for Human Septic Shock (APROCCHSS) trial and the Adjunctive Corticosteroid Treatment in Critically Ill Patients with Septic Shock (ADRENAL), both reported in the latest issue of NEJM, are landmark studies detailing the largest analyses of hydrocortisone use in patients with septic shock.

Both of these trials were massive, with over 5,000 patients combined, which is much larger than all previous studies according to Anthony Suffredini, MD, of the National Institutes of Health. An additional useful feature of these trials was that they had clear criteria for entry into the study. These criteria included "vasopressor-dependent shock and respiratory failure leading to the use of mechanical ventilation, details of antimicrobial therapy, assessment of survival at 90 days, and well-defined secondary outcomes and analyses of adverse events."

The ADRENAL and APROCCHSS had vastly different 90-day mortality rates: ADRENAL had mortality rates of 27.9% with hydrocortisone and 28.8% with placebo ($P = .50$), while APROACCHSS had mortality rates of 43.0% with hydrocortisone plus fludrocortisone and 49.1% with placebo ($P = .03$). Despite this, they both display the beneficial effect anti-inflammatory therapies, such as hydrocortisone, have on secondary outcomes of shock reversal and the reduction in duration of mechanical ventilation. "It is unlikely that in the near future sufficiently powered trials will provide us with better data" than the ADRENAL and APROCCHSS trials, Dr. Suffredini wrote.

Dr. Suffredini made these comments in an editorial accompanying this study in the New England Journal of Medicine. He is the deputy chief of the critical care medicine department at the National Institutes of Health Clinical Center, and he has served on the executive committee of the Department of Veteran Affairs Cooperative Studies Program. He has no other relevant financial disclosures to report.

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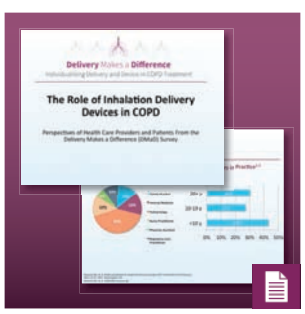

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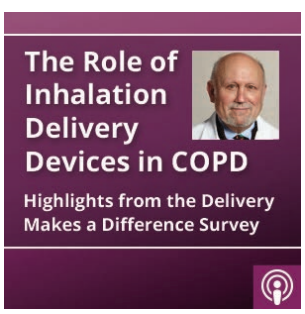

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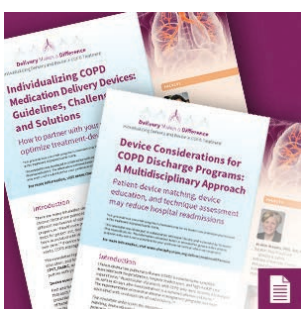

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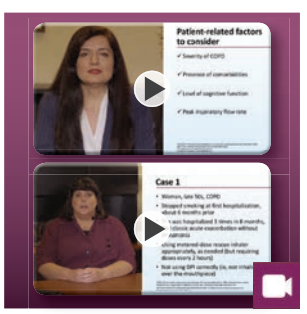

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Death rate steady with pediatric early warning system

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – Use of a pediatric early warning system reduced the incidence of late ICU admissions among hospitalized pediatric patients, but did not reduce the rate of all-cause hospital mortality, according to results of a large, multicenter trial.

Taken together, the findings of the trial do not support the use of the Bedside Pediatric Early Warning System (BedsidePEWS) to reduce hospital mortality, noted investigator Christopher S. Parshuram, MBChB, DPhil, during a presentation at the Critical Care Congress sponsored by the Society of Critical Care Medicine.

BedsidePEWS is a documentation-based care system that combines a validated severity of illness score, a specialized documentation record, and specific recommendations for care escalation.

The multicenter randomized cluster study, called the EPOCH trial, included 21 hospitals in seven countries that provided inpatient pediatric care. Ten of the hospitals delivered the BedsidePEWS intervention, while the remaining 11 provided usual care. The study data included 144,539 patient discharges comprising 559,443 patient days. Enrollment began Feb. 28, 2011, and ended on June 21, 2015.

For the BedsidePEWS group, all-cause hospital mortality was 1.93 per 1,000 patient discharges, versus 1.56 per 1,000 patient discharges for usual care (adjusted odds ratio, 1.01; 95% confidence interval, 0.61-1.69; $P = .96$), according to a report on this study that was published in JAMA.

Taken together, the findings of the trial do not support the use of the Bedside Pediatric Early Warning System to reduce hospital mortality, according to the study investigators led by Dr. Parshuram.

However, the BedsidePEWS group had a significant improvement in the secondary outcome of significant clinical deterioration events, a composite outcome reflecting late ICU admissions.

In the BedsidePEWS group, the rate of significant clinical deterioration events was 0.50 per 1,000 patient-days, compared with 0.84 per 1,000 patient-days at hospitals with usual care (adjusted rate ratio, 0.77; 95% CI, 0.61-0.97; $P = .03$), the investigators wrote.

The goal of the EPOCH trial was to determine whether BedsidePEWS could reduce rates of all-cause hospital mortality and significant clinical deterioration among hospitalized children, according to the researchers.

"The BedsidePEWS versus usual care did improve processes of care and early detection of critical illness, aligned with the notion of providing the right care, right now," Dr. Parshuram, associate professor of critical care medicine and pediatrics at the University of Toronto, said during his presentation at the meeting. "Certainly more vital signs were documented, and anecdotally there were reports of culture change.

"However, when we looked further, there was no difference in hospital mortality, nor hospital resource utilization," Dr. Parshuram added.

The Canadian Institutes of Health Research funded the study. Dr. Parshuram is an inventor of BedsidePEWS and owns shares in a company that is commercializing it.

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SOURCE: Parshuram CS et al. JAMA. 2018 Feb 27. doi: 10.1001/jama.2018.0948.

Marik proclaims end to corticosteroid monotherapy for sepsis

BY ANDREW D. BOWSER
Frontline Medical News

SAN ANTONIO – While critical care specialists await more data on a so-called sepsis cocktail with varying degrees of hope and skepticism, Paul E. Marik, MD, FCCP, has proclaimed the dawning of a new era.

Dr. Marik became a celebrity in the critical care medicine community after he and his colleagues reported the results of his retrospective study evaluating the combination of hydrocortisone, vitamin C, and thiamine for treatment of severe sepsis and septic shock (Chest. 2017 Jun. doi: 10.1016/j.chest.2016.11.036).

Since this study, several physicians have already been putting Dr. Marik's method to practice, the investigator and audience members noted during a session at the Critical Care Congress sponsored by the Society of Critical Care Medicine.

"My point is, steroids work, but they don't work well alone, and the era of glucocorticoid monotherapy has come to an end," Dr. Marik said in his presentation at the meeting.

These comments echoed Dr. Marik's May 2017 editorial in Critical Care Medicine, in which he suggested that critically ill and injured patients may benefit from combination therapy with hydrocortisone and vitamin C (Crit Care Med. 2017 May;45[5]910-1).

Andrew D. Bowser/Frontline Medical News

Dr. Paul E. Marik

That editorial was quickly followed by the report on Dr. Marik and colleagues' before-after study, in which hospital mortality was 8.5% versus 0.4% in the treatment and control groups, respectively (P less than .001). This finding led the investigators to suggest that intravenous vitamin C administered along with corticosteroids and thiamine is "effective" in reducing mortality, in their paper published in CHEST®.

During Dr. Marik's presentation at the meeting, he noted that he had been "misquoted" with regard to the finality of his study's results. The final line of the CHEST® paper reads, "Additional studies are required to confirm these preliminary findings," he emphasized.

Nevertheless, Dr. Marik alluded to a "big paradigm shift" in the treatment of sepsis.

"Our experience has been echoed by now hundreds, if not thousands, of clinicians across the world," said Dr. Marik, chief of the division of pulmonary and critical care medicine, Eastern Virginia Medical School, Norfolk.

He recounted an anecdotal case submitted by "Josh from Ohio" describing an elderly man who was "started on cocktail and within a day his pressor requirements melted away and he was extubated." Quoting "Josh from Ohio," Dr. Mark continued, "Tomorrow he will probably leave the ICU with no residual organ dysfunction, no volume overload, [and] no ICU complications."

Eddy Gutierrez, MD, of Jacksonville, Fla., noted in a question-and-answer period that he has had "positive results" with a similar approach.

"When we first learned about the vitamin C and the 'Marik protocol,' so to speak, I was in fellowship and I got laughed at," Dr. Gutierrez said. "Nobody would let me try it."

Others are taking a wait-and-see approach.

Greg S. Martin, MD, secretary of the Society of Critical Care Medicine, said in an interview that there are "at least two schools of thought" among critical care specialists regarding the use of hydrocortisone, vitamin C, and thiamine for treatment of sepsis and septic shock.

"One school of thought is that this is incredibly important if this is even fractionally as effective as what [Dr. Marik] showed, because we have not found an effective therapy for sepsis," said Dr. Martin, associate professor of medicine at Grady Memorial Hospital, Atlanta.

"The contrarian approach is to say, 'yes, but this seems remarkably unlikely to be as effective as what he has shown,'" Dr. Martin added. "Particularly in sepsis, people are very skeptical of whether a drug or a drug combination is going to be as effective when you really get down to a high-quality randomized controlled trial that would be the definitive level of evidence."

The wait may not be long for at least some data. Multiple clinical trials are recruiting or planned, according to Dr. Marik. These included a 140-patient U.S. randomized, double-blind trial of vitamin C, hydrocortisone, and thiamine vs. placebo that started in February 2018, according to the study's ClinicalTrials.gov listing.

As part of his presentation, Dr. Marik reported a disclosure related to Baxter (advisory board).

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MOMENTUM 3 HeartMate 3 LVAD 'practice changing'

BY BRUCE JANCIN
Frontline Medical News


Frontline Medical News

"I think this is going to open the gates for more referrals ... for destination therapy in patients who are deemed ineligible for transplant," noted Dr. Mandeep R. Mehra (right).

ORLANDO – The HeartMate 3 magnetically levitated left ventricular assist device (LVAD) provided far superior outcomes, compared with the widely used HeartMate II axial-flow pump at 2 years of follow-up in patients with advanced heart failure in the large multicenter MOMENTUM 3 trial, Mandeep R. Mehra, MD, reported at the annual meeting of the American College of Cardiology.

HeartMate 3 recipients had a 90% lower risk of undergoing reoperation to replace or remove their device because of malfunction, and a stroke rate half that in the HeartMate II group.

"This was the lowest rate of stroke ever seen in any LVAD trial," according to Dr. Mehra, medical director of the Brigham and Women's Hospital Heart and Vascular Center, Boston, and professor of medicine at Harvard Medical School.

"We believe this is a practice-changing result in the field, and that the real implication of our findings is to reassure those who refer or treat patients with advanced heart failure that it is perhaps going to be ignorant not to refer patients for consideration for destination therapy," he said at a press conference highlighting the MOMENTUM 3 results, also presented in a late-breaking clinical trials session.

The HeartMate 3 is a miniaturized centrifugal-flow device that fits entirely within the chest, whereas the HeartMate II requires creation of a pocket in the abdomen. The HeartMate 3 was designed to prevent pump thrombosis – a common limiting problem with the HeartMate II and other LVADs – by employing three innovations: use of wide blood-flow passages to reduce shear stress and minimize disruption of red blood cells as they pass through the pump; reliance on magnetic levitation technology to create a frictionless pump with no mechanical bearings, which are subject to wear and tear; and incorporation of an artificial fixed pulse that speeds up and slows every 2 seconds in order to minimize blood stasis, which promotes thrombosis, the cardiologist explained in a video interview.

MOMENTUM 3 is the largest-ever randomized trial of LVAD therapy, involving 1,028 advanced heart failure patients at 69 U.S. centers. The study population is a mix of bridge-to-transplant patients and others who weren't eligible for heart transplantation and are using their device as lifelong destination therapy. In an earlier report on the first 294 patients to reach 6 months of follow-up post implantation, Dr. Mehra and his coinvestigators showed that the HeartMate 3 group had a significantly lower incidence of the composite endpoint of disabling stroke or reoperation to replace or remove the device (N Engl J Med. 2017 Feb 2;376[5]:440-50).


Bruce Jancin/Frontline Medical News

Dr. James L. Januzzi Jr.

At ACC 2018, he presented the prespecified 2-year analysis of results in the first 366 patients to reach that benchmark. The rate of survival free of disabling stroke or reoperation for device malfunction was 79.5% in the HeartMate 3 group and 60.2% with the HeartMate II, for a highly significant 54% reduction in the risk of bad outcome. Reoperation for device malfunction occurred in 1.6% of HeartMate 3 patients versus 17% of those with a HeartMate II, for a 92% reduction in risk. Two-year survival was 82.8% in the HeartMate 3 group and 76.2% in HeartMate II recipients.

The overall stroke rate was 10% with the HeartMate 3, compared with 19% with the older, axial-flow LVAD. The incidence of disabling stroke was 3% in the HeartMate 3 group and at 2% with the HeartMate II; however, nondisabling stroke occurred in only 3% of HeartMate 3 recipients, compared with 14% of patients with the HeartMate II.

"There has always been this notion that, 'There are so many complications with this device, so let's suffer with the disease rather than suffer with the pump.' Now we're showing that you don't suffer with the pump as with the earlier-generation devices. I think this is going to open the gates for more referrals ... for destination therapy in patients who are deemed ineligible for transplant."

Discussant James L. Janzuzzi Jr., called the MOMENTUM 3 results "a very-much-needed step forward."

"Perhaps the most dramatic observation in this study is the dramatic reduction in thrombosis events requiring reoperation. In essence, this problem was entirely prevented by the use of this magnetically levitated centrifugal-flow device. Reoperation for thrombosis accounted for two-thirds of the reoperations in the HeartMate II group and the rate was zero in the HeartMate 3 population. Essentially, with this technology we've addressed a very important unmet need by reducing the onset of pump thrombosis, which is the precursor to either pump dysfunction or embolic stroke," commented Dr. Januzzi, professor of medicine at Harvard Medical School, Boston.

Given the 83% survival rate at 2 years in the HeartMate 3 group in the MOMENTUM 3 trial, the on-average 50% survival at 10 years for heart transplant recipients, and the perpetual enormous shortage of donor organs, it's time to consider a randomized trial of an advanced LVAD such as the HeartMate 3 versus heart transplantation, with quality-of-life outcomes front and center, he noted.

The MOMENTUM 3 trial is funded by Abbott. Dr. Mehra reported receiving research funds from and serving as a consultant to the company.

The 2-year results of MOMENTUM 3 were published online at NEJM.org (doi: 10.1056/NEJMoa1800866) during the presentation.

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SOURCE: Mehra MR et al. ACC 18.

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments:
The reported 2- year follow-up results of MOMENTUM 3 trial on the new generation HeatMate-III magnetically levitated LVAD gives more hope to patients with end-stage heart failure for a better quality of life and longer survival and opens new doors for potentially becoming an alternative to cardiac transplantation for patients with a long waiting time on the transplant list.

New frontier in TAVR is bicuspid disease

BY BRUCE JANCIN
Frontline Medical News

DENVER – Thirty-day transcatheter aortic valve replacement (TAVR) outcomes in real-world clinical practice using the Evolut R self-expanding valve were as good in patients treated for bicuspid disease as for tricuspid disease, according to a retrospective analysis of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) national registry.

This is encouraging news because at present only tricuspid aortic valve disease is an approved indication for TAVR. Bicuspid disease isn't an approved indication because of a lack of supporting evidence regarding safety and efficacy. The new STS/ACC TVT registry data, which capture all commercial TAVR procedures done in the United States, lay the groundwork for an announced Medtronic-sponsored prospective study of Evolut Pro TAVR in patients with bicuspid disease aimed at winning an expanded indication for the device, which would open the door to on-label TAVR for patients with bicuspid disease, Jeffrey J. Popma, MD, explained at the Transcatheter Cardiovascular Therapeutics annual educational meeting (www.crf.org/tct).

BRUCE JANCIN/FRONTLINE MEDICAL NEWS

Dr. Jeffrey J. Popma

"I've always been insecure about whether we have the right technology to be able to treat bicuspid disease. This registry data is reassuring to me that we might. I think it may be time to do a prospective registry for low-surgical-risk patients with bicuspid disease and see if we can emulate these kinds of results," said Dr. Popma, the director of interventional cardiology at Beth Israel Deaconess Medical Center and a professor of medicine at Harvard Medical School, both in Boston.

"I think that the one limitation to recruitment in our low-risk TAVR trial is patients with bicuspid disease. Probably 25%-30% of low-risk patients are bicuspid, so we can't include them right now in our low-risk trial," he added at the meeting sponsored by the Cardiovascular Research Foundation.

Even though TAVR for patients with bicuspid disease is off label, operators do perform the procedure. All of these cases are captured in the STS/ACC TVT registry. Dr. Popma reported on 6,717 patients who underwent TAVR with placement of the Evolut R valve at 305 U.S. centers during 2014-2016. The pur-

pose of this retrospective study was to compare 30-day outcomes in the 191 TAVR patients with native valve bicuspid disease with the outcomes in the 6,526 with tricuspid disease.

The two groups were evenly matched in terms of key baseline characteristics, including aortic valve mean gradient, severity of aortic, mitral, and tricuspid regurgitation, and comorbid conditions – with the exception of coronary artery disease, which was present in 48% of the bicuspid group versus 65% of those with tricuspid disease. Also, the bicuspid disease group was younger by an average of nearly 9 years, and their mean baseline left ventricular ejection fraction of 52.5% was lower than the LVEF of 55.5% seen in the tricuspid group.

Procedure time averaged 126 minutes in the bicuspid group and 116 in the tricuspid group. Femoral access was utilized in 87% of the bicuspid patients and in 92% of tricuspid patients. The device was implanted successfully in 97% of the bicuspid group and in 99% of the tricuspid group. More than one valve was required in 3.7% of the bicuspid disease group, a rate similar to that in the tricuspid group. Total hospital length of stay was roughly 6 days in both groups.

Rates of symptomatic improvement at 30 days were closely similar in the two groups. Preprocedurally, two-thirds of patients in both

Continued on following page

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groups had a New York Heart Association class III; at 30 days, however, that was true for a mere 2.4% of the bicuspid patients and 10.3% of the tricuspid patients. By day 30, 52% of the bicuspid group and 48% of the tricuspid group were NYHA class I.

Also, 30-day rates of all-cause mortality, stroke, MI, major bleeding, and major vascular complications were similar in the two groups. The only striking difference in 30-day clinical outcomes involved the need for aortic valve reintervention, which occurred in 1.8% of the bicuspid versus only 0.2% of tricuspid patients.

No or only trace aortic regurgitation was present at 30 days in 62% of the bicuspid group and in 61% of the tricuspid group, while mild aortic regurgitation was noted in 31% and 33%, respectively.

Thirty-day mean aortic valve gradient improved to a similar extent in the two groups: from a baseline of 47.2 mm Hg to 9.4 mm Hg in the bicuspid group and from 42.9 mm Hg to 7.5 mm Hg in the tricuspid group.

Dr. Popma noted that an earlier analysis he carried out comparing outcomes of TAVR using the earlier-generation CoreValve in bicuspid versus tricuspid disease showed suboptimal rates of paravalvular regurgitation and an increased need for multiple valves in the bicuspid group.

"The lesson is 'Thank God we've got new technology!' because the new technology has made a big difference for us," the cardiologist observed. "We think that the advancement in the technique and the advancement in the valves is going to give us fairly comparable outcomes with Evolut in bicuspid and tricuspid patients."

Discussant Hasan Jilaihawi, MD, a codirector of transcatheter valve therapy at New York University, pronounced the short-term outcomes in patients with bicuspid aortic valve disease "better than I would have expected," adding that he, too, thinks it's time for a prospective registry study of the Evolut valve in such patients.

Dr. Popma's study was supported by Medtronic. He reported having received research grants from Medtronic and other medical device companies.

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SOURCE: Popma JJ. TCT 2017.

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments: This retrospective study is an encouraging report on 30-day outcomes of a new generation TAVR valve, Evolut R, in patients with bicuspid aortic valve stenosis. The bicuspid valve sample size was small compared to the tricuspid group (191 vs. 6,526) and, not unexpectedly, much younger than the tricuspid valve group. It is worth noting that, despite the younger age, "Femoral access was utilized in 87% of the bicuspid patients and in 92% of tricuspid patients." The bicuspid group also had a significantly higher rate of aortic valve reintervention at 30 days than the tricuspid cohort (1.8% vs. 0.2%). We should await the longer-term follow-up results to see if these reported short-term outcomes would last beyond 1 year.

Dabigatran effective for myocardial injury after noncardiac surgery

BY MITCHEL L. ZOLER
Frontline Medical News

ORLANDO – Treating patients who developed myocardial injury after noncardiac surgery with the anticoagulant dabigatran significantly cut the rate of subsequent major vascular complications in a randomized, multicenter trial with 1,754 patients, a result that gives surgeons and physicians the first evidence-based intervention for treating a common postsurgical condition.

"Because we have not systematically followed noncardiac surgery patients, it's easy to presume that everyone is okay, but all the epidemiology data show that these patients [who develop myocardial injury after noncardiac surgery] don't do okay. We need to be aggressive with secondary prophylaxis," P.J. Devereaux, MD, said at the annual meeting of the American College of Cardiology. "The unfortunate thing is that right now, we don't do much for these patients," said Dr. Devereaux, professor of medicine and director of cardiology at McMaster University in Hamilton, Ont.

Results from prior epidemiology studies have shown that, among the roughly 200 million patients who undergo noncardiac surgery worldwide each year, 8% will develop MINS (myocardial injury after noncardiac surgery) (Anesthesiology. 2014 Mar;120[3]:564-78). The myocardial injury that defines MINS is identified by either an overt MI that meets the universal definition, or an otherwise unexplained rise in serum troponin levels from baseline in the first couple of days after surgery. In the new study, Dr. Devereaux and his associates identified 80% of MINS by a troponin rise and 20% by a diagnosed MI.

The challenge in diagnosing MINS and then administering dabigatran will be implementation of this strategy into routine practice, commented Erin A. Bohula May, MD, a cardiologist at Brigham and Women's Hospital in Boston. "The problem is, troponin is not routinely measured in postoperative patients. It will be hard to change practice," she noted.

Dr. Devereaux agreed that a significant barrier is convincing clinicians, especially surgeons, to routinely measure a patient's troponin levels just before and immediately after surgery. "People are lulled into a false sense of security because patients [who develop MINS] usually don't have chest pain," he said in a video interview. "When we first showed that patients with MINS have bad outcomes, that convinced some [surgeons] to measure troponin after surgery. "Showing we can do something about it" is another important step toward fostering more awareness of and interest in diagnosing and treating MINS.

The Management of Myocardial Injury After Noncardiac Surgery Trial (MANAGE) enrolled 1,754 patients at 82 centers in 19 countries. Researchers randomized patients to treatment with either 110 mg dabigatran b.i.d. or placebo. A majority of patients in both arms also received aspirin and a statin, treatments that Dr. Devereaux should be used along with dabigatran in routine practice, based on observational findings, although the efficacy of these drugs for MINS patients has not been tested in randomized studies. The study's primary endpoint was the incidence of major vascular complications, a composite that included vascular mortality, nonfatal MI, nonfatal and nonhemorrhagic stroke, peripheral arterial thrombosis, amputation, or symptomatic venous thromboembolism.

After an average follow-up of 16 months, the primary endpoint occurred in 11% of the dabigatran-treated patients and in 15% of controls, which represented a 28% risk reduction that was statistically significant. The study's primary safety endpoint was a composite of life-threatening, major, and critical organ bleeds, which occurred in 3% of the dabigatran-treated patients and in 4% of controls, a nonsignificant difference. The dabigatran-treated patients showed a significant excess of both minor bleeds – 15% compared with 10% in controls – and "nonsignificant" lower gastrointestinal bleeds, 4% with dabigatran and 1% in the controls. The dabigatran-treated patients also had a significantly higher incidence of dyspepsia.

MANAGE was funded by the Population Health Research Institute and had no commercial funding. Dr. Devereaux has received research support from Abbott Diagnostics, Boehringer Ingelheim, Philips Healthcare, and Roche Diagnostics. Dr. May has been a consultant to Daiichi Sankyo, Merck, and Servier and has received research funding from Eisai.

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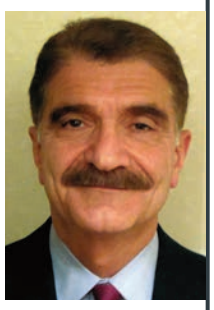
SOURCE: Devereaux P et al. ACC 18.

MITCHEL L. ZOLER/FRONTLINE MEDICAL NEWS

"We need to be aggressive," Dr. P.J. Devereaux noted.

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments:



Myocardial injury after on-cardiac surgery procedures could be a hallmark of significant yet asymptomatic coronary artery disease. The reported results of a significantly lower rate of vascular complications with dabigatran treatment are encouraging and especially, in the face of the similar safety endpoints to those of the control group. What remains is convincing the surgeons to change their practice.

Shift work's influence on cardiometabolic risk

BY DOUG BRUNK
Frontline Medical News

LOS ANGELES – Current and previous night workers had significantly increased levels of hemoglobin A_{1c}, compared with diurnal workers, preliminary results from an ongoing study showed. The finding sheds further insight into the link between environmental light, circadian rhythms, and metabolic disorders.

"To date, observational studies on bright light have revealed that evening bright light is associated with increased appetite and that bedroom light intensity is correlated with obesity," Massimo Federici, MD, said at the World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease. "It's also been reported that artificial light is correlated with type 2 diabetes in the home setting and that daytime light exposure is positively correlated with body mass index. However, no studies have directly investigated the effect of acute light on human glucose metabolism."

At the same time, observational studies of shift workers have shown that shift work is associated with metabolic disorders, but evidence for a causal relationship is limited, said Dr. Federici, professor of medicine and nutritional science at the University of Rome Tor Vergata. One study of night shift workers revealed reduced meal frequency but increased consumption of high energy snacks, physical activity, and altered sleep pattern, while a separate analysis found that permanent night shift workers showed only partial adaptation in 24-hour circadian rhythm of glucose and insulin levels (Am J Physiol Endocrinol Metab.

Continued on page 42

Phosphodiesterase-5 inhibitors prescribed incorrectly

BY NICOLA GARRETT
Frontline Medical News

While most veterans with pulmonary hypertension are treated in accordance with clinical guidelines, almost two-thirds who are prescribed therapy are being treated with pulmonary vasodilators inappropriately, an analysis of veteran prescription data reveals.

Little was known about how pulmonary vasodilators were used in practice prior to the publication of this study. While pulmonary vasodilators are considered effective for group 1 pulmonary hypertension (PH), clinical guidelines and advice from the Choosing Wisely campaign recommend against their routine use for PH patients classified into the most common types of PH – groups 2 and 3 – because of a lack of benefit, potential for harm, and high cost, the authors wrote. The report was published in Annals of the American Thoracic Society.

The new analysis shows that patients with PH are potentially being exposed to unnecessary harm, according to study author Renda Soylemez Wiener, MD, MPH, of the Center for Healthcare Organization & Implementation Research at Bedford (Mass.) Veterans Affairs Medical Center, and her colleagues. Their findings also reveal that inappropriate prescribing of pulmonary vasodilators, mostly by specialist clinicians, is contributing to the financial burden of an already stretched health system.

The research team looked at prescription data for veterans prescribed a phosphodiesterase-5 inhibitor (PDE5i), which causes pulmonary vasodilation, between 2005 and 2012 at any VA site. The primary outcome of the study was the proportion of patients who received potentially inappropriate PDE5i as classified in guideline recommendations. Patients with group 1 PH were deemed to have been treated appropriately, while those with group 2 and 3 PH were deemed to have been potentially treated inappropriately. Those with groups 4 and 5 PH were thought to have received treatment of "uncertain value."

Among 108,777 veterans with at least one ICD-9CM diagnosis code for PH, 2,790 (2.6%; 95% confidence interval, 2.5-2.7%) received daily treatment with PDE5is. Among these, 541 (19.4%; 95% CI, 18.0%-20.9%) were being treated appropriately, 1,711 (61.3%; 95% CI, 59.5%-63.1%) were receiving potentially inappropriate treatment, and 358 (12.8%; 95% CI, 11.6%-14.1%) were receiving treatment of uncertain value.

In a chart abstraction analysis from a randomly selected subset of PDE5i-treated patients, half (110/230, 47.8%; 95% CI, 41.3%-54.5%) had documented right heart catheterization to confirm the presence of PH. After factoring this into their algorithm, the investigators determined that only 11.7% (95% CI, 8.0%-16.8%) of these patients received clearly appropriate treatment.

Over the 8-year study period, the number of patients with PH group 2 or 3 prescribed PDE5i rose more than 14-fold, the researchers said. They speculated that this figure was likely to continue to rise with the increasing use of echocardiography and detection of PH.

According to the authors, the cost of treating one PH patient for 1 year with PDE5i therapy was between $10,000 and $13,000.

The 1,711 PH patients classified as being treated inappropriately in the study translated into a cost of over $20 million, if each patient were treated for only 1 year, but many of the patients were treated for a longer period of time.

The researchers suggested that there were several reasons why clinicians might choose to deviate from the guidelines, including lacking familiarity with them or disagreeing with them.

"While guidelines do allow trials of PDE5i in treatment for groups 2 or 3 PH on a case-by-case basis after consultation with a PH expert and a confirmatory [right heart catheterization], even PH experts disagree about whether a trial of PDE5i therapy is reasonable and appropriate for patients with group 3 PH," they wrote.

They may also overestimate the potential benefits of treatment and/or underestimate potential harm.

Clinicians may believe that guidelines developed for a general population do not apply to the patients they are treating.

"It is understandable why clinicians may offer unproven therapies like PDE5i in hopes of providing relief to very sick patients with groups 2 or 3 PH, especially if they do not believe the recommendation applies to their individual patient or they are not convinced about the potential harms of pulmonary vasodilators," they said.

The authors expressed concern about VA clinicians' allowing patients to take PDE5i therapy that had been initially prescribed by clinicians outside of VA hospitals. The researchers said such drugs, which potentially had been prescribed inappropriately, "were continued by VA clinicians without much apparent scrutiny."

The chart abstraction analysis also showed that specialists prescribed the majority of potentially inappropriate PDE5i treatment, suggesting "that other interventions to prevent inappropriate use may be required."

The researchers concluded that "[the] time has come to develop interventions to optimize prescribing for PH in order to improve the value, quality, and safety of care."

One potential intervention suggested by the researchers was to require patients with PH to be evaluated at a PH expert center, as recommended by treatment guidelines.

The study was funded by the Department of Veterans Affairs with resources from the Edith Nourse Rogers Memorial VA Hospital. Elizabeth S. Klings, MD, one of the study's authors, declared receiving research support from several pharmaceutical companies.

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SOURCE: Wiener RS et al. Ann Am Thorac Soc. 2018 Feb 27. doi: 10.1513/AnnalsATS.201710-762OC.

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2000;278[3]:E413-20).

Although few metabolic intervention studies using light have been done, Dr. Federici mentioned three of note. One, in patients with seasonal affective disorder and type 2 diabetes, showed reduced insulin requirements after light therapy (Lancet. 1992;339[8800]:1065-6). Another, a short-term study of 25 obese subjects treated with 5,000 lux bright light therapy in addition to exercise, showed reduced body fat after 6 weeks (Obesity. 2007; 15[7]:1749-57). A third, in 34 obese subjects who were exposed to 1,300 lux bright light every morning for 3 weeks, showed a small but significant reduction in fat mass (Obes Facts. 2013;6:28-38).

As part of an ongoing project known as EuRhythDia, researchers including Dr. Federici set out to identify metabolic and molecular variables associated with shift work, and to test the effect of a lifestyle intervention that comprised light exposure, exercise, and melatonin. He presented unpublished results from one aspect of the trial: a cross-sectional analysis of 273 nurses divided into one of three groups: 64 diurnal workers (DW), 111 active night shift workers (aNW), and 98 prior night shift workers (pNW). Those with diabetes or taking oral antidiabetic drugs were excluded from the study.

The analysis showed that nurses in the pNW group were significantly older, at a mean of 39.7 years, than those in the DW group, whose mean age was 37 years, and the aNW group, who averaged 36.1 years. Those in the pNW group also had a significantly greater body mass index, compared with their counterparts in the aNW and DW groups (a mean of 25.7 kg/m^2, vs. 24.8 and 23.7, respectively) as well has a higher mean waist circumference (a mean of 87.2 cm, vs. 84.6 cm and 82 cm).

The mean HbA_{1c} was higher in the nurses with prior and active night shift work, at 5.3% each, than in the diurnal workers (5.1%, *P* less than .001).

When Pittsburgh Sleep Quality Index scores were used to evaluate sleep quality independent of work status, more than half of the study subjects (163) were classified as being "good sleepers," while 110 were considered to be "bad sleepers." Bad sleepers had a significantly higher mean HbA_{1c} level compared with good sleepers (5.3% vs. 5.2%). Bad sleepers also had higher levels of HDL cholesterol (a mean of 60.8 mg/dL vs. 56.3 mg/dL).

Dr. Federici highlighted preliminary findings from a study of 32 aNW subjects who were assigned to treatment with warm light therapy at 1,000 lux for 30 minutes at 30 cm every morning for 3 months. They observed a mild improvement in the area under the curve of the oral glucose tolerance test at 24 weeks (12 weeks' washout after 12 weeks of light therapy). "However, the effect was obtained not at the end of the intervention but at the end of the washout period," he said.

He called for more studies going forward that take into account the effect of seasons as well as the effects of diet and exercise.

Dr. Federici disclosed that he receives editorial fees from Springer Nature group.

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Swamp coolers not linked to dust-mite sensitization in atopic children

BY THOMAS R. COLLINS
Frontline Medical News

ORLANDO – Swamp coolers – a low-cost alternative to air-conditioning in dry regions – weren't found to increase sensitization to house dust mites or mold in atopic pediatric patients, researchers reported.

Neema Izadi, MD, and his associates say the findings, seen in a pediatric Colorado population in a study evaluating data over 10 years, could mean that not everyone at risk of dust-mite and mold sensitization needs to avoid these cooling systems.

Swamp coolers, or evaporative coolers, draw water from a reservoir with a pump and the water is placed on a cooling pad. Then a fan pulls the air through the pad. This cools the air inside the home, but also increases the moisture in the air.

"Evaporative coolers have been shown to raise relative humidity by about 10%," said Dr. Izadi, a pediatric allergy and immunology fellow at National Jewish Health, Denver, presenting at the joint congress of the American Academy of Asthma, Allergy and Immunology and the World Asthma Organization. "They work best in environments where the air is very warm and dry."

House dust mites and mold thrive in higher humidity. Small studies performed in Colorado, Utah, and other locations have shown that the swamp coolers increase house dust-mite allergen content, but there have been very few studies that have looked at actual sensitization. One smaller study in Nevada did find that the coolers increased sensitization to dust mites and mold.


DR. IZADI

In this study – thought to be the largest ever to look at this question – Dr. Izadi and his colleagues assessed data on patients aged 21 years and younger who were seen at National Jewish Health during 2008-2017 and who had at least one positive environmental skin-prick test. The average age was about 9 years. The cohort included 8,503 patients with sensitization to house dust mites and 9,286 with sensitization to mold. Researchers examined data on swamp coolers in their homes.

The researchers found that 29% of those with swamp coolers were dust-mite positive on skin testing, and 28% of those without one were positive. This was not a significant difference ($P = .85$). They found that 45% of those with the coolers were positive for sensitization to any mold, compared with 44% without one – also not a significant difference ($P = .43$).

They also found no difference according to age group, sex, or individually for atopic dermatitis, asthma, or allergic rhinitis.

He acknowledged that the study had no way to reliably account for patients who were transplants to Colorado, having moved there from somewhere else. The study also didn't examine the age of homes, whether it had carpeting, or other factors.

He noted that the amount of time the coolers were run in the home was not examined and that "it might matter how much it is on." This, he said, might account for differences in these results, compared with the Nevada study that did find a sensitization increase cause by the coolers.

"Evaporative coolers or swamp coolers are a great low-cost alternative in semiarid and arid environments – they can cut costs from 15% from 35%," Dr. Izadi said. "These data may indicate that it may be unnecessary to recommend that patients remove their swamp cooler, at least from a dust-mite and mold sensitization standpoint."

Dr. Izadi had no relevant financial disclosures.

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SOURCE: Izadi N et al. AAAAI/WAO Joint Congress, Abstract 586.

VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments: Swamp coolers are used in semi-arid and arid climates like Arizona, where I did my fellowship training but they didn't work well to keep apartments and homes cool enough if over about 100°F outside! The system is cheaper than air conditioning. So it is great to know that this type of cooling system does not cause more mold and dust mite allergies.

Artificial intelligence streamlines asthma care

BY THOMAS R. COLLINS
Frontline Medical News

ORLANDO – Reviewing patient charts for asthma risk factors using natural language processing can be done 8 times faster than reviewing the charts by hand, and with high levels of accuracy, researchers reported here.

Natural language processing (NLP) is a kind of artificial intelligence in which computers are "trained" through a reiterative process to understand human language.

Researchers at Mayo Clinic previously have shown that a program created in-house can successfully and quickly determine patients' asthma status. In this study, they turned to assessment of asthma risk factors, Chung-Il Wi, MD, assistant professor of pediatrics at Mayo said in a presentation at the joint congress of the American Academy of Allergy, Asthma, and Immunology and the World Asthma Organization.

They used a convenience sample of 177 patient charts to train the NLP system. The system extracted – from key terms and sentences in the electronic health record (EHR) – data such as breastfeeding history and history of atopic conditions such as allergic rhinitis, eczema, and food allergy. From parent charts, the system extracted terms related to family history of asthma and other atopic conditions. The performance of the NLP algorithm was assessed by comparison with results of a manual chart review in a test cohort of 220 patient charts.


DR. WI

Researchers found a high level of agreement between the NLP analysis and the manual review. For breastfeeding, the positive predictive value (PPV) of the NLP was 98% and the negative predictive value (NPV) was 86%. For history of atopic conditions the PPV was at or near 100%, with a NPV of 97%-99%, depending on the condition.

For family history of atopic conditions, the PPV was 91%-100%, depending on the condition, and the NPV was 96%-99%.

"Childhood asthma risk factors identified (an) NLP algorithm using EHR has excellent concordance with chart review," researchers wrote.

Using an average time per chart, researchers found that it would take 7 hours to complete a manual review for the information presented in the study, compared to 50 minutes for the NLP.

The findings, thought to be the first demon-

Continued on page 48

VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments: This article brings mixed emotions. On one hand, using artificial intelligence brings a more thorough evaluation regarding asthma risk. On the other hand, our pediatric pulmonary subspecialty has gotten diluted over the last 3 decades. We used to regularly do arterial puncture, thoracentesis, and chest tube placement procedures. Now a computer might replace another aspect of our job, too? The practice of medicine is an art and that art should not be lost.

Yellow-zone management - What is the best plan for asthma?

BY BIANCA NOGRADY
Frontline Medical News

Significantly escalating the dose of inhaled glucocorticoids at the first sign of an imminent asthma exacerbation has had mixed results in preventing the exacerbation from occurring, according to the results of two trials in adults and children.

Presented at the joint congress of the American Academy of Allergy, Asthma, and Immunology and the World Asthma Organization and simultaneously published in the March 3 online edition of the New England Journal of Medicine, one study explored the effect of quadrupling the inhaled glucocorticoid dose in adults and adolescents with asthma, while the other looked at quintupling the dose in children.

The first study involved 1,922 participants who were aged 16 years or above, who were receiving inhaled glucocorticoids, and who had experienced at least one asthma exacerbation in the previous year. They were randomized to a self-management plan that instructed them to either take quadruple their usual dose of inhaled glucocorticoids at the first sign of worsening asthma – more use of reliever inhaler, difficult sleeping, or reduced peak flow – or to continue using their usual dose of inhaled glucocorticoids.

At 1 year, there was a significantly lower incidence of severe asthma exacerbations in the group who used the higher dose of inhaled glucocorticoids (45% vs. 52%; hazard ratio, 0.80; P = .001) after adjustment for age, sex, and peak flow measures at randomization, according to Tricia McKeever, PhD, from the department of epidemiology and public health at the University of Nottingham (England), and her coauthors.

Researchers also saw a lower percentage of participants using systemic glucocorticoids in the quadruple-dose group, compared with the normal-dose group (33% vs. 40%), and the quadruple-dose group also showed a 14% lower incidence of unscheduled health care consultations.

At the end of the 12-month follow-up, the estimated mean total dose of inhaled glucocorticoids was 385 mg in the quadruple-dose group and 328 mg in the normal-dose group.

The most common serious adverse event was hospitalization for asthma, which occurred three times in the quadruple-dose group and 18 times in the normal-dose group. However the incidence of oral candidiasis and dysphonia – both potentially treatment related – was significantly higher in the quadruple-dose group (36 events vs. 9 events).

Overall, the number needed to treat with the quadruple dose to prevent one severe asthma exacerbation was 15.

The second study, which was double blinded, investigated whether quintupling the dose of inhaled glucocorticoids might avoid exacerbations in children. They randomized 254 children who had mild-moderate persistent asthma and had had at least one exacerbation treated with systemic glucocorticoids in the previous year to manage "yellow-zone" early-warning signs with either normal dose or five times their usual dose of inhaled glucocorticoids.

The rate of severe asthma exacerbations did not differ significantly between the quintuple-dose and normal-dose groups at the 1-year follow-up (0.48 vs. 0.37; P = .3), nor did the time to the first severe exacerbation or the rate of emergency department or urgent care visits.

The four hospitalizations for asthma all occurred in the high-dose group. However, there was a lower growth rate seen in children in the high-dose group than in the low-dose group (5.43 cm/yr vs. 5.65 cm/yr; P = .06). There were no significant differences between the two groups in other adverse events.

However, Daniel J. Jackson, MD, and his coauthors noted that there were fewer yellow-zone episodes and fewer exacerbations in both groups than they had anticipated.

"It is important to recognize that our findings are specific to school-age children with mild to moderate persistent asthma regularly treated with daily low-dose inhaled glucocorticoids (with good adherence)," wrote Dr. Jackson from the department of pediatrics at the University of Wisconsin–Madison and his coauthors.

Possible subgroup benefit from high-dose inhaled steroids

These two trials address the important question of whether substantial escalation of regularly used inhaled glucocorticoids prevents exacerbations if started at the first sign of deterioration, as this so-called yellow zone has long been thought the perfect time to initiate more aggressive care, noted Philip G. Bardin, PhD, of the Monash Lung and Sleep Unit at the Monash University Medical Centre in Melbourne in an editorial. However glucocorticoids have serious side effects, and there is some preclinical evidence that they may enhance viral replication.

One trial shows that an escalating dose in this yellow zone does not prevent exacerbations in children with the early signs of asthma instability. The second trial is more complex and more controversial, as the open-label design may have biased the outcome, and the degree of benefit is debatable, Dr. Bardin noted in the New England Journal of Medicine (2018 Mar 3. doi: 10.1056/NEJMe1800152).

Together, these studies suggest that high doses of inhaled glucocorticoids either do not prevent exacerbations or only do so in a small subgroup of patients with as-yet-undefined baseline and exacerbation characteristics, he added in the editorial, which was published in the same issue as these two studies.

The first study was supported by the National Institute for Health Research. Six authors declared grants, personal fees, and other funding and support from the pharmaceutical industry outside the submitted work.

The second study was supported by the National Heart, Lung, and Blood Institute. Fifteen authors declared grants, personal fees and other funding from the pharmaceutical industry, as well as other private industry, outside the submitted work. Several also declared grants from organizations including the National Institutes of Health.

Dr. Bardin reported personal fees from GlaxoSmithKline outside the submitted work.

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SOURCES: McKeever T et al. N Engl J Med. 2018 Mar 3. doi: 10.1056/NEJMoa1714257; Jackson DJ et al. N Engl J Med. 2018 Mar 3. doi: 10.1056/NEJMoa1710988.

VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments: The STICS trial reported by Jackson, et al has been heavily discussed since hitting the press at the AAAAI meeting! The STICS trial focused on children whereas the NEJM paper authored by McKeever, et al included patients who were age 16 and above but the mean age was 56 years. The STICS study showed no difference in the primary outcome for patients who had significantly elevated inhaled steroid dosing in the yellow zone compared with controls. The primary outcome was the rate of severe asthma exacerbations treated with systemic glucocorticoids. Also, the P value for difference in linear growth per year was .06, but they did a subset analysis of children younger than 8 years of age. The younger children who received the significantly higher dose of inhaled steroids in their yellow zones had a 0.12 cm per year lower growth per yellow-zone episode than the control patients with a p value of 0.02. This landmark study is making us all re-think how we build an asthma action plan for our pediatric patients.

Continued from page 43

strating NLP's value for this purpose, suggest "the huge potential of leveraging NLP for asthma care and research," researchers said.

Dr. Wi said the system can be applied to any EHR system. He said it only makes sense to put an algorithm to use in this way – it saves both clinical time and time in doing research projects.

"Whenever we do asthma research we need to collect asthma risk factors anyway, but we don't want to do manual chart review anymore in this EMR era," he said. "Now, the computer can do it."

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SOURCE: Wi C-I. AAAAI/WAO Joint Congress 2018, Abstract 637.

TB in 2017: Good news and bad news

BY RICHARD FRANKI
Frontline Medical News

The rate and number of new tuberculosis cases in the United States for 2017 were the lowest since national surveillance started in 1953, but news on the TB elimination front is not so good, according to the Centers for Disease Control and Prevention.

Those new lows – TB incidence of 2.8 per 100,000 persons and 9,093 new cases – continue a downward trend that started in 1993, but the current rate of decline is much lower than the threshold needed to eliminate TB by the year 2100, Rebekah J. Stewart and her associates at the CDC's Division of Tuberculosis Elimination, Atlanta, wrote in the Morbidity and Mortality Weekly Report.

TB incidence for 2017 was, in fact, 28 times higher than the U.S. elimination threshold of less than one case per 1,000,000 persons, and the average annual rate of decline since 2014, 2.0%, is only about half the sustained annual decline of 3.9% needed to eliminate TB by the year 2100. "Ongoing efforts to prevent TB transmission must be sustained, and efforts to detect and treat [latent TB infection], especially among groups at high risk, must be increased," they said.

Geographically, at least, the states with populations at the highest risk are Hawaii, which had a TB incidence of 8.1 per 100,000 persons in 2017, and Alaska, with an incidence of 7.0 per 100,000. California and the District of Columbia were next, each with an incidence of 5.2. The states with the lowest rates were Montana and Wyoming at 0.3 per 100,000, the investigators reported, based on data from the National Tuberculosis Surveillance System as of Feb. 12, 2018.

Groups most affected by TB include persons housed in congregate settings – homeless shelters, long-term care facilities, and correctional facilities – and those from countries that have high TB prevalence. Overall incidence for non–U.S. born residents was 14.6 per 100,000 in 2017, compared with 1.0 for the native born, with large discrepancies seen between U.S. and non–U.S. born blacks (2.8 vs. 22.0), native Hawaiian/Pacific Islanders (6.5 vs. 21.0), and Asians (2.0 vs. 27.0), Ms. Stewart and her associates said.

"Increased support of global TB elimination efforts would help to reduce global … prevalence, thereby indirectly reducing the incidence of reactivation TB in the United States among non–U.S. born persons from higher-prevalence countries," they wrote.

The issue of global action on TB was addressed by the Forum of International Respiratory Societies in a statement recognizing World TB Day (March 24). "TB is the world's most common infectious disease killer, yet is identifiable, treatable and preventable; what is missing is the political will to dedicate the resources necessary to eradicate it, once and for all," said Dean E. Schraufnagel, MD, the organization's executive director.

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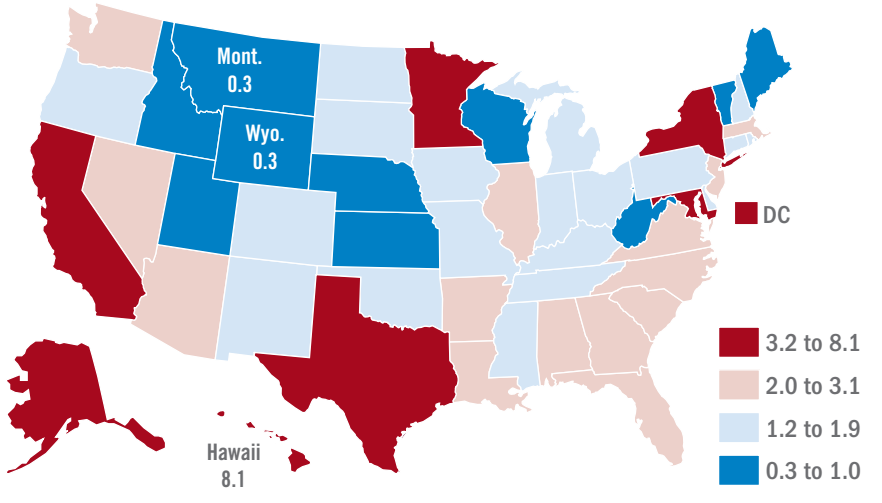
Tuberculosis incidence per 100,000 persons, 2017



Note: Based on cases reported to the National Tuberculosis Surveilance System.
Source: MMWR. 2018 Mar 23;67(11):317-23

SOURCE: Stewart RJ et al. MMWR. 2018 Mar 23;67(11):317-23.

CDC: Flu levels highest since pandemic year 2009

BY RICHARD FRANKI
Frontline Medical News

Influenza activity continued to increase in the week ending Jan. 20, and the 2017-2018 flu season continues to look a lot like the 2009-2010 pandemic, according to data from the Centers for Disease Control and Prevention.

That season was dominated by influenza A (H3N2), and the 2017-2018 season seems to be going down that same path. For the week ending Jan. 20, the proportion of outpatient visits for influenza-like illness increased to 6.6%, which is, for the second consecutive week, the highest level reported since October of – you guessed it – 2009, when it hit 7.7%, the CDC said in its weekly flu surveillance report.

The level reported last week, 6.3%, has been revised downward and now stands at an even 6%.

It turns out that 2018 is something of a milestone for the H3N2 virus. The virus first emerged in 1968, so it has reached its 50th anniversary, Dan Jernigan, MD, director of the influenza division at the CDC's National Center for Immunization and Respiratory Diseases, Atlanta, said on Jan. 26 in a weekly briefing.

H3N2 must not be happy about hitting the big 5-0, however, because the map of influenza-like illness activity looks pretty red and angry. For the week ending Jan. 20, there were 30 states at the highest level of flu activity on the CDC's 1-10 scale, with another nine in the "high" range at levels 8 and 9.

Dr. Jernigan did suggest that activity may have peaked in some areas of the country, with California among them.

There were seven pediatric deaths reported for the week ending Jan. 20, although six occurred in previous weeks. There have been 37 flu-related deaths among children so far during the 2017-2018 season, the CDC said.

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Alternative oxygen therapy reduces treatment failure in bronchiolitis

BY RANDY DOTINGA
Frontline Medical News

High-flow oxygen therapy outside the ICU boosts the likelihood that infants with bronchiolitis will avoid treatment failure and an escalation of treatment, a study finds.

"High flow can be safely used in general emergency wards and general pediatric ward settings in regional and metropolitan hospitals that have no immediate direct access to dedicated pediatric intensive care facilities," study coauthor Andreas Schibler, MD, of University of Queensland in Australia, said in an interview. The findings were published March 22 in the New England Journal of Medicine.

Bronchiolitis is quite common in children, and a 2002 report found that respiratory syncytial virus (RSV) bronchiolitis was the most common reason for infants under the age of 1 year to be hospitalized in the United States during 1997-1999 (Pediatr Infect Dis J. 2002 Jul;21[7]:629-32).

"The typical treatment for bronchiolitis is supportive therapy, providing nutrition, fluids, and if needed, respiratory support including provision of oxygen," Dr. Schibler said.

The prognosis is generally good thanks to improvements in intensive care, he said, which some infants need because the standard oxygen therapy provided in general pediatric wards is insufficient. The new study examines whether high-flow oxygen therapy through a cannula – which he said has become more common – reduces the risk of treatment failure in non-ICU therapy, compared with standard oxygen treatment.

Dr. Schibler and his colleagues tracked 1,472 patients under 12 months with bronchiolitis and a need for oxygen treatment who were randomly assigned to high-flow or standard oxygen therapy to maintain their oxygen saturation at 92%-98% or 94%-98%, depending on policy at the hospital. The subjects were patients at 17 hospitals in Australia and New Zealand.

A total of 739 infants received high-flow treatment that provided heated and humidified oxygen at a rate of 2 L/kg of body weight per minute. The other 733 infants received standard oxygen therapy up to a maximum 2 L/min.

The treatment failed, requiring an escalation of care, in 87 of 739 patients (12%) in the high-flow group and 167 of 733 (23%) in the standard-therapy group. (risk difference = –11% points; 95% confidence interval, –15 to –7; *P* less than .001).

"The ease of use and simplicity of high flow made us recognize and think that this level of respiratory care can be provided outside intensive care," Dr. Schibler said. "This was further supported by the observational fact that most of these infants with bronchiolitis showed a dramatically improved respiratory condition once on high flow."

Dr. Schibler said there haven't been any signs of adverse effects from high-flow oxygen therapy. As for the cost of the treatment, he said it is "likely offset by a reduced need for intensive care therapy or costs associated with transferring to a children's hospital."

What should physicians and hospitals take from the study findings? "If a hospital explores the option to use high flow in bronchiolitis, then start the therapy early in the disease process or once an oxygen requirement is recognized," Dr. Schibler said. "Implementation of a solid and structured training program with a clear hospital guideline based on the evidence will ensure the staff who care for these patients will be empowered and comfortable to adjust the oxygen levels given by the high-flow equipment. The greater the confidence and comfort level for the nursing and respiratory technician staff, the better for these infants, as they will sooner observe those infants who are not responding well and may require a higher level of care such as intensive care or they will recognize the infant who responds well."

The National Health and Medical Research Council (Australia) and the Queensland Emergency Medical Research Fund provided funding, and sites received grant funding from various sources. Fisher & Paykel Healthcare, a respiratory care company based in Auckland, New Zealand, donated high-flow equipment and consumables and travel/accommodation support. Study authors reported various grants and other support.

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SOURCE: Franklin D et al. N Engl J Med. 2018 Mar 22;378(12):1112-31.

Xenon imaging could detect lung involvement after HSCT

BY SHARON WORCESTER
Frontline Medical News

SALT LAKE CITY – Hyperpolarized xenon-129 magnetic resonance imaging, or ^{129}Xe MRI, showed strong promise for revealing early lung ventilation deficits in pediatric hematopoietic stem cell transplant (HSCT) patients in a proof-of-concept study.

The use of hyperpolarized xenon gas in this setting remains investigational, but is emerging as a safe nonionizing approach for mapping and quantifying regional airway obstruction in the pediatric population. It has been shown to be more sensitive to early disease than the current clinical gold standard of measuring forced expiratory volume in 1 second (FEV_1) by spirometry, Laura L. Walkup, PhD, said at the combined annual meetings of the Center for International Blood & Marrow Transplant Research and the American Society for Blood and Marrow Transplantation.

The ^{129}Xe MRI provides regional information that spirometry cannot, allowing for a targeted approach to planned procedures such as bronchoscopy, said Dr. Walkup of Cincinnati Children's Hospital Medical Center.

"We hypothesized that hyperpolarized ^{129}Xe MRI would be sensitive to lung abnormalities in the pediatric HSCT population," she said.

Of 13 patients aged 6-13 years (mean, 10 years) who were enrolled in the study and underwent ^{129}Xe-MRI, 9 also completed spirometry successfully, and the average FEV_1 in those patients was 83% of the predicted value.

Ventilation deficits were apparent on the ^{129}Xe MRI imaging in 8 of the 13 subjects and varied in regional distribution. The whole-lung ^{129}Xe ventilation defect percentage for the HSCT group was 14%, which was significantly greater than the approximately 6% ventilation defect percentage in a cohort of age-matched controls, Dr. Walkup said, noting that ventilation deficits were seen in three of four subjects who were unable to complete reliable spirometry.

"So those are lung abnormalities that may have otherwise gone undetected," she said, adding that hyperpolarized xenon gas also highlighted the wide individual variation in ventilation, even among cases with similar FEV_1 percentages.

The findings are notable, because pulmonary complications such as bronchiolitis obliterans are a major source of morbidity and mortality in the pediatric HSCT population, and an accurate and early diagnostic tool identifying the location and severity of suspected obstructive lung pathology following HSCT is desperately needed, she said.

The HSCT patients in the current study included four boys and nine girls. Isotopically-enriched xenon gas (86% ^{129}Xe) was hyperpolarized using a commercial polarizer and images were acquired during a breath hold of up to 16 seconds and up to 1 L of xenon gas. Conventional anatomic MR images also were acquired.

The ^{129}Xe ventilation was quantified using a less than 60% mean whole-lung ^{129}Xe signal threshold, and was compared to FEV_1 percentage predicted as measured via spirometry.

The procedure was well tolerated by all patients, Dr. Walkup said, noting that no patients withdrew from the study, and all were able to maintain the required breath hold.

Drops in blood oxygen saturation level did occur, but were transient and resolved within 10-30 seconds of normal breathing. Further, there were no changes in heart rate during imaging, and any side effects related to xenon, such as tingling in extremities, dizziness, or euphoria, were also quickly resolved with normal breathing, she said.

"There were no serious adverse events related to the study ... these results are in good agreement with

Continued on following page

Hurricane relief and patient care

BY LTC HERBERT KWON, MC, USA

In October 2017, in support of the Federal Emergency Management Agency's response to assist the Governor and people of Puerto Rico, three Department of Defense (DOD) military hospital platforms were deployed; one each, by the US Army, Navy, and Air Force. They arrived on the island at different times with predominantly wartime surgical capabilities and augmented the Federal Emergency Management Agency (FEMA), US Public Health Service, National Guard, and Puerto Rico Department of Health efforts. My perspective is that of patient care and transport between the Centro Medico hospital complex in San Juan, the larger regional hospitals, the Veterans Administration hospital, the DOD response, FEMA Disaster Medical Assistance Teams (DMAT), and FEMA Federal Medical Shelters about 4 to 6 weeks after Hurricanes Maria and Irma struck. Based upon this experience, I would like to offer the following.

Pre-Disaster: All clinicians have a few patients that teeter "on the edge." When basic services go away, these patients fall over that edge and become inpatients. Establish a list of patients who require oxygen and devices such as vests, cough-assist, or ventilation. If evacuation before the disaster is possible, those patients need to leave. If they refuse, or are unable to leave, they need to be able to supply their own generated power for a prolonged period of time, as batteries will run out prior to power restoration. They must be able to use oxygen concentrators, as tank re-supply may not be readily available. By law, FEMA cannot give generators to individuals, so individuals must prepare for themselves. In a hurricane-prone area where seasonal risk can be established, planning medication refills at the beginning of the season or giving a larger than normal supply may prove useful. In an area prone to sudden disaster, such as earthquake or tornado, then counseling patients to request refills at least 2 weeks early may be adequate.

Post-Disaster: The most reliable form of communication will be text. You likely already have text contacts for your staff and family members; add other providers, responders, planners, pharmacists, and oxygen suppliers to your text contacts. While you may wish to share a text point of contact with patients, understand that your ability to actually help during the initial disaster will likely be limited. Identify possible language translation needs and possible translators among your staff and/or friends as telephone services will be limited or absent following the disaster. Finally, identify your local emergency response planners on Facebook, Twitter, or other social media feeds. This will allow you to direct others to these sites for accurate information after the disaster.

Responder Recommendations: A single social media post can DESTROY your plans and hamper your efforts. Advertise a single contact point and an information resource (eg, bulletin board, webpage) early and often. Publicly and accurately declare the means by which people will access health care and health-care services, such as medications, dialysis, and oxygen. There will be nongovernment organizations (NGOs), friends, and other well-meaning individuals who will try to assist people in need through unconventional channels. Yet, by requesting assistance through nonroutine channels, those efforts tend to delay assistance, cause confusion, and/or squander resources. Continue to direct those requests through the established response channels, ie, the local 911 equivalent.

Plan to use cellular texts to communicate. While satellite telephones are great in concept, in execution, they are difficult to utilize when transmitting complex medical information. If you have an expansive budget, there are now devices available that allow for Iridium satellite-based text communications that require batteries but not intact cellular towers.

Facilities with electricity, water, oxygen, medications, laboratory testing, and CT scanners need to be identified and advertised within the responder community. If FEMA is involved, these resources will be identified and updated on a routine basis. The information will be distributed to their DMAT teams. Those DMAT teams will be distributed throughout the response area. Additionally, if the resources and budgeting are approved, then FEMA will also help re-establish medical transport, as well as Federal Medical Shelters (FMS). The FMS can temporarily house patients who can perform basic activities of daily living but require power, oxygen, or medication administration. For those patients in need of medications without insurance, FEMA may activate medication assistance through the Emergency Prescription Assistance Program. This will allow up to 30 days of medication to be distributed at no cost to the individual through participating pharmacies.

External responders will obviously need to pair with local providers/professionals who can navigate the system and, if necessary, can translate medical terms and care plans. Additionally, external responders will be targets for individuals looking to obtain resources for secondary gain or profit. Establishing a plan or consistently redirecting people to the appropriate resources for those needs may limit the inevitable damage these individuals will cause. Additionally, understand that the efficiencies of the modern society will be gone, and tasks will take much longer than expected. Even if you can communicate by text, the transporting of patients, delivering supplies, meeting with groups, and assessing sites will take far longer than you are used to when none of the stoplights are functional or if gasoline is in limited supply.

Finally, there will be patients for whom no solution, short of an intact, well-resourced medical system, exists—those with severe congenital issues, patients with advanced dementia, patients with advanced cancer, and those with multiple-antibiotic-resistant osteomyelitis are a few of the patients that this response encountered. If transport out of the area is unavailable, NGOs and other charities may be the best, and at times, the only resource for these patients. During this response, I observed NGO and charities helping individual patients and their families with their power, shelter, and medical needs that could not be legally provided by federal government response.

While I hope you may never need to use them, preparations for evacuation, medication, power, and communications before a potential disaster occurs will prove helpful to your patients. After the disaster, consistent and simple communications to the public will be necessary to limit the damage from the social media rumor mill. Working within the organized response framework and leveraging local knowledge and targeted NGO involvement will maximize the effect of your efforts.

Dr. Kwon is Chief, Pulmonary-Critical Care-Sleep Medicine Service, Madigan Army Medical Center, Tacoma, Washington. The views expressed are those of the author and do not reflect the official policy of the Department of the Army, the Department of Defense, or the US Government.

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previously published safety assessments of xenon in kids and in adults, and at our institution we routinely perform xenon imaging in children as young as age 6," she added.

The findings, which are consistent with those seen in studies of other conditions such as cystic fibrosis, asthma, and chronic obstructive pulmonary disease, suggest that ^{129}Xe MRI is an emerging modality with strong translational potential for detecting early pulmonary involvement following HSCT, she said.

"The real power of the xenon MRI is the spatial information that it provides; we can use that information to plan targeted procedures like bronchoscopy and biopsies ... and since it is nonionizing, it may be used serially to assess disease progression or response to an intervention," Dr. Walkup said.

She noted, however, that, because it is not yet approved by the Food and Drug Administration and because it requires specialized expertise and hardware, it is available at only a handful of centers worldwide.

There is a long way to go before the technology will be widely clinically implemented, but work is ongoing at Cincinnati Children's Hospital to determine how xenon MRI may play a role in pulmonary screening of patients, she said.

Dr. Walkup reported having no financial disclosures.

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SOURCE: Walkup LL et al. 2018 BMT Tandem Meetings, Abstract 56.

Higher rifampin doses for pulmonary TB discussed

BY NEIL OSTERWEIL
Frontline Medical News

BOSTON – Current daily doses of rifampin for treating pulmonary tuberculosis may be too low and could be safely increased, results of a randomized phase 2 study suggest.

"Back in the 1970s, rifampin was an expensive drug, and attempts to shorten TB therapy using higher but intermittent doses of rifampin were unsuccessful at that time because of increased toxicity. That line of inquiry was essentially dormant for 40 years," said Gustavo Velásquez, MD, from Brigham & Women's Hospital in Boston.

Neil Osterweil/Frontline Medical News

Dr. Gustavo Velásquez

More recent controlled trials have evaluated higher daily doses of rifampin, but none thus far have looked at concentration-dependent drug activity in Latin American patients or at efficacy as a function of the parameter that is thought to best predict rifampin activity, which is the ratio of the area under the curve to the maximum inhibitory concentration (AUC/MIC) of rifampin, he said at the Conference on Retroviruses and Opportunistic Infections.

To get a better idea of optimal rifampin dosing for the treatment of pulmonary TB, Dr. Velásquez and his colleagues conducted the HIRIF (High-Dose Rifampin in Patients With TB) trial. The phase 2 study was designed to evaluate the pharmacokinetics, efficacy, and safety of higher daily rifampin doses for pulmonary TB.

They looked at the three parameters across three treatments arms: 10 mg/kg rifampin (the current standard of care), 15 mg/kg, or 20 mg/kg.

Patients in Peru were screened, enrolled, and randomized in cohorts of 60 patients each to one of the three specified dose levels, which they received either as additional rifampin tablets or placebo for the first 8 weeks of treatment, after which all patients were continued on rifampin 10 mg/kg to complete a 6-month regimen. All patients were followed for an additional 6 months for assessment of TB recurrence.

Rifampin total doses ranged from as low as 300 mg for patients in the 30-kg to 37-kg weight range, to as high as 1,500 mg for those weighing more than 70 kg.

The efficacy analysis was by

modified intention to treat, excluding 6 patients who had insufficient $\log_{10}$ colony-forming units (CFUs) of TB, and a per-protocol analysis excluding an additional 42 patients whose doses of rifampin were affected by three study halts for adverse events. After each halt and review by the data safety–monitoring board, the trial was allowed to resume, but because enrollment and experimental dosing also were suspended, patients in the 15- and 20-mg/kg arms received 10 mg/kg during the 2- to 5-week halts. The number of patients in the 10-, 15-, and 20-mg/kg doses included in the per-protocol analysis were 56, 38, and 38, respectively,

Controlled trials have evaluated higher daily doses of rifampin, but none thus far have looked at concentration-dependent drug activity in Latin American patients or at efficacy as a function of the parameter that is thought to best predict rifampin activity.

Pharmacokinetic evidence from this study, previously published, showed that the median maximum drug concentration (C_{max}) in serum

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in the experimental arms reached the lower end of the targeted range of 8 mcg/mL or greater, whereas the median in the standard-of-care arm was 6.2 mcg/mL. Only 33% of patients in the 10-mg/kg arm reached the minimum 8-mcg/mL level, Dr. Velásquez noted, vs. 72% and 81% of patients in the 15- and 20-mg/kg doses, respectively.

In the modified intention-to-treat population, for every 5-mg/kg increase in rifampin dose, there was a nonsignificant trend toward faster decline in TB CFUs in sputum. Similarly, for every 1-log increase in rifampin AUC/MIC, there was a trend, albeit nonsignificant, toward faster decline.

However, in patients in the per-protocol analysis, every 5-mg/kg dose increase and 1-log increase in rifampin AUC was associated with significantly faster declines in CFUs (P = .022 and .011, respectively).

An analysis of treatment outcomes at 12 months, a secondary endpoint, showed that there were five cases of treatment failure, including three in the control arm and one each in 15- and 20-mg/kg arms, and six cases of recurrence after cure, which occurred in three, one, and two patients, respectively,

The safety analysis by intention-to-treat showed that the incidence of grade 2 or greater rifampin-related adverse events

(AEs) were 43.3%, 51.7%, and 38.3% in the 10-, 15-, and 20-mg/kg doses, differences that were not statistically significant.

In addition, there were no significant differences among the treatment arms in either time to first grade 2 or greater rifampin-related AEs, the occurrence of one or more grade 2 or greater hepatic rifampin AEs, or time to first hepatic rifampin-related AEs of grade 2 or above.

"[With] high-dose rifampin, I think we have a really very robust body of literature to which this study can be added, demonstrating the safety of high-dose rifampin in the context of TB treatment," noted Dr. Benson.

Dr. Velásquez noted that the study was limited by the possibility that the study halts could have biased efficacy effect estimates toward null and by differences in weight distribution among the three treatment arms.

"This actually is the first trial that shows not only a dose response of rifampin but also an exposure response of rifampin in combination therapy," he said. "Our study supports that even higher doses of rifampin beyond what we studied of 20 mg/kg should be studied for potential treatment shortening." The evidence also suggests that the current 10-mg/kg dose is low and could be safely increased to a 15- or 20-mg/kg dose, he concluded.

In a media briefing following the presentation, moderator Constance Benson, MD, from the University of California San Diego, who was not involved in the study, commented that, with "high-dose rifampin, I think we have a really very robust body of literature to which this study can be added, demonstrating the safety of high-dose rifampin in the context of TB treatment."

"There are some circumstances where I think using a much higher dose than we've been using would be an appropriate thing to do," she added.

Examples of patients who might benefit include patients with disseminated TB or people with more serious TB than the average case, she said.

The study was supported by the National Institute of Allergy and Infectious Diseases. Dr. Velásquez and Dr. Benson reported no relevant conflicts of interest.

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SOURCE: Velásquez G et al. CROI 2018, Abstract 39LB.

Women working in medicine shout #MeToo

BY CHRISTINA JEWETT
Kaiser Health News

Annette Katz didn't expect to be part of a major social movement. She didn't set out to take on a major health organization. But that all began to change when a coworker saw her fighting back tears and joined Ms. Katz to report to her union what amounted to a criminal sexual offense at a Cleveland Veterans Affairs Medical Center in 2012 and 2013.

Four years later, Ms. Katz, a licensed practical nurse at the hospital, testified in a court deposition that a male nursing assistant had shoved her into a linen closet and groped her and subjected her to an onslaught of lewd comments.

In speaking out and taking legal action, Ms. Katz joined a growing group of women who are combating sexual harassment in the medical field at every level, from patients' bedsides to the executive boardroom.

Much as the #MeToo moment has raised awareness of sexual harassment in business, politics, media, and Hollywood, it is prompting women in medicine to take on a health system where workers have traditionally been discouraged from making waves and where hierarchies are ever present and all commanding. While the health care field overall has far more women than men, in many stations of power the top of the pyramid is overwhelmingly male, with women occupying the vast base.

In a recent survey, 30% of women on medical faculties reported experiencing sexual harassment at work within the past 2 years, said Reshma Jagsi, MD, who conducted the poll. That share is comparable to results in other sectors, and as elsewhere, in medicine it had been mostly taboo to discuss before last year.

"We know harassment is more common in fields where there are strong power differentials," said Dr. Jagsi, director of the Center for Bioethics and Social Sciences in Medicine at the University of Michigan, Ann Arbor. "And we know medicine is very hierarchical."

Workers in the health care and social assistance field reported 4,738 cases of sexual harassment from fiscal 2005 through 2015, eclipsed only by fields such as hospitality and manufacturing, where men make up a greater proportion of the workforce, according to data gathered by the Equal Employment Opportunity Commission.

A Kaiser Health News review of dozens of legal cases across the United States shows similar patterns in the waves of harassment cases that have cropped up in other fields, from entertainment to sports to journalism: The harassers are typically male; the alleged harasser supervises or outranks the alleged victim; there are slaps on the butt, lewd comments, and requests for sex; and when superiors are confronted with reports of bad behavior, the victims, mostly women, are disbelieved, demoted, or fired.

But recently, physicians have taken to Twitter using the #MeTooMedicine tag, sharing anecdotes and linking to blogs that chronicle powerful doctors harassing them or disrobing at professional conferences.

Women who work in cardiology recently told the cardiology trade publication TCTMD that they felt the problem was particularly widespread in their specialty, where females account for 14% of the physicians. A Los Angeles anesthesiologist made waves in a blog post urging "prettier" women to adopt a "professional-looking, even severe, hair style" to be taken seriously and to consider self-defense classes.

Among those speaking out is Jennifer Gunter, MD, a San Francisco obstetrician-gynecologist who recently wrote a blog post about being groped in 2014 by a prominent colleague at a medical conference – even naming him.

In a recent survey, 30% of women on medical faculties reported experiencing sexual harassment at work within the past 2 years, said Dr. Jagsi, who conducted the poll. That share is comparable to results in other sectors.

"I think nothing will change unless people are able to name people and institutions are held accountable," she said in an interview. "I don't think without massive public discourse and exposure that things will change."

Lawsuits, many settled or still making their way through the courts, describe encounters.

A Florida nurse claimed that in 2014, a surgeon made lewd comments about her breasts, asking her in a room full of people whether he should "refer to her as 'JJ' or 'Jugs,'" the nurse's lawsuit says. The nurse said she "responded that she wished to be called by her name."

In other cases: A phlebotomist in New York alleged in a lawsuit that a doctor in her medical practice gave her a box of Valentine's Day candy and moved in for an unwanted kiss on the mouth. A Florida medical resident alleged that a supervising doctor told her she looked like a "slutty whore." A Nebraska nurse claimed that a doctor she traveled with to a professional conference offered to buy her a bikini, if he could see her in it, and an extra night in a hotel, if they could share the room. She declined.

A Pennsylvania nurse described the unsatisfying response she got after reporting that a colleague had pressed his pelvis against her and flipped through her phone for "naked pictures." A supervisor to whom she reported the conduct expressed exasperation, saying "I can't deal with this" and "What do you want?"

Kayla Behbahani, DO, chief psychiatry resident at University of Massachusetts Memorial Medical Center, Worcester, did not file a lawsuit but recently wrote about sexual harassment committed by a subordinate. In an interview, she said her instincts were to pity the man and also to follow a dictate that's drilled into medical students: Don't make waves. So, she disclosed the harassment only after another woman's complaint launched an investigation.

"As a professional, I come from a culture where you go with the flow," Dr. Behbahani said. "You deal with what you're dealt. In that regard, it was a dilemma for me."

Ms. Katz, the Veterans Affairs nurse, initially didn't complain about the harassment. A single mother with two children, she needed her job. Her attacker, M.D. Garrett, was also a nursing assistant but had more seniority, was a veteran, and was friends with her boss.

"I really did feel that I would lose my job," Ms. Katz said in an interview. "I would be that troublemaker."

But as the abuse escalated, she went to the VA inspector general and the Cleveland police.

She estimated that five times Mr. Garrett pushed her into a closet where he would ask for sex. She would "tell him 'no' and fight my way out of [his] grip," her statement said. He shoved her into an unconscious patient's bathroom and would "try to restrain me, but I eventually could break free."

After one such assault, a colleague noticed tears in Ms. Katz's eyes. The coworker shared with Ms. Katz that she, too, had been a target of Mr. Garrett's lewd behavior.

Ms. Katz and the colleague filed complaints in March 2013 with their union, with the police, and with their managers. That July, Mr. Garrett was indicted by a grand jury and later pleaded guilty to three counts of sexual imposition and one count of unlawful restraint. He was also dismissed from his job.

Reached by phone, Mr. Garrett said he agreed to the plea because he was facing multiple felonies and didn't know what a jury would do. He said that, even though he pleaded guilty to four misdemeanors, he did not commit the crimes of which he was accused. "There was no harassment; she and I were friends," he said.

In 2013, Ms. Katz sued the VA, alleging that it failed to protect her from harassment and retaliated against her by refusing to give her a job-site transfer before firing her for not showing up to work.

The VA attorneys argued that the department had no direct knowledge of harassing behavior before Ms. Katz reported it and that, once it was informed, immediate action was taken. Veterans Affairs Deputy Press Secretary Lydia Blaha said in an email that anyone engaged in sexual harassment is swiftly held accountable.

The U.S. Department of Veterans Affairs agreed in February 2018 to pay $161,500 to settle Ms. Katz's lawsuit.

Ms. Katz said it was costly and emotional to press on with her legal case but hopes it helps other women see that seeking justice is worthwhile. "I do think there are a lot of women who just suffer in silence," she said.

Dr. Gunter, the San Francisco physician-blogger, said that needed change will come only when people who are more established across all professions stand up for those who are more junior.

KHN's coverage of these topics is supported by the John A. Hartford Foundation and The David and Lucile Packard Foundation. Kaiser Health News is a nonprofit news service covering health issues. It is an editorially independent program of the Kaiser Family Foundation that is not affiliated with Kaiser Permanente.

CHEST™ Physician
THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

Gender bias in academic medicine is treatable

BY TED BOSWORTH
Frontline Medical News

TAMPA – Gender bias that disadvantages women from rising in academic medicine might require specific habit-changing strategies rather than efforts that draw on goodwill alone, according to new follow-up data from a randomized trial discussed and reevaluated at the annual meeting of the American College of Psychiatrists.

One premise of this trial, supported by other research, is that entrenched gender stereotypes drive both male and female behavior and must be addressed directly for change, said Molly Carnes, MD, professor of psychiatry at the University of Wisconsin, Madison.

The initial results of the trial, which randomized academic departments at the University of Wisconsin to participate in habit-changing workshops or to serve as controls, were published almost 3 years ago (Acad Med. 2015 Feb;90[2]:221-30). It is the most recent follow-up (Devine et al. J Exp Soc Psychol. 2017 Nov;73:211-5) that corroborates that long-term changes are possible with intervention.

The published findings showed that, when 1,137 faculty members from 46 departments in the experimental arm were compared with 1,153 faculty members from 46 departments in the control arm, there were significant improvements in the experimental arm in surveyed attitudes reflecting personal bias awareness ($P = .001$) and willingness to support gender equity ($P = .013$).

These changes in attitude translated into concrete changes in new female faculty hires in the most recent analysis. From 32% in a 2-year period before the workshops, the new female hires climbed to 46% in the 2-year period after the workshops – a relative increase of 44% in the departments participating in the experimental arm. In the control departments, female new faculty hires remained at 32% in both time periods.

"Basically, there are 20 new women faculty members at the University of Wisconsin because of this study," Dr. Carnes said.

The training was not designed to change just male faculty perceptions but perceptions of both males and females. The result was a fundamental change in culture within departments randomized to the experimental arm, according to data generated by a variety of study analyses.

"When we looked at questions about department climate, we found that both male and female faculty members in the experimental groups were significantly more likely to say they fit in their department, they felt respected for their research and scholarship by their colleagues, and they felt comfortable raising personal and family issues even if they conflicted with departmental activities," Dr. Carnes said.

This general attitude change is important because, Dr. Carnes emphasized, women share the cultural biases that can result in reduced female career opportunities in clinical and academic medicine. In addition, women generally are aware that stereotypical positive "agentic" adjectives for men, such as decisive, competitive, and ambitious, often are viewed negatively and generate backlash when applied to women. They therefore act on this awareness.

"Stereotype-based bias is a habit that can be broken, but it requires more than good intentions," said Dr. Carnes, who emphasized that "gender-based assumptions and stereotypes are deeply embedded in the patterns of thinking of both men and women."

As one example, Dr. Carnes cited her work evaluating female resident behavior when leading in-hospital code resuscitations. There are data to show that there is no difference in the effectiveness of male and female resident code leaders, but women typically feel that the assertive, aggressive behavior required for code leadership is "counternormative." After the code, some women feel compelled to apologize to team members for being demanding or assertive, a step that Dr. Carnes attributed at least in part to fear of backlash from stepping out of gender-expected behavior.

The fix is not necessarily suppression of gender-related attributes. Dr. Carnes cited evidence that the stereotypical positive communal adjectives for women, such as nurturing, supportive, and sympathetic, might explain why studies suggest that women are more likely than men to be transformational leaders who inspire team members to contribute beyond their own self-interest in achieving goals.

Ultimately, the fix is replacement of stereotypes that keep men as well as women from defusing biases that "lead to subtle unintentional advantages in academic career advancement for Jack not afforded to Jill," Dr. Carnes said. Based on the low numbers of female leaders in academic medicine decades after medical schools began enrolling women in substantial numbers, she concluded that meaningful change in gender bias is not likely to occur without implementation of specific proactive strategies aimed at challenging current perceptions. Her published study confirms that such strategies can help.

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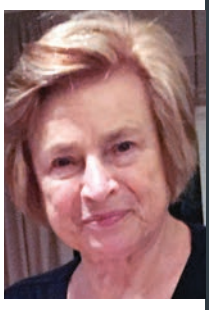
VIEW ON THE NEWS

Giving women a start on university science faculties



Hiring of women increased in the intervention group, compared with the control (odds ratio, 2.23). However, since women faculty left at a higher rate than did men during the same period, the gender distribution within these STEMM departments did not change. It seems that this one-time short workshop altered behavior to allow more highly educated women to get a first faculty position at a prominent university. This is a good start but does not address the problem of women getting to the top on the faculty.

Bevra H. Hahn, MD, is Distinguished Professor of Medicine (emeritus) at the University of California, Los Angeles.

Cyberliability insurance: Should you purchase a policy?

BY ALICIA GALLEGOS
Frontline Medical News

As hackers become more sophisticated, these cybercriminals are finding novel ways to access protected health data, leaving health care providers to pick up the costly pieces of their crimes.

In 2017, there were at least 477 publicly reported health data breaches in the United States, affecting some 5.6 million patients, up from 450 health care breaches in 2016, according to Protenus, a health care cybersecurity vendor that tracks data breaches reported to the U.S. Department of Health & Human Services.

When medical files are stolen, physicians are on the hook for more than just a possible ransom request; they also face thousands of dollars in potential fines, fees, and legal costs, said Joshua R. Cohen, JD, a medical malpractice defense attorney based in New York. To mitigate the consequences, cybersecurity experts say physicians should consider purchasing cyberliability insurance, a relatively new coverage policy that protects against data breaches and subsequent lawsuits.

"A breach is very expensive," said Mr. Cohen, chair for the New York City Bar Association Committee on Medical Malpractice. "You have the fine to the Office for Civil Rights, which can be in the millions of dollars, and you're going to have to ameliorate the breach, which can be hundreds of dollars per person, let alone deal with lawsuits from the patients."

Cyberliability: What's the risk?

Cyberliability refers to legal dangers arising from data breaches, privacy law violations, and ransomware/cyberextortion threats, as well as data loss and business interruption from computer system failures.

Of the 477 breaches in 2017 analyzed by Protenus, 37% were from hacking, 37% resulted from insider incidents, and 16% stemmed from data loss or theft. About 10% of cases resulted from unknown causes, according to the report.

Data breaches caused by hackers and malware attacks are rising in the health care sector, said Katherine Keefe, global head of breach response services for Beazley, a national cyberliability insurer and risk management company. Beazley handled 2,615 data breaches in 2017, more than half of which were health care related, Ms. Keefe said in an interview. The top three causes of health care breaches reported to Beazley in 2017 were accidental disclosure, hack or malware, and insider incidents, according to a recent report from that company

Ms. Keefe noted that Beazley has seen a recent surge of phishing emails – electronic attempts to gain sensitive information for malicious reasons by disguising the sender as a trusted source. The emails often request that employees click on a link and change a password in an effort to steal data or gain access to medical records.

"We see an awful lot of that," Ms. Keefe said. "There's been a real surge in successful phishing emails and social engineering that enables criminals to identify medical practice leaders. It's not hard to dress up an email to look like it's coming from a specific individual. There are all kinds of increasingly sophisticated tactics to trick people into letting criminals into their systems or tricking people into forwarding money or valuable information."

Hackers frequently use phishing emails to get employees to download a payload, the portion of malware that performs malicious actions, Mr. Cohen added. Once downloaded, payloads can do significant damage to a medical practice.

"Once you get hit with these payloads, not only can they start pulling information out of the computer system, they can also start doing things such as turning on laptop cameras, reading emails, listening in on computer microphones," he said. "All they need is one employee to click."

Cybercoverage: Is it needed?

To protect themselves from potential breach expenses, more medical practices are purchasing cyberliability insurance policies. A 2017 survey of 270 insurance brokers and 125 underwriters found that health care has more first-time buyers of standalone cyberliability insurance than does any other industry.

However, Mr. Cohen advises that practices should do their research before buying and be aware of the different types of policies, coverage limits, and insurance options.

"Be careful about what it covers," he said. "Are they going to pay for all the amelioration for all the patients affected? Some policies will cover 'repairing and disinfecting the system,' but they will not likely cover all the [Office for Civil Rights] fines."

The Doctors Company, a national medical liability insurer, provides $50,000 in cybersecurity coverage to all its insured physician members and the option to increase coverage by $1 million in additional protection, according to Crystal Brown, senior vice president of underwriting for the Doctors Company. The coverage protects against regulatory and liability claims arising from theft, loss, or accidental transmission of patient or financial information, as well as the cost of data recovery. Another policy offered protects against claims arising from administrative actions pertaining to utilization, licensing, credentialing, and misconduct.

"In health care, data breaches are not a matter of 'if' but 'when,'" Ms. Brown said in an interview. "With the costs of breach response and potential HIPAA violations now reaching several hundred dollars per stolen medical record, we urge physicians to carefully evaluate their risks and make certain they are adequately protected."

Meanwhile, national medical liability insurer ProAssurance offers health providers a basic cyberliability coverage endorsement in most states on its medical professional liability policy. The insurer also has a branded cyberprogram that allows clients to buy additional and broader coverage at a discounted premium.

"In today's electronic environment, we are hearing about breaches occurring at both small and large health care practices," said Melanie Tullos, vice president for ProAssurance. "Small physician practices are just as vulnerable, if not more so, to a cyberbreach and should take the necessary steps to protect patient data against an attack at all measures, including, but not limited to, purchasing cyberliability coverage.

The price of cyberliability insurance varies by risk and other factors, Ms. Tullos said. Generally, the cost of a $1 million cyberliability policy for a single physician practice is less than $1,000, whereas a group of 10 physicians can pay up to $8,000-$9,000, she said in an interview.

Beazley offers policies that cover the expenses and services associated with investigating whether a data breach has occurred, responding to breaches, and handling liability that may arise from the breach, said Ms. Keefe, of Beazley, which works with companies such as the Doctors Company to provide coverage and also works with state-run malpractice programs to offer a cyberliability component for a small additional premium, she said.

Ms. Keefe stressed that cyberliability coverage can ensure that physician practices don't run up a hefty bill in the event of a data breach by paying for separate specialists and damage control.

"One of the reasons doctors should have cyberliability coverage are the costs associated with figur-

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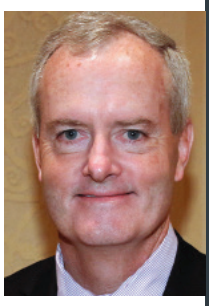
VIEW ON THE NEWS



Michael E. Nelson, MD, FCCP, comments: Being old enough to remember a paper chart and scheduling book, I can't help but marvel at the how the electronic health record (EHR) has fallen short of its expectations and added to the cost of medical care. Well, let's add cybersecurity insurance to the cost of doing business. While I love the ability to look at a chest x-ray or CT without a viewbox, I can't think of many other things that the EHR has done to make me a more efficient physician. It has, however, spawned many cottage industries that provide "must have" services with their attendant fees. The ever-increasing regulatory and administrative burdens and costs placed on physicians' practices is making it impossible for smaller practices to remain financially viable, leaving smaller communities without medical services. I don't think this was the intent when we decided to "modernize" medicine. It makes me want to go back to those Halcyon days of the paper chart – try phishing one of those, you hackers.

Expert argues for improving MACRA, not scrapping it

BY DENISE FULTON
Frontline Medical News

Even given the notable problems and challenges associated with Medicare's Merit-Based Incentive Payment System (MIPS), the program should be improved via pilot programs and demonstration projects, according to Gail R. Wilensky, PhD, economist and senior fellow at Project Hope and a former top health aide to President George H.W. Bush.

The Medicare Payment Advisory Committee (MedPAC) is set to recommend to Congress that the MIPS portion of the value-based reforms enacted under the Medicare Access and CHIP Reauthorization Act (MACRA) be eliminated and replaced with a Voluntary Value Program. MedPAC's report is due to Congress in March.

"Although I agree with MedPAC about the problems it has identified, I am also concerned about the commission's proposal," Dr. Wilensky wrote in an editorial published in the New England Journal of Medicine (doi: 10.1056/NEJMp1801673). She noted that a lack of support from major medical associations, combined with the impending midterm elections, means that it would be challenging to get a legislative fix through Congress.

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VIEW ON THE NEWS

Michael E. Nelson, MD, FCCP, comments: Dr. Wilensky made some cogent arguments as to why scrapping MIPS may not be such a good idea. In my mind, however, the final paragraph of the editorial was the most important. "Practicing physicians need make their views about the MIPS and its alternatives known to their representative medical groups and, if necessary, to their representatives in Congress as well. In the past, practicing clinicians have been woefully bad at making their voices heard. Now is a good time for that to change." Your future is being decided without you. The squeaky wheel gets the grease.

Continued from previous page

ing out what to do if patient records are lost or stolen," she said. "The cost of hiring a lawyer, hiring a forensics investigator to assess the situation, the cost of notifying the patients, and taking all the steps required by HIPAA can really add up. Most practices don't have those costs built into their annual budgets. A cyberpolicy acts as a buffer against those expenses."

Risk: Can it be managed?

Of course, there is plenty that practices can do to prevent – and protect themselves from – a health data breach before it happens. Providing employee awareness training is an important step, said Craig Musgrave, chief information officer of the Doctors Company. Institute a training program for staff at all levels and go over the basics, such as refraining from opening emails from senders they don't know, Mr. Musgrave wrote in a recent column. Updating all software regularly and backing up data is also essential. And Mr. Musgrave emphasizes the importance of "whitelisting."

"Health care systems are fragmented in their management of systems and data," Mr. Musgrave wrote in his column. "Their ability to patch legacy systems and employ cybersecurity staff varies enormously. Therefore, application whitelisting is essential. Rather than blacklisting known malicious software, an application whitelist prevents the launching of any executable program (known or unknown) that does not have explicit authorization. This, in combination with strong firewalls and network segmentation tools like micro-segmentation, provides stronger security."

In addition, consider implementing data security policies and incident response protocols, as well as employee training on securing patient data, ProAssurance's Ms. Tullos said.

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MedPAC to Congress: Eliminate MIPS

BY GREGORY TWACHTMAN
Frontline Medical News

The Medicare Payment Advisory Commission has formally recommended to Congress that it repeal the Merit-based Incentive Payment System track of Medicare's Quality Payment Program.

MedPAC "has concluded that ... the Merit-Based Incentive Payment System (MIPS) will not fulfill its goals and therefore should be eliminated," the commission said in its March 15 report to Congress. MedPAC added that the "basic design of MIPS is fundamentally incompatible with the goals of a beneficiary-focused approach to quality measurement."

The commission notes that the design of MIPS measures quality and adjusts payments based on measures chosen by the individual physician. "But a system built on this design will be inequitable, because clinicians will be evaluated and compared on dissimilar measures. In addition, many clinicians will not be evaluated at all because, as individuals, they will not have a sufficient number of cases for statistically reliable scores."

MedPAC adds that, by the Centers for Medicare & Medicaid Services' own estimates, more than half of clinicians will be exempt from reporting on MIPS based on the low-volume threshold that exempts providers who bill for $90,000 or less in Medicare claims or see 200 or fewer Medicare patients.

The advisory panel also highlighted other flaws. Those include MIPS' onerous reporting burden; measures that do not allow for meaningful comparisons among clinicians; differing rules for clinicians depending on location, practice size, and other factors; and payment adjustments that could vary wildly from year to year, creating financial uncertainty for physicians.

The commission, which voted 14-2 in favor of eliminating MIPS, also recommended it be replaced with a "voluntary value program." But it has offered Congress only a conceptual direction for that replacement program.

"This voluntary value program (VVP) is based on the premise that patient outcomes rely on the combined contributions of clinicians and emphasizes that quality improvement is a collective effort," according to the report.

The VVP would measure all clinicians based on the same set of measures: clinical quality, patient experience, and value. And it would do so on a population level, rather than the individual patient level.

MedPAC sees the VVP not as an end goal in the transition to paying for value but rather a stepping stone to get clinicians more comfortable with value-based payments en route to moving into the QPP's advanced alternative payment model (A-APM) track.

MedPAC "has concluded that ... the Merit-based Incentive Payment System (MIPS) will not fulfill its goals and therefore should be eliminated," the commission said.

"A VVP's penalties and rewards might not be significant enough to meaningfully change clinician behavior," the report stated. "However, the intent is to get clinicians comfortable with being measured in a manner similar to the way they would be in A-APMs. With that experience, clinicians would be poised to form or join robust A-APMs, under which the risk and reward are more meaningful, and the potential for true delivery system reform is within reach."

There was a near unanimous consensus among MedPAC commissioners that MIPS is flawed, but not all commissioners were ready to give up on it – especially considering how much clinicians have already invested in the program.

MedPAC also heard from the American Medical Association, which voiced opposition to the idea of ending MIPS. In addition, the commission received written feedback from physicians against its proposal.

Other experts, such as Gail R. Wilensky, PhD, support preserving MIPS. (Some of Dr. Wilensky's comments on this topic are summarized in a separate article on this page.)

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CHEST NETWORKS

Palliative care screening, sleep devices, novel biologics

Palliative and end-of-life care

Nurse-driven palliative care screening

Palliative care (PC) aims to improve quality of life for patients with a life-threatening illness, providing holistic patient-centered support along the continuum of the disease process. Although frequently implemented in critical care settings, integrating PC in the neuro ICU has been difficult to adopt in practice due to the uncertainty in prognostication of definitive outcomes and practice culture beliefs such as the self-fulfilling prophecy (Frontera, et al. *Crit Care Med.* 2015;43[9]:1964; Rubin, et al. *Curr Opin Crit Care.* 2017;23[2]:134; Knies, et al. *Semin Neurol.* 2016;36[6]:631).

DR. McCAMEY

At our institution, a nursing education project was conducted to pilot nurse-driven PC screenings on admission to the neuro ICU. The project evaluated nurse comfort and knowledge with identifying and recommending PC consults. Pre- and post-intervention surveys revealed that education and introduction of a PC screening tool significantly increased nurse comfort and knowledge of PC eligibility.

The screening also revealed that 62% of patients demonstrated a PC need. This pilot highlighted the neuro ICU patient population's need for routine PC screenings and that nurse-driven screenings can provide early identification of potential PC consultations.

PC in the neuro ICU can exist to contribute to successful outcomes in patient and family care. Within neurocritical care, incorporating PC is essential to provide extra support to patients and families (Frontera, et al. 2015).

For these reasons and data from the project, nurse-driven screening may encourage appropriate early PC consults. Patient-centered care is the ultimate goal in the management of our patients. Nurse-driven PC screening can help bring various unmet PC needs to the health-care team for opportunities that might not have been met or otherwise assessed. Consider implementing nurse-driven PC screening protocols at your institution to aid in collaborative and proactive interdisciplinary care.

Danielle McCamey, ACNP
Steering Committee Member

Sleep medicine

Diagnostics, devices, and sleep

The past several months have been busy for the Sleep Medicine NetWork. We have been working to represent the interests of our membership and our patients in many arenas.

Devices coded as **E0464**, defined as life support mechanical ventilators used with mask-based ventilation in the home are being more frequently used. According to the Office of the Inspector General (OIG), there has been an 89-fold increase in billing for **E0464** ventilators for Medicare and its beneficiaries between 2009 and 2015, increasing from $3.8M to $340M. In response, the Agency for Healthcare Research and Quality (AHRQ) requested a response to specific questions related to these devices.

DR. DAS

The CHEST Sleep Medicine NetWork, in conjunction with NAMDRC, submitted a document emphasizing the unique needs of patients of differing disease states (ie, how someone with neuromuscular disease differs from one with COPD) and why some patients may require an **E0464** device. The ability of CHEST staff and leadership to streamline evaluation and response allowed our voice to be heard in real-time.

In 2018, the CHEST Sleep Medicine NetWork will be participating in a Federal Drug Association-sponsored workshop entitled "Study Design Considerations for Devices including Digital Health Technologies for Sleep-Disordered Breathing (SDB) in Adults," along with other national organizations and leaders in our field. This workshop will address available technologies for the diagnosis, monitoring, and treatment of SDB, as well as trends for digital health technologies and clinical trial design considerations.

Finally, the Sleep Medicine NetWork has wasted no time after a successful CHEST 2017 in Toronto in planning for the next annual meeting in San Antonio. We are excited to present an exciting curriculum in Sleep Medicine at CHEST 2018, so stay tuned.

Aneesa M. Das, MD, FCCP
NetWork Chair

Occupational and environmental health

Post-deployment lung disease

Since the early 1990s, ongoing military deployments to Southwest Asia remain a unique challenge from a pulmonary symptomology and diagnostic perspective.

Various airborne hazards in the deployment environment include geologic dusts, burn pit smoke, vehicle emissions, and industrial air pollution. Exposures can give rise to both acute respiratory symptoms and, in some instances, chronic lung disease. Currently, data are limited on whether inhalation of airborne particulate matter by military personnel is linked to increases in pulmonary diseases (Morris MJ, et al. *US Army Med Dep J.* 2016:173).

Over the last 17 years, we learned that acute eosinophilic pneumonia and exacerbation of preexisting asthma is well documented, and the development of uncommon pulmonary disorders, such as constrictive bronchiolitis, remains controversial (Morris MJ, et al. *Ther Adv Respir Dis.* 2013;7[4]:235).

Ongoing research by the Veterans Affairs continues to enroll post-deployed personnel in an Airborne Hazard and Burn Pit Registry. Past approaches in evaluation of deployed individuals ranged from common tests such as spirometry, HRCT scanning, full PFTs, bronchoprovocation challenges, and, in some instances, lung biopsies (Krefft SD, et al. *Fed Pract.* 2015;32[6]:32). More novel evaluations of postdeployment dyspnea include impulse oscillometry, exhaled nitric oxide, bronchoscopy, and cardiopulmonary exercise testing (Huprikar, et al. *Chest.* 2016;150[4]:S934A).

Members of the CHEST Occupational and Environmental Health NetWork are currently updating comprehensive approaches to evaluate military personnel with chronic respiratory symptoms from deployments. Continued emphasis, however, should be placed on diagnosing and treating common diseases such as asthma, exercise-induced bronchospasm, GERD, and upper airway disorders.

Pedro F. Lucero, MD, FCCP
Steering Committee Member

Clinical pulmonary medicine

Biologics – Birth of a new era of precision management in asthma

An estimated 10% to 20% of patients with severe uncontrolled asthma do not respond to maximal best standard treatments, leading to substantial health-care costs. A paradigm shift is now underway in our approach to the care of these patients with the emergence of novel biologics targeting the complex and interconnected inflammatory pathways in asthma that result in a diverse profile of asthma endotypes and phenotypes (Fig 1).

Current FDA-approved biologics primarily target patients with a T2 high phenotype (Table1).

Table 1: Biologics currently approved in asthma

Biologic agent	Target	Route	Dosage	Anaphylaxis warning	CPT code J code
Omalizumab	IgE	SC	Based on weight & IgE 150-375 mg every 2-4 weeks	Yes	**96372 J2182**
Mepolizumab	IL-5	SC	100 mg every 4 weeks	No	**96372 J2357**
Reslizumab	IL-5	IV	3 mg/kg every 4 weeks	Yes	**96365 J2786**
Bernalizumab	IL-5 Receptor-a	SC	30 mg every 4 weeks for 1st 3 doses then every 8 weeks	Yes	**96372 J3490** (temp)

Table 2: Biologics in development

	Target
Quilizumab	IgE M1 epitope
Legelizumab	IgE Ce3 domain
Pitrakinra	IL-4/ IL-13
Altrakincept	IL-4 / IL-13
Pascolizumab	IL-4
Lebrikizumab	IL-13
Trakolinumab	IL-13
Anrukinzumab	IL-13

Dupilumab binds to the alpha unit of the IL-4 receptor and blocks both IL-4 and IL-13. It shows potential efficacy in patients with T2 high asthma

Continued on following page

AMA Insights

As many who read *CHEST® Physician* may know, we have a nucleus of dedicated volunteers who give unselfishly of their time and talent to represent our members in the area of "regulatory advocacy" and "policy advocacy" in the areas of pulmonary, critical care, and sleep medicine. It is our goal to recognize and support this valuable group of individuals who represent us in the space of coding and reimbursement, RUC activities, relationships with organizations like the ACP and the AMA, as well as our sister societies, such as ATS, SCCM, NAMDRC, CCNA, APSR, ALAT, and ERS, among others.

One of our goals, in addition to recognizing this group, is to identify and mentor the next generation of representatives. A great example of this mentorship is reflected in our involvement with the AMA. Dr. Bob McCaffree has represented CHEST for 22 years and is now mentoring Dr. Raj Desai who will be assuming this role of AMA Delegate this year. Special thanks to Dr. McCaffree for his unselfish service in this capacity and for his mentorship of Dr. Desai. I hope that you enjoy this and future *CHEST® Physician* articles summarizing and reflecting on the activities pertinent to CHEST at the AMA.

John Studdard, MD, FCCP
CHEST President

Collaborating with societies: CHEST and AMA

BY NEERAJ R. DESAI, MD, MBA, FCCP; AND D. ROBERT MCCAFFREE, MD, MSHA, MASTER FCCP

While the American Medical Association (AMA) is the oldest and largest national medical association, many physicians, both members and nonmembers, have limited understanding of the policies, processes, and strategic foci of the AMA. It is our goal to inform our membership about the workings of the AMA and how those interact with the goals of CHEST and our members. We hope to do this by publishing periodic articles in *CHEST® Physician*. One of the authors (DRM) has been the CHEST delegate to the AMA for more than 20 years, and the other (NRD) is CHEST's new delegate.

The AMA was founded in 1847 at a convocation of physicians following a call by Dr. Nathan Davis at the New York Medical Society for such a convocation to establish a national organization of physicians "to promote the science and art of medicine and the betterment of public health." One early focus was the development of a Code of Ethics, which remains a major focus of the AMA. The current strategic plan has three major goals:

- Create thriving physician practices.
- Create the medical school of the future.
- Improve health outcomes.

We will expand on these in future articles.

The AMA is both an individual member organization and a federation of geographic, ie, county and state, societies and specialty societies, as well as the uniformed services and the VA. It is this federation that comprises the House of Delegates (HOD or House), which is the principle policy-making body of the AMA. The number of delegates from each member organization (now numbering more than 170 organizations) depends on the number of individual AMA members among that organization's members. Due to recent bylaws changes, CHEST now has two delegates. The HOD meets twice per year to establish policy on health, medical, professional, and governance matters, as well as the principles within which the AMA's business activities are conducted.


DR. DESAI


DR. McCAFFREE

Most policies originate via resolutions submitted by individuals or societies. These resolutions then go to one of several Reference Committees for open discussion. These committees then report their recommendations back to the House, which then discusses and votes on the recommendations. In some instances, the question is referred for further studies by one of several councils, whose reports go to the Board of Trustees or back to the House.

Most member societies meet in caucuses or Section Councils prior to the voting in the House to discuss the pending business. The Specialty and Service Society (SSS) is the largest caucus in the AMA's House of Delegates. The SSS meets twice annually in conjunction with the Interim and Annual Meetings of the HOD. There are two categories of groups in the SSS: those societies that have seats in the HOD and those seeking admission to the house.

SSS groups in the HOD include:

- 119 national medical specialties
- 2 professional interest medical associations
- 5 military service groups

An association must first be represented in the SSS for 3 years and meet the required number of AMA members before it is eligible to seek admission to the HOD.

The American College of Chest Physicians (CHEST) is an active member of the SSS but also joins with other societies of similar interests in the Section Council on Chest and Allergic Diseases. This caucus includes the ATS, SCCM, ASSM, and several allergy societies. Through the HOD, the SSS, and the Section Council, CHEST can partner with the AMA and other societies, such as ATS, to support each other's resolutions or important regulatory issues.

In summary, the AMA plays an important role in many areas of interest to our members. And, it can be a useful forum for connecting with societies with similar interests in directing advocacy and setting policy. We plan to continue this update in future issues of *CHEST® Physician*.

References

1. https://www.ama-assn.org/content/ama-house-delegates Accessed: January 28, 2018
2. https://www.ama-assn.org/practice-management/ama-steps-forward-practice-improvement-strategies Accessed: January 28, 2018

Continued from previous page

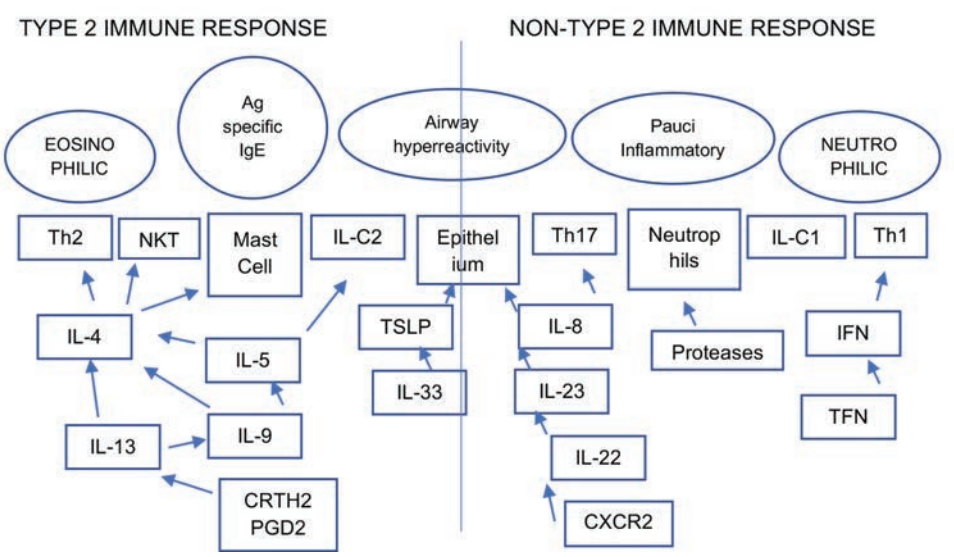
with or without eosinophilia but has not yet received FDA approval.

Multiple newer biologics are currently in development (Table 2).

Pulmonologists need to get familiar with the logistics of administration of these novel agents. The two common methods of administering biologics are (1) buy and bill – where the provider buys the drug directly from the distributor; and (2) assignment of benefits (typically administered by a Pharmacy Benefit Manager) - specific dose of the medication is shipped to the physician's office and physician only bills for the administration. CPT and J codes are shown in Table 1.

Shyamsunder Subramanian, MD, FCCP
Steering Committee Member

Figure 1: Inflammatory pathways in asthma and endotype.



SAVE LIVES: Clean your hands

WHO's global annual call to action for health-care workers

The World Health Organization (WHO) has announced its annual SAVE LIVES: Clean Your Hands 2018 campaign (Saito, et al. *J Hosp Infect.* 2018;98[4]:321), designating May 5, 2018, as world hand hygiene day.

Health-care-associated infections are a major patient safety problem. Unfortunately, their spread is common in hospitals and ICUs around the globe. The vehicle for these infections, including multidrug-resistant organisms, is frequently the contaminated hands of health-care workers. Health-care-acquired infections, as any other infection, can lead to sepsis and death. Infections acquired in the ICU are especially deadly, with mortalities that can be as high as 80%. Proper hand hygiene, despite being simple and inexpensive, is the single most important means of reducing the prevalence of hospital-acquired infections and the spread of antimicrobial resistance.

We have known about the significance of hand washing since the early 19th century. More recent data show that hand washing can reduce the overall prevalence of hospital-acquired infections and the cross-transmission of multidrug-resistant organisms. It is estimated that we can prevent 15% to 30% of these infections with adequate hand washing alone.

Despite the clear benefit and the understanding of the importance of hand washing, compliance with this simple intervention is only about 50%. Health-care workers tend to overestimate these rates, self-reporting a compliance of 75%. Even the latter number represents a lot of missed opportunities, and we must do something about it.

A multifaceted approach that combines education with written material, reminders, and continued feedback on performance can have an important effect on hand washing compliance and rates of hospital-acquired infections.

Sepsis is the single most important cause of death in hospitals in the United States. The campaign (http://www.who.int/infection-prevention/campaigns/clean-hands/en/), sponsored by the World Health Organization, should serve as a reminder to all health-care workers about the importance of adequate hand washing and as an opportunity to improve our compliance moving forward.

Despite the progress made, there is still a lot of room for improvement. We can have an impact on the number of deaths from sepsis by preventing them to occur in the first place. Wash your hands and do it well, it does not cost us anything.

Remember: It is in our hands – prevent sepsis and save lives!

Shruti Gadre, MD
Steering Committee Member, Critical Care NetWork
Angel Coz, MD, FCCP
Chair, Critical Care NetWork

In memoriam

W. Gerald Rainer, MD, FCCP, died November 14, 2017, one day after his 90th birthday Dr. Rainer was President of the American College of Chest Physicians in 1982-1983. He practiced thoracic and cardiovascular surgery for 50 years with St. Joseph Hospital in Denver as his professional home.

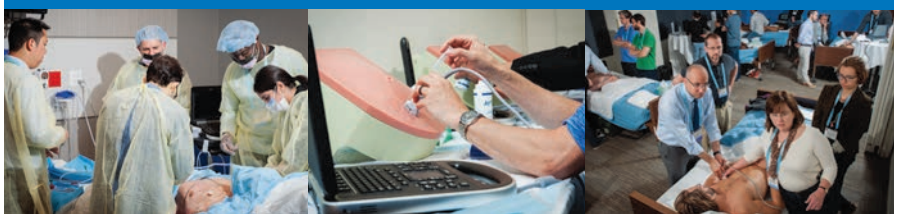
He was a respected leader, researcher, and educator, helping and mentoring countless residents, fellows, and many other health-care professionals. Dr. Rainer was also a distinguished clinical professor of surgery at the University of Colorado School of Medicine and served on many University boards and committees.

He published prolifically in many respected surgical journals and was able to masterfully blend his private practice with strong academic involvement.

As President of the American College of Chest Physicians and many other respected medical and surgical organizations, he was also actively involved in international professional societies. CHEST extends its condolences to Dr. Rainer's wife of 67 years, Lois, and to his family and friends.

CHEST®

2018 Education Calendar



Live Learning Courses

Courses held at the CHEST Innovation, Simulation, and Training Center in Glenview, Illinois.

Bronchoscopy Procedures for the ICU
May 5-6

Advanced Critical Care Echocardiography
June 1-3

Difficult Airway Management
June 8-10 | September 7-9

Lung Cancer: A Multidisciplinary Course for Pulmonologists Covering Current Paradigms for Diagnosis and Management
July 13-15

Bronchoscopy and Pleural Procedures for Pulmonary and Critical Care Medicine Fellows
July 20

Mechanical Ventilation: Advanced Critical Care Management
July 26-28

Advanced Diagnostic and Therapeutic Bronchoscopy
August 4-5

Cardiopulmonary Exercise Testing (CPET)
August 10-12

Critical Skills for Critical Care: A State-of-the-Art Update and Procedures for ICU Providers
August 24-26

Ultrasonography: Essentials in Critical Care
September 13-15
November 29-December 1

Comprehensive Bronchoscopy With Endobronchial Ultrasound
September 20-22

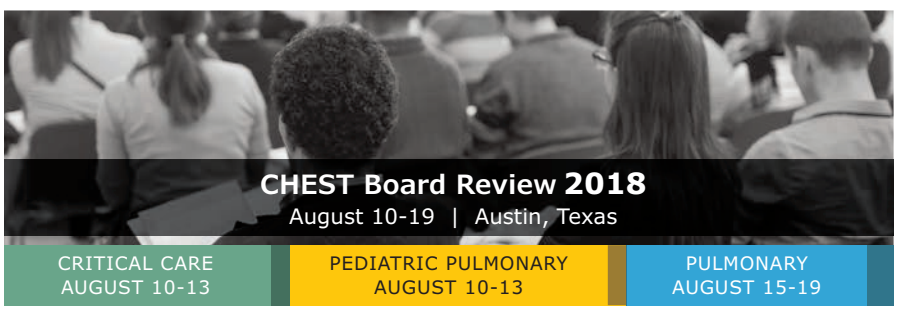
Comprehensive Pleural Procedures
November 3-4

Critical Care Ultrasound: Integration Into Clinical Practice
November 9-11

Extracorporeal Support for Respiratory and Cardiac Failure in Adults
December 7-9

Advanced Critical Care Board Review Exam Course
December 7-9

Learn More **livelearning.chestnet.org**



Calendar subject to change. For most current course list and more information, visit livelearning.chestnet.org.

This month in the journal *CHEST*®

Editor's Picks

RICHARD S. IRWIN, MD, MASTER FCCP
Editor in Chief, the journal CHEST®

GIANTS IN CHEST MEDICINE
Professor Emeritus Elizabeth F. Juniper, MCSP, MSc
By Dr. P. M. O'Byrne

ORIGINAL RESEARCH
A Population-Based Cohort Study on the Drug-Specific Effect of Statins on Sepsis Outcome.
By Dr. C-C Lee, et al.

A Multicenter Randomized Trial of a Checklist for Endotracheal Intubation of Critically Ill Adults.
By Dr. D. R. Janz, et al.

Determinants of Unintentional Leaks During CPAP Treatment in OSA.
By Dr. M. Lebret, et al.

EVIDENCE-BASED MEDICINE
Screening for Lung Cancer: CHEST Guideline and Expert Panel Report.
By Dr. P. J. Mazzone, et al.

Treating Cough Due to Non-CF and CF Bronchiectasis With Non-pharmacological Airway Clearance: CHEST Expert Panel Report.
By Dr. A. T. Hill, et al.

New strategic plan for CHEST

We are pleased to announce the completion of a new, multiyear strategic plan for CHEST. Over the past few years, key stakeholders have provided essential input, resulting in a plan that identifies a very focused set of priorities we'll pursue to help achieve our overarching strategy. Having selected these priorities, which leverage our strengths and strategic advantages, we are committed to dedicating sufficient resources toward their accomplishment over the next several years.

Each year, the plan will be reviewed and modified to reflect changes to CHEST priorities.

A strategic plan is an important tool for our organization because it truly does focus and direct our efforts and resources. Guided by our 2013-2017 strategic plan, we were able to accomplish the following:

- Developed events, products, and services that produced meaningful education for the CHEST community and generated positive financial margins;
- Optimized our membership model to increase engagement of all clinicians on the health-care team;
- Enhanced our global presence through guideline development and increased educational offerings;
- Launched a new Association Management System (AMS) and made strides to becoming a data-driven organization;
- Built and moved into a new building that enhanced our ability to develop and host courses in the CHEST Innovation, Simulation, and Training Center;
- Increased our visibility through our rebrand as "CHEST";
- Fostered relationships and collaborated with other organizations to promote lung health through the CHEST Foundation; and
- Met our budget goals and financial covenants with our bank, and increased the CHEST Foundation's corpus for grants and awards.

This new strategic plan can be found on chestnet.org under the "About" section. As members of CHEST, we invite you to review what's outlined and become familiar with what the plan encompasses. This plan provides details to help you understand the future direction of CHEST, and we know you'll support us in these important endeavors.

CRITICAL CARE COMMENTARY

Life after angiotensin II

BY JONATHAN CHOW, MD; AND ASHISH K. KHANNA, MD, FCCP

Hypotension is an often-underestimated adversary. Even brief periods of intraoperative mean arterial pressure (MAP) <65 mm Hg increase the odds of both myocardial ischemia and acute kidney injury in the postoperative period. The threshold may be even higher in the postoperative critically ill population (Khanna, et al. *Crit Care Med.* 2018;46(1):71). Hypotension that is refractory to high-dose vasopressors is associated with an all-cause mortality of 50% to 80%.

The vasopressor toolbox centers around escalating doses of catecholamines with or without the addition of vasopressin. High-dose catecholamines, albeit a frequent choice, is associated with adverse cardiac events (Schmittinger, et al. *Intensive Care Med.* 2012;38[6]:950) and is an independent predictor of ICU mortality (Sviri, et al. *J Crit Care.* 2014;29[1]:157).

The evidence behind angiotensin II

Angiotensin II (AT II) is a naturally occurring hormone in the renin-angiotensin-aldosterone (RAA) system that modulates blood pressure through direct arterial vasoconstriction and direct stimulation of the kidneys and adrenal cortex to release vasopressin and aldosterone, respectively.

Positive results from the recent phase 3 trial for AT II have offered hope that this agent would add the needed balance to the current scarcity of vasopressor options (Khanna, et al. *N Engl J Med.* 2017;377[5]:419). AT II would provide the missing piece in the jigsaw that would allow the intensivist to manage refractory hypotension, while keeping a multimodal vasopressor dosing regimen within therapeutic limits.

Irvine Page and coworkers are credited with most of the initial work on AT II, which they did nearly 70 years ago. Anecdotal use in humans has been reported since the early 1960s (Del Greco, et al. *JAMA* 1961;178:994). After a prolonged period of quiescence, the Angiotensin II in High-Output Shock (ATHOS) pilot study, which was done in 2014 as a single-center "proof of concept" study of 20 patients, reinvigorated clinical enthusiasm for this agent (Chawla, et al. *Crit Care.* 2014;18[5]:534). ATHOS demonstrated the effectiveness of AT II at decreasing norepinephrine (NE) requirements of patients in vasodilatory shock (mean NE dose in AT II group 7.4 ug/min vs 27.6 ug/min in placebo, *P*=.06). These promising results were followed by ATHOS-3, a phase 3, double-blind, multicenter randomized controlled trial of stable human synthetic AT II. This trial was conducted under a special protocol assessment agreement with the US Food and Drug Administration (FDA). A total of 344 patients with predefined criteria for vasodilatory shock were randomized to AT II or placebo as the intention-to-treat population. The primary end-point was a response in MAP by hour 3 of AT II initiation; response was defined as either a MAP rise to 75 mm Hg or an increase in MAP ≥ 10 mm Hg. The primary end-point was reached more frequently in the AT II group than in the placebo group (69.9% AT II vs 23.4% placebo, OR 7.95, 95% CI 4.76-13.3, *P*<.001). The AT II group had significantly lower cardiovascular sequential organ failure assessment (SOFA) scores at 48 hours and achieved a consistent decrease in background vasopressor doses. Post-hoc data analysis found that the highest benefit was in patients who were AT II deficient (high ratio of AT I:AT II) (Wunderink, et al. *Intensive Care Med Exp.* 2017;5(Suppl 2):44). The patients who were AT II depleted and received placebo had a higher hazard ratio of death (HR 1.77, 95% CI 1.10-2.85, *P*=.019), while those who were AT II depleted and received AT II had a decreased risk of mortality (HR 0.64, 95% CI 0.41-1.00, *P*=.047). The data suggest not only that AT II levels may be predictive of mortality in vasodilatory shock but also that exogenous AT II administration may favorably modulate mortality in this population. Further, a subset data analysis of severely ill patients (APACHE II scores > 30) showed that those who received AT II and standard vasopressors had a significantly lower 28-day mortality compared with patients who only received standard vasopressors (Szerlip, et al. *Crit Care Med.* 2018;46[1]:3). Considering that the endothelial cells in the lungs and kidneys are locations where AT I is hydrolyzed by angiotensin-converting enzyme (ACE) into AT II, patients receiving ACE-inhibitors and individuals with pulmonary or renal disease are at greatest risk for AT II deficiency. As such, the use of AT II in the extra-corporeal membrane oxygenation (ECMO), post cardiopulmonary bypass, acute respiratory distress syndrome (ARDS), and renal failure populations are of future interest.

DR. CHOW

DR. KHANNA

Is there a downside?

Appropriate caution is necessary when interpreting these outcomes. One criticism that ATHOS-3 received was the use of a MAP goal of 75 mm Hg, a higher value than currently recommended by clinical guidelines, in the first 3 hours of AT II administration. Because this was a phase 3 trial, both the safety and efficacy of the drug were examined. These goals are difficult to accomplish if simultaneously manipulating other variables. Therefore, to isolate the effects of drug efficacy and safety, a higher MAP goal (75 mm Hg) was established to minimize any effect from varying background vasopressor doses during the first 3 hours of the study.

Furthermore, ATHOS-3 did find an increase in venous and arterial thromboembolic events in patients who received AT II (13% AT II vs 5% placebo). Previously, a systematic review of over 30,000 patients did not report this increased thromboembolic risk (Busse, et al. *Crit Care.* 2017;21[1]:324). According to the package insert, all patients receiving AT II should receive appropriate thromboembolic prophylaxis if medically indicated.

Where does AT II fit in our algorithm for resuscitation and the vasopressor toolbox?

Data from Wunderink et al indicate a potential mortality benefit in populations who are AT II depleted. However, we can only infer who these patients may be, as no commonly available assay can measure AT I and AT II levels. ATHOS and ATHOS-3 used AT II late during resuscitation, as did the Expanded Access Program (EAP) of the FDA, which gave physicians preliminary access to AT II while it was undergoing FDA review. Using similar inclusion criteria as ATHOS-3, the EAP did not permit patients to receive AT II until doses greater than or equal to 0.2 ug/kg/min of NE-equivalents were reached.

In a recently published case report, AT II was successfully used in a patient with septic shock secondary to a colonic perforation (Chow, et al. Accepted for e-publication: *A&A Practice.* April 2018.). This individual was in vasodilatory shock despite standard resuscitation, 0.48 ug/kg/min of NE, and 0.04 units/min of vasopressin. Methylene blue and hydroxocobalamin had failed to relieve the vasoplegia, and only after the initiation of AT II at 40 ng/kg/min, the patient could be relieved of vasopressors and survived to be discharged from the hospital. In our opinion, best clinical practices would allow for an early multimodal vasopressor regimen that should include AT II at the earliest sign of rapid clinical decline (Jentzer, et al. *Chest.* 2018. Jan 9. pii: S0012-3692(18)30072-2. doi: 10.1016/j.chest.2017.12.021. [Epub ahead of print]).

Angiotensin II was recently approved by the FDA in December 2017 and is now available on the market for management of vasodilatory shock. This will undoubtedly have a profound impact on the way clinicians treat vasodilatory shock. Previously, we were confined to agents such methylene blue and hydroxocobalamin to rescue patients from profound vasoplegia. However, none of these agents are supported by robust evidence from randomized control trials.

Now, we can openly welcome a new challenger to the campaign, a new hue to the palette of vasopressor colors. This new class of vasopressor makes complete physiological sense and will provide an invaluable tool in our daily battle against sepsis and vasodilatory shock.

Continued on following page

"No consequence" Knowledge Check-In expands

In 2018, ABIM is introducing the new Knowledge Check-In assessment option, an every-2-year assessment option serving as an alternative to the 10-year assessment model. Initially, for 2018, this option will be piloted for both Internal Medicine and Nephrology. In 2019, the Knowledge Check-In will expand to several additional specialties, including Pulmonary Disease. The remaining specialties, including Critical Care Medicine, will become available in 2020.

Previously, ABIM announced that physicians taking the Knowledge Check-In in 2018—the initial year it is offered in Internal Medicine or Nephrology—would have another chance to take it again 2 years later if they were unsuccessful, even if they were due to pass the exam that year. Based on feedback ABIM received from the physician community, this feature is now being extended to include all other Internal Medicine subspecialties in the future. Therefore, if a physician opts to take the Knowledge Check-In the first year it is offered in their subspecialty and is unsuccessful, they will get at least one additional opportunity to take it 2 years later.

For more information visit www.abim.org/checkin.

Continued from previous page

Dr. Chow is Assistant Professor, Division of Critical Care Medicine, Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD; Dr. Khana is Assistant Professor of Anesthesiology, Staff Intensivist, Vice-Chief for Research, Center for Critical Care, Department of Outcomes Research & General Anesthesiology, Anesthesiology Institute, Cleveland Clinic, Cleveland, OH.

Editor's note

For decades, our options to treat patients with profound vasoplegia have been limited to high-dose catecholamines and vasopressin. Clinicians are often faced with the need to initiate multiple catecholamine agents knowing that these drugs stimulate similar receptors. The recent ATHOS-3 trial introduces AT II as a new option for the management of patients with refractory vasodilatory shock. This drug has a distinct mechanism of action that complements the effect of other vasopressors. Moreover, recent data suggest that this new agent is most beneficial in patients who are AT II deficient. Just like cancer therapies have evolved to precision medicine, will we perhaps face the need to better understand and promptly identify patients with AT II deficiency? For now, we have a new player on our vasopressor team.

Angel Coz, MD, FCCP
Section Editor

FDA to host meeting about sleep apnea devices

You are invited to attend this open meeting on April 16, held at the FDA White Oak Campus in Silver Spring, Md. (https://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm596147.htm). The FDA is soliciting ideas or opinions about criteria or processes for FDA review of medical devices to diagnose or treat sleep apnea. CHEST is represented by Dr. Neil Freedman (neilfreedman@comcast.net) and Dr. Barbara Phillips (bphil020@gmail.com) who also welcome your input by email prior to the meeting. Home testing, "apps," and the criteria to diagnose sleep apnea and/or its resolution are among the topics to be discussed.

Bringing respiratory care to asthma clinics in Guyana

BY SHARON ARMSTEAD, EMBA, RRT

How it all started

The study abroad project was truly a goal and vision that came about after returning to Guyana after approximately 46 years. I was born in Guyana but left as a child and returned later and joined a mission group. In 2015, I began a personal journey of missionary service with the team of Bridge Global Medical Missions (BGMM) in Georgetown, Guyana. I was the first respiratory therapist to join the team.

I remember during the first few days in the hospitals I was told that there was "a lot of wheezing" in the EDs. Treating patients consisted of just administrating short-acting nebulizer treatments, but I remember being very impressed with the ICU at the main public hospital, Georgetown Public Hospital Corporation (GPHC), because they had the ventilators I could use. However, physicians only managed the patients while the nurses were left to monitor the ventilators and equipment, which they did not understand.

At the Linden Hospital in Guyana, the ED was constantly full of the "wheezers," and the ICU only had ventilators that were basically nonfunctioning due to language barriers or a lack of biomed professionals. One of my fondest memories was fixing two ventilators from China. I could get the ventilators to work and explain the basic modes because in my mind, it was just a ventilator, and they could see the modes. The problem was the language was all in Chinese! So, we all got together: a Cuban doctor, a Cuban biomed, and a nurse with a translation program and, finally, changed the language to English. It was an interesting day!

When we were on our study abroad trip this past January, I was able to place an intubated patient on that same ventilator. After my first visit to Linden Hospital, I addressed a few of my observations with the medical director, and I will never forget his comment. He said, "I thought respiratory would just come do some nebulizer treatments and show us oxygen."

Study abroad and respiratory care

Then the vision of my project began, because I needed to show him the scope of the practice of a respiratory therapist. I asked Dr. Heyliger-Thomas of BGMM if she could assist me in promoting a study abroad program in Guyana with the Ministry of Health. It was very important for me to bring my students to Guyana for many reasons, the most important being the profession was needed there, and our students would be excellent representatives.

In 2015, the study "Introduction of spirometry into clinical practice in Georgetown, Guyana: quality and diagnostic outcomes" highlighted increased physician referral to the country's only COPD/asthma clinic. I wanted to promote the importance of study abroad and international mission work, especially when promoting the care of asthma and the pulmonary patient, which I believe we did. The main project during study abroad was to test the school-aged children in Linden, thereby showing that there was undiagnosed asthma.

The 2 days that we were in Linden brought the largest sign-up for their clinic. When we did our screening at Mackenzie High School, we were able to utilize the portable spirometers and printer purchased by the CHEST Foundation community service grant. We are still collecting data, but the one thing that was revealed was the difficulty in obtaining medication for the treatment of asthma and COPD in some areas.

This project was also a learning experience for our students in many ways: in how they performed their interviews, how the culture affected the way their patients answered their questionnaires, and even how they performed on the tests. The value to the student and the individual of working within a different culture, far away from the norms of North America, allows them to appreciate their patients, the work they do, and their interprofessional team in a whole new light.

I want this experience to have an impact on each student's life. You are a teacher, an instructor, a mentor, professor, and much more when traveling with 10 students. The most satisfying moment is the transformation you see in them. They are no longer timid and unsure of themselves; they have greater confidence in their abilities and a deeper understanding of the needs of a patient. They finally understand the importance of culture as it pertains to health care.

Students at Mackenzie High School thanking CHEST Foundation donors for their support of a lung screening event at their institution.

Clinicians at Linden Hospital in Guyana in training with Ms. Armstead's team.

Sharon Armstead, EMBA, RRT, is a winner of the 2017 CHEST Foundation Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP. Sharon acts as a Clinical Assistant Professor and is the Director of Clinical Education at Texas State University's Department of Respiratory Care.

The effect of the CHEST Foundation grant

Applying for the CHEST Foundation community service grant was the largest grant I had ever attempted. Having a support system behind you is the most important piece of advice I can give to future grant applicants. I could not have completed my grant without our grant team at Texas State University. They truly had my back; and close to the deadline when it seemed insurmountable, they helped push me through it. The other piece of advice is to have a true vision and stick to that vision. The most difficult part of my project was the budget, prioritizing the things or people that I needed. Honestly, I needed help here, because for me, I needed everything. I had to make choices and leave some things out. I focused on what the actual need was for the many.

My ultimate goal for Guyana is to promote and show the need for respiratory care professionals to have that education offered at the University of Guyana as part of its allied health program and assist those in the application to the International Fellowship Program of the American Association of Respiratory Care—there has never been a fellow from Guyana. I believe that Guyana will have the resources, and with assistance, could achieve the goal. My vision and goal started in 2016, and I want to achieve it in the next 10 years.

I would like to thank all the CHEST Foundation donors from the bottom of my heart. This project was real and, as a CHEST member myself, it encourages me to be a better donor. Thank you—for it was and is much appreciated. Finally, I would like to express my thanks to my Co-Assistant Program Director, Holly Wise (Mass Communications) and Amber Hazelett, RRT (RC assistant), and the BGMM team for their entire support throughout the study abroad journey.

(This article was previous published in CHEST Thought Leaders.)

This grant is supported in full by the CHEST Foundation. Donors like you make grants like this possible. Thank you for your generosity and passion for community service and moving the needle forward on improving patient outcomes. To support community service initiatives, and the next generation of lung health champions, please go to foundation.chestnet.org/donate

New lung cancer screening guideline from CHEST

BY PETER MAZZONE, MD, FCCP

An update to CHEST's lung cancer screening guideline, *Screening for Lung Cancer: CHEST Guideline and Expert Panel Report*, has just been published online in the journal *CHEST*®. This update was made possible by the hard work of my co-authors and the amazing support of the CHEST staff.

Our goal was to update the evidence base for the benefit, harms, and implementation of low-radiation dose chest CT screening, then use this evidence base to produce meaningful and usable recommendations. The process for developing the guideline followed the rigorous methodological standards of CHEST in which the evidence was gathered from a systematic literature review, and the overall quality of the body of evidence was assessed using the GRADE approach. Recommendations were developed and graded based on this assessment.

There are a few aspects of the new guidelines to highlight. First, we have updated some of the core recommendations; second, we have developed new recommendations related to the implementation of high-quality screening; and third, the CHEST approach to guideline development has evolved to allow us to provide recommendations in which the evidence allows and statements based on experience and expert consensus in which it does not. Through this process, we developed six graded recommendations and nine ungraded consensus-based statements.

In this update, a few changes to the core recommendations about who should be screened are worthy to note:

- We have recommended an increase to the upper age of the screen-eligible cohort from 74 to 77, in line with CMS coverage and reflecting the oldest age of participants in the National Lung Screening Trial at the end of the screening period.
- We have directly addressed the cohort of individuals who are at high risk for having/developing lung cancer based on clinical risk prediction calculators but do not meet the current eligibility criteria. We recommended that this cohort should not be routinely screened given the greater potential for this cohort to have comorbid conditions that would influence morbidity from the evaluation and treatment of screen-detected findings and death from any cause. We did, however, state that there will be individuals within the cohort deemed to be at high risk for lung cancer from a clinical risk prediction calculator who are healthy enough to benefit from lung cancer screening and that low-radiation dose CT screening could be considered in these individuals.
- We recommended against low-radiation dose CT screening in cohorts at low risk of developing lung cancer and in individuals with comorbidities that adversely influence their ability to tolerate the evaluation of screen-detected findings, tolerate treatment of an early stage screen-detected lung cancer, or that substantially limit their life expectancy.
- We also highlighted that screening is reserved for patients without symptoms that could be caused by the presence of lung cancer, stressing that all symptomatic patients should receive an appropriate diagnostic evaluation.

Our remaining recommendation and statements are focused on aspects of screening implementation that influence the balance of benefit and harms of screening and lend to an approach to screening that respects patient values. An extensive literature review, followed by a recommendation or statement, is provided to guide programs in the following areas:

- the choice of nodule size to define what constitutes a positive test;
- maximizing compliance with annual screening exams;
- developing a comprehensive approach to lung nodule management;
- minimizing overtreatment of potentially indolent lung cancers;
- the provision of evidence-based tobacco cessation treatment;
- providing effective counseling and shared decision-making visits prior to the low-radiation dose CT scan;
- how to perform the low-radiation dose CT scan;
- structured reporting of the exam results, management of non-nodule findings on the low radiation dose CT; and
- the development of data collection and reporting tools that are capable of assisting with quality improvement initiatives.

Throughout the recommendations and statements, we have tried to be sensitive to the variety of acceptable approaches to screening program organization, ranging from program structures that are entirely decentralized (test ordering, counseling, and management of the findings by the referring provider) to those that are entirely centralized (test ordering, counseling, and management of the findings by the screening program).

Though we have attempted to comprehensively evaluate the literature and balance available evidence with pragmatism and the needs of our patients, we recognize that well-intentioned and informed experts can have different opinions about aspects of our guidelines. This highlights the need for further research to guide the screening community. Most will agree that it is time to increase access to high- quality lung cancer screening programs across the country. We hope that the updated CHEST lung cancer screening guidelines can help catalyze this.

Coinciding with the publication of the guideline, CHEST has developed new e-learning modules on the benefits and harms of CT screening for lung cancer. The modules are based on the CHEST 2018 educational session on the Screening for Lung Cancer Guidelines. The modules are available at chestnet.org/lungcancerscreening.

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Five things to do around the convention center at CHEST 2018

Planning to attend CHEST 2018? We know you're always on the go, so we've come up with a few quick things to do in San Antonio without having to go more than a few blocks outside of the convention center.

KYLE MONAHAN

FLICKR

Whataburger

While some may be hardcore In-N-Out fans, there's another well known burger joint in Texas with a location that happens to be next to the convention center on E Commerce St. Head on over to Whataburger and experience what the company calls a "bigger, better burger."

San Antonio Riverwalk

Want to experience the San Antonio, Texas atmosphere but don't have time for a long excursion? The Henry B. Gonzalez Convention Center is a few steps away from the Riverwalk, which winds throughout the city. Off of the northwest corner of the convention center, take a stroll and experience the picturesque beauty of the San Antonio river, the restaurants, and the bright colorful surroundings.

La Villita Historic Arts Village

Interested in art? Interested in architecture? La Villita, located on the west side of the convention center on S Alamo St, is on the US government's National Register of Historic Places as a Historic District. Take a look at different architectural styles, like adobe, early Victorian, and Texas vernacular limestone buildings. You'll find markers throughout La Villita with information about each building's history. You'll also find local artists, custom art, and unique dining options.

Tower of the Americas

Exit the south end of the convention center to go to the Tower of the Americas for a spectacular view of the city. This 750-foot tall tower has an observation deck, revolving restaurant with panoramic views, a stationary bar, and a 4D theater adventure ride great for the whole family. This is a great stop for lunch, dinner, or a nice afternoon activity.

The Alamo

Lastly, if you have an hour to spare, take a tour of the Alamo that commemorates the 1836 siege and battle. There are free and ticketed activities, including audio or guided tours (ticketed) or history talks, visiting the Alamo Church, exhibitions, and more! Don't forget to stop at the gift shop for a souvenir or two to take home.

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1 Sterling, K. "Long-term Results of the OPTALYSE PE trial" as presented at the International Symposium on Endovascular Therapy (ISET) meeting, Hollywood, FL Feb 2018

2 Piazza, G., et al., A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: the Seattle II study." *Journal of the American College of Cardiology: Cardiovascular Interventions* 2015; 8: 1382-92.

3 Tapson, et al, "Optimum Duration and Dose of r-tPA with the Acoustic Pulse Thrombolysis Procedure for Submassive Pulmonary Embolism: OPTALYSE PE," American Thoracic Society (ATS) Meeting, Washington, DC, May 2017.

The EkoSonic™ Endovascular System is not available for sale in Canada.

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