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Courtesy Susan Millard, MD

“This oral drug therapy is actually treating the underlying problem, as opposed to many of the therapies we have that take hours to nebulize and only work locally in the airways.”

Dr. Susan Millard of Helen DeVos Children's Hospital in Grand Rapids, Mich.

New cystic fibrosis therapy raises hopes for specialists, patients

BY KERRY DOOLEY YOUNG

MDedge News

A newly approved triple-combination modulator to treat cystic fibrosis (CF) has raised expectations of a treatment turning point among patients and specialists. If the early results are sustained, elexacaftor/ivacaftor/tezacaftor (Trikafta) could prove to be the rare case of a much-touted new medicine that meets high expectations.

“CF even in infants causes inflammation, so we know that lung damage can start early and progress,” said Susan Millard, MD, FCCP, of Helen DeVos Children's Hospital in Grand Rapids, Mich., and the local clinical research director for

the pediatric pulmonary and sleep medicine section. “This oral drug therapy is actually treating the underlying problem, as opposed to many of the therapies we have that take hours to nebulize and only work locally in the airways.”

Dr. Millard is the recent past pediatric editor for Chest Physician and has been a local principal investigator at Helen DeVos Children's Hospital for many Vertex-sponsored clinical studies.

The pivotal studies

The Food and Drug Administration approval of Trikafta rested on two pivotal phase 3, placebo-controlled studies, one in patients with two copies of the most common CF mutations, F508del, and

CYSTIC FIBROSIS // continued on page 4

Measles cases surge in 2019

BY THERESE BORDEN

MDedge News

Measles made a comeback in 2019. The Centers for Disease Control and Prevention reported that, in 2019, 1,282 individual cases of measles were confirmed in 31 states, the largest number since 1992. This number is a major uptick in cases, compared with previous years since 2000 when the CDC declared measles eliminated from the United States. No deaths have been reported for 2019.

Three-quarters of these cases in 2019 were linked to recent outbreaks in New York and occurred in primarily in underimmunized, close-knit communities and in patients with links to international travel. A total of 128 of the people who got measles this year were hospitalized, and 61 reported having complications, including pneumonia and encephalitis. The overall median patient age was 6 years (31% aged 1-4 years, 27% aged 5-17 years, and 29% aged at least 18 years).

The good news is that most of these cases occurred in unvaccinated patients. The national vaccination rate for the almost 4 million kindergartners reported as enrolled in 2018-2019 was 94.7% for two doses of the MMR vaccine, falling just short of the CDC recommended 95% vaccination rate threshold. The CDC reported an

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INSIDE HIGHLIGHT



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ABIM's assessment option anticipated to launch in 2022

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Cystic fibrosis patients see improved quality of life // continued from page 1

the second in patients with one copy of F508del and a second mutation that was called a “minimal-function” mutation. The findings have ignited the hopes of many people with CF and their physicians. The drug was approved in October 2019 for patients aged 12 years and older who

have at least one F508del mutation of the cystic fibrosis transmembrane conductance regulator gene. About 90% of patients in the United States have at least one copy of F508del. In the study looking at patients with one copy of F508del, the mean predicted forced expiratory volume in 1 second

increased 13.8% in patients taking the drug versus placebo (N Engl J Med. 2019 Oct 31. doi: 10.1056/NEJ-Moa1908639).

The number of pulmonary exacerbations decreased by 63% in the Trikafta group, compared with placebo. Pulmonary exacerbations were

described as a change in specific symptoms that required treatment with a new oral, intravenous, or inhaled antibiotic. Serious adverse drug reactions that occurred more frequently in patients receiving Trikafta, compared with placebo, were rash and influenza events.

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In the study that included patients with two copies of F508del, on average, the lung function increased 10% versus patients on ivacaftor/tezacaftor at 4 weeks. In addition, there was a 45.1-mmol/L on average decrease in the sweat chloride level in the Trikafta group, compared with ivacaftor/tezacaftor.

A hopeful start

Robert Giusti, MD, a pediatric pulmonologist at New York University Langone Health, is also hopeful. “This could be the kind of treatment that will make a revolution in terms of [cystic fibrosis] care if it can be started very early in life shortly after diagnosis. We anticipate that patients will be disease free for a

longer period of time.”

The Cystic Fibrosis Foundation’s (CFF) “venture philanthropy” initiative played an important role in the development of the drug by Vertex Pharmaceuticals. The CFF has invested many millions of dollars in research by drug companies since the 1980s and was an early backer of Vertex. According to a statement



Dr. Robert Giusti

on the CFF website, the Foundation sold its royalty rights for treatments developed by Vertex for \$3.3 billion in 2014. The drug has a list price of about \$311,000 a year. Payment issues may arise in the future, but for now, Vertex has stated that insurers and some Medicaid programs began paying claims for Trikafta.

Specialists who treat CF now are watching to see how well patients tolerate this highly anticipated drug – and how well it meets expectations. The Therapeutic Development Network, the clinical research division of the CFF, is enrolling patients taking Trikafta in an observational study to follow for long-term follow-up.

Meeting expectations

“[Long-term efficacy is] something that we’re always concerned about. When the drug comes to market, is it going to be as effective as we thought it might be?” said Ryan Thomas, MD, director of the Cystic Fibrosis Center at Michigan State University, East Lansing. The MSU Cystic Fibrosis Center receives funding from the Cystic Fibrosis Foundation.

The FDA called its October approval of Trikafta a “landmark approval.” The agency used several of its programs to prioritize and accelerate the review of Trikafta, giving the medicine fast-track status and a “breakthrough therapy” designation. But this also was the case with another Vertex drug for CF, lumacaftor/ivacaftor (Orkambi), which the FDA approved in 2015. That medicine also had fast-track status and breakthrough therapy designation.

Almost one in five patients could not tolerate treatment with Orkambi, most often because of adverse breathing events, according to a French study published in the American Journal of Respiratory and Critical Care Medicine. The investigators wrote: “Among the 845 patients (292 adolescents, 553 adults) who initiated lumacaftor/

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Dr. Ryan Thomas

Continued from previous page

ivacaftor, 18.2% (154 patients) discontinued treatment, often due to respiratory (48.1%, 74 patients) or nonrespiratory (27.9%, 43 patients) adverse events” and that the discontinuation rate was considerably higher than previously reported in clinical trials.

“We thought [Orkambi] was going to be something that could have a big effect,” Dr. Thomas said. “It turned out that it was harder for people to tolerate than we thought and the improvements weren’t as sustained as we thought they might be. I really don’t think this will end up being the case with Trikafta.”

Longer term data are starting to emerge, which may ease some of the concerns inherent in working with a newer medicine. “These [data] suggest that this is going to be a game changer,” Dr. Thomas said. “If Trikafta is this efficacious, well, we’re talking about having people with CF who will live full lifespans without a lung transplant, and that is so rare.”

The decrease in hospitalizations, improved CT scans, and lower rates of lung function decline suggest it could be “the Holy Grail,” Dr. Thomas said.

A different disease

Trikafta is the latest in a series of improvements of CF treatment in recent decades, recalled Dr. Giusti, who has been in this field for about 3 decades. “It used to be that I attended many funerals for children with CF. Now with patients living longer and healthier lives I am invited to attend their weddings and even their children’s baptisms and bris ceremonies. It is a very different disease than it used to be.”

The promise of Trikafta leaves behind the minority of patients for whom the drug won’t work. This is for the 10% of patients that have rare mutations. That can lead to difficult conversations with parents about why this new option is not a choice for their child, Dr. Millard said. “It

just crushes you, but the Cystic Fibrosis Foundation is committing a lot of new research in that direction. Their mantra is ‘until it is done.’”

Realistic expectations

William (Randy) Hunt, MD, FAAP, FACP, assistant professor of medicine in the Division of Pulmonary, Allergy, Critical Care and Sleep, Emory University School of Medicine, Atlanta, agrees that Trikafta is an exciting development in CF treatment. He noted, “Starting this medication early in life may very well significantly attenuate the disease, but it is not a cure. For individuals who already have significant disease, we may not see the same level of improvements in lung function as what we saw in the studies. The studies generally excluded individuals with $ppFEV_1 < 40\%$. Nevertheless, I remain optimistic and have been prescribing it to nearly everyone that qualifies after a discussion.”

Dr. Hunt added, “Patients are asking if they can stop their current



Dr. William (Randy) Hunt

chronic CF therapies once they start Trikafta. The answer is ‘no, at least not right now.’ While all the relatively short-term data around Trikafta are very promising, we do not yet know how sustained the long-term benefits will be. Still, safely removing therapeutic burden from our patient population is a real interest. There are plans underway by the CFF and other institutions to systematically research whether discontinuing chronic CF therapies is safe in the setting of Trikafta.”

He concluded that 10% of individuals with CF mutations still do not respond to the modulators currently available. “We will not leave that population behind, but treating these remaining mutations is going to take continued efforts and likely modulators that are therapeutically differently from the mechanism of actions of those that are currently available,” he said.

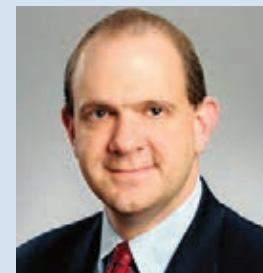
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approximate 2.5% rate of vaccination exemptions among school-age children.

The bad news is that, despite the high rate of MMR vaccination among U.S. children, there are gaps in measles protection in the U.S. population because of factors leaving patients immunocompromised and antivaccination sentiment that has led some parents to defer or refuse the MMR.

In addition, adults who were vaccinated prior to 1968 with either inactivated measles vaccine or measles vaccine of unknown type may have limited immunity. The inactivated measles vaccine, which was available in 1963-1967, did not achieve effective measles protection.

A global measles surge

While antivaccination sentiment contributed to the 2019 measles cases, a more significant factor may be the global surge of measles. More than 140,000 people worldwide died from measles in 2018, according to the World Health Organization and the CDC.

“[Recent data on measles] indicate that during the first 6 months of the year there have been more measles cases reported worldwide than in any year since 2006. From Jan. 1 to July 31, 2019, 182 countries reported 364,808 measles cases to the WHO. This surpasses the 129,239 reported during the same time period in 2018. WHO regions with the biggest increases in cases include the African region (900%), the Western Pacific region (230%), and the European region (150%),” according to a CDC report.

Studies on hospitalization and complications linked to measles in the United States are scarce, but two outbreaks in Minnesota (2011 and 2017) provided some data of what to expect if the measles surge continues into 2020. The investigators found that poor feeding was a primary reason for admission (97%); additional complications included otitis media (42%), pneumonia (30%), and tracheitis (6%). Three-quarters received antibiotics, 30% required oxygen, and 21% received vitamin A. Median length of stay was 3.7 days (range, 1.1-26.2 days) (*Pediatr Infect Dis J.* 2019 Jun;38[6]:547-52. doi: 10.1097/INF.0000000000002221).

‘Immunological amnesia’

Infection with the measles virus appears to reduce immunity to other pathogens, according to a paper published in *Science* (2019 Nov 1;366[6465]:599-606).

The hypothesis that the measles virus could cause “immunological amnesia” by impairing immune memory is supported by early research showing children with measles had negative cutaneous tuberculin reactions after having previously tested positive.

“Subsequent studies have shown decreased interferon signaling, skewed cytokine responses, lymphopenia, and suppression of lymphocyte proliferation shortly after infection,” wrote Michael Mina, MD, from Brigham and Women’s Hospital in Boston, and coauthors.

“Given the variation in the degree of immune repertoire modulation we observed, we anticipate that future risk of morbidity and mortality after measles would not be homogeneous but would be skewed toward individuals with the most severe elimination of immunological memory,” they wrote. “These findings underscore the crucial need for continued widespread vaccination.”

In this study, researchers compared the levels of around 400 pathogen-specific antibodies in blood samples from 77 unvaccinated children, taken before and 2 months after natural measles infection, with 5 unvaccinated children who did not contract measles. A total of 34 children experienced mild measles, and 43 had severe measles.

They found that the samples taken after measles infection showed “substantial” reductions in the number of pathogen epitopes, compared with the samples from children who did not get infected with measles.

This amounted to approximately a 20% mean reduction in overall diversity or size of the antibody repertoire. However, in children who experienced severe measles, there was a median loss of 40% (range, 11%-62%) of antibody repertoire, compared with a median of 33% (range, 12%-73%) range in children who experienced mild infection. Meanwhile, the control subjects retained approximately 90% of their antibody repertoire over a similar or longer time period. Some children lost up to 70% of antibodies for specific pathogens.

Maternal-acquired immunity fades

In another study of measles immunity, maternal antibodies were found to be insufficient to provide immunity to infants after 6 months.

The study of 196 infants showed that maternal measles antibodies had dropped below the protective threshold by 3 months of age – well before the recommended age of 12-15 months for the first dose of MMR vaccine.

The odds of inadequate protection doubled for

each additional month of age, Michelle Science, MD, of the University of Toronto and associates reported in *Pediatrics* (2019 Dec 1. doi: 10.1542/peds.2019-0630).

“The widening gap between loss of maternal antibodies and measles vaccination described in our study leaves infants vulnerable to measles for much of their infancy and highlights the need for further research to support public health policy,” Dr. Science and colleagues wrote.

The researchers randomly selected 25 samples for each of eight different age groups: up to 30 days old, 1 month (31-60 days), 2 months (61-89 days), 3 months (90-119 days), 4 months, 5 months, 6-9 months, and 9-11 months.

Just over half the babies (56%) were male, and 35% had an underlying condition, but none had conditions that might affect antibody levels. The conditions were primarily a developmental delay or otherwise affecting the central nervous system, liver, or gastrointestinal function. Mean maternal age was 32 years.

To ensure high test sensitivity, the researchers used the plaque-reduction neutralization test to test for measles-neutralizing antibodies instead of using enzyme-linked immunosorbent assay, because “ELISA sensitivity decreases as antibody titers decrease,” the investigators wrote. They used a neutralization titer of less than 192 mIU/mL as the threshold for protection against measles.

When the researchers calculated the predicted standardized mean antibody titer for infants with a mother aged 32 years, they determined their mean to be 541 mIU/mL at 1 month, 142 mIU/mL at 3 months (below the measles threshold of susceptibility of 192 mIU/mL), and 64 mIU/mL at 6 months. None of the infants had measles antibodies above the protective threshold at 6 months old, the authors noted.

Children’s odds of susceptibility to measles doubled for each additional month of age, after adjustment for infant sex and maternal age (odds ratio, 2.13). Children’s likelihood of susceptibility to measles modestly increased as maternal age increased in 5-year increments from 25 to 40 years.

Children with underlying conditions had greater susceptibility to measles (83%), compared with those without a comorbidity (68%, $P = .03$). No difference in susceptibility existed between males and females or based on gestational age at birth (ranging from 37 to 41 weeks).

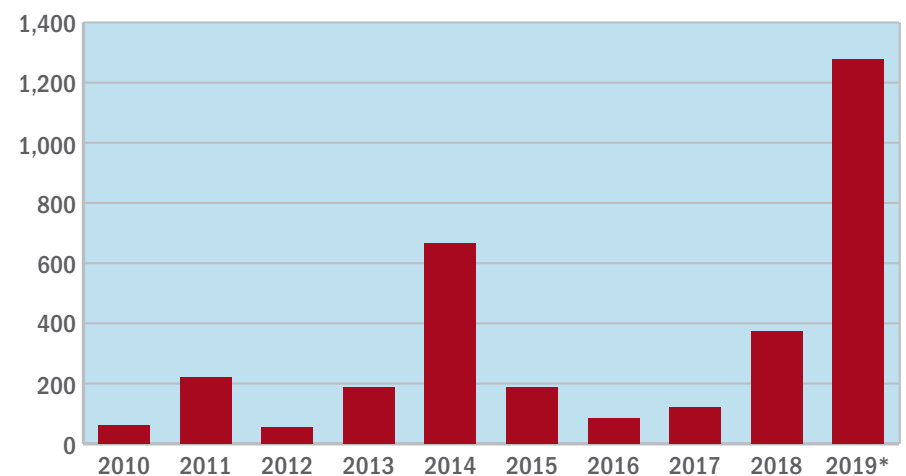
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Despite the high rate of MMR vaccination among U.S. children, there are gaps in measles protection in the U.S. population because of antivaccination sentiment and factors leaving patients immunocompromised.

Number of measles cases reported to the CDC, 2010-2019



*Cases as of Dec. 5.

Source: National Center for Immunization and Respiratory Diseases, Division of Viral Diseases

Ask patients with respiratory symptoms about vaping

BY ANDREW D. BOWSER

MDedge News

One of the most important questions health care providers can ask patients who present with respiratory symptoms this winter is “Do you vape?”

Vaping-related lung injuries cause symptoms such as fever, cough, headache, and fatigue, making it challenging to differentiate them from influenza or respiratory infections, according to the Centers for Disease Control and Prevention.

Accordingly, providers need to ask patients with respiratory, gastrointestinal, or constitutional symptoms about their use of e-cigarette or vaping products, according to one of several new CDC recommendations that appear in the Morbidity and Mortality Weekly Review.

“E-cigarette or vaping product use-associated lung injury (EVALI) remains a diagnosis of exclusion because, at present, no specific test or marker exists for its diagnosis, and evaluation should be guided by clinical judgment,” the CDC report reads.

As of Dec. 27, 2019, the CDC reports that 2,561 patients have been hospitalized with EVALI since March 31, 2019, and 55 deaths have been confirmed in 27 states and the District of Columbia. The outbreak appears to have peaked in September, but cases are still being reported.

Revised clinical recommendations

At least a quarter of rehospitalizations for vaping-related lung injuries occurred within 2 days of initial discharge, and 13.5% of all deaths have occurred after patients left the hospital, according to the CDC.

Those who required rehospitalization for e-cigarette or vaping product use-associated lung injury and those who died after discharge were more likely to have one or more chronic conditions than were other EVALI patients, and those “who died also were more likely to have been admitted to an intensive care unit, experienced respiratory failure necessitating intubation and mechanical ventilation, and were significantly older,” Christina A. Mikosz, MD, and associates wrote in the Morbidity and Mortality Weekly Report.

Their analysis included the 1,139 EVALI patients who were discharged on or after Oct. 31, 2019. Of

that group, 31 (2.7%) patients were rehospitalized and subsequently discharged and another 7 died after the initial discharge. The median age was 54 years for those who died, 27 years for those who were rehospitalized, and 23 for those who survived without rehospitalization, said Dr. Mikosz of the CDC National Center for Injury Prevention and Control, Atlanta, and associates.

Those findings, along with the rates of one or more comorbidities – 83% for those who died, 71% for those who were rehospitalized, and 26% for those who did not die or get readmitted – prompted the CDC to update its guidance for postdischarge follow-up of EVALI patients.

That update involves six specific recommendations to determine readiness for discharge, which include “confirming no clinically significant fluctuations in vital signs for at least 24-48 hours before discharge [and] preparation for hospital discharge and postdischarge care coordination to reduce risk of rehospitalization and death,” Mary E. Evans, MD, and associates said in a separate CDC communication (MMWR. 2019 Dec. 20. 68[early release]:1-6).

Further recommendations

Beyond asking about vape use, providers should evaluate suspected EVALI with pulse oximetry and chest imaging, and should consider outpatient management for patients who are clinically stable, according to the recommendations.

The agency said influenza testing should be “strongly considered,” especially during influenza season, given that EVALI is a diagnosis of exclusion and that it may co-occur with other respiratory illnesses. Antimicrobials (including antivirals) should be given as warranted, they added.

Corticosteroids may be helpful in treating EVALI, but may worsen respiratory infections typically seen in outpatients, and so should be prescribed with caution in the outpatient setting, the CDC recommended.

Behavioral counseling, addiction treatment services, and Food and Drug Administration-approved cessation medications are recommended to help patients quit vaping or using e-cigarette products, CDC said.

Health care providers should emphasize the importance of an annual flu shot for all patients 6 months of age or older, including those who use e-cigarette or vaping products, according to the agency.

VIEW ON THE NEWS

Daniel Ouellette, MD, FCCP, comments: The first lung transplant for a patient with severe lung disease from vaping occurred recently at my hospital. I was proud of the team that had saved this young person’s life, and happy that he survived. The incident, however, made me reflect. A generation ago, respiratory physicians and medical societies like CHEST advocated for increased public awareness of the adverse consequences of tobacco use, bans on advertisements and use in public spaces, and package warning labels on tobacco products. We need to learn more about the dangers of vaping and about how to take care of patients with critical illness resulting from vaping. We may also need to be advocates for our patients and the public health.



“It is not known whether patients with EVALI are at higher risk for severe complications of influenza or other respiratory infections,” the report reads.

Vitamin E acetate as likely culprit

In a report published in the New England Journal of Medicine (2019 Dec 20. doi: 10.1056/NEJMoa1916433), CDC investigators found vitamin E acetate in fluid from the lungs of 94% of patients with electronic cigarette, or vaping, product use-associated lung injury, data from a convenience sample of 51 patients indicate.

Benjamin C. Blount, PhD, of the National Center for Environmental Health at the CDC, and colleagues sought to further clarify potential toxic ingredients in patients with EVALI, the researchers examined bronchoalveolar-lavage (BAL) fluid from 51 EVALI patients and 99 healthy controls.

After using isotope dilution mass spectrometry on the samples, 48 of the 51 patients (94%) showed vitamin E acetate in their BAL fluid. No other potential toxins including plant oils, medium-chain triglyceride oil, petroleum distillates, and diluent terpenes were identified; the samples of one patient each showed coconut oil and limonene.

A total of 47 of 51 patients for whom complete laboratory data were available either reported vaping tetrahydrocannabinol products within 90 days of becoming ill, or showed tetrahydrocannabinol or its metabolites in their BAL fluid. In addition, 30 of 47 patients showed nicotine or nicotine metabolites in their BAL fluid.

The average age of the patients was 23 years, 69% were male. Overall, 25 were confirmed EVALI cases and 26

were probable cases, and probable cases included the three patients who showed no vitamin E acetate.

The safety of inhaling vitamin E acetate, which is a common ingredient in dietary supplements and skin care creams, has not been well studied, but it could contribute to lung injury when heated in e-cigarette products by splitting the acetate to create the reactive compound and potential lung irritant ketene, the researchers said.

The study findings were limited by several factors including the possibility that vitamin E acetate is a marker for exposure to other toxicants, a lack of data on the impact of heating vitamin E acetate, and the inability to assess the timing of the vitamin E acetate exposure compared to BAL sample collection, the researchers noted.

The research was supported by the National Cancer Institute, the FDA Center for Tobacco Products, and Ohio State University Pelotonia Intramural Research. The researchers had no financial conflicts to disclose.

The need for this additional clinical guidance was assessed in anticipation of the seasonal uptick in influenza and other respiratory infections, according to the CDC, which said the recommendations were based in part on individual clinical perspectives from nine national experts who participated in a previously published clinical guidance on managing patients with EVALI.

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SOURCES: Jatlaoui TC et al. MMWR Morb Mortal Wkly Rep. 2019 Nov 19. doi: 10.15585/mmwr.mm6846e2; Chatham-Stephens K et al. MMWR Morb Mortal Wkly Rep. 2019 Nov 19. doi: 10.15585/mmwr.mm6846e1.

Richard Franki contributed to this story.

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Heavy cannabis use heightens stroke, arrhythmia risks

BY NEIL OSTERWEIL

MDedge News

PHILADELPHIA – Young cigarette smokers who are heavy marijuana users are at a nearly three-fold increased risk for stroke, and people with cannabis use disorder are at a 50% greater risk of being hospitalized for arrhythmias, according to new research to be presented at the American Heart Association scientific sessions.

An analysis of pooled data on nearly 44,000 participants in a



DR. PAREKH



DR. PATEL

cross-sectional survey showed that, among the 13.6% who reported using marijuana within the last 30 days, the adjusted odds ratio for young-onset stroke (aged 18-44 years), compared with nonusers, was 2.75, reported Tarang Parekh, MBBS, a health policy researcher of George Mason University in Fairfax, Va., and colleagues.

In a separate study, a retrospective analysis of national inpatient data showed that people diagnosed with cannabis use disorder – a pathological pattern of impaired control, social impairment, risky behavior, or physiological adaptation similar in nature to alcoholism – had a 47%-52% increased likelihood of hospitalization for an arrhythmia, reported Rikinkumar S. Patel, MD, a psychiatry resident at Griffin Memorial Hospital in Norman, Okla.

“As these [cannabis] products

become increasingly used across the country, getting clearer, scientifically rigorous data is going to be important as we try to understand the overall health effects of cannabis,” said AHA President Robert Harrington, MD, of Stanford (Calif.) University in a statement.

Stroke study

In an oral presentation with simultaneous publication in the AHA journal *Stroke*, Dr. Parekh and colleagues presented an analysis of pooled data from the Behavioral Risk Factor Surveillance System (BRFSS), a nationally representative cross-sectional survey collected by the Centers for Disease Control and Prevention in 2016 and 2017.

They looked at baseline sociodemographic data and created multivariable logistic regression models with state fixed effects to determine whether marijuana use within the last 30 days was associated with young-onset stroke.

They identified 43,860 participants representing a weighted sample of 35.5 million Americans. Of the sample, 63.3% were male, and 13.6% of all participants reported using marijuana in the last 30 days.

They found in an unadjusted model that marijuana users had an odds ratio for stroke, compared with nonusers, of 1.59 (*P* less than .1), and in a model adjusted for demographic factors (gender, race, ethnicity, and education) the OR increased to 1.76 (*P* less than .05).

When they threw risk behavior into the model (physical activity, body mass index, heavy drinking, and cigarette smoking), they saw that the OR for stroke shot up to 2.75 (*P* less than .01).

Arrhythmias study

Based on recent studies suggesting that cannabis use may trigger car-

diovascular events, Dr. Patel and colleagues studied whether cannabis use disorder may be related to arrhythmias, approaching the question through hospital records.

“The effects of using cannabis are seen within 15 minutes and last for around 3 hours. At lower doses, it is linked to a rapid heartbeat. At higher doses, it is linked to a too-slow heartbeat,” he said in a statement.

Dr. Patel and colleagues conducted a retrospective analysis of the Nationwide Inpatient Sample from 2010-2014, a period during which medical marijuana became legal in several states and recreational marijuana became legal in Colorado and Washington. The sample is a database maintained by the Healthcare Cost and Utilization Project of the U.S. Office of Disease Prevention and Health Promotion.

They identified 570,557 patients aged 15-54 years with a primary diagnosis of arrhythmia, and compared them with a sample of 67,662,082 patients hospitalized with no arrhythmia diagnosed during the same period.

They found a 2.6% incidence of cannabis use disorder among patients hospitalized for arrhythmias. In regression analysis adjusted for demographics and comorbidities, cannabis use disorder was associated with higher odds of arrhythmia hospitalization in young patients, at 1.28 times among 15- to 24-year-olds (95% confidence interval, 1.229-1.346) and 1.52 times for 25- to 34-year-olds (95% CI, 1.469-1.578).

“As medical and recreational cannabis is legalized in many states, it is important to know the difference between therapeutic cannabis dosing for medical purposes and the consequences of cannabis abuse. We urgently need additional research to understand these issues,” he said.

VIEW ON THE NEWS

Eric Gartman, MD, FCCP,
comments: As the prevalence of

marijuana use accelerates with a changing legal climate, the health effects on the larger population will begin to be



elucidated. It has been well stated previously that several factors have disadvantaged scientific study in this field (most significantly by the inability to study real-world use with federal research money), and our research efforts are lagging way behind use patterns. Further, characteristics of modern marijuana and methods of use (e.g., very high THC potency, cutting with other substances, vaping) leave a very large gap in our knowledge base, and it is very likely that what we know about marijuana use from studies from decades ago no longer applies. Unfortunately, similar to the current vaping discussion, we will likely be informing in retrospect after some significant damage has been done.

“What that means for clinicians is that, if you’re seeing a patient who is presenting with a symptomatic arrhythmia, adding cannabis usage to your list of questions as you begin to try to understand possible precipitating factors for this arrhythmia seems to be a reasonable thing to do,” Dr. Harrington commented.

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Guidelines recommend changes to MDR-TB treatment

BY MARK S. LESNEY

MDedge News

At least five drugs should be used in the intensive phase of treatment and four drugs in the continuation phase of treatment of multidrug-resistant tuberculosis (MDR-TB), according to new clinical guidelines jointly released by the American Thoracic Society, the Centers for Disease Control and Prevention, the European Respiratory Society, and the Infectious Diseases Society of America.

The guidelines were published in the *American Journal of Respiratory and Critical Care Medicine* (2019. 200[10]:e93-e142).

The committee assessed published systematic reviews, and meta-analyses, including a new individual patient data meta-analysis from 12,030 patients, in 50 studies, across 25 countries with confirmed pulmonary rifampin-resistant TB.

With these data, they developed 21 Population, Intervention, Comparator, and Outcomes (PICO) questions and generated 25 GRADE-based recommendations. “Certainty

the evidence was judged to be very low, because the data came from observational studies with significant loss to follow-up and imbalance in background regimens between comparator groups,” according to Payam Nahid, MD, and colleagues on behalf of the societies. Despite these limitations, the guidelines described good practices in the management of MDR-TB and proposed a clinical strategy tool for building a treatment regimen for MDR-TB, as well as recommendations on the role of surgery in treat-

Continued on following page

Continued from previous page

ment of MDR-TB, for treatment of contacts exposed to MDR-TB, and for the treatment of isoniazid-resistant TB.

Six ungraded good practice statements, which the writing committee had high confidence in, were emphasized:

1. Consultation should be requested with a TB expert when there is suspicion of or confirmation of drug-resistant TB.

2. Molecular drug susceptibility testing should be obtained for rapid detection of mutations associated with resistance.

3. Regimens should include only drugs to which the patient's particular *Mycobacterium tuberculosis* isolate has documented, or high likelihood of, susceptibility.

4. Treatment response should be monitored clinically, radiographically, and bacteriologically, with cultures obtained at least monthly for pulmonary TB.

5. Patients should be educated about their condition and asked about adverse effects at each visit. Adverse effects should be investigated.

6. Patient-centered strategies and interventions should be used to minimize barriers to treatment.

In terms of treatment, key recommendations included the use of at least five drugs in the intensive phase of treatment and four drugs in the continuation phase of treatment.

For patients with isoniazid-resistant TB, they suggested adding a later-generation fluoroquinolone to a 6-month regimen of daily rifampin, ethambutol, and pyrazinamide.

Another meta-analysis of 22 randomized controlled trials of directly observed therapy (DOT) and other interventions to improve adherence reported significant increases in cure with DOT (18%) and with patient education and counseling (16%). In addition, compared with the complementary groups, loss to follow-up was 49% lower with DOT, 26% lower

with financial incentives, and 13% lower with patient education and counseling. However, there was no significant reduction in mortality, according to the committee.

For contacts with presumed MDR latent TB infection (LTBI) due to exposure to an infectious patient with MDR-TB, treatment for LTBI vs. following with observation alone

was recommended, comprising a 6- to 12-month treatment with a fluoroquinolone alone or with a second drug, on the basis of source-case isolate drug susceptibility testing, the researchers stated.

“We anticipate that use of regimens that incorporate injectables will decline over time, and it is likely that both WHO and ATS/

CDC/ERS/IDSA recommendations on treatment duration will change in the near future and the distinction between an initial and continuation phase will be reduced further in the context of newer, more potent all-oral regimens emerging,” the committee concluded.

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Postextubation laryngeal injury has lasting effects

BY JIM KLING

MDedge News

More than half of patients who undergo prolonged mechanical ventilation ex-

perience an acute laryngeal injury (ALGI), and the injury is associated with worse breathing and speaking at 10 weeks, according to a study published in *Critical Care Medicine* (2019 Dec;47[12]:1669-

706). The researchers, led by Alexander Gelbard, MD, of Vanderbilt Medical Center, Nashville, Tenn., found that higher body mass index, diabetes, and larger endotracheal tube (ETT) size were all

associated with heightened risk.

The investigators assert that comparatively scarce data are available about how patients fare after receiving mechanical ventilation, and how adverse effects might interfere

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with recovery and return to daily activity. The larynx is rarely examined after extubation, and laryngeal injury may initially appear to be minor. Restricted glottic mobility therefore tends to be diagnosed after discharge, leaving critical care specialists unaware of the long-term impact.

The findings of the study should

be a wake-up call for the development of guidelines for recognition and management of laryngeal injuries, according to John Robert Gowardman, MD, of Royal Brisbane (Australia) and Women's Hospital, who wrote an accompanying editorial (Crit Care Med. 2019 Dec;47[12]:1802-4).

Findings that ETT size, diabetes,

and BMI represent risk factors for injury should help identify patients at risk, and the "practice of 'putting in the biggest ETT just in case' needs to be balanced against the dangers of an undersized ETT. ...We should ask, 'can my patient be safely managed with a smaller ETT?'" wrote Dr. Gowardman.

The researchers followed 100

consecutive adult patients who were examined with nasolaryngoscopy following an intubation of greater than 12 hours at Vanderbilt University Medical Center. They recorded baseline comorbidities and other factors. Fifty seven patients had an ALGI, defined as having glottic mucosal ulceration/granulation or subglottic granulation tissue/stenosis at the time of endoscopy. Nineteen patients had granulation tissue, 48 had posterior glottic ulceration, and 8 had subglottic mucosal ulceration.

Ten weeks after extubation, all patients were contacted by phone and asked to answer the Voice

The larynx is rarely examined after extubation, and laryngeal injury may initially appear to be minor. Restricted glottic mobility therefore tends to be diagnosed after discharge, leaving critical care specialists unaware of the long-term impact.

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Handicap Index (VHI)-10 and the Clinical Chronic Obstructive Pulmonary Disease Questionnaire (CCQ). The questioner did not know the results of the patient's endoscopy. Patients with ALGI were heavier on average (mean difference, 14 kg; BMI difference, 3.8 kg/m²), were more likely to have type 2 diabetes (46% versus 21%), and had more severe illness (median Charlson Comorbidity Index, 3.00 versus 2.00).

Sixty-seven patients completed the 10-week questionnaires, including 40 patients with ALGI and 27 without ALGI. Injury was associated with reports of worse breathing (median CCQ, 1.05 versus 0.20; P less than .001), as well as worse patient-reported voice outcomes (median VHI, 2 versus 0; P = .005).

ETT size appeared to be an important factor, according to multivariate analyses. Use of a 7.0 ETT was associated with lower frequency of injury than 7.5 (adjusted odds ratio, 0.04; P = .004) and 8.0 (OR, 0.03; P = .004). There was no significant difference between the 7.5 and 8.0 sizes.

The Vanderbilt Institute for Clinical and Translational Research funded the study. Dr. Gowardman has no relevant disclosures.

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SOURCE: Shinn JR et al. Crit Care Med;2019 Dec;47(12):1669-706.

Transcatheter TR repair tops medical management

BY M. ALEXANDER OTTO

MDedge News

SAN FRANCISCO – Survival after 12 months was more likely with transcatheter repair of tricuspid regurgitation instead of guideline-directed medical therapy, and patients were less likely to be rehospitalized with heart failure, in a propensity-matched case-control study presented at the Transcatheter Cardiovascular Therapeutics annual meeting.

Tricuspid regurgitation carries a substantial



Dr. Taramasso

burden of morbidity and mortality, but there hasn't been great success with surgical approaches, so several trials are underway assessing transcatheter repair. It's unclear at the moment whether it will beat medical management, which generally includes diuretics and symptom relief, said lead investigator Maurizio Taramasso, MD, PhD, a cardiac surgeon and interventional cardiologist at the University Hospital of Zürich.

Dr. Taramasso and colleagues wanted to take a look at the issue pending results of the ran-

domized trials. "There's still a lot of uncertainty in regard to what we can do for the patient by reducing tricuspid regurgitation. [There are] no data showing that reducing tricuspid regurgitation improves survival," he said at the meeting.

The investigators matched 268 patients from the international Transcatheter Tricuspid Valve Therapies registry treated during 2016-2018 with 268 medical-management patients from the Mayo Clinic in Rochester, Minn., and Leiden (the Netherlands) University, based on age, European System for Cardiac Operative Risk Evaluation II scores, and systolic pulmonary artery pressure, the major predictor of poor outcomes in tricuspid regurgitation.

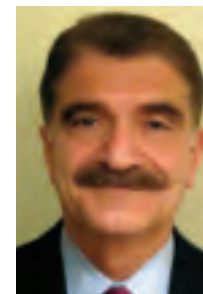
Even with matching, transcatheter patients were worse off, which is probably why they had valve repair in the first place, Dr. Taramasso said at the meeting sponsored by the Cardiovascular Research Foundation. The baseline burden of right ventricular dysfunction, heart failure, mitral regurgitation, atrial fibrillation, and pacemaker placement were all significantly higher in the transcatheter group.

Even so, transcatheter patients had lower 1-year mortality (23% vs. 36%; $P = .001$) and fewer heart failure rehospitalizations (32% vs. 49%, P less than .0001). Transcatheter repair was associated with greater survival and freedom from heart failure rehospitalization (HR, 0.60; 95% CI, 0.46-0.79; $P = .003$), which remained significant after adjusting for sex, New York Heart Association functional class, right ventricular dysfunction, and atrial fibrillation (HR, 0.39; 95% CI, 0.26-0.59; P less than .0001), and after further adjustment for mitral regurgitation and pacemaker/defibrillator placement (HR, 0.35; 95% CI, 0.23-0.54; P less than .0001). Subgroup analyses based on mitral regurgitation severity, pulmonary artery pressure, and other factors all favored repair.

"This is an important set of data to show that, indeed, fixing the tricuspid valve does lead to better outcomes, and perhaps we can do that with a transcatheter approach," said Robert Bonow, MD, a professor of cardiology at Northwestern

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments: Surgical intervention for tricuspid valve regurgitation has been associated with a high mortality rate. As alluded to in this report, the patients who undergo intervention are very high risk at baseline. The results of this study are encouraging for the role of transcatheter valve technology in repair of TV even though the 1-year mortality rate was still quite high at 23%, albeit lower than the mortality with medical therapy at 36%.



University, Chicago, after hearing the presentation.

The fact that transcatheter patients were sicker when they were treated is reassuring, added moderator Ajay Kirtane, MD, an interventional cardiologist and associate professor of medicine at Columbia University, New York.

The success rate for the procedure, which was to be alive at the end of it, with the device successfully implanted, the delivery system retrieved, and residual tricuspid regurgitation (TR) less than 3+, was 86%, and 85% of patients were treated with MitraClip, most with two or three clips. Outcomes were similar, but not worse, than medical management when TR wasn't significantly reduced.

No company funding was reported. Dr. Taramasso is a consultant for Abbott Vascular, Boston Scientific, 4TECH, and CoreMedic; and has received speaker fees from Edwards Lifesciences.

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SOURCE: Taramasso M et al. *J Am Coll Cardiol.* 2019 Sep 24. doi: 10.1016/j.jacc.2019.09.028.

Icosapent ethyl approved for CV risk reduction

BY CATHERINE HACKETT

MDedge News

Icosapent ethyl (Vascepa) has gained an indication from the Food and Drug Administration for reduction of cardiovascular events in patients with high triglycerides who are at high risk for cardiovascular events.

It is "the first FDA-approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy," the agency announced.

The decision, announced on Dec. 13, 2019, was based primarily on results of REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial), which tested icosapent ethyl in 8,179 patients with either established cardiovascular disease or diabetes and at least one

additional cardiovascular disease risk factor. It showed that patients who received icosapent ethyl had a statistically significant 25% relative risk reduction in the trial's primary, composite endpoint (*N Engl J Med.* 2019 Jan 3;380[1]:11-22).

In a November meeting, the FDA's Endocrinologic and Metabolic Drugs Advisory Committee voted unanimously for approval.

The agency notes that, in clinical trials, icosapent ethyl was linked to an increased risk of atrial fibrillation or atrial flutter requiring hospitalization, especially in patients with a history of either condition. The highly purified form of the ethyl ester of eicosapentaenoic acid was also associated with an increased risk of bleeding events, particularly in those taking blood-thinning drugs that increase the risk of bleeding, such as aspirin, clopidogrel, or warfarin.

The most common side effects reported in the clinical trials for icosapent ethyl were musculoskeletal pain, peripheral edema, atrial fibrillation, and arthralgia.

The complete indication is "as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride levels (at least 150 mg/dL) and established cardiovascular disease or diabetes mellitus and two or more additional risk factors for cardiovascular disease," according to a statement from Amalin, which markets Vascepa.

The drug was approved in 2012 for the indication of cutting triglyceride levels once they reached at least 500 mg/dL.

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ISCHEMIA trial hailed as practice changing

BY BRUCE JANCIN

MDedge News

PHILADELPHIA – The eagerly awaited results of the ISCHEMIA trial – the largest-ever randomized trial of an initial invasive versus conservative management strategy for patients with stable ischemic heart disease – were emphatically declared practice changing by interventional cardiologists and noninterventionalists alike at the American Heart Association scientific sessions.

At a median 3.3 years of follow-up of 5,179 participants with baseline moderate or severe ischemia at 320 sites in 37 countries in ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches), an initial invasive strategy accompanied by optimal medical therapy (OMT) didn't reduce the risk of the primary composite endpoint of cardiovascular death, MI, hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest, compared with a conservative strategy of OMT alone. The rates at 4 years were 15.5% with the conservative strategy and 13.3% with the invasive strategy, reported study chair Judith S. Hochman, MD, professor of medicine and senior associate dean for clinical sciences at New York University.

Nor was there a significant between-group difference in the major secondary endpoint of cardiovascular death or MI: 13.9% with the conservative strategy, 11.7% with invasive management.

"The probability of at least a 10% benefit of the invasive strategy on all-cause mortality was less than 10%, based on a prespecified Bayesian analysis," she added.

Prior to enrollment and randomization, CT angiography was routinely performed to rule out left main coronary artery disease.

Fifty-four percent of participants in the National Heart, Lung, and Blood Institute-funded trial had severe ischemia on a baseline non-invasive stress test. To the investigators' surprise, patients with more severe ischemia or more extensive

multivessel involvement didn't do better with the invasive approach.

Almost a quarter (23%) of patients in the conservative management group crossed over to revascularization within 4 years.

Quality-of-life results

An invasive strategy did result in significantly greater improvement in angina control and quality of life, as measured using the Seattle Angina



Dr. Hochman



Dr. Spertus



Dr. Levine



Dr. Jacobs

Questionnaire, than OMT alone in patients who had angina at least once a month at baseline.

"We have 100% confidence that there is a treatment benefit associated with an invasive approach early as well as late after randomization," said John A. Spertus, MD, co-principal investigator for the ISCHEMIA quality of life analysis.

Indeed, he calculated that, for patients with weekly angina, the number needed to treat with revascularization instead of OMT alone for one to be angina-free at 3 months was three.

However, in the 35% of ISCHEMIA participants who reported no angina within the past month at baseline, the invasive strategy offered no quality of life advantage, he added.

"I really think we need to hit 'pause' on asymptomatic revascularization. I just don't see any benefit in patients without symptoms, left main disease excluded," commented Dr. Spertus, director of health

outcomes research at St. Luke's Mid-America Heart Institute and professor of medicine at the University of Missouri, Kansas City.

The reaction

ISCHEMIA addressed a key clinical issue that's long been surrounded by equipoise because of a paucity of high-quality data. As such, it was deemed worthy of its own AHA Late-Breaking Science session.

The assembled discussants agreed the results will change their clinical practice.

"Based on the trial results to date in the patient population studied in the trial, I as a clinician would feel comfortable advising my patients not to undergo the invasive strategy if their angina was absent or controlled or tolerated. I don't think we should feel obligated to take them to the cath lab," said Alice K. Jacobs, MD, an AHA past-president and professor of medicine and director of the cardiac catheterization laboratory and interventional cardiology at Boston Medical Center.

The ISCHEMIA trial has been the target of criticism because of its cost, prolonged duration, and shifting endpoints, but

Glenn L. Levine, MD, praised the ISCHEMIA investigators for achieving "as well-designed and -executed a trial as one could practically do in the real world." ISCHEMIA will undoubtedly be incorporated into AHA/American College of Cardiology guidelines on chest pain and on revascularization that are now in the process of being updated, predicted the cardiologist, who has chaired writing panels for numerous AHA/ACC guidelines.

"As someone who has been intimately involved with our national guidelines for the last 6 years, I say thank you to all the investigators and participants," added Dr. Levine, professor of medicine at Baylor College of Medicine and director of the cardiac care unit at the Michael E. DeBakey Medical Center, Houston.

"I'll just say that this definitely will change my practice," commented Brahmajee K. Nallamothu, MD, an interventional cardiologist and professor of medicine at the University of

VIEW ON THE NEWS

G. Hossein Almassi, MD, FCCP, comments: The results of the ISCHEMIA trial were unexpected and contrary to the long held beliefs and the established practice of invasive interventions for patients with ischemic heart disease. The study is a major game changer in the field of cardiovascular disease. The findings, however, should be interpreted in the context of the study design where patients with stable ischemic heart disease confirmed on noninvasive stress test were enrolled. They do not apply to patients with unstable angina or significant angina burden. It is worth noting that, in patients with angina once a week, there was significant improvement in the quality of life as stated by the co-principal investigator, Dr. Spertus, at a post meeting interview.

Michigan, Ann Arbor. "Just like the COURAGE trial taught me that not every blockage needs to have a stent in it right away, I think this is teaching me that not every patient with moderate to severe ischemia needs to go right away to the cath lab."

Session cochair James de Lemos, MD, declared, "My take home is this is a remarkable finding. It's medical proof that revascularization does not appear to have a marked effect."

"I think the downstream implications of ISCHEMIA with regard to noninvasive testing are massive. I think that's where will see more of an impact in our practice," according to Dr. de Lemos, professor of medicine at the University of Texas Southwestern Medical Center and chief of the cardiology service at Parklawn Hospital in Dallas.

Numerous panelists expressed hope that the National Institutes of Health will fund a long-term extension of ISCHEMIA to learn if the results hold up.

The ISCHEMIA trial was funded by the National Heart, Lung, and Blood Institute. Dr. Spertus holds the copyright for the Seattle Angina Questionnaire.

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SOURCE: Hochman JS. AHA Late Breaking science session.

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Novel analysis links insomnia to first-onset major depressive disorder

BY HEIDI SPLETE

MDedge News

Severity of insomnia, specifically difficulty initiating sleep, was a significant predictor of major depressive disorder, a prospective study of 768 adults with a history of depression suggests.

Insomnia has been identified as a risk factor for depression, but the impact of lifetime depression history and the role of insomnia in major depressive disorder (MDD) remains unclear, wrote Tessa Blanken, MSc, of the Netherlands Institute for Neuroscience, Amsterdam, and colleagues. Studies of this relationship have been hampered by the difficulty of isolating the impact of insomnia as an independent predictor of MDD from depression and other disorders.

In a study published in *Sleep*, the researchers reviewed data from 768 adults aged 18-65 years who were participants in the Netherlands Study of Depression and Anxiety, a multicenter, longitudinal study that included four assessments over 6 years. The participants had no current or prior diagnosis of MDD.

The investigators used Network Outcome Analysis to study the link between insomnia and MDD. The investigators wrote, "Network modeling techniques provide a unique framework to study the interactions among symptoms and their role in the development and maintenance of psychiatric disorders. Using network analysis we can estimate the unique association between pairs of symp-

toms, while controlling for the state and associations of all other symptoms."

Over 6-years' follow-up, 141 participants (18%) were diagnosed with first-onset MDD. Overall, insomnia severity was a significant predictor of first-onset MDD (hazard ratio 1.11, 95% confidence interval). The analysis showed that the predictive effect of insomnia on first-onset MDD was driven solely by the item "Did you have trouble falling asleep" (hazard ratio, 1.33; 95% confidence interval, 1.12-1.57; observed range, 0-4). Those individuals who had trouble falling asleep 3-4 times or more than 4 times a week were 2.3 or 3.2 times, respectively, more likely to develop first-onset MDD. None of the other sleep complaints, such as nocturnal and early morning awakening, significantly increased the risk of first-onset MDD.

The study findings were limited by several factors including the full impact of short sleep duration and lack of chronotype assessment. However, "the identification of 'difficulty initiating sleep' as a risk factor is particularly promising because a recent meta-analysis showed that cognitive behavioural therapy, the treatment of choice for insomnia, is highly effective," the researchers wrote.

The study was supported by the European Research Council. The researchers had no disclosures.

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SOURCE: Blanken T et al. *Sleep*. 2019 Dec 2. doi: 10.1093/sleep/zsz288.

FDA okays lemborexant to treat insomnia

BY JAKE REMALY

The Food and Drug Administration has approved lemborexant (Dayvigo) for the treatment of insomnia in adults. The agency approved the drug for the treatment of insomnia characterized by difficulties with sleep onset or sleep maintenance.

Lemborexant will be available in 5-mg and 10-mg tablets after the Drug Enforcement Administration

schedules the drug, which is expected to occur within 90 days, according to a statement from Eisai.

Lemborexant is an orexin receptor antagonist. Its approval is based on two phase 3 studies, SUNRISE 1 and SUNRISE 2, that included approximately 2,000 adults with insomnia. Investigators assessed lemborexant versus active comparators for as long as 1 month and versus placebo for 6 months.

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Disentangling sleep problems and bipolar disorder

BY BRUCE JANCIN

MDedge News

COPENHAGEN – Sleep spindle density is diminished in euthymic patients with bipolar disorder, suggesting that this sleep architecture abnormality might offer potential for early differentiation of bipolar from unipolar depression, Philipp S. Ritter, MD, said at the annual congress of the European College of Neuropsychopharmacology.

“Hopefully in the future our finding, if replicated, might have clinical utility. It might be a kind of soft biomarker that could be used in early detection, or, in people having their first depressive episode, you could perhaps use this to risk-stratify. And if you see there’s a great reduction in spindle density then a patient might have a higher likelihood of a bipolar disorder, so you might not want to treat with antidepressants that have a high switch rate,” explained Dr. Ritter, a psychiatrist at Technical University of Dresden (Germany).

Sleep spindles are a specific sleep architecture formation evident on the sleep EEG. They are sudden high-amplitude bursts occurring in stage N2 sleep. They are thought to



Dr. Philipp S. Ritter

be associated with sensory gating and memory processes. Other investigators have repeatedly demonstrated that patients with schizophrenia, as well as their asymptomatic first-degree relatives, have a reduced density of fast spindles greater than 13 Hz, compared with the general population. In contrast, patients with unipolar depression do not display this polysomnographic abnormality.

These findings prompted Dr. Ritter and his coinvestigators to conduct an all-night polysomnographic study in 24 euthymic patients with

bipolar disorder and 25 healthy controls. The bipolar patients demonstrated a reduced density and mean frequency of fast sleep spindles, but not slow spindles (*Acta Psychiatr Scand.* 2018 Aug;138[2]:163-72).

These sleep spindle findings implicate thalamic dysfunction as a potential neurobiologic mechanism in bipolar disorder, since spindles are generated in the thalamus and spun off in thalamocortical feedback loops, Dr. Ritter observed.

Which comes first?

Sleep problems are a prominent issue in patients with bipolar disorder, even when they are euthymic.

“Anybody who deals with bipolar patients knows that sleep is a constant issue. You are always talking to your patients about their sleep. They’re sleeping too much, or not enough, or they’re sleeping just about right but it’s unsatisfactory. They do not sleep well. And if there’s something that disrupts their sleep, it can precipitate episodes,” Dr. Ritter said.

He wondered whether sleep problems are an intrinsic part of the bipolar illness, or a byproduct of the stress of having a severe mental

disorder, perhaps a medication side effect, or whether the disordered sleep actually precedes the clinical expression of the mood disorder. So he and his coinvestigators turned to a Munich-based cohort sample of 3,021 adolescents and young adults assessed via the standardized Composite International Diagnostic Interview four times during 10 years of prospective follow-up.

Among 1,943 participants in the epidemiologic study who were free of major mental disorders at entry, the presence of sleep disturbance at baseline as quantified using the Symptom Checklist-90-Revised doubled the risk of developing bipolar disorder within the next 10 years. After the researchers controlled for potential confounders, including parental mood disorder, gender, age, and a history of alcohol or cannabis dependence, poor sleep quality at baseline remained independently associated with a 1.75-fold increased chance of subsequently developing bipolar disorder (*J Psychiatr Res.* 2015 Sep;68:76-82).

Dr. Ritter reported having no financial conflicts regarding these studies.

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Study shows ADHD/sleep disorder link may be bidirectional

BY CHRISTINE KILGORE

MDedge News

Insomnia, restless legs syndrome (RLS), and frequent snoring were significantly associated with subsequent ADHD symptoms in a large longitudinal study of adolescents in China.

Investigators twice assessed 7,072 middle and high school students participating in the larger longitudinal Shandong Adolescent Behavior & Health Cohort – in 2015 and 1 year later in 2016 – for sleep, mental health, psychosocial factors (using the self-administered Adolescent Health Questionnaire, or AHQ), and for ADHD symptoms (using the Youth Self-Report, or YSR, of the Achenbach Child Behavior Checklist).

At baseline, ADHD symptoms were reported by 7.6% of adolescents and were significantly correlated, after adjusting for adolescent and family covariates, with all the sleep variables studied: sleep duration of 7 hours or less per night, insomnia symptoms, poor sleep quality, RLS symptoms, frequent snoring, and hypnotic use, reported Xianchen Liu, MD, PhD, of Shandong (China) University, and coinvestigators. They noted a dose-response relationship between sleep duration and the odds of having ADHD symptoms.

At 1-year follow-up, 4.5% of the 6,531 participants who did not have ADHD symptoms at

baseline now reported them. After adjustments for covariates, any insomnia (odds ratio, 1.48), difficulty initiating sleep (one of the insomnia symptoms) (OR, 2.09), RLS (OR, 1.47), and frequent snoring (OR, 2.30) at baseline were each significantly associated with development of incident ADHD symptoms and with ADHD severity at 1 year, they reported in *Sleep*.

“Given the fact that sleep disorders in adolescents are often underdiagnosed and untreated primarily in the primary care setting, our findings highlight that clinicians should assess and manage short sleep duration and sleep problems for effective treatment of ADHD in adolescents,” as well as for prevention, they wrote.

The AHQ includes questions that assess nocturnal sleep duration and sleep problems during the past month. The adolescent and family variables that were selected as covariates and controlled for include cigarette smoking, alcohol use, use of mental health services, chronic physical diseases, and parental education and occupation. Depression was also a covariate but was assessed through a different scale.

The YSR measures eight ADHD symptoms during the past 6 months on a 3-point scale (not true, somewhat or sometimes true, and very true or often true). The adolescent participants of this study were in grades 7, 8, and 10 at baseline. Their mean age at baseline was 15 years; half

were male. They were part of the larger Shandong Adolescent and Behavioral Cohort, a longitudinal study of almost 12,000 adolescents.

Growing evidence has demonstrated a bidirectional relationship between sleep problems and ADHD symptoms in pediatric populations, the investigators wrote, and further research is needed to examine the “mediators, moderators, and biological mechanisms of the sleep-ADHD link [in adolescents].”

While there are multiple potential pathways for this link, sleep problems may sometimes result in a cluster of behavioral and cognitive symptoms that are not true ADHD but that mimic the disorder, they noted.

The investigators also noted that approximately 67% of adolescents who had clinically relevant ADHD symptoms at baseline no longer had these symptoms at 1-year follow-up – a finding that “supports the [idea]” that ADHD symptoms with onset in adolescence may be transient or episodic rather than persistent.

The study was funded in part by the National Natural Science Foundation of China. The authors reported that they have no conflicts of interest.

chestphysiciannews@chestnet.org

SOURCE: Liu X et al. *Sleep*. 2019 Dec 2. doi: 10.1093/sleep/zsz294.

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not available for the digital edition.**



Dr. Abraham Verghese: Patients need physicians who see and feel beyond the EMR

BY KARI OAKES

MDedge News

CHICAGO – Speaking to a rapt audience of radiologists, an infectious disease physician who writes and teaches about the importance of human touch in medicine held sway at the opening session of the annual meeting of the Radiological Society of North America.

It wasn't hard for Abraham Verghese, MD, to find points of commonality between those who sit in dark reading rooms and those who roam the wards.

The EMR, Dr. Verghese said, is a “system of epic disaster. It was not designed for ease of use; it was designed for billing. ... Frankly, we are the highest-paid clerical workers in the hospital, and that has to change. The Stone Age didn't end because we ran out of stone; it ended because we had better ideas.”

The daily EMR click count for physicians has been estimated at 4,000, and it's but part of the problem, said Dr. Verghese, professor of medicine at Stanford (Calif.) University. “For every hour of cumulative patient care, physicians spend 1½ hours on the computer, and another hour of our personal time at home dealing with our inbox,” he said. EMR systems may dominate clinical life for physicians, “but they were not built for our ease.”

Dr. Verghese is a practicing physician and medical educator, and is also the author of a body of fiction and nonfiction literature that delineates the physician-patient relationship. His TED-style talk followed opening remarks from Valerie Jackson, MD, the president of the Radiological Society of North America, who encouraged radiologists to reach out for a more direct connection with patients and with nonradiologist colleagues.

The patient connection – the human factor that leads many into the practice of medicine – can be eroded for myriad reasons, but health care systems that don't elevate the physician-patient relationship do so at the peril of serious physician burnout, said Dr. Verghese. By some measures, and in some specialties, half of physicians score high on validated burnout indices – and a burned-out physician is at high risk for leaving the profession.

Dr. Verghese quoted the poet Anatole Broyard, who was treated for prostate cancer and wrote extensively about his experiences.

Wishing for a more personal connection with his physician, Mr. Broyard wrote: “I just wish he would brood on my situation for perhaps 5 minutes, that he would give me his whole mind just once, be bonded with me for a brief space, survey my soul as well as my flesh, to get at my illness, for each man is ill in his own way.”

It's this opportunity for connection and contemplation that is sacrificed when, as Dr. Verghese said, “the patient in the bed has become a mere icon for the ‘real’ patient in the computer.”

Dr. Jackson, executive director of the American Board of Radiology, and Dr. Verghese both



Dr. Verghese said, “The patient in the bed has become a mere icon for the ‘real’ patient in the computer.”

acknowledged that authentic patient connections can make practice more rewarding and reduce the risk of burnout.

Dr. Verghese also discussed other areas of risk when patients and their physicians are separated by an electronic divide.

“We are all getting distracted by our peripheral brains,” and patients may suffer when medical errors result from inattention and a reluctance to “trust what our eyes are showing us,” he said. He and his colleagues solicited and reported 208 vignettes of medical error. In 63% of the cases, the root cause of the error was failure to perform a physical examination (*Am J Med.* 2015 Dec;128[12]:1322-4.e3). “Patients have a front side – and a back side!” he said, to appreciative laughter. A careful physical exam, he said, involves inspecting – and palpating – both sides.

The act of putting hands on an unclothed patient for a physical exam would violate many societal norms, said Dr. Verghese, were it not for the special rules conferred on the physician-patient relationship.

“One individual in this dyad disrobes and allows touch. In any other context in this society, this is assault,” he said. “The very great privilege of our profession ... is that we are privileged to examine [patients'] bodies, and to touch.”

The gift of this ritual is not to be squandered, he said, adding that patients understand the special rhythm of the physical examination. “If you come in and do a half-assed probe of their belly and stick your stethoscope on top of their paper gown, they are on to you.”

Describing his own method for the physical exam, Dr. Verghese said that there's something that feels commandeering and intrusive about beginning directly at the head, as one is taught. Instead, he offers an outstretched hand and begins with a handshake, noting grip strength, any tremor, hydration, and condition of skin and nails. Then, he caps the handshake with his other hand and slides two fingers over to the radial pulse, where he gathers more information,

all the while strengthening his bond with his patient. His exam, he said, is his own, with its own rhythms and order which have not varied in decades.

Whatever the method, “this skill has to be passed on, and there is no easy way to do it. ... But when you examine well, you are preserving the ‘person-ality,’ the embodied identity of the patient.”

From the time of William Osler – and perhaps before – the physical examination has been a “symbolic centering on the body as a locus of personhood and disease,” said Dr. Verghese.

Dr. Jackson encouraged her radiologist peers to come out from the reading room to greet and connect with patients in the imaging suite. Similarly, Dr. Verghese said, technology can be used to “connect the image, or the biopsy report, or the lab test, to the personhood” of the patient. Bringing a tablet with imaging results or a laboratory readout to the bedside or the exam table and helping the patient place the findings on or within her own body marries the best of old and new.

He shared with the audience his practice for examining patients presenting with chronic fatigue – a condition that can be challenging to diagnose and manage.

These patients “come to you ready for you to join the long line of physicians who have disappointed them,” said Dr. Verghese, who at one time saw many such patients. He said that he developed a strategy of first listening, and then examining. “A very interesting thing happened – the voluble patient began to quiet down” under his examiner's hands. If patients could, through his approach, relinquish their ceaseless quest for a definitive diagnosis “and instead begin a partnership toward wellness,” he felt he'd reached success. “It was because something magical had transpired in that encounter.”

Neither Dr. Verghese nor Dr. Jackson reported any conflicts of interest relevant to their presentations.

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FROM AACN

Recognize PTSD signs to enhance well-being of colleagues and yourself

Since nursing is a high-stress profession, it's important to recognize signs of post-traumatic stress disorder (PTSD) in yourself or your fellow nurses.

"Nurses and PTSD: Combine Professional Care With Self-Care," in American Nurse Today notes that one in four nurses will experience PTSD at some point. Symptoms can include agitation, irritability, self-destructive behavior, social isolation, fear, loneliness, and severe anxiety.

Nurse leaders can support their staff by seeking resources, advocating for assistance, and engaging with them. "When you listen, encourage, and support them, you develop trust, which can go a long way toward getting them the help they need," the article adds.

Within the article is a link to "Wellness 101," a self-care series that details nine dimensions of wellness to help nurses set goals for the well-being of themselves and others. "Wellness 101: 9 dimensions of wellness," an introductory article in the series, summarizes each type of wellness:

Physical

Exercise, eat healthy, reduce stress, address medical issues and maintain healthy practices every day.

Emotional

Cognitive behavioral skills and mindfulness can relieve stress and anxiety.

Financial

Plan well and control spending to change how you feel.

Intellectual

Learn a new skill or concept, understand different viewpoints or exercise your mind with puzzles and games.

Career

Engage in work that provides satisfaction and matches your values.

Social

Build a support network based on mutual respect and trust among friends, family and co-workers.

Creative

Doodle, dance or sing without worrying about whether you're doing it well.

Environmental

Appreciate your responsibility to preserve and protect the environment and connect to nature.

Spiritual

Be open to quiet self-reflection, reading and dialogue. Explore your beliefs and respect those of others.

What are CHEST NetWorks?

NetWorks are special interest groups that focus on particular areas of chest medicine. Join any of CHEST's 22 NetWorks to connect with others who have similar interests; help plan educational sessions; take on leadership roles; and participate in the development of policies, opinions, and position statements. Joining and staying involved in CHEST NetWorks provides a pathway to leadership roles.

Primary and secondary

Join as many NetWorks as you would like, and designate (up to) two primary NetWorks and limitless secondary NetWorks. Primary NetWork designation gives you access to News From Your NetWork, a bi-yearly communication from your NetWork Chair with

relevant education course offerings, key events in the CHEST community, and up-to-date information on happenings in your NetWork.

Join multiple NetWorks or change your NetWork affiliation any time by logging in to My Account, and indicate your preferences on the NetWorks page.

Leadership positions

NetWork membership is a benefit for all CHEST members. If interested in joining a NetWork Steering Committee, visit the Apply for CHEST Leadership page, to learn more about how to get involved.

Questions?

networks@chestnet.org.



CHEST Foundation welcomes new trustees

At CHEST 2019 in New Orleans, the CHEST Foundation was pleased to formally welcome to its Board of Trustees new CHEST President Stephanie Levine, MD, FCCP, and Executive Committee Chair of the Council of Global Governors, Sai Haranath, MBBS, MPH, FCCP – who were appointed to their positions – as well as Roozehra Khan, DO, FCCP; Burton Lesnick, MD, FCCP; and Jill Popovich – who were elected to their positions. Guided by life-changing experiences with public service, memories of loved ones struggling with lung disease, and a pure and overwhelming desire to help the most

vulnerable populations around the world acquire the resources they need to survive, the new CHEST Foundation Board members understand enhancing the CHEST Foundation's impact on global health over the coming years to be their greatest shared priority.

The CHEST Foundation is delighted to see so many ambitious visions of awareness, international community building, and technologic innovation already coming to life, thanks to the efforts of its newly elected trustees and other board members.

To support their and other initiatives, donate today at chest-foundation.org/donate.

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CHEST NETWORKS

POCUS. Fungal infections. Pleural interventions.

Cardiovascular Medicine and Surgery

Evolution of point of care ultrasound (POCUS) education: cardiovascular, pulmonary, and beyond

A recent *CHEST Physician* article noted the ubiquity of POCUS employment but lamented inconsistencies and possible inadequacies of POCUS education amongst AC-GME specialty fellowships (Satterwhite L. An update on the current standard



Dr. Baeten

for ultrasound education in fellowship. *CHEST Physician*, December 2019, p. 34). POCUS education/training is no longer limited to physician fellowships but has percolated into the undergraduate medical education curricula of first-year medical students and physician assistant (PA) programs (Hoppmann RA, et al. *Crit Ultrasound J*. 2011;[3]:1; Rizzolo D, et al. *J Physician Assist Educ*. 2019;30[2]:103). Some PA residencies have long-incorporated POCUS training to varying degrees, providing emergency/critical care/cardiovascular ultrasound training comparable to that of physician residencies (Daymude ML, et al. *J Physician Assist Educ*. 2007;18[1]:29). A 12-month POCUS fellowship, which mirrors physician POCUS fellowship curricula, is also available for PAs at Madigan and Brooke Army Medical Centers and allows graduates the opportunity to earn RDMS/RDCS credentials (Monti J. *J Physician Assist Educ*. 2017;28[1]:27). POCUS employment is not limited to physicians and PAs, however. Respiratory therapists and other allied health professionals are also exploring the value of pulmonary, cardiovascular, and other critical care POCUS applications in their respective practices (Karthika M, et al. *Respir Care*. 2019;64[2]:217). Meanwhile, POCUS devices continue to evolve toward inexpensive handheld machines that incorporate machine learning/artificial intelligence, further mitigating barriers to integration of POCUS into routine

clinical practice (Tsay D, et al. *Circulation*. 2018;138[22]:2569). With the expansion of POCUS across the full spectrum of health care, leadership from multiprofessional organizations, such as CHEST and the Society of Point-of-Care Ultrasound (SPOCUS), are well-positioned to leverage their diverse leadership to govern the training and safe employment of POCUS.

Robert Baeten II, DmSc, FCCP
Steering Committee Member

Chest Infections

New laboratory testing guidelines for diagnosing fungal infections

Secondary to a growing number of immunosuppressed individuals, the incidence of invasive fungal infections (IFI) is increasing. IFIs can be difficult to treat and are associated with a high mortality rate. Effective treatment is predicated on early recognition and accurate diagnosis (Limper AH, et al. *Am J Respir Crit Care Med*. 2011;183[1]:96). Therefore, the American Thoracic Society created a clinical practice guideline on laboratory diagnosis of the most common fungal infections (Hage CA, et al. *Am J Respir Crit Care Med*. 2019;200[5]:535). The most important diagnostic considerations for clinicians are summarized below:



Dr. Carmona

1 Serum galactomannan and serum aspergillus PCR are recommended in severely immunocompromised patients suspected of having invasive pulmonary aspergillosis (IPA).

2 Galactomannan and aspergillus PCR in bronchoalveolar lavage (BAL) are recommended for patients who are strongly suspected of having IPA, especially if serum is negative. In less severe immunocompromised patients, the BAL sensitivity of galactomannan is better compared with serum, without reducing specificity.



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3 Due to low specificity/high false-positive rate, 1,3-B-D-glucan should not be used in isolation to diagnose invasive candidiasis.

4 No single best test exists for the diagnosis of blastomycosis or coccidioidomycosis; rather, more than one diagnostic test including fungal smear, culture, serum antibody, and antigen testing should be used for suspected blastomycosis or coccidioidomycosis.

5 Urine or serum antigen testing is recommended for patients with suspected disseminated or acute histoplasmosis. For immunocompetent patients suspected of pulmonary histoplasmosis, serologic testing is recommended; antigen testing may increase the diagnostic yield.

While these recommendations provide a basis for laboratory testing for the most common IFIs, they must be integrated into the clinical context to ensure accurate diagnosis.

Kelly Pennington, MD, Steering Committee Member

Eva M. Carmona, MD, PhD, Net-Work Member

Clinical Pulmonary Medicine Definitive pleural interventions in malignant pleural effusions

Malignant pleural effusions (MPEs) contribute significantly to symptom burden, and an emphasis on patient-centered outcomes prioritizes palliation of symptoms and definitive management with pleurodesis. Clinical guidelines (Feller-Kopman DJ, et al. *Am J Respir Crit Care Med.* 2018;198[7]:839) for MPE recommend an indwelling pleural catheter



Dr. Faiz



Dr. Warner

(IPC) or chemical pleurodesis as first-line definitive pleural intervention. In a recent prospective study, Bhatnagar and colleagues (Bhatnagar R, et al. *JAMA.* 2019 Dec 5. doi: 10.1001/jama.2019.19997) evaluated the effectiveness of thoracoscopy with talc poudrage compared with chest tube placement with talc slurry. The authors randomized 330 patients with MPE and expandable lung, and the primary outcome was pleurodesis failure at 90 days after randomization. There was no significant difference in primary outcome, and pleurodesis failure at 90 days was 22% with talc poudrage and 24% with talc slurry. Similar results for pleurodesis failure at 30 and 180 days were noted. Secondary outcomes for all-cause mortality, quality of life measures, symptom (chest pain, dyspnea) scores, hospital days, and radiographic opacification also showed no difference. This supports an earlier study by Dresler and associates (Dresler CM, et al. *Chest.* 2005 Mar;127[3]:909) that reported similar efficacy of talc poudrage and talc slurry. Interestingly, Bhatnagar's group (Bhatnagar R, et al. *N Engl J Med.* 2018 Apr 5;378[14]:1313) previously demonstrated administration of talc slurry via IPC was safe and effective in the outpatient

setting, but no direct comparison of IPC combined with talc poudrage or talc slurry is available. These studies provide support for flexibility in MPE management, and selection of definitive pleural intervention can be tailored for each individual patient.

Saadia Faiz, MD, FCCP, Steering Committee Member

Mark Warner, MD, FCCP, NetWork Member

Interprofessional Team Interprofessional team and noninvasive ventilation in COPD exacerbation

Noninvasive ventilation (NIV) is a standard of care for treatment of COPD exacerbations, resulting in reduced need for mechanical ventilation, length of hospital stay, and mortality. Patient selection is as im-



Dr. Farmer



Dr. Luthra

portant to success as is choice of an appropriate interface, maintenance of synchrony, and a dedicated interprofessional team. Prior studies have identified that necessary factors for successful implementation of NIV in exacerbations of severe COPD include adequate equipment, sufficient numbers of qualified respiratory therapists, flexibility in

staffing, provider buy-in, respiratory therapist autonomy, interdisciplinary teamwork, and staff education (Fisher et al. *Ann Am Thorac Soc.* 2017;14[11]:1674). These studies also suggest that efforts to increase the use of NIV in COPD need to account for the complex and interdisciplinary nature of NIV delivery and the need for team coordination. The authors further point out that although NIV is a cornerstone of treatment for patients with severe exacerbations of COPD with proven reduced need for intubation, hospital length of stay, and mortality and despite high-quality evidence and strong recommendations in clinical guidelines, use of NIV varies widely across hospitals. Since interdisciplinary teamwork, respiratory therapy autonomy, and staff education have been identified as important factors in appropriate implementation of NIV, investigators are currently studying the effectiveness, acceptability, and feasibility of interprofessional education for physicians, respiratory therapists, and nurses vs online education for increasing the delivery of NIV in patients hospitalized with COPD exacerbation (R01 HL 146615 – 01 Implementation of interprofessional training to improve uptake of noninvasive ventilation in patients hospitalized with severe COPD exacerbation). More importantly, this work will further elucidate the interdisciplinary nature of NIV therapy and the benefit of an interprofessional approach to team education.

Mary Jo Farmer, MD, PhD, FCCP, Steering Committee Member
Munish Luthra, MD, FCCP, Steering Committee Member

Welcome new CHEST Physician Editorial Board members

The new Editorial Board members will be assisting in reviewing content for CHEST Physician.

A. Christine Argento, MD, FCCP

Dr. Argento is an Assistant Professor of Medicine and Thoracic Surgery, is the Director of Interventional Pulmonary and the Interventional Pulmonary Fellowship Program Director at Northwestern University, Feinberg School of Medicine. She has been very involved in simulation training and education, particularly with respect to bronchoscopy, interventional pulmonary, and pleural procedures. She is the current Secre-



Dr. Argento

tary-Treasurer of the Association of Interventional Pulmonary Program Directors (AIPPD) and a member of the CHEST Bronchoscopy Domain Task Force.

David L. Bowton, MD, FCCP

Dr. Bowton is Professor Emeritus in the Department of Anesthesiology, Section on Critical Care at Wake Forest University Baptist Medical Center in Winston Salem, North Carolina. He was formerly Head of the Section on Critical Care in the Department of Anesthesiology and the Medical Director of Respiratory Care, the Neurocritical Care ICU, and the Cardiovascular Surgical ICU. His current inter-



Dr. Bowton

ests are in critical care education, especially with respect to simulation education in the areas of mechanical ventilation and airway management. He is the current Chair of the CHEST Cardiovascular Medicine and Surgery NetWork.

Mary Cataletto, MD, FCCP

Dr. Cataletto is a pulmonologist in the Department of Pediatrics at NYU Health and the current chair of the Pediatric Chest Medicine NetWork at CHEST. Dr. Cataletto is Professor of Clinical Pediatrics at both the NYU Grossman School of Medicine and the Renaissance School of Medicine at Stony Brook University. She



Dr. Cataletto

Continued on following page

Continued from previous page

has a long standing interest in medical education and medical publishing - serving as Editor in Chief of *Pediatric Allergy, Immunology and Pulmonology*, as well as on the editorial boards of multiple subspecialty texts and review books. Her research interests include sleep and breathing in children with craniofacial abnormalities, including those with Trisomy 21 and Prader-Willi syndrome.

Megan Conroy, MD

Dr. Conroy is Chief Pulmonary and Critical Care Fellow at The Ohio State University in Columbus, Ohio. Upon completion of her training, she will join The Ohio State University Division of Pulmonary, Critical Care, and Sleep Medicine as an Assistant Professor of Clinical Medicine. Her clinical expertise is in severe asthma and critical care medicine. She serves as the CHEST Fellow-in-Training member of the Airways Disorders NetWork Steering Committee and as a member of the Trainee Work Group. She is the first fellow to serve on the *CHEST Physician* Editorial Board, and she will work with several board members to provide new



Dr. Conroy

perspectives in her area of expertise when reviewing articles.

Sachin Gupta, MD, FCCP

Dr. Gupta is a Pulmonary and Critical Care physician in group private practice in the San Francisco, Bay Area. His clinical expertise is in the fields of pulmonary hypertension, interstitial lung diseases, and non-tuberculous mycobacterial infections. He is actively participating in several societies, including the Pulmonary Hypertension Association, California Thoracic Society, and CHEST. In addition to his clinical interests, he has been an international medical volunteer and highly involved in the Bay Area in digital health tech consulting.



Dr. Gupta

Mangala Narasimhan, DO, FCCP

Dr. Narasimhan works for Northwell Health as the Regional Director of Critical Care Services and is an attending in the Division of Pulmonary, Critical Care, and Sleep Medicine. She is the Medical Director of the Northwell Acute Lung Injury Center/VV ECMO program and ICU Director of the Medical ICU at Long Island Jewish Medical Center. She is a Profes-

sor of Medicine at the Zucker School of Medicine at Hofstra/Northwell. She has been teaching ultrasound and advanced echo nationally and internationally for 15 years. Her research interests include point of care ultrasound in the critically ill, ECMO for acute lung injury, and outcomes research in the ICU.



Dr. Narasimhan

Brandon M. Seay, MD, MPH

Dr. Seay is a Pediatric Pulmonologist and Sleep Specialist for the Children's Physician Group Pulmonology in Atlanta, Georgia. His clinical interests include asthma, cystic fibrosis, sleep apnea, and behavioral insomnia of childhood. Other interests include medical education through social media and health advocacy via legislative and social media efforts. He is currently a member of the CHEST Social Media Work Group as a lead on video efforts.



Dr. Seay

Meet the FISH Bowl finalists

CHEST 2019 marked the inaugural FISH Bowl competition for attendees.

Inspired by Shark Tank, our kinder, gentler, yet still competitive and cutting-edge FISH Bowl (Furthering Innovation and Science for Health) featured CHEST members disrupting our beliefs about how clinical care and education are performed. As health-care providers, they presented innovative ideas pertaining to education and clinical disease for pulmonary, critical care, and sleep medicine. Six finalists were chosen from dozens of submissions, and three emerged winners!

In this limited series, we introduce you to several of them - beginning with finalist Dr. Ernest Chan.

Name: Ernest G. Chan, MD, MPH

Institutional Affiliation:

Department of Cardiothoracic Surgery at the University of Pittsburgh Medical Center

Position: PGY-4 Integrated Cardiothoracic Surgery Resident

Brief Summary of Submission:

My innovative idea for the CHEST FISH Bowl Competition

2019 was a device that monitors the use of the incentive spirometry, as well as makes its use interactive with a postoperative surgical patient. Our device would have several modules that monitor the frequency, volume, and quality of each breath. All of the information will be sent to the electronic medical records, so patients can get feedback from the surgical team in real time. There will also be programmable alarms so that we can create unique treatment plans personalized to each patient.

All of these functions will ultimately allow us as physicians to study this incentive spirometry better.

1 What inspired your innovation? What inspired my innovation is the world we live in today. Everything is automated from your toaster oven to self-driving cars. This automation allows for improved adherence and minimization of confounding variables.

2 Who do you think can benefit most from it, and why? I think the people who would benefit most are the patients.

When you are at your most vulnerable state after surgery, it is important to feel like someone is looking after you. Right now with incentive spirometry, you are given the device, someone tells you how to use it one time, and you are supposed to use it correctly. With our device, not only are you constantly reminded of using the device, as well as using correctly, the medical team is being fed these data to ensure what you are doing maximizes the benefits.

3 What do you see as challenges to your innovation gaining widespread acceptance? How can they be overcome?

I think the initial challenge will be the acceptance in spending more money. Physiologically and scientifically, the use of incentive spirometry should help decrease postoperative pulmonary complications, but the current data are controversial, at best.

I think that if we can show improvement in these postoperative complications, taking on extra upfront cost in investing in our device will ultimately pay off in the end.

4 Why was it meaningful for you to emerge as a finalist in FISH Bowl 2019?

I believe CHEST to be one of if not the most premiere medical organizations in the world. To become a finalist in the inaugural FISH Bowl Competition is a complete honor. Throughout every CHEST annual conference, there is innovation in every corner and every presentation.

I hope that becoming a finalist at the FISH Bowl competition is just the first in my participation with CHEST.

5 What future do you envision for your innovation beyond FISH Bowl 2019?

I hope that my innovation will inspire young thinkers to look at any medical device, procedure, or protocol and say, "How can I apply technology to this to make this better, safer, or more efficient?"

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Eduardo Bossone, MD, PhD, FCCP

The lecture is generously funded by the CHEST Foundation.

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Children Are Not Just Little Adults – Except Sometimes
Howard Panitch, MD, FCCP

The Margaret Pfrommer Memorial Lecture in Home-Based Mechanical Ventilation is generously supported by International Ventilator Users Network of Post-Polio Health International and the CHEST Foundation.

Pasquale Ciaglia Memorial Lecture in Interventional Medicine

Medical Thoracoscopy: Past, Present, and Future
Pyng Lee, MD, PhD
The lecture is generously funded by the CHEST Foundation.

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Mark J. Rosen, MD, Master FCCP Memorial Lecture

Remembering a Giant in Chest Medicine: The Mark J. Rosen Memorial Lecture

Lisa Moores, MD, FCCP

CHEST FOUNDATION GRANT AWARDS

The GlaxoSmithKline Distinguished Scholar in Respiratory Health

Kamran Mahmood, MBBS, FCCP
Lymphocyte Exhaustion Markers in Malignant Pleural Effusions of Lung Cancer

This grant is supported by an endowed fund from GlaxoSmithKline.

CHEST Foundation Research Grant in Lung Cancer

James Tsay, MD
Effect of the Inflammation Signaling Pathway on Lung Microbiome and Lung Cancer

This grant supported in full by the CHEST Foundation.

CHEST Foundation Research Grant in Pulmonary Arterial Hypertension

Mona Alotaibi, MD
Metabolic Derangements Underlying SSC-PAH

This grant supported in full by the CHEST Foundation.

CHEST Foundation and the Alpha-1 Foundation Research Grant in Alpha-1 Antitrypsin Deficiency

Derek Russell, MD
Neutrophil-Elastase Positive Exosomes and Emphysema in Alpha-1 Antitrypsin Deficiency

This grant supported by the Alpha-1 Foundation and the CHEST Foundation.

CHEST Foundation Research Grant in Women's Lung Health

Neelima Navuluri, MD, MPH
Evaluation of Chronic Hypoxemia

From Cardiopulmonary Disease Among Patients in Western Kenya and Perspectives on Oxygen Therapy

This grant supported in full by the CHEST Foundation.

CHEST Foundation Research Grant in Pulmonary Fibrosis

Eric Abston, MD
Noninvasive Quantification of Pulmonary Fibrosis Due to Radiation Induced Lung Injury Using [68Ga]CBP8 Type 1 Collagen Probe

Karthik Suresh, MD
Safety and Efficacy of High-Flow Air for Long-term Oxygen Therapy Delivery in Patients With Pulmonary Fibrosis

These grants are supported by a scientific advancement agreement from Boehringer Ingelheim Pharmaceuticals, Inc and by a grant from Genentech.

CHEST Foundation Research Grant in Chronic Obstructive Pulmonary Disease

Chris Mosher, MD
Identifying Treatment Outcomes and Early Predictors of Failure in 600 Hospitalized Patients With Acute Exacerbation of COPD Treated with Noninvasive Ventilation

This grant supported in full by the CHEST Foundation.

CHEST Foundation Research Grant in Nontuberculous Mycobacteria Diseases

Elsje Pienaar, PhD
A Computational Bridge Between In Vitro MIC and In Vivo Efficacy of Antibiotics Against MAC Infection

Elisa Ignatius, MD
Early Bactericidal Activity of Standard Drugs Used to Treat Mycobacterium Avium Complex: A Pilot Study

Supported by a research award

grant by Insmmed Incorporated.

CHEST Foundation Research Grant in Venous Thromboembolism

Mitchell Cahan, MD
A Translational Approach to Understanding Venous Thromboembolism in Post-Surgical Patients Using MicroRNAs in the American Black Bear

This grant supported in full by the CHEST Foundation.

CHEST Foundation Research Grant in Severe Asthma

Vickram Tejwani, MD
Peripheral Immune Cell Landscape in Obese Children With Severe Asthma

Sunita Sharma, MD, MPH
Predictors of Anti-IL-5 Treatment Failure in Severe Asthmatics
Supported by an independent educational grant from AstraZeneca LP.

CHEST Foundation Research Grant in Cystic Fibrosis

Kathleen Ramos, MD, MS
Underweight Individuals With Cystic Fibrosis and Implications for Lung Transplantation
This grant supported by Vertex Pharmaceuticals Incorporated.

John R. Adrizzo, MD, FCCP Research Grant in Sarcoidosis

Divya Patel, DO
Pharmacogenetic Predictors of Therapeutic Response to Methotrexate in Patients With Sarcoidosis

Nicholas Arger, MD
Using Serum Interferon-Induced Chemokines to Predict Sarcoidosis Outcomes

This grant is in honor of John R. Adrizzo, MD, and is supported in full by the Adrizzo Family, their

friends, and the CHEST Foundation.

CHEST Foundation Research Grant in Sleep Medicine

Irene Telias, MD
Influence of Sleep-Wakefulness Abnormalities on Patient-Ventilator Dyssynchrony: A Step Towards Improvement of Sleep Quality in Critically Ill Patients

Sushmita Pamidi, MD, MSc
Maternal Sleep-Disordered Breathing in Pregnancy and Risk of Adverse Health Outcomes in Children: A Follow-Up Study of the 3D Pregnancy and Birth Cohort
This grant supported by Apria Healthcare and Jazz Pharmaceuticals.

CHEST Foundation Community Service Grant Honoring D. Robert McCaffree, MD, Master FCCP

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Improving Critical Care Capacity in Sierra Leone

Dana Hickman, ARNP-C, FNP-BC
Living With COPD: Empowering Individuals, Families, and Caregivers
Ann Salvator, MS
Pediatric Asthma Screenings and Education on the Navajo Reservation

Tisha Wang, MD
PAP Foundation Education Days: A Project to Reach Patients, Caregivers, and Physicians
Grants supported in full by the CHEST Foundation.

Winners: CHEST Challenge Championship 2019

1st Place

Ohio State University

Elie Homsy, MD
Rachel Quaney, MD
Ryan Story, MD

Program Director: Jennifer McCallister, MD, FCCP

2nd Place

Walter Reed National Military Medical Center

Jeannette Collins, MD
Ian Grasso, MD
Arthur Holtzcalw, MD

Program Director: Aaron Holley, MD, FCCP

3rd Place

Maimonides Medical Center

Sushil Gupta, MBBS
Ankur Sinha, MD
Vignesh Ponnusamy, MD

Program Directors: Yizhek Kupfer, MD, and Stephan Kamholz, MD, FCCP

Winners: Abstract awards

Alfred Soffer Research Award Winners

Johnathan Chung: *Evaluating clinical utility of a UIP genomic classifier in subjects with and without a HRCT pattern of UIP*

Girish Nair, MD: *Quantitative lung function imaging using novel integrated Jacobian ventilation method in a healthy cohort with no respiratory symptoms*

Young Investigator Award Winners

Marvi Bikak, MD: *Application of Markov modeling to assess outcomes in COPD*

Arunima Bera, MD: *Soluble intracellular adhesion molecule-1 (ICAM-1) predicts mortality in children with ARDS and sepsis*

Abstract Poster

Winner: Rachel Naramore: *Causes of mortality post single vs double lung transplantation for COPD*

Runner-Up: Arjun Srinivasan: *Feasibility and safety of day care thoracoscopy for undiagnosed exudative pleural effusions*

Case Report Slide Winners

Catherine A. Gao, MD: *Nocardia Abscess and pulmonary alveolar proteinosis masquerading as lung cancer with lymphangitic spread in a 57-yo patient with 80 py smoking history*, in Fellows session - Interesting Presentations of Infectious Diseases

Sangita Goel, MD: *Successful single lung transplant of a hepatitis C positive donor to an HIV seropositive recipient with pulmonary fibrosis*, in Fellows Session, - Pulmonary Pathology

Matthew Lyons, MD: *Familial pulmonary fibrosis secondary to short telomere syndrome*, in Medical Student/Resident Session - Diffuse Lung Disease

Sarika Savajiyani, DO: *Management of secondary hyperfibrinolysis in extracorporeal membrane oxygenation as identified by thromboelastography*, in Fellows Session - Clinical Conundrums In ECMO

Chase A. Baxter, DO: *Polybiopsy Fulminans: pulmonary lymphomatoid granulomatosis*, in Medical Student/Resident Session - Pulmonary Pathology

Jason Low, MBBS: *The Hurricane Effect: An unusual phenomenon*

in the pulmonary artery, in Fellows Session - Bronchoscopic Procedures

Jacob Hupp, MD: *ECMO-related hemolytic anemia: A case series illustrating the role of plasmapheresis in management*, in Fellows Session - Plasmapheresis To The Rescue

Nichole A. Smith, MD: *Bilateral chylothorax secondary to spontaneous thoracic duct aneurysm*, in Fellows Session - Disorders of the Pleura

Ritu Modi, MD: *A florist's occupational exposure*, in Fellows Session - Chest Infections: Find The Fungus

Ly Tran, DO: *A rare case of paraneoplastic edematous dermatomyositis associated with small cell lung cancer*, in Medical Student/Resident Session - Lung Cancer: Unusual Presentations

Abdelhamid Ben Selma, MD: *Primary synovial sarcoma of the lung complicated with post biopsy tumor spread to the tracheal wall*, in Medical Student/Resident Session - Pulmonary Pathology II

Dhaval Thakkar, MD: *A curious manifestation of sarcoidosis*, in Fellows Session - Pulmonary Manifestations of Systemic Disease

Isaac N. Biney, MBChB: *Acute pulmonary embolism associated with a mobile right atrial thrombus managed by suction thrombectomy*, in Fellows Session - Pulmonary Vascular Disease

Tie: José Antonio J. Meade Aguilar: *Crossfit Training-related spontaneous diaphragmatic rupture: A case report* and Abigail R. Sullivan, DO: *A rare case of culture-negative Whipple's endocarditis*, in Medical Student/Resident Session - Cardiovascular Cases

Yameena T. Jawed: *Blue inside and out: A novel case of hypothermic shock salvaged by methylene blue*, in Fellows Session - Unusual Cases and Treatments in the ICU

Rahul Dasgupta, MD: *Superior vena cava (SVC) -tracheal fistula: an unusual case of hemoptysis*, in Medical Student/Resident Session - Lung Cancer: Expect The Unexpected

Akshay Bhatnagar, MD: *A case of clinically amyopathic dermatomyositis-related interstitial lung disease due to anti-MDA5 antibody and hepatitis B infection*, in Fellows Session - Diffuse Lung Diseases



CHEST[®] Annual Meeting 2019

Kathleen Twomey, MD: *A case of recurrent encephalopathy in a gastric bypass patient*, in Medical Student/Resident Session - Critical Care Complications

Jennifer Sunny, DO: *Massive bee envenomation treated by plasmapheresis*, in Medical Student/Resident Session - Critical Care Devices

Hafiz B. Mahboob, MD: *Pazopanib associated secondary spontaneous pneumothorax: Natural disease progression or drug safety concern?* in Fellows Session - Lung Cancer

Tie: Andrew Demaio, MD: *A case of pulmonary tuberculosis and persistent intestinal inflammation and hemorrhage: TB or not TB?* and Joanna M. Scoon: *Attack of the wild boars*, in Fellows Session - Chest Infections

Danielle El Haddad, MD: *A right to left extracardiac shunt from a chronic superior vena cava thrombus in a prothrombotic patient*, in Medical Student/Resident Session - Pulmonary Vascular Disease

John Shumar, DO: *Make no bones about it: A rare case of osseous sarcoidosis presenting twenty years after initial diagnosis*, in Medical Student/Resident Session - Pulmonary Manifestations Of Systemic Disease

Case Report Poster Winners

Jad Sargi, MD: *Atypical presentation of posterior reversible encephalopathy syndrome (PRES syndrome)*

Ankur Sinha, MBBS: *Listeria monocytogenes brain abscess in an immunocompetent adult*

Carla Emille D. Barbon, MD: *Giant primary liposarcoma of the pleura resected through hemi-clamshell thoracotomy*

Hope F. Johnson, RRT: *Bronchoscopic treatment of early and late presentation of iron pill aspiration*

Humna Abid Memon, MD: *Autologous stem cell transplantation: A possible treatment for pulmonary hypertension in Poems syndrome*

Jordanna Hostler, MD, FCCP: *Beyond steroids: Mepolizumab for chronic eosinophilic pneumonia*

Zahra Zia, MD, MBBS: *Extracorporeal membrane oxygenation (ECMO) for emergent surgical treatment of anaerobic purulent pericarditis causing cardiac tamponade, bronchomediastinal fistula, and ARDS*

Brooke A. McDonald: *Fatal central pulmonary cement embolism after kyphoplasty*

Mary E. Richert, MD: *A case of rasburicase-induced methemoglobinemia due to glucose-6-phosphate dehydrogenase deficiency treated with hyperbaric oxygen therapy*

Shiva M. Arjun, MD: *Aortobronchial fistula due to graft failure: A rare cause of hemoptysis*

Harshwant Grover, MD: *Black mediastinum: Primary mediastinal melanoma*

Neha Agarwal, MD: *Posttransplant pulmonary Kaposi sarcoma presenting as chylothorax*

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ABIM's longitudinal assessment option anticipated to launch in 2022

BY MICHAEL E. NELSON, MD, FCCP

CHEST Physician Editorial Board Member

Physicians have asked for more flexible and convenient ways to maintain their ABIM Board certification, and the recently announced longitudinal assessment option is being designed to accomplish these requests. It is anticipated to launch in 2022 in as many specialties as possible, allowing time prior to launch for engagement with the medical community to produce the best possible experience.

How will the new longitudinal assessment option be different? Question delivery will be structured to allow physicians greater ease of use and mobility, enabling access from virtually anywhere. Answer feedback will be immediate, and physicians will see the rationale behind the answer, along with links to educational material. The preferred pace for answering questions during each administration window will be determined by the examinee, and access to all the resources you use in practice, such as journals or websites, will also be allowed.

Engaging the community

As a Council member, I can attest to the fact that the ABIM has spent a lot of time thinking through key features that are “must haves” in the new option, but there are details that are still being defined. ABIM has prioritized engaging the community, and the suggestions, insights, and questions coming out of these efforts are being used to guide the development of the new longitudinal assessment option.

Following the initial announcement in August, nearly 1,400 physicians submitted comments about the new option. ABIM conducted 69 one-on-one interviews with board-certified physicians and ran user-testing on existing longitudinal assessment platforms from other Boards. ABIM staff attended society meetings throughout the fall and also assembled a Physician Advisory Panel of 11 physicians from members of our Community Insights



Dr. Nelson

Network. We want to ensure the features we are considering work well for physicians and provide the high quality experience they deserve.

How can you get involved?

Physicians interested in giving ABIM feedback are invited to connect with us through our Community Insights Network. By joining the Network, you'll have an opportunity to share your ideas through surveys, interviews, and user tests and be a member of our online community “ABIM Engage.”

ABIM staff will also be in attendance at society meetings to provide individualized guidance and answer your questions. We had a booth at CHEST this past October, and you can find upcoming society meetings staff who will be attending on the ABIM website.

What Should You Do Now?

All current ABIM MOC program requirements and policies remain in effect, and ABIM will communicate

any program changes well in advance of implementation. If you have an assessment due in 2020 or 2021, you can choose from the options currently available in your discipline.

Registration for all 2020 MOC assessments opened December 1, and physicians may have several pathways to choose from, including taking the Knowledge Check-In at home, office, or testing center or the traditional point-in-time assessment taken at a PearsonVUE center.

The next Knowledge Check-In in Pulmonary Disease will be offered in 2021. ABIM's website lists the full schedule of available assessment options (<https://tinyurl.com/t5bfg55>). You can find all of your MOC program requirements and deadlines by signing into your Physician Portal at abim.org.

To keep up to date with developments in ABIM's longitudinal assessment program, visit the new longitudinal FAQ webpage (<https://tinyurl.com/u5bbdgw>) that is updated as information becomes available.

This month in the journal CHEST®

Editor's Picks

BY PETER J. MAZZONE, MD, MPH, FCCP

Editor in Chief

Editorials

Right Ventricle to Left Ventricle Ratio at CTPA Predicts Mortality in Interstitial Lung Disease

By Dr. S. Gaine, et al.

Lung Ultrasound for the Diagnosis of Acute Heart Failure in the Emergency Department: A Step Forward.

By Dr. P. Le Conte, et al.

Original research

The Burden of Substance Abuse-Related Admissions to the Medical ICU

By Dr. D. Westerhausen, et al.

Accuracy of Several Lung Ultra-



sound Methods for the Diagnosis of Acute Heart Failure in the Emergency Department: A Multicenter Prospective Study

By Dr. T. Choulhed, et al.

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Mark J. Rosen, MD, Master FCCP Endowment

Mark J. Rosen, MD, Master FCCP, was dedicated to championing lung health through volunteering, philanthropy, and education. Support the legacy of Dr. Rosen by contributing to the Mark J. Rosen, MD, Master FCCP Endowment. Funds raised will support international young professionals' travel to the United States to attend the annual meeting.

To learn more and to support the Mark J. Rosen, MD, Master FCCP Endowment, visit bit.ly/MarkJRosenEndowment.

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