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# **Section** CHEST Physician®

Scanning electron micrograph of patient-isolated SARS-CoV-2 viruses emerging from cultured cells.

### **COMMENTARY Questions about post-COVID-19** lung injury – what we know so far

BY AARON B. HOLLEY, MD, FCCP

ven as the COVID-19 pandemic continues, the post-COVID-19 syndrome pandemic has already begun. What is post-COVID-19 syndrome (or long-haulers or long COVID)? Is it standard postviral fatigue? Prolonged deconditioning following debilitating illness? Permanent lung or vascular injury? Common sense and past experience say it's all of these.

In theory, the burden of actual lung injury post COVID-19 should be the easiest to quantify, so let's discuss what we think we know. I've heard experts break post-COVID-19 lung injury into three broad categories:

- Preexisting lung disease that is exacerbated by acute COVID-19 infection.
- Acute COVID-19 infection that causes acute respiratory distress syndrome (ARDS) or other acute lung injury (ALI).
- Non-critically ill acute COVID-19 with residual lung damage and abnormal repair. These categories are necessarily imprecise,

making it challenging to fit some patients neatly into a single definition.

For patients in the first category, management will be dictated largely by the nature of the preexisting lung disease. For those in category two, we already know a lot about what LUNG INJURY // continued on page 7

> CHEST 202' ANNUAL MEETING | OCTOBER 17-20

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

### **OSA** in women: Different symptoms, risks, and consequences

BY CHRISTINE KILGORE MDedge News

he reported prevalence and severity of obstructive sleep apnea in women is lower, compared with men, but the consequences of the disease are "at least the same, if not worse," with women appearing to have greater susceptibility to adverse OSA-related cardiovascular consequences - particularly as it pertains to endothelial dysfunction, Reena Mehra, MD, MS, said at the virtual annual meeting of the Associated Professional Sleep Societies.

Women more so than men have endothelial dysfunction associated with OSA, "suggesting there is an enhanced sensitivity of the female vascular endothelium to intermittent hypoxia," said Dr. Mehra, director of sleep disorders research at the Cleveland Clinic and professor of medicine at Case Western Reserve University, also in Cleveland.

Sex-specific differences in the anatomic and physiological characteristics of the upper airway, in fat distribution, and in respiratory stability as they relate to OSA have been documented

**SLEEP** // continued on page 4





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### Sleep apnea // continued from page 1

for some time – and today, these and other differences relating to the diagnosis, treatment, and consequences of sleep apnea continue to be studied and elucidated, said Dr. Mehra, Anita Rajagopal, MD, and Chitra Lal, MD, in a session on OSA in women. Each spoke about the breath and implications of these differences, and of increasing recognition of the significance of OSA in women.

### Likely underdiagnosis

Epidemiologic studies have suggested a three- to fivefold higher prevalence of OSA in men than in women in the general population. But it has also been estimated that 17%-25% of women have sleep apnea, and the prevalence reported in various studies has generally increased with time, said Dr. Rajagopal, department medical director for sleep medicine at Community Physician Network in Indianapolis, and medical director of the Community Health Network Sleep/Wake Disorders Center, also in Indianapolis.

One population-based study in Sweden, reported in 2013, found OSA (defined as an apnea-hypo-



pnea index [AHI]  $\geq$  5) in 50% of women aged 20-70 (Eur Respir J. 2013;41[3]:610-5), she noted.

It's quite possible women are being misdiagnosed or underdiagnosed because of their reporting of different symptoms, Dr. Rajagopal said. The Epworth Sleepiness Scale, commonly used to screen for OSA, has not been validated for use in women and has not been strongly associated with daytime sleepiness in women in population-based studies, she said, noting that women who report similar levels of daytime sleepiness to men are less likely to have an ESS score greater than 10.

"We shouldn't rule out obstructive sleep apnea in women with a low ESS," Dr. Rajagopal said in an interview after the meeting. Attentiveness to the symptoms more often reported by women – generalized daytime fatigue/lack of energy, insomnia, morning headaches, mood disturbances, and nightmares – is important, as is performance of overnight polysomnography when a home sleep study is negative and there



### SCHEST Physician

is clinical suspicion of OSA.

Respiratory disturbances in women are frequently associated with arousals – which induce less ventilatory instability in women than in men – rather than oxygen desaturations, leading to underestimation of OSA on home sleep testing. Insomnia associated with OSA in women may also increase the likelihood of a false– negative result, Dr. Rajagopal said at the meeting.

"It's really important [in sleep testing] to consider your AHI values in women," she said. "The AHI value may not provide a true indication of the degree of sleep fragmentation being expe-

"The long-term effects of REM disruption contribute to greater symptomatology at lower AHI values in women compared to men."

rienced by patients." That OSA symptoms manifest in women with lower AHIs has been elucidated in research showing, for instance, that those with an AHI of 2-5 per hour have a similar level of symptoms to men with an AHI of at least 15 per hour, she said.

Women tend to have a clustering of apnea during REM sleep, and it's possible that "the longterm effects of REM disruption contribute to greater symptomatology at lower AHI values in women compared to men," Dr. Rajagopal said.

Also at play are when it comes to testing and diagnosis are several other key sex differences, she said. For one, the upper airways in women are less collapsible and more stable during sleep (most evident during non-REM sleep), and respiratory events during sleep are less frequently associated with complete upper airway collapse.

Women also have shorter apneic episodes, but "the longest apneas are associated with a more severe oxygen desaturation," she said. Moreover, they have more episodes of upper airway resistance during sleep, which in and of itself "has been shown to produce clinical symptoms such as daytime fatigue and clinical depression."

Continued on following page

#### Continued from previous page

In her presentation, Dr. Mehra similarly commented on a likely underdiagnosis of OSA in women. In addition to differing symptoms, including palpitations, "women are less likely to have arousals, and have a lesser degree of nocturnal hypoxia compared to men ... perhaps leading to even more of an underdiagnosis."

#### **Unique consequences**

Differences in upper airway physiology and other sex-specific differences impacting OSA susceptibility are at least partly attributable to sex hormones, said Dr. Mehra and Dr. Lal, associate professor of medicine at the Medical University of South Carolina, Charleston.

A significant increase in prevalence is seen after menopause, category as well as an increase in left ventricular mass thickness, and a 30% increased risk of heart failure or death in women with moderate/ severe OSA, compared with women without OSA or with mild OSA, Dr. Mehra said. These findings were not observed in men (Circulation. 2015;132:1329-37).

The dominance of REM-related OSA in women raises risk because sleep disturbances during REM sleep are associated with adverse cardiometabolic outcomes including prevalent and incident hypertension, Dr. Mehra noted. "REM-related OSA may also adversely impact glucose metabolism," she said, "even in the absence of non-REM obstructive sleep apnea."

Regarding OSA treatment and responsivity, Dr. Mehra said that preliminary, post hoc data from



and research has shown that each additional year in menopause is associated with a greater AHI – a "dose-response effect," Dr. Lal said. An inverse association between hormone replacement therapy and OSA severity has been seen in epidemiological studies including the Sleep Heart Health Study, Dr. Mehra said. But in prospective studies, Dr. Lal noted, hormone replacement therapy has not been shown to decrease AHI.

Experimental and clinical studies suggest that the vascular endothelium is influenced by sex hormones, Dr. Mehra said. Estrogen is known to improve endothelial function by inducing increased nitric oxide bioavailability – important in the setting of hypoxemia, which leads to reduced bioavailability of nitric oxide.

"Alterations of sex-specific hormones in OSA may represent a key factor in increasing vulnerability to vascular dysfunction," Dr. Mehra added.

The Sleep Heart Health Study also documented sex-specific differences, showing a graded increase of troponin with increasing OSA severity a randomized, controlled trial of the impact of continuous positive airway pressure therapy on cardiovascular biomarkers showed a sex-specific effect. "There were differences in men versus women in terms of responsiveness with regards to biomarkers of inflammation and oxidative stress ... with reductions from CPAP observed in women but not in men," said Dr. Mehra, a co-investigator of the study.

The data suggest, she said, that "these biomarkers may be more responsive to treatment and a reversal of sleep apnea pathophysiology in women."

Women also appear to respond better than men to upper airway nerve stimulation, she said, referring to an international registry study showing a 3.6-fold higher odds of responsiveness to the therapy relative to men (Eur Resp J. 2019;53[1]:1801405). Women in the study were 60% less likely to be approved by insurance for UAS, however, making it "a public policy issue, said Dr. Mehra, a coinvestigator.

Dr. Rajagopal, Dr. Mehra, and Dr. Lal all reported that they had no potential conflicts of interest.

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### A faster, fitter, variant tied to increasing hospitalization: Why Delta has doctors worried

### BY BRENDA GOODMAN, MA

atherine O'Neal, MD, an infectious disease physician, took to the podium of the Louisiana governor's press conference recently and did not mince words.

"The Delta variant is not last year's virus, and it's become incredibly apparent to health care workers that we are dealing with a different beast," she said.

Louisiana is one of the least vaccinated states in the country. In the United States as a whole, 48.6% of the population is fully vaccinated. In Louisiana, it's just 36%, and Delta is bearing down.

Dr. O'Neal spoke about the pressure that rising COVID cases were already putting on her hospital, Our Lady of the Lake Regional Medical Center in Baton Rouge. She talked about watching her peers, 30- and 40-year-olds, become severely ill with the latest iteration of the new coronavirus – the Delta variant – which is sweeping through the United States with astonishing speed, causing new cases, hospitalizations, and deaths to rise again.

Dr. O'Neal talked about parents who might not be alive to see their children go off to college in a few weeks. She talked about increasing hospital admissions for infected kids and pregnant women on ventilators.

"I want to be clear after seeing what we've seen the last 2 weeks. We only have two choices: We are either going to get vaccinated and end the pandemic, or we're going to accept death and a lot of it," Dr. O'Neal said, her voice choked by emotion.

### Where Delta goes, death follows

Delta was first identified in India, where it caused a devastating surge in the spring. In a population that was largely unvaccinated, researchers think it may have caused as many as three million deaths. In just a few months' time, it has sped across the globe.

Research from the United Kingdom shows that Delta is highly contagious. It's about 60% more easily passed from person to person than the Alpha version (or B.1.1.7, which was first identified in the United Kingdom).

Where a single infected person might have spread older versions of the virus to two or three others, mathematician and epidemiologist Adam Kucharski, PhD, an associate professor at the London School of Hygiene and Tropical Medicine, thinks that number – called the basic reproduction number – might be around six for Delta, meaning that, on average, each infected person spreads the virus to six others.

"The Delta variant is the most able and fastest and fittest of those viruses," said Mike Ryan, executive director of the World Health Organization's Health Emergencies Programme, in a recent press briefing.

Early evidence suggests it may also cause more severe disease in people who are not vaccinated.

"There's clearly increased risk of ICU admission, hospitalization, and death," said Ashleigh Tuite, PhD, MPH, an infectious disease epidemiologist at the University of Toronto in Ontario.

In a study published ahead of peer review, Dr. Tuite and her coauthor, David Fisman, MD, MPH, reviewed the health outcomes for more than 200,000 people who tested positive for SARS-CoV-2 in Ontario between February and June of 2021. Starting in February, Ontario began screening all positive COVID tests for mutations in the N501Y region for signs of mutation.

Compared with versions of the coronavirus that circulated in 2020, having an Alpha, Beta, or Gamma variant modestly increased the odds that an infected person would become sicker. The Delta variant raised the risk even higher, more than doubling the odds that an infected person would need to be hospitalized or could die from their infection.

Emerging evidence from England and Scotland, analyzed by Public Health England, also shows an increased risk for hospitalization with Delta. The increases are in line with the Canadian data. Experts caution that the picture may change over time as more evidence is gathered.

"What is causing that? We don't know," Dr. Tuite said.

### **Enhanced virus**

The Delta variants (there's actually more than one in the same viral family) have about 15 different mutations compared with the original virus. Two of these, L452R and E484Q, are mutations to the spike protein that were first flagged as problematic in other variants because they appear to help the virus escape the antibodies we make to fight it.

It has another mutation away from its binding site that's also getting researchers' attention – P681R.

This mutation appears to enhance the "springiness" of the parts of the virus that dock onto

Continued on following page

### Lung injury // continued from page 1

their recovery from ARDS will look like (N Engl J Med. 2003 Feb 20. doi: 10.1056/NEJMoa022450; N Engl J Med. 2011 Apr 7. doi: 10.1056/NEJMoa1011802).

There's no longer reason to believe that COVID-19-related ARDS is particularly unique, and all things being equal, lung recovery should mimic that seen with non-COVID-19 ARDS (Ann Am Thorac Soc. 2021. doi: 10.1513/ AnnalsATS.202008-1076OC).

It's going to take patience and time, and beyond targeted rehabilitation it's not clear that we have anything available to expedite the process.

The third category of patients is the most intriguing. Is there a group of patients who have residual lung injury but didn't have evident ARDS/ ALI during their acute COVID-19 infection? Anecdotally we think so, but we know little about prevalence and less about management. A recent study published in Annals of the American Thoracic Society addresses both issues (2020. doi: 10.1513/ AnnalsATS.202008-1002OC). In an observational report on patients recovering after being hospitalized with COVID-19 infection, 3.6% of patients had residual lung injury that improved with 3 weeks of corticosteroid treatment.

The report is hardly definitive. It's observational, and patients required extensive screening and identification by a multidisciplinary committee of experts in interstitial lung disease. Patients were diagnosed as having organizing pneumonia (OP) as their "lung injury" if certain radiographic criteria were met. There were no biopsies. Last, there was no control group. Still, this report is critically important. It tells us that at 6 weeks post discharge, about 3.6% of patients who were hospitalized for COVID-19 will have persistent symptoms, radiographic abnormalities, and a plateau in their recovery.

Beyond that, it tells us little. Did these patients really have OP? It's impossible to know. The CT findings used to establish the diagnosis are nonspecific (Chest. 2011. doi: 10.1378/chest.10-0883). Response to steroids is consistent with OP, but the treatment course was quite short (Curr Opin Pulm Med. 2005. doi: 10.1097/01. mcp.0000175521.41729.07). If truly OP, one would expect a high relapse rate after steroid withdrawal. Patients weren't followed long enough to monitor recurrence rates. Also, as appropriately discussed in the accompanying editorial, there's no control group so we can't know whether the patients treated with steroids would have recovered without treatment (doi: 10.1513/

AnnalsATS.202101-048LE). There was objective improvement in lung function for the two to three patients they followed who did not receive steroids. However, it was of lesser magnitude than in the steroid group.

Post–COVID-19 symptoms will remain a challenge for the foreseeable future. More than 30 million patients have been diagnosed with COVID-19 in the United States and close to half will experience persistent dyspnea (JAMA. 2020. doi: 10.1001/ jama.2020.12603). The vast majority will likely not have identifiable lung injury that will benefit from steroids. I wish I could prescribe patience to both physicians and patients.

Dr. Holley is associate professor of medicine at Uniformed Services University and program director of pulmonary and critical care medicine at Walter Reed National Military Medical Center.

### 'Long-haul' recovery worse than cancer rehab for some

### BY DAMIAN MCNAMARA

Some people recovering from COVID-19 fare worse than current or previous cancer patients when referred to outpatient rehabilitation services, a new study from the CDC demonstrates.

People experiencing ongoing or "long-haul" symptoms after COVID-19 illness were more likely to report pain, challenges with physical activities, and "substantially worse health," compared with people needing rehabilitation because of cancer, lead author Jessica Rogers-Brown, PhD, and colleagues report.

The study was published online July 9 in Morbidity and Mortality Weekly Report (MMWR) (2021. doi: 10.15585/mmwr.mm7027a2).

The CDC investigators compared the self-reported physical and mental health symptoms, physical endurance, and use of health services of 1,295 outpatients recovering from COVID-19 and a control group of another 2,395 outpatients rehabilitating from a previous or current cancer diagnosis who had not experienced COVID-19.

Researchers used electronic health record data from January 2020 to March 2021 in the Select Medical network of outpatient clinics. The study included patients from 36 states and the District of Columbia. Compared with people referred

*"Antibodies don't* 

penetrate inside the

cell. If these viruses are

going from one cell to

another by just fusing to

each other, antibodies

become less useful."

for cancer rehabilitation, those with COVID-19 symptoms lasting beyond 4 weeks were 2.3 times more likely to report pain, 1.8 times more likely to report worse physical health, and 1.6 times more likely to report difficulty with physical activities, an adjusted odds ratio analysis reveals.

The COVID-19 rehabilitation group also performed significantly worse on a 6-minute walk test, suggesting less physical endurance than people recovering from cancer (P < .001). They also used more rehabilitation services overall.

The researchers suggest services tailored to the unique physical and mental health rehabilitation needs of the post–COVID-19 patient population could be warranted.

The study does not suggest all people recovering with COVID-19 will fare worse than people recovering from cancer, the authors caution. They note that "these results should not be interpreted to mean that post–COVID-19 patients overall had poorer physical and mental health than patients with cancer."

"Instead, results indicate that post-COVID-19 patients specifically referred to a large physical rehabilitation network had poorer health measures than those referred for cancer, which indicates that some patients recovering from COVID-19 had substantial rehabilitation needs."

### Continued from previous page

our cells, said Alexander Greninger, MD, PhD, assistant director of the UW Medicine Clinical Virology Laboratory at the University of Washington in Seattle. So it's more likely to be in the right position to infect our cells if we come into contact with it.

Another theory is that P681R may also enhance the virus's ability to fuse cells together into clumps that have several different nuclei. These balls of fused cells are called syncytia.

"So it turns into a big factory for making viruses," said Kamran Kadkhoda, PhD,

thology at the Cleveland Clinic in Ohio.

This capability is not unique to Delta or even to the new coronavirus. Earlier versions and other viruses can do the same thing, but according to a recent paper in Nature, the syncytia that Delta creates are larger than the ones created by previous variants. Larger syncytia may help the

virus copy itself quickly, so a person's viral load builds up faster. That may enhance the ability of the virus to transmit from person to person.

And at least one recent study from China supports this idea. That study, which was posted ahead of peer review on the website Virological. org, tracked 167 people infected with Delta back to a single index case.

China has used extensive contact tracing to identify people that may have been exposed to the virus and sequester them quickly to tamp down its spread. Once a person is isolated or quarantined, they are tested daily with gold-standard PCR testing to determine whether or not they were infected.

Researchers compared the characteristics of Delta cases with those of people infected in 2020 with previous versions of the virus.

This study found that people infected by Delta tested positive more quickly than their predecessors did. In 2020, it took an average of 6 days for someone to test positive after an exposure. With Delta, it took an average of about 4 days.

When people tested positive, they had more than 1,000 times more virus in their bodies, suggesting that the Delta variant has a higher growth rate in the body. This gives Delta a big advantage and may help explain why Delta is so much more contagious.

Beyond transmission, Delta's ability to form syncytia may have two other important consequences. It may help the virus hide from our immune system, and it may make the virus more damaging to the body.

"Antibodies don't penetrate inside the cell. If these viruses are going from one cell to another by just fusing to each other, antibodies become less useful," Dr. Kadkhoda said.

### **Escape artist**

Recent studies show that Delta is also able to escape antibodies made in response to vaccination more effectively than the Alpha, or B.1.1.7 strain. The effect was

more pronounced in older adults, who tend to have weaker responses to vaccines in general.

This evasion of the immune system is particularly problematic for people who are only partially vaccinated. Data from the United Kingdom show that a single dose of vaccine is only about 31% effective at preventing illness with Delta, and 75% effective at preventing hospitalization.

After two doses, the vaccines are still highly effective – even against Delta – reaching 80% protection for illness, and 94% for hospitalization, which is why U.S. officials are begging people to get both doses of their shots, and do it as quickly as possible.

Finally, the virus's ability to form syncytia may leave greater damage behind in the body's tissues and organs. "Especially in the lungs," Dr. Kadkhoda said. The lungs are very fragile tissues. Their tiny air sacs – the alveoli – are only a single-cell thick. They have to be very thin to exchange oxygen in the blood. "Any damage like that can severely affect any oxygen exchange and the normal housekeeping activities of that tissue," he said. "In those vital organs, it may be very problematic."

The research is still early, but studies in animals and cell lines are backing up what doctors say they are seeing in hospitalized patients.

A recent preprint study from researchers in Japan found that hamsters infected with Delta lost more weight – a proxy for how sick they were – compared with hamsters infected with an older version of the virus. The researchers attribute this to the virus's ability to fuse cells together to form syncytia.

Another investigation, from researchers in India, infected two groups of hamsters – one with the original "wild-type" strain of the virus, the other with the Delta variant of the new coronavirus.

As in the Japanese study, the hamsters infected with Delta lost more weight. When the researchers performed necropsies on the animals, they found more lung damage and bleeding in hamsters infected with Delta. This study was also posted as a preprint ahead of peer review.

German researchers found that cells infected with the Delta variant formed more and larger syncytia compared with cells infected with the wild type strain of the virus. The authors write that their findings suggest Delta could "cause more tissue damage, and thus be more pathogenic, than previous variants."

Researchers say it's important to remember that, while interesting, this research isn't conclusive. Hamsters and cells aren't humans. More studies are needed to prove these theories.

Scientists say that what we already know about Delta makes vaccination more important than ever.

"The net effect is really that, you know, this is worrisome in people who are unvaccinated and then people who have breakthrough infections, but it's not ... a reason to panic or to throw up our hands and say you know, this pandemic is never going to end," Dr. Tuite said, "[b]ecause what we do see is that the vaccines continue to be highly protective."

### Nintedanib slows ILD progression in patients with RA

### BY TED BOSWORTH

MDedge News

n a new subgroup analysis of a previously published multinational trial, the preservation of lung function with nintedanib (Ofev) was about the same in patients with interstitial lung disease related to rheumatoid arthritis (RA-ILD) as it was in patients with other



etiologies, according to data presented at the annual European Congress of Rheumatology.

"There was no significant heterogeneity across any of several characteristics we eval-

Dr. Kelly

uated," reported Clive Kelly, MBBS, of the Institute of Cellular Medicine at Newcastle (England) University.

The INBUILD trial, which enrolled more than 600 patients in 15 countries with a range of fibrosing lung diseases, was published almost 2 years ago (N Engl J Med. 2019;381:1718-27. doi: 10.1056/ NEJMoa1908681). On the primary endpoint of rate of decline in forced vital capacity (FVC), the medians were -80.8 mL per year among those randomized to nintedanib and -187.8 mL per year (P < .001) on placebo.

The INBUILD study provided evidence that fibrosing lung diseases have a common pathobiologic mechanism that can be slowed by targeting intracellular kinases. Nintedanib inhibits several growth factor receptors as well as nonreceptor tyrosine kinases, but its exact mechanism for slowing fibrosing lung diseases remains unclear.

Nintedanib initially received ap-

provals from the FDA for systemic sclerosis–associated ILD in 2019 and for chronic fibrosing ILD with progressive phenotypes in 2020 after being initially approved for the treatment of idiopathic pulmonary fibrosis in 2014.

When asked for comment, Paul F. Dellaripa, MD, an associate professor of medicine in the division of rheumatology, immunology, and allergy at Harvard Medical School, Boston, indicated these data are helpful in considering strategies for RA patients with ILD, but he encouraged collaboration between joint and lung specialists.

"Antifibrotic agents for patients with progressive ILD in autoimmune diseases like RA is a welcome addition to our care of this challenging complication," said Dr. Dellaripa, who has published frequently on the diagnosis and treatment of lung diseases associated with RA. Yet, treatment must be individualized, he added.

"It will be incumbent for rheumatologists to incorporate lung health as a critical part of patient care and work closely with pulmonologists to consider when to institute antifibrotic therapy in patients with ILD," he said.

### **Details of subanalysis**

In the RA-ILD subpopulation of 89 patients, there was no further decline in FVC from 24 weeks after randomization to the end of 52 weeks for those on nintedanib, but the decline remained steady over the full course of follow-up among those in the placebo group The decline in the placebo group reached –200 mL at the end of 52 weeks. As a result, the between-group relative reduction in FVC at 52 weeks of 116.7 mL favoring nintedanib over placebo (*P* 



CT scan shows extensive pulmonary fibrosis in the mid and lower zones (note the extensive honeycombing).

< .037) slightly exceeded the 107mL reduction (P < .001) observed in the overall INBUILD study population.

Among other subgroups the investigators evaluated, outcomes with nintedanib did not differ when patients were split into groups with higher or lower baseline levels of high-sensitivity C-reactive protein, regardless of whether the groups were defined by levels above and below 1 mg/L or 3 mg/L. The same was true for those who were taking nonbiologic disease-modifying antirheumatic drugs or glucocorticoids.

However, for these latter analyses, Dr. Kelly conceded that the differences were based on small numbers of patients and so cannot be considered conclusive.

The adverse event most closely associated with nintedanib in the RA-ILD population was diarrhea, just as in the overall study, and it was more than twice as frequent in the RA-ILD patients receiving the active therapy, compared with placebo (54.8% vs. 25.5%). Nausea was also more common (21.4% vs. 10.6%), and so was decreased appetite (11.9% vs. 2.1%) and weight reduction (9.5% vs. 2.1%).

Lung-related adverse events, such as bronchiolitis (21.4% vs. 17.0%) and dyspnea (11.9% vs. 10.6%), were only slightly more frequent in the nintedanib group. Nasopharyngitis (7.1% vs. 12.8%) was less common. Side effects leading to treatment discontinuation were higher on nintedanib (19.0% vs. 12.8%)

The RA-ILD subgroup represented 13.4% of those randomized in INBUILD. The mean time since diagnosis of RA was about 10 years. More than 60% were smokers or former smokers. At baseline, the mean FVC of predicted was 71%. More than 85% had a usual interstitial pneumonia (UIP) radiologic pattern.

Acute exacerbations and death were not evaluated in the RA-ILD subpopulation, but these were secondary endpoints in the published INBUILD study according to the presence or absence of a UIP-like fibrotic pattern. For the combined endpoint of acute exacerbation of ILD or death, the protection associated with nintedanib approached statistical significance for the population overall (odds ratio, 0.68; 95% confidence interval, 0.46-1.01) and reached significance for those with a UIP pattern (OR, 0.61; 95% CI, 0.38-0.98).

Nintedanib led to lower death rates at 52 weeks in the overall population (8.1% vs. 11.5% with placebo) and in the group with a UIP pattern (9.7% vs. 15.0% with placebo).

Dr. Kelly has financial relationships with multiple pharmaceutical companies, including Boehringer Ingelheim, which provided funding for INBUILD and this subpopulation analysis. Dr. Dellaripa reported financial relationships with Bristol-Myers Squibb and Genentech.

### Children and COVID: Vaccinations drop as the cases rise

### BY RICHARD FRANKI

Mdedge News

With only a quarter of all children aged 12-15 years fully vaccinated against COVID-19, first vaccinations continued to drop and new cases for all children rose for the second consecutive week.

Just under 25% of children aged 12-15 had completed the vaccine regimen as of July 12, and just over one-third (33.5%) had received at least one dose. Meanwhile, that age group represented 11.5% of people who initiated vaccination during the 2 weeks ending July 12, down from 12.1% a week earlier, the Centers for Disease Control and Prevention said. The total number of new vaccinations for the week ending July 12 was just over 201,000, compared with 307,000 for the previous week.

New cases of COVID-19, however, were on the rise in children. The 19,000 new cases reported for the week ending July 8 were up from 12,000 a week earlier and 8,000 the week before that, according to a report from the American Academy of Pediatrics and the Children's Hospital Association.

That report also shows that children made up

22.3% of all new cases during the week of July 2-8, compared with 16.8% the previous week, and that there were nine deaths in children that same week, the most since March. COVID-related deaths among children total 344 in the 46 jurisdictions (43 states, New York City, Puerto Rico, and Guam) that are reporting such data by age.

Children aged 16-17 years, who became eligible for COVID vaccination before the younger age group, are further ahead in the process. Among the older children, almost 46% had gotten at least one dose and 37% were fully vaccinated by July 12.

### **Political support of permanent DST concerns experts**

**BY CHRISTINE KILGORE** *MDedge News* 

he reintroduction of congressional bills that aim to end seasonal time change and move permanently to daylight saving time (DST) – and action on the issue by 19 states in the last 4 years – signal political momentum and up the ante on sleep medicine to educate others and to more uniformly weigh in on the health consequences of such a change.

This was the message of several sleep scientists and physicians who participated in moderated discussions of DST at the virtual annual meeting of the Associated Professional Sleep Societies.

A position paper issued about a year ago by the American Academy of Sleep Medicine objected to the proposed switch and instead called for elimination of DST in favor of permanent standard time (ST). While there are detrimental health effects with time changes in either direction, there is "abundant" evidence that the transition from standard time to daylight saving time is worse, the AASM statement says (J



Clin Sleep Med. 2020;16[10]:1781-84).

Some experts have questioned, however, whether the evidence is weighty and comprehensive enough to drive a change in national policy. Others, such as SLEEP 2021 discussant Karin Johnson, MD, say there is unawareness outside of sleep medicine – and even within – of a growing body of literature on circadian misalignment and its associated health risks.

"There's an educational gap for what's out there [in the literature]," Dr. Johnson, medical director of the Baystate Health regional sleep

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program and Baystate Medical Center sleep laboratory in Springfield, Mass., said in an interview after the meeting.

Calls for more research, particularly on the chronic effects of DST and ST, are concerning because discussions of abolishing seasonal time change are "moving forward with or without us," Kenneth Wright Jr., PhD, director of the chronobiology laboratory at the University of Colorado in Boulder and professor in the university's department of integrative biology, said at the meeting.

"We don't have time ... to have the studies we'd need to prove unequivocally that permanent standard time [is best]. We need to consider the scientific evidence before us – what's known about human biology and health with respect to light and circadian timing," Dr. Wright said. "The argument that pushing our clocks later is going to be healthier is not tenable. We cannot support that given the vast amount of scientific evidence we have from circadi-

an and sleep science." Underscoring the sense of urgency to be engaged in the issue were the messages of Rep. Raymond Ward, MD, PhD, a Utah legislator in the state's House of Representatives who introduced a bill to permanently observe DST, pending the amendment of federal law to permit such a change, and provided that five other Western states enact the same legislation.

"I chose to support DST because I became convinced this is the only thing that's politically possible," said Rep. Ward, a family practice physician at the Ogden Clinic in Bountiful. National polls have shown a "strong preference" to end seasonal time change, he said, and a poll conducted in his district showed that nearly 80% "wanted to stop changing the clocks, and 65% wanted the summer time schedule."

"To me, the train seems to be

moving in one direction," said Rep. Ward. "The bills open in Congress in both the House and the Senate don't have enough support yet, but every time another state legislature passes [legislation to establish permanent DST], they pick up a few more supporters."

The Sunshine Protection Act of 2021 introduced in the House in January by Rep. Vern Buchanan (R-Fla.) has 23 cosponsors, and a bill of the same name introduced in the Senate in March by Marco Rubio (R-Fla.) has 14 cosponsors. Both bills have bipartisan support and are reintroductions of legislation initially put forth in 2019. A press release issued by Sen. Rubio's office says that "extending DST can benefit the economy and our overall health."

According to the National Conference of State Legislatures, 19 states have enacted legislation or passed resolutions in the last several years to provide for year-round DST, if Congress were to allow such a change. And according to a Congressional Research Service (CRS) report on DST updated in September 2020, at least 45 states have, since 2015, proposed legislation to change their observance of DST.

These efforts include proposals to exempt a state from DST observance, which is allowable under existing law, and proposals that would establish permanent DST, which would require Congress to amend the Uniform Time Act of 1966, the CRS report says.

### The state of the science

Shifting from ST to DST has been associated with an increase in cardiovascular morbidity (heart attacks and atrial fibrillation), increased missed medical appointments, increased ED visits, increased mood disturbances and suicide risk, increased risk of fatal car crashes and medical errors – and sleep loss, said Elizabeth Klerman, MD, PhD, professor of neurology in the division of sleep medicine at Harvard Medical School, Boston.

These associations are covered in AASM statement, along with acknowledgment that most studies on the chronic effects of DST have "either been retrospective or addressed the issue indirectly."

For Dr. Johnson, who refers to DST as "sleep deprivation time," the most convincing data regarding the dangers of permanent DST come

### SLEEP MEDICINE Sleep disordered breathing in neuromuscular disease: Early noninvasive ventilation needed

### BY CHRISTINE KILGORE

MDedge News

Solution in patients with neuromuscular disease and is increasingly addressed with noninvasive ventilation, but its patterns go beyond obstructive sleep apnea (OSA) and include hypoventilation, hypoxemia, central sleep apnea, pseudocentrals, periodic breathing, and Cheyne-Stokes respiration, Gaurav Singh, MD, MPH said at the virtual annual meeting of the Associated Professional Sleep Societies.

The prevalence of sleep-related disordered breathing surpasses 40% in patients diagnosed with neuromuscular disease, but "sleep disordered breathing [in these patients] does not equal obstructive sleep apnea," said Dr. Singh, staff physician at the Veteran Affairs Palo Alto (Calif.) Health Care System in the section of pulmonary, critical care and sleep medicine, and an affiliated clinical assistant professor at Stanford (Calif.) University.

"The most common sleep-related breathing disorder in neuromuscular disease is probably hypopnea and hypoventilation with the sawtooth pattern of dips in oxygen saturation that occur during REM sleep," he said. As neuromuscular diseases progress, hypoventilation may occur during non-REM sleep as well.

Evaluation is usually performed with polysomnography and pulmonary function testing, he *Continued on following page* 

#### Continued from previous page

from studies comparing locations within time zones. "The farther you're off from the meridian, the more you have that 'social jet lag' or circadian misalignment [between the innate circadian rhythm, which is synchronized with solar time, and school or work schedules]," she said at the meeting.

Researchers reported in 2017 (Cancer Epidemiol Biomarkers Prev. 2017;26[8]:1306-11), for instance, that the risk for all cancers and many specific cancers increased from east to west within a time zone, as solar time is progressively delayed. "They documented changes in risk for every 5 degrees west from the meridian," she said.

Dr. Johnson is a case in point of the "educational gap" that she believes needs attention. Two years ago, as chair of the sleep section of the American Academy of Neurology, she delved into the literature after the AAN asked the section whether it should endorse the AASM's position paper on DST. "I didn't know the literature even as a sleep scientist until I got into this," she said.

"If you're asked me 2 years ago," she added in the later interview, "I would have said that permanent DST is fine."

The sleep section recommended that the AAN endorse permanent ST, but the AAN ultimately decided it "didn't feel strongly enough to say that standard time is unequivocally the better option," Dr. Johnson said in an interview. "They agreed that there's science [in favor of it], but ... it's a big public policy decision."

Jamie Żeitzer, PhD, associate professor of psychiatry and behavioral sciences at Stanford (Calif.) University's Center for Sleep Sciences and Medicine, voiced similar concerns at the meeting about currently advocating a shift in either direction. It's "absolutely clear that switching clocks, especially since it's occurring at a population level, is deleterious and we need to get rid of it," he said. "But before we put forth dictates on public health [with a shift to permanent ST], I think we better be sure we're correct."

"I think we're getting close. I think the data thus far [are indicating] that permanent standard time is better for health," Dr. Zeitzer said. "But I don't think there's a cumu-

lative amount of evidence to really say that we have to subvert all other interests because this is so important for public health. We need at

least a few more studies."

There is not enough evidence, for instance, to conclude that the body clock does not eventually adjust to DST, he said, and it is not yet clear what roles electric light and sunlight each play in the body's circadian time.

"And we need to think about north-south. What may be important for the upper Midwest, and for Maine, and for Washington, may not be ... good for Florida and Texas and southern California," Dr. Zeitzer said. "You have very different patterns of light exposure, especially when it deals with seasons."

### **Historical considerations**

In his comments at the meeting, Muhammad Rishi, MBBS, the lead author of the AASM's position statement, added that circadian misalignment – that "asynchrony between the internal and external clocks" – is associated in studies with an increased risk of obesity, metabolic syndrome, and depression. But he also emphasized that the "historical evidence" against permanent DST is at least as strong as the medical evidence.

"The U.S. has gone on permanent daylight savings time several times in the past, most recently in the 1970s during the OPEC [oil embargo], and it was so unpopular," said Dr. Rishi, of the department of pulmonology, critical care, and sleep medicine at the Mayo Clinic Health System in Eau Claire, Wis. "England

> also did it in the 1960s and then abolished it, and most recently Russia did it ... it became so unpopular with increased depression and mood disorders

that they abolished it."

Rep. Ward said that China has offered a large natural experiment with its move decades ago from five time zones to one time zone – Beijing time. "I don't think we've seen any sweeping changes in their health because they have one large time zone," he said.

Dr. Klerman took issue, saying she "knows someone in China who is trying to get that data about health outcomes and is unable to get it."

Arguments that DST saves energy hold little to no weight upon scrutiny of the data, Dr. Johnson said. Moreover, research other than oft-cited, older Department of Transportation studies suggests that "permanent DST is bad for energy and bad for the climate," she said. "This really needs to be more fully evaluated by the government and others."

Dr. Johnson said after the meeting that it's important for experts from the energy and climate sectors, education, and medicine – including pediatrics, oncology, and other specialties with "a stake in this" – to come together and share information so "we won't all be in our silos." She and other sleep experts in the neurology field are planning to host a summit in 2022 to do just this.

Dr. Johnson and Kin Yuen, MD, of the Sleep Disorders Center at the University of California, San Francisco, both expressed concern at the meeting that adoption of permanent DST would negate the benefits of delayed school start times in middle and high school students.

There is some evidence that delayed start times have led to decreased tardiness and absences, Dr. Yuen said. To have the same impact with permanent DST, "instead of starting at 8:30 a.m., you'd have to start at 9:30," Dr. Johnson added after the meeting.

The first discussion of DST at the SLEEP 2021 meeting was led by Erin E. Flynn-Evans, PhD, MPH, director of the Fatigue Countermeasures Laboratory at the National Aeronautics and Space Administration Ames Research Center. Dr. Yuen led a later second question-and-answer session. They and each of the eight participants reported that they had no relevant conflicts of interest.

Dr. Yuen and Dr. Flynn-Evans are both coauthors of the AASM's position statement on DST. Dr. Klerman is a coauthor of the Society for Research on Biological Rhythms 2019 position paper on DST (J Biol Rhythms. 2019;34[3]:227-30).

The AASM's statement has been endorsed by 19 organizations, including the American College of Chest Physicians, the SRBR, the American Academy of Cardiovascular Sleep Medicine, the Society of Behavioral Sleep Medicine, the National PTA, and the American College of Occupational and Environmental Medicine.



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### Obesity hypoventilation: Moving the needle on underrecognition

**BY CHRISTINE KILGORE** *MDedge News* 

besity hypoventilation syndrome (OHS) is bound to be increasing because of the rising obesity epidemic but is underrecognized and "frequently underdiagnosed," Saiprakash B. Venkateshiah, MD, said at the virtual annual meeting of the Associated Professional Sleep Societies.

The condition, which can cause significant morbidity and mortality, is defined by the combination of obesity and awake alveolar hypoventilation (PaCO<sup>2</sup>  $\ge$  45 mm Hg), with the exclusion of alternative causes of hypoventilation. Sleep disordered breathing (SDB) is almost universally present, with approximately 90% of individuals with OHS also having obstructive sleep apnea (OSA), most often severe, and approximately 10% having sleep-related hypoventilation, or a "pure hypoventilation subtype, if you will," said Dr. Venkateshiah, assistant professor of medicine at

Emory University, Atlanta. The prevalence of OHS in the general population is unknown, but its prevalence in patients who present for the evaluation of SDB has ranged from 8% to 20% across multiple studies, he said, referring

Sleep disordered breathing is almost universally present, with approximately 90% of individuals with OHS also having obstructive sleep apnea, most often severe.

to a review published in Chest (2016;149[3]:856-68). Up to 40% of patients with OHS present for the first time with acute hypercapnic respiratory failure, which has an in-hospital mortality of 18%.

Postmenopausal women appear to have a higher prevalence, compared with premenopausal women and men, he noted, and women appear to be more likely than men to present with the clinical phenotype of OHS without associated OSA.

The arterial blood gas measurement needed to document alveolar hypoventilation and definitively diagnosis OHA is a "simple and economical test," he said, "but it is logistically very difficult to obtain [these measurements] routinely in all patients in the clinic ... and is one of the reasons why OSH is underdiagnosed."

### **Guideline advice**

A practice guideline published in 2019 by the American Thoracic Society suggests that, for obese patients with SDB and a low to moderate probability of having OSH, a serum bicarbonate level be measured first (Am J Respir Crit Care Med. 2019:200[3]:e6-24). "In patients with serum bicarbonate less than 27 mmol/L, clinicians might forgo measuring PaCO<sup>2</sup>, as the diagnosis in them is very unlikely," Dr. Venkateshiah said, referring to the guideline. "In patients with a serum bicarbonate greater than 27, you might need to measure PaCO<sup>2</sup> to confirm or rule out the diagnosis of OHS."

(Patients strongly suspected of having OHS, with more than a low to moderate probability – those in whom arterial blood gases should be measured – are "usually severely obese with typical signs and symptoms such as dyspnea, nocturia, lower-extremity edema, excessive daytime sleepiness, fatigue, loud disruptive snoring, witnessed apneas, as well as mild hypoxemia during wake and/or significant hypoxemia during sleep," the ATS guideline says.)

The guideline panel considered the use of oxygen saturation measured with pulse oximetry during wakefulness to screen for OHS and decided to advise against it because of the paucity of evidence-based literature, Dr. Venkateshiah noted. (In making its five conditional recommendations, the guideline panel cited an overall *Continued on following page* 

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said, but supplementary testing including serum bicarbonate levels, arterial blood gases, and echocardiography to assess for left ventricular ejection fraction and cardiomyopathy may be useful as well.

While a sleep study is not required per Centers for Medicare & Medicaid coverage criteria for the use of respiratory assist devices in patients with neuromuscular disease, polysomnography is valuable for identifying early nocturnal respiratory impairment before the appearance of symptoms and daytime abnormalities in gas exchange, and is better than home testing for distinguishing different types of events (including pseudocentrals). It also is helpful for determining the appropriate pressures needed for venti latory support and for assessing the need for a backup rate, Dr. Singh said.

Commonly used types of noninvasive ventilation include bilevel positive airway pressure on the spontaneous/timed or pressure control modes, with or without volume-assured pressure support, he said.

Expiratory positive airway pressure (EPAP) is usually set low initially to help decrease the work of breathing and improve triggering, then titrated up to ensure that upper airway obstructive events are treated. Pressure support (the difference between the inspiratory positive airway pressure and EPAP) is set to achieve target tidal volume and to rest the respiratory muscles. And inspiratory time is set "on the longer end" to achieve maximal target volume and ensure appropriate gas exchange, Dr. Singh said.

Data from randomized controlled trials evaluating the effectiveness of NIV are limited, he said. A study published 15 years ago (Lancet Neurol. 2006;5[2]:140-7) showed a survival benefit and improvement in quality of life measures in patients with amyotrophic lateral sclerosis (ALS) with normal or moderately impaired bul-

Sleep disturbances "may be the earliest sign of muscle weakness in [patients with neuromuscular disease], sometimes being detected before their underlying neuromuscular disease is diagnosed."

bar function but not in those with severe bulbar weakness.

Regarding the timing of initiating NIV, a retrospective study published several years ago (Eur J Neurol. 2018;25[3]:556-e33) looked at almost 200 ALS patients and evaluated differences in survival amongst those started earlier with NIV (forced vital capacity  $\geq$  80%) and those started later (FVC < 80%).

At 36 months from diagnosis, mortality was 35% for the early group and 53% for the later group. "Improved survival was driven by ben-

efit in patients with non-bulbar-onset ALS, compared with bulbar-onset disease," Dr. Singh said.

"This study and several other similar studies seem to indicate that the earlier NIV [noninvasive ventilation] is started in patients with neuromuscular disease, the better in terms of improving survival and other relevant measures such as quality of life," he said.

Asked about Dr. Singh's presentation, Michelle Cao, DO, clinical associate professor at Stanford University, said that NIV is an "invaluable tool in the treatment of conditions leading to chronic respiratory failure," such as neuromuscular disease, and that it's important to incorporate NIV training for future pulmonary, critical care and sleep physicians. Dr. Cao directs the adult NIV program for the neuromuscular medical program at Stanford Health Care.

Saiprakash B. Venkateshiah, MD, of Emory University, Atlanta, also said in introducing Dr. Singh at the meeting that earlier diagnosis and appropriate NIV therapy "may improve quality of life and possibly even lower survival in certain disorders."

In addition, he noted that sleep disturbances "may be the earliest sign of muscle weakness in [patients with neuromuscular disease], sometimes being detected before their underlying neuromuscular disease is diagnosed."

Dr. Singh, Dr. Cao, and Dr. Venkateshiah each reported that they had no potential conflicts of interest.

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very low quality of evidence.)

Symptoms of OHS overlap with those of OSA (for example, daytime hypersomnolence, witnessed apneas, loud snoring, and morning headaches), so "symptoms alone cannot be used to discriminate between the two disorders," he advised. Signs of OHS commonly seen in clinical exams, however, are low resting daytime oxygen saturations and lower-extremity edema. A sleep study, he added, is needed to document and characterize SDB in patients with OHS.

Positive airway pressure therapy is the first-line treatment for OHS, and long-term outcomes of patients

### *Positive airway pressure therapy*

is the first-line treatment for OHS, and long-term outcomes of patients with OHS on PAP treatment are significantly better, compared with untreated individuals.

with OHS on PAP treatment are significantly better, compared with untreated individuals.

There is no strong evidence to recommend one form of PAP therapy over another for patients with OHS and concomitant severe OSA, he said, but "the bottom line" from both short- and long-term randomized clinical trials comparing CPAP with noninvasive ventilation "is that CPAP is equivalent to noninvasive ventilation as far as outcomes are concerned."

The ATS guideline panel recommends CPAP therapy for patients with OHS and severe OSA. And for OHS with nonsevere OSA, bilevel PAP is traditionally used – including pure hypoventilators, Dr. Venkateshiah said.

Weight-loss interventions are paramount, since "the primary driver of OHS is obesity," he said at the meeting. There are only a few studies that have looked at bariatric surgery in patients with OHS, he said, "but they did note significant improvements in gas exchange, sleep apnea, lung volumes and pulmonary hypertension."

The ATS guideline suggests weight-loss interventions that produce sustained weight loss of 25%-30% of the actual body weight. Such interventions are "most likely required to achieve resolution of hypoventilation," Dr. Venkateshiah said.

#### **OHS or COPD?**

In a separate presentation on OHS, Michelle Cao, DO, clinical associate professor at Stanford (Calif.) University, emphasized the importance of distinguishing the patient with OHS from the patient with hypercapnic chronic obstructive pulmonary disease. Spirometry and the flow volume curve can help rule out hypercapnic COPD and other conditions that cause daytime hypoventilation.

A study published in 2016 of 600 hospitalized patients determined to have unequivocal OHS found that 43% had been misdiagnosed as having COPD and none had been previously diagnosed with OHS (Obesity Science & Practice. 2016;2[1]:40-7), Dr. Cao noted. Patients in the study had a mean age of 58 and a mean body mass index of 48.2 kg/m<sup>2</sup>; 64% were women.

Dr. Venkateshiah and Dr. Cao had no relevant disclosures.

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### First KRAS mutation drug for lung cancer approved

The new drug, sotorasib

(Lumakras), specifically

targets the KRAS

G12C mutation, which

accounts for about 13%

of NSCLC mutations.

### **BY ZOSIA CHUSTECKA**

he first drug to target KRAS mutations in non-small cell lung cancer (NSCLC) has been approved by the Food and Drug Administration.

KRAS mutations are the most common mutations to occur in NS-CLC tumors, accounting for about 25% of them, but for a long time they appeared to be resistant to drug therapy.

The new drug, sotorasib (Lumakras), specifically targets the KRAS G12C mutation, which accounts for about 13% of NSCLC mutations.

It is considered to be something of a breakthrough in cancer research. When clinical data on the new drug (from 126 patients) were presented last year at the World Conference on Lung Cancer, lung cancer experts greeted the results enthusiastically, as reported to this news organization at the time.

"This is a historic milestone in lung cancer therapy. After four decades of scientific efforts in targeting KRAS, sotorasib has potential to be the first targeted treatment option for this patient population with a high unmet need," Bob T. Li, MD, PhD, of Memorial Sloan Kettering Cancer Center in New York, said at the time.

Now, in a press release from the manufacturer, Amgen, he said: "Sotorasib represents a major advancement in oncology and changes the treatment paradigm for patients with KRAS G12C-mutated non-small cell lung cancer.

"Patients with non-small cell lung cancer who have progressed beyond first-line treatment face a poor prognosis and have limited treatment options available to them. Sotorasib delivers a new option for these patients, and it is the first KRAS-targeted therapy to be approved after nearly four decades of research," he added.

### **Details of clinical data**

This is an accelerated approval based on response rate data.

The FDA notes that the clinical data come from a study of 124 patients with locally advanced or metastatic KRAS G12C-mutated

> NSCLC with disease progression after receiving an immune checkpoint inhibitor and/or platinum-based chemotherapy.

The major outcome measured was overall response rate, which was 36%. Of the patients who responded, tion of response of 6

58% had a duration of response of 6 months or longer.

Sotorasib was approved at a dose of 960 mg, and this dose was based on available clinical data as well as pharmacokinetic and pharmacodynamic modeling, the FDA noted. As part of the evaluation for this accelerated approval, the agency is requiring a postmarketing trial to investigate whether a lower dose will have a similar clinical effect.

The most common side effects include diarrhea, musculoskeletal pain, nausea, fatigue, liver damage, and cough. Sotorasib should not be used if patients develop symptoms of interstitial lung disease, and should be permanently discontinued if interstitial lung disease is confirmed.

Patients on sotorasib should have liver function tests prior to starting and while taking the drug; if liver damage develops, the drug should be stopped or the dose reduced. Patients should avoid taking acid-reducing agents, drugs that induce or are substrates for certain enzymes in the liver, and drugs that are substrates of P-glycoprotein.

### **Companion diagnostic tests**

Along with the new drug, the FDA approved two companion diagnostic tests – the QIAGEN therascreen KRAS RGQ PCR kit (approval granted to QIAGEN GmbH) for analyzing tumor tissue and the Guardant360 CDx (approval granted to Guardant Health) for analyzing plasma specimens to determine if the KRAS G12C mutation is present. The agency notes that. if the plasma test comes back negative, the patient's tumor tissue should be tested.

### Long COVID symptoms reported in 6% of pediatric patients

### **BY TARA HAELLE**

Persistent long COVID symptoms affect approximately 6% of children 3 months after infection with SARS-CoV-2, according to new research.

The prevalence of long COVID in children has been unclear and is complicated by the lack of a consistent definition, said Anna Funk, PhD, an epidemiologist at the University of Calgary (Alba.), during her online presentation of the findings at the 31st European Congress of Clinical Microbiology & Infectious Diseases.

In the several small studies conducted to date, rates range from 0% to 67% 2-4 months after infection, Dr. Funk reported.

To examine prevalence, she and her colleagues, as part of the Pediatric Emergency Research Network (PERN) global research consortium, assessed more than 10,500 children who were screened for SARS-CoV-2 when they presented to the ED at 1 of 41 study sites in 10 countries – Australia, Canada, Indonesia, the United States, plus 3 countries in Latin America and 3 in Western Europe – from March 2020 to June 15, 2021.

PERN researchers are following up with the more than 3,100 children who tested positive 14, 30, and 90 days after testing, tracking respiratory, neurologic, and psychobehavioral sequelae.

Dr. Funk presented data on the 1,884 children

who tested positive for SARS-CoV-2 before Jan. 20, 2021, and who had completed 90-day follow-up; 447 of those children were hospitalized and 1,437 were not.

Symptoms were reported more often by children admitted to the hospital than not admitted (9.8% vs. 4.6%). Common persistent symptoms were respiratory in 2% of cases, systemic (such as fatigue and fever) in 2%, neurologic (such as headache, seizures, and continued loss of taste or smell) in 1%, and psychological (such as new-onset depression and anxiety) in 1%.

"This study provides the first good epidemiological data on persistent symptoms among SARS-CoV-2-infected children, regardless of severity," said Kevin Messacar, MD, a pediatric infectious disease clinician and researcher at Children's Hospital Colorado in Aurora, who was not involved in the study.

And the findings show that, although severe COVID and chronic symptoms are less common in children than in adults, they are "not nonexistent and need to be taken seriously," he said in an interview.

After adjustment for country of enrollment, children aged 10-17 years were more likely to experience persistent symptoms than children younger than 1 year (odds ratio, 2.4; P = .002).

Hospitalized children were more than twice

as likely to experience persistent symptoms as nonhospitalized children (OR, 2.5; P < .001). And children who presented to the ED with at least seven symptoms were four times more likely to have long-term symptoms than those who presented with fewer symptoms (OR, 4.02; P = .01).

### 'Some reassurance'

"Given that COVID is new and is known to have acute cardiac and neurologic effects, particularly in children with [multisystem inflammatory syndrome], there were initially concerns about persistent cardiovascular and neurologic effects in any infected child," Dr. Messacar explained. "These data provide some reassurance that this is uncommon among children with mild or moderate infections who are not hospitalized."

But "the risk is not zero," he added. "Getting children vaccinated when it is available to them and taking precautions to prevent unvaccinated children getting COVID is the best way to reduce the risk of severe disease or persistent symptoms."

The study was limited by its lack of data on variants, reliance on self-reported symptoms, and a population drawn solely from EDs.

No external funding source was noted. Dr. Messacar and Dr. Funk disclosed no relevant financial relationships.

### Vaping and pregnancy: Inhaled toxins among risks

### BY JAKE REMALY

MDedge News

imited emerging data from animal experiments and human epidemiologic studies suggest that vaping may have negative effects on fertility and pregnancy. "Even if these impacts are less severe than

conventional smoking, we really should be thinking about alternative options that may be safer for our patients than inhalation of this aerosol," said Blair J. Wylie, MD, MPH, a maternal-fetal medicine physician at Beth Israel Deaconess Medical Center in Boston.

Dr. Wylie reviewed what is known about vaping, including chemicals other than nicotine that have been detected in vape aerosols, and pregnancy at the 2021 virtual meeting of the American College of Obstetricians and Gynecologists.

In a separate study presented at the ACOG meeting, Nicole Izhakoff, a researcher at Florida International University, Miami, and colleagues evaluated the association between e-cigarette use during pregnancy and unfavorable birth outcomes, such as preterm birth, low birth weight, or extended hospital stay for the newborn.

The investigators used 2016-2017 survey data from the Pregnancy Risk Assessment Monitoring System. In all, 71,940 women completed the survey, including 859 who reported e-cigarette use during pregnancy.

After adjusting for age, race, ethnicity, insurance, maternal education, prenatal care, abuse during pregnancy, and complications during pregnancy, the researchers estimated that the odds of an unfavorable birth outcome were 62% greater among women who used e-cigarettes during pregnancy, compared with those who did not.

"Physicians of all subspecialties, especially those of obstetrics-gynecology and pediatrics, need to increase the implementation of screening for past or current e-cigarette use in at-risk patients," Ms. Izhakoff and coauthors concluded.

Dr. Wylie coauthored another study related to this topic that was published online May 24, 2021, in the Journal of Maternal-Fetal & Neonatal Medicine (doi: 10.1080/14767058.2021.1929156).

The researchers examined birth

weights of children whose mothers use e-cigarettes alone, those whose mothers used both e-cigarettes and conventional cigarettes, and those whose mothers smoked conventional cigarettes only. Their estimates were imprecise, but signaled that e-cigarette use may reduce birth weight. The use of e-cigarettes

> alone appeared to have less of an impact on birth weight than the dual use of conventional cigarettes and e-cigarettes did.

Dr. Wylie cautioned that outcomes like birth weight are "pretty crude measures of whether an exposure is okay or not in pregnancy. Many of these toxins that we know that are in the

aerosols can cause harm, but they may not be reflected in the absolute value of the birth weight."

Answering the question of which is safer is a challenge anyway because researchers likely have incomplete information about who vapes, who smokes, and who does both.

Still, the new research illustrates that "people are starting to think about this and beginning to do some analysis that is really hypothesis generating at this point," Dr. Wylie said. Such studies may prompt clinicians to ask their patients about e-cigarette use.

"Marijuana is sort of a similar thing where patients' perception of safety, because things are legal, can lead to use during pregnancy without ... letting their care teams know," she said. "Things are changing so rapidly in terms of what's available to people to use that we need to stay on top of that as obstetricians and ask the right questions and try to understand what the risks are and potential benefits."

"What is frightening, I think, about these electronic cigarettes is that you're heating this liquid to extraordinarily high temperatures to create the vapor," and the extreme heat vaporizes plastics and metals as well as nicotine, Dr. Wylie said.

An ACOG committee opinion discusses approaches to smoking and vaping cessation such as counseling, behavioral therapy, and medication. The publication also lists a host of elements have been isolated from vape aerosol, including "carbonyl compounds (formaldehyde, acetaldehyde, acetone, and acrolein); volatile organic compounds (benzene and toluene); nitrosamines; particulate matter; and heavy metals such as copper, lead, zinc, and tin."

In addition to the nicotine in e-cigarette liquids, which is harmful in itself, there is "all of this other company that it keeps," including solvent byproducts, known carcinogens, and lung irritants, Dr. Wylie said.

People who vape have increased cough, wheezing, and phlegm production, compared with people who do not vape. Vaping also may worsen underlying lung disease like asthma. Lung function on spirometry decreases after e-cigarette use, studies have shown.

In 2019, researchers described e-cigarette or vaping product use– related acute lung injury (EVALI), which has caused more than 60 deaths in the United States. The condition may be related to vitamin E acetate, a component that had been used in some liquids used by patients with EVALI.

And the nicotine in e-cigarettes can accelerate atherogenesis and affect blood pressure, heart rate, and arterial stiffness.

Animal models provide other rea-

sons for caution. One experiment in mice [J Endocr Soc. 2019 Sep 5;3(10):1907-16] showed that exposure to e-cigarette aerosol impaired implantation and fetal health. The results suggest "that there might be some negative impacts across generations," Dr. Wylie said.

Another study has suggested the possibility that women who currently use e-cigarettes may have slightly diminished fecundability (Am J Epidemiol. 2021 Feb 1;190[3]:353-61). The results were not statistically significant, but the study "gives us pause about whether there could be some impact on early pregnancy and fertility," Dr. Wylie said.

In mouse models, prenatal exposure to e-cigarette aerosol has decreased fetal weight and length, altered neurodevelopment and neuroregulatory gene expression, and increased proinflammatory cytokines. E-cigarette aerosol also has caused birth defects in zebrafish and facial clefting in frogs. Whether and how these data relate to human pregnancy is unclear.

Dr. Wylie had no relevant financial disclosures. Ms. Izhakoff and coauthors had no disclosures.



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Dr. Wylie

### Advancing bronchoscopy: Reaching the unreachable

### BY SANDEEP JEWANI, MD; AND JESSICA JOHNSON, MD

s of 2019, lung cancer remained the leading cause of cancer death in the United States. In March 2021, the USPSTF updated the guidelines for lung cancer screening, increasing the number of eligible patients in order to identify malignancies in the early stages when more treatment options exist. With the growth of lung cancer screening, increasingly smaller pulmonary nodules are being identified in more peripheral locations previously thought to be unreachable with bronchoscopy. While bronchoscopy has been utilized for over a century for therapeutic interventions, the development of the fiberoptic bronchoscope in 1967 ushered in an era of evolving diagnostic functions. From the initial endobronchial and transbronchial biopsy techniques, to the introduction of endobronchial ultrasound, and now the latest navigational and robotic modalities, these advances have opened a new realm of interventions available in our diagnostic approach to lung cancer.

Bronchoscopy has become essential in the diagnosis of thoracic malignancies, providing both di-



Dr. Jewani

agnostic and staging information in one procedural setting. By first assessing the mediastinal and hilar lymph nodes with endobronchial ultrasound and transbronchial needle aspiration, involved lymph nodes can give both diagnosis and staging information required to guide treatment. This is particularly important in the case of non-small cell lung cancer, which utilizes the TNM staging system. Through the use of convex probe endobronchial ultrasound (CP-EBUS), combined with rapid on-site evaluation (ROSE) by pathologic condition, we can more accurately target the individual lymph nodes for biopsy without the need for any additional procedures





Dr. Johnson

that are often more complex and invasive, such as mediastinoscopy. It is important to note the role of CP-EBUS extends beyond the lymph node assessment and can also be utilized for the evaluation of other mediastinal lesions, such as central parenchymal masses. These would otherwise be difficult to access due to the lack of a clear airway to the lesion (Argento and Puchalski. *Respir Med.* 2016;116:55-8).

While EBUS has improved the sampling of lymph nodes, advanced imaging technologies and subsequent increases in lung cancer screening have increased the number of lung malignancies identified in earlier stages before extension to the lymph nodes occurs. This scenario requires a direct biopsy of the primary nodule or lung mass.

While CP-EBUS can be utilized for some central parenchymal lesions, peripheral nodules pose a greater challenge to the bronchoscopist as they cannot be directly visualized with the conventional bronchoscope. These lesions are amenable to traditional sampling techniques such as bronchial brushings and washings in addition to transbronchial needle aspiration and transbronchial biopsy.

However, the yield for peripheral lesions is less than that for central tumors and depends on lesion size, distance from hilum, spatial positioning from bronchus, and operator experience. To help localize peripheral lesions, a separate form of endobronchial ultrasound is available that can be used in combination with fluoroscopy to target a lesion. Radial probe endobronchial ultrasound (RP-EBUS) utilizes a rotating ultrasound transducer that can be advanced either through the working channel of the broncho-

scope or through a guide sheath to extend to airways beyond what the conventional bronchoscope can reach. This assists the bronchoscopist with locating the correct airway and, therefore, increases the yield of sampling techniques. The use of RP-EBUS has reported diagnostic vields of almost 85% if the ultrasound is located within the lesion, but less than 50% if adjacent to the lesion (Chen et al. Ann Am Thorac Soc. 2014;11[4]:578-82). While this improves the yield beyond that achieved with conventional bronchoscopy alone, it continues to challenge the bronchoscopist to locate an accessible airway from a series of branching bronchi that are beyond the level of direct visualization.

Due to the historical difficulty in accurately reaching peripheral lesions, alternative technologies for sampling these lesions, such as image-guided biopsies or surgical resection, were employed. While CT scan-guided biopsies traditionally have high diagnostic yields, they also carry a higher rate of complications, including pneumothorax and bleeding. This has led to a significant increase over the past 2 decades in new bronchoscopic technologies targeting safer and more accurate sampling of increasingly smaller, peripheral lesions.

Traditionally, any new technologies created were intended to be used alongside flexible fiberoptic bronchoscopy. The more recently introduced technologies, however, aim to provide a safer, more accurate procedure through virtual bronchoscopy.

By obtaining CT scan images prior to the procedure, a 3D visualization is constructed of the tracheobronchial tree, allowing for directed guidance of endobronchial accessories to more distal airways. Where the bronchoscopist was previously limited in navigating the bronchial tree to the subsegmental bronchi, virtual bronchoscopy can depict the airways up to the 7th order subdivision. This is a significant improvement in airway visualization - however, only when partnered with guidance technologies can the model be accurately navigated.

One modality that is often coupled with virtual bronchoscopy to accurately reach peripheral lesions is electromagnetic navigation bron-*Continued on following page* 

### **NEWS FROM CHEST** -

### Continued from previous page

choscopy (ENB). Multiple ENB software systems have been created and continue to be highly utilized by bronchoscopists to target peripheral lesions, as it has often been likened to a GPS for the lungs. With the addition of specific hardware components, a magnetic field

is created around the patient where the sensor position can be elicited to within 1-mm accuracy. When overlaid with the CT scan images, the bronchoscopist can have real-time positioning of the probe in all

With increasing technologies and equipment available, bronchoscopy has quickly become an essential step in the diagnosis of lung cancer.

tient-based studies (Agrawal et al. *J Thorac Dis.* 2020;12[6]:3279-86). More data related to the robotic-assisted bronchoscopy systems can be expected in the future as more experience is gained, but initial results are promising in the system's ability to diagnose early lung cancers safely and accurately.

With increasing

high rates of lesion localization,

greater than 85%, with varying

diagnostic yields from 69-79%.

Some cadaver studies that utilized

diagnostic yields – over 90% – but

artificial tumors reported higher

this was not seen in initial pa-

three planes and guide the necessary sampling tools to the lesion of interest. The reported yields for ENB vary but have been shown to increase in the presence of specific image findings such as a positive bronchus sign – an air-filled bronchus leading into the lesion.

The presence of this finding can increase the yield up to almost 75% from just under 50% in the absence of a positive bronchus sign (Ali et al. *Ann Am Thorac Soc.* 2018;15[8]:978-87). However, regardless of this finding, the overall diagnostic yields for ENB continue to fall below that seen with other image-guided biopsy techniques.

The procedural complications, however, are significantly less and, therefore, many physicians continue to advocate for ENB as the initial procedure in attempt to decrease risk for the patient.

The newest technology to be introduced to target peripheral lung lesions and to improve upon the shortcomings of other techniques is robotic-assisted bronchoscopy. While surgical specialties have seen success with robotic techniques over many years, the first robotic bronchoscopy system was not introduced until 2018.

At present, there are two systems available: the Monarch<sup>\*</sup> system by Auris Health and the Ion Endoluminal<sup>\*</sup> System by Intuitive Surgical. These systems allow for increased bronchoscope stability, improved visualization, adjustable angulation of biopsy tools, and an improved ability to make even subtle turns in the airways. Early studies on both systems were cadaver based, but an increasing number of patient trials are now being reported or actively enrolling. Both systems have shown technologies and equipment available, bronchoscopy has quickly become an essential step in the diagnosis of lung cancer. While other techniques exist beyond those described here, these are some of the more widely used options currently available. It is not possible at this time to define one technology as the best tool for the diagnosis of lung cancer, as patient factors will always have to be taken into consideration to ensure safety and accuracy. However, with constantly changing technologies, the bronchoscopist now has a variety of tools available to help target previously "unreachable" lesions as we aim to decrease the historically

high mortality rates of lung cancer. Dr. Jewani and Dr. Johnson are from Loyola University Medical Center, Department of Pulmonary and Critical Care Medicine, Maywood, Illinois.

#### References

1. Agrawal A. et al. Robotic bronchoscopy for pulmonary lesions: a review of existing technologies and clinical data. *Thorac Dis.* 2020;12(6):3279-3286.

2. Ali MS, et al. Computed Tomography Bronchus Sign and the Diagnostic Yield of Guided Bronchoscopy for Peripheral Pulmonary Lesions. A Systematic Review and Meta-Analysis. *Ann Am Thorac Soc.* 2018 Aug;15(8):978-987. doi:10.1513/AnnalsATS.201711-8560C.

 Argento AC, Puchalski J. Convex probe EBUS for centrally located parenchymal lesions without a bronchus sign. *Respir Med.* 2016 Jul;116:55-8. doi: 10.1016/j. rmed.2016.04.012. Epub 2016 Apr 29.
Chen A, et al. Radial probe endobronchial ultrasound for peripheral pulmonary lesions.
A 5-year institutional experience. *Ann Am Thorac Soc.* 2014 May;11(4):578-82. doi:10.1513/AnnalsATS.201311-3840C.



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### CRITICAL CARE COMMENTARY

## Delirium in the ICU: Best sedation practices lead to the best outcomes

BY MATTHEW F. MART, MD, MSCI

elirium is a frequent form of organ failure among the critically ill, impacting up to 80% of mechanically ventilated patients (Ely EW et al. JAMA. 2004;291[14]:1753-62). Its cardinal manifestations include disturbances in attention and cognition that occur acutely (e.g., hours to days) that are not better explained by another disease process (such as a toxidrome or dementia) (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders. 5th ed. 2013). Duration of delirium in the intensive care unit (ICU) is independently associated with poor outcomes, such as mortality and hospital length of stay, even when accounting for comorbidities, coma duration, sedative use, and severity of illness. Delirium during critical illness is an important bellwether for a patient's clinical status, often serving as a harbinger for severe or worsening disease.

Over the last two decades, the critical care community has come to understand the importance of recognizing delirium, which is often underdiagnosed, as well as delirium prevention. In the ICU, several factors coalesce to form the perfect environment for the development of delirium. Patients often have preexisting comorbidities that predispose to delirium, such as preexisting cognitive impairment, and the severity of critical illness increases the risk of delirium further. There are also bedside factors, however, that are \_\_\_\_\_\_ important for



the intensivist to address, many of which are modifiable. These include routinely screening for delirium and assessing level of consciousness, implementing early mobility

and rehabilitation, targeting light sedation, and avoiding deliriogenic medications such as benzodiazepines. These evidence-based care practices form the foundation of the 2018 Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU (i.e., PADIS guidelines), which aim to reduce delirium and iatrogenesis from critical care (Devlin JW et al. Crit Care Med. 2018;46[9]:e825-e873). The severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) pathogen that has caused the coronavirus disease 2019 (COVID-19) pandemic, however, has brought unprecedented challenges to critical care. One unfortunate side effect has been



increased use of deep sedation and, thus, a greater incidence of delirium (Pun BT et al. Lancet Respir Med. 2021;9[3]:239-50). While the impact of the pandemic is unprecedented, thoughtful and careful sedation use remains vital to providing optimal care for the critically ill patient.

### The link between sedation and delirium

The advent of modern mechanical ventilation brought critical care medicine into a period of rapid growth. Practices derived from the operating room, such as deep sedation and paralysis, became commonplace. Yet, starting in the late 1990s and early 2000s, evidence started growing regarding the impact of delirium and the unique aspects of the ICU that made it so prevalent. Delirium is strongly linked to inpatient mortality in mechanically ventilated adults, and it is best understood as an additional form of organ failure, much like other organ failures commonly recognized and treated by intensivists, such as respiratory or renal failure. Certain medications and sedation practices are associated with the development and duration of delirium. Benzodiazepines, a common sedative medication, are strongly linked to the development of delirium. In a study comparing commonly used sedative and analgesic agents, the use of lorazepam was associated with a greater risk of delirium the following day among critically ill, mechanically ventilated patients (Pandhariphande PP et al. Anesthesiology. 2006;104[1]:21-6). Given how commonly benzodiazepines are used and delirium develops in the ICU, this association has striking implications for clinical care and outcomes such as mortality. It is also significant, given that benzodiazepine use has increased during the pandemic, potentially creating significant downstream consequences. Benzodiazepines should be actively avoided when at all possible, given their propensity to lead to delirium, in accordance with the most recent guidelines.

### Which sedation agent to choose?

While the negative effects of benzodiazepine-based sedation are well established, the optimal sedation agent remains unclear. Several other drugs are commonly used in the ICU, including propofol, dexmedetomidine, and opioid agents such as fentanyl and morphine. Propofol and dexmedetomidine are used specifically for their sedative properties, though they have dramatically different effects on the depth of sedation and different mechanisms of action. Opioid agents are most commonly used for their analgesic effect; however, in higher doses or combined with other medications, they have the secondary effect of inducing sedation. No particular sedation agent, however, beyond the avoidance of benzodiazepines has been recommended for use in the most recent guidelines. In the PRODEX and MIDEX studies, dexmedetomidine was noninferior to both midazolam and propofol in achieving targeted light to moderate sedation, and dexmedetomidine was associated with a shorter duration of mechanical ventilation compared to midazolam (Jakob SM et al. JAMA. 2012;307[11]:1151-60). More recently, the SPICE-III trial studied dexmedetomidine vs. usual care and found no difference in 90-day mortality (Shehabi Y et al. N Engl J Med. 2019;380[26]:2506-17).

In choosing the best sedation agent to avoid delirium, the largest and most applicable trial to date is the "Maximizing the Efficacy of Sedation and Reducing Neurological Dysfunction and Mortality in Septic Patients with Acute Respiratory Failure," or MENDS2 trial (Hughes CG et al. N Engl J Med. 2021;384:1424-36). This study was a double-blind, multicenter randomized controlled trial of dexmedetomidine vs propofol in critically ill patients with sepsis receiving mechanical ventilation. The primary outcome was days alive without delirium or coma over the 14-day intervention period. The study enrolled 438 patients between 13 sites, with 422 patients receiving either dexmedetomidine or propofol. Hughes and colleagues found no difference in the primary outcome of days alive without delirium or coma between the dexmedetomidine and the propofol arms. The study also found no

### **CHEST** website redesign puts the user first

ou've probably noticed that we recently rolled out a new website - one that is updated, streamlined, and user-friendly (and if you haven't, go check it out!). Our goal for this project was to ensure that chestnet.org remains your go-to resource when it comes to pulmonary, critical care, and sleep medicine, and to accomplish that, we recognized that some major changes were needed. In short, while we were on



the cutting-edge of chest medicine, our website definitely was not.

That's why we've redesigned everything from the ground up. Our very best tools, resources, and offerings are now front and center, which means that you'll be able to find everything you're looking for, plus some extras you aren't, with a few simple clicks.

While there are a lot of new features on the site that we can't wait for you to discover, here are the upgrades that we're most excited about.

### **Mobile responsiveness**

One of the biggest changes to the site is that it is now mobile responsive. That means you'll have a seamless experience regardless of what device you're on. Whether that's a phone or a tablet,

you'll be able to log in to your account, view any of our resources, and purchase products functions that used to be only accessible from a desktop.

### **Intuitive navigation**

We have so much content to offer that finding a place for everything can be difficult, and, in the past, resources often got buried within the naviga-

tion. That's why we spent months taking an inventory of our entire site so that we could reorganize all of our resources in a way that would make more sense to you – our users.

### **Community-centered**

We know that you joined CHEST for more than our top-tier resources; you joined to be part of a community. That's why the new site includes more community-based hubs and opportunities for peer-to-peer interaction. We'll continue to add more features like blog commenting and Twitter feeds

so that you can continue to engage with your colleagues, let your voice be heard, and expand your circle of peers.

### **User-focused design**

What are you hoping to find when coming to our site? What do you want to accomplish? What features would make that easier? By asking these questions, employing a succinct set of design principles, and completing several rounds of member prototype testing, we believe that we redesigned the site not only for you, but with you.

While we've made some major upgrades, we're not done yet. We'll continue to enhance the site in the upcoming month with one goal in mind to ensure you're getting more out of your membership than ever before.

This month in the journal CHEST®

Editor's Picks

BY PETER J. MAZZONE, MD, MPH, FCCP

Editor in Chief Peak inspiratory flow as a predictive therapeutic biomarker in COPD. By Drs. D. Mahler and D. Halpin.

Family presence for critically ill patients during a pandemic. By Drs. J. Hart and S. Taylor.

Executive summary: diagnosis and evaluation of hypersensitivity pneumonitis: CHEST guideline and expert panel report. By Dr. L. Fernandez Perez et al.

The usefulness of chest CT imaging in patients with suspected or diagnosed COVID-19: A review of literature. By Dr. S. Machnicki et al.

Oxygen therapy in sleep-disordered breathing. By Dr. S. Zeineddine et al.



### *Continued from previous page*

difference in secondary outcomes, including ventilator-free days, 90day mortality, and 6-month global cognition, as well as no difference in safety endpoints. Importantly, there was excellent compliance with guideline-recommended practices of spontaneous awakening and breathing trials and early mobility, both of which are associated with reduced sedation exposure. The study did have some notable nuances, however. The overall doses of trial drugs were relatively low, and there was a moderate use of rescue sedation. There was also a small amount of crossover use of propofol and dexmedetomidine between treatment arms (10%), although the authors note that this was lower than in

prior related studies. Overall, the MENDS2 study suggests there is likely clinical equipoise between propofol and dexmedetomidine in terms of delirium outcomes when combined with best practices, such targeted light sedation, paired awakening and breathing trials, and early mobility.

### How should we manage sedation to prevent delirium?

Building off of the recent MENDS2 study and earlier work in the field, along with the 2018 PADIS guidelines, the general paradigm of sedation management should be focused on using light sedation with sedation interruptions to minimize overall sedation exposure. Based on the best available evidence to date,

targeting less overall sedation leads to improved outcomes in critically ill patients, including mortality and duration of mechanical ventilation. Benzodiazepines should be avoided due to their association with delirium, but currently there is no evidence to suggest one nonbenzodiazepine sedative is better than another. Intensivists can feel comfortable choosing between agents based on a patient's individual clinical needs, especially when patients are receiving paired spontaneous awakening and breathing trials and early rehabilitation. These same principles should be applied to sedation management and delirium patients in COVID-19 patients as well. While certain circumstances will necessitate deeper sedation at

times (e.g., refractory hypoxemia due to ARDS from COVID-19), clinicians should continually reassess the actual sedation needs of the patient with the goal of reducing overall sedation. Focusing effort on these evidence-based practices will help reduce the incidence of delirium and ultimately improve patient outcomes.

Dr. Mart is with the Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University Medical Center; Critical Illness, Brain Dysfunction, and Survivorship (CIBS) Center; and VA Tennessee Valley Healthcare System Geriatric Research Education and Clinical Center (GRECC), Nashville, Tennessee.

## Medicare rules for CPAP penalize low-income patients for nonadherence

Report from the CHEST Health Policy and Advocacy Committee (HPAC) Conference

### BY TED BOSWORTH

he relationship between adherence and benefit for those prescribed continuous positive airway pressure (CPAP) devices is clear. However, a Medicare-reimbursement rule that demands adherence blind to circumstances appears to be denying access to many low-income patients, according to an analysis delivered at the annual CHEST Health Policy and Advocacy Committee (HPAC) conference sponsored by the American College of Chest Physicians.

Over the past several years, adherence to CPAP has improved substantially following a series of studies that demonstrated the device must be used at least 4 hours per night to achieve improved outcomes. Medicare defines adherence as using the device more than 4 hours per night for 70% of nights (21 nights) during a consecutive 30-day period any time in the first 3 months of initial usage.

However, the studies that show improved adherence show a lag among those in the lowest income quartile, according to Sairam Parthasarathy, MD, FCCP, of the Center for Sleep and Circadian Sciences at the University of Arizona, Tucson. When patients are followed for a year after being prescribed CPAP, the lag for the low-income patients is not seen immediately. Rather, adherence studies show a steady climb in adherence in all income groups initially, but "right at 90 days, there is a marked change," according to Dr. Parthasarathy.

This change happens to coincide with Medicare policy that denies reimbursement for CPAP after 90 days if patients are not using CPAP at least 4 hours per night, which is the threshold associated with benefit.

The correlation between this policy and income disparity is "observational" rather than proven, but Dr. Parthasarathy is confident it is valid. He believes it is a prime example of a health inequity driven by poorly conceived policy.

"The 90-day rule needs to go," he said, calling the choice of threshold "man-made."

"This is the only disease condition for which a therapy is withheld if it is not used according to some magical threshold," he said. "I cannot think of a more draconian policy."

In an effort to illustrate the problem, Dr. Parthasarathy likened this policy to withholding insulin in a diabetes patient judged nonadherent because of a persistently elevated Hb1Ac.

At 90 days, adherence rates remain at a relatively early point in their upwards trajectory in all income groups. One year later, adherence rates are more than twice as high in the highest income relative to the lowest quartile and approaching twofold greater in quartiles 2 and 3.

"It takes time to get used to these devices," Dr. Parthasarathy explained. Given studies demonstrating that "more is better" with CPAP, whether measured by sleep scales or quality of life, Dr. Parthasarathy advocates strategies to improve adherence, but he questioned an approach that penalizes low-income patients for a definition of nonadherence at an arbitrary point in time. He suggested it is just one example of health policies that ultimately penalize individuals with lower incomes.

"There are millions of dollars spent every year on understanding the genetics of disease, but the biggest influence on how long you live is the ZIP code of where you live," said Dr. Parthasarathy, referring to zip codes as a surrogate for socioeconomic status.

This is not to imply, however, that genetics are Continued on following page



### **NetWorks**

### Disaster medicine in the pandemic. Telehealth and post pandemic care. Rise in lung transplants for older patients. Women's lung health.

#### **Disaster response**

Advancing disaster medicine and global health in times of pandemic Worldwide hardships due to COVID-19 have revealed opportunities for improvement. Disaster education, telemedicine, knowledge





Dr. Miller

Dr. Patil

sharing, and resource allocation have been highlighted as such areas. In an August 2020 publication, Hart et al. argue, "Every hospital needs a Disaster Medicine physician now" (Hart et al. "Why Every US Hospital Needs a Disaster Medicine Physician Now" https://doi.org/10.1017/ dmp.2020.302).

Every physician must be prepared to be the expert in times of disaster. A survey of U.S. medical students showed that despite few respondents (<27%) feeling adequately educated, >90% are willing to respond to a natural disaster or a pandemic (Kaiser et al. Disaster Med Pub Health Prep. 2009;3[4]:210-16). While natural disasters have increased by almost 35% since the 1990s, a robust approach to disaster education is not routinely implemented across the fields of medicine, nursing, allied health, and health administration (Freebairn. World Disasters Report 2020: Executive Summary. 2020 ed. IFRC. https:// tinyurl.com/bsbhsm9v). Notably, disaster education provides opportunities for multidisciplinary team-building where learners build a foundation of knowledge together. While no ideal educational model has been fully adopted, high-quality educational opportunities include National Disaster Life Support Foundation courses, SALT triage, and ATLS (Homer et al. Prehospital and Disaster Medicine https://doi. org/10.1017/s1049023x00056028).

Telemedicine has emerged as a very effective means of disaster support through both direct patient encounters and provider education. Tele-triage used to delineate patients requiring urgent hospitalization from those who can be managed at home has proven effective in areas with limited health care facilities (World Health Organization. Coronavirus disease. https://www.who. int/emergencies/diseases/novel-coronavirus-2019). Knowledge sharing opportunities from organizations like Project ECHO have allowed for >368,000 learners from 146 countries to exchange information during >8,000 learning sessions (Project ECHO COVID-19 response. https://

hsc.unm.edu/echo/institute-programs/covid-19-response).

Physicians of all specialties should continue to develop skills in triage, surge capacity management, ethical/ legal issues surrounding disasters, organizational interoperability, and telemedicine, and emphasize skills to ensure their own personal protection. *Christopher Miller, DO, MPH Steering Committee Fellow-in-Training Member Sarang Patil, MD Steering Committee Member* 

#### **Practice operations**

**Telehealth and postpandemic care** Telehealth is the use of electronic information and telecommunication technologies to provide care when

the physician

are not in the

Telehealth has

been available

The COVID-19

pandemic forced

health care pro-

viders, systems,

for 40 years.

same place.

and the patient



Dr. Baxter

and patients to quickly adapt to virtual audio and visual visits, new documentation parameters, billing, and reimbursement structures. Emergency rules have removed the barriers to adoption of home-based diagnostics and virtual visits. It is expected that 20% to 30% post-pandemic care will be provided via telehealth.

Telehealth is particularly beneficial in providing counseling services or managing chronic illnesses, such as COPD and heart failure. There has been an explosion of monitoring devices both wearable and implantable. Some devices, which monitor PA pressure, have been shown to reduce heart failure hospitalizations and all-cause hospitalizations (Shavelle DM, et al. Circ Heart Fail. 2020;13: e006863). Studies have been conducted on home spirometry and oximetry devices in postlung transplant, ILD (Russell AM et al. Am J Respir Crit Care Med. 2016 Oct 15; 194[8]:989-997), and CF patients (Compton M et al. Telemed J E Health . 2020 Aug;26[8]:978-84). As we move forward, we will have to ascertain what data acquisition is relevant and develop processes to address it in real time.

In this changing landscape of health care delivery, we can anticipate an increase in virtual visits and a trend toward e-consults, which will necessitate further advancements in remote monitoring and assessment and will require us to adopt new practice models.

> Caitlin Baxter, MBBS Steering Committee Fellow-in-Training Namita Sood, MBBCh, FCCP Steering Committee Member Continued on following page

#### Continued from previous page

irrelevant, Dr. Parthasarathy said. He pointed to data linking genetic traits that determine melanin levels and circadian rhythms. He noted one genotype associated with later bedtimes that is more commonly found in African Americans and Hispanics.

This has relevance to a variety of sleep disorders and other health conditions, but it might serve as a fundamental disadvantage for children with this genotype, Dr. Parthasarathy maintained. He cited a study conducted at his center that found Hispanic children sleep on average 30 minutes less than white children (Sleep Med. 2016;18:61-66). The reason was simple. Hispanic children went to bed 30 minutes later but rose at the same time.

The later bedtimes and reduced sleep could potentially be one obstacle among many, such as

the need for lower income patients to hold several jobs, that prevent these patients from becoming accustomed to CPAP at the same speed as wealthier patients, according to Dr. Parthasarathy.

The current Medicare policy that withholds CPAP on the basis of a single definition of nonadherence appears to lead directly to an inequity in treatment of sleep apnea, Dr. Parthasarathy maintained. Dr. Parthasarathy, who was a coauthor of a recently published paper on addressing disparities in sleep health (Chest. 2021;159:1232-40), described this issue as part of a larger problem of the failure to deliver health care that is sensitive to the cultural and racial differences underlying these inequities.

Kathleen Sarmiento, MD, FCCP, Director, VISN 21 Sleep Clinical Resource Hub for the San Francisco VA Health Care System, agreed. Dr. Sarmiento, a member of the CHEST Health Policy and Advocacy Committee and the moderator of the session in which Dr. Parthasarathy presented his data, said, "This type of issue is exactly what our Committee [HPAC] would like to address."

The association between the 90-day Medicare rule for CPAP reimbursement and reduced access to this therapy among patients of lower economic status is compelling, she indicated. Within the goal of advocacy for health policies that will reduce inequities, Dr. Sarmiento explained that the committee is attempting to identify and reverse the source of these types of disparity.

"Specific rules or regulations are actionable targets to effect broader change in health care access and health care delivery," said Dr. Sarmiento, alluding to the mission of HPAC.

Dr. Parthasarathy and Dr. Sarmiento report no relevant conflicts of interest.

### NEWS FROM CHEST -

### **SCHEST**



### **2021** COURSES CHEST Global Headquarters | Glenview, IL

August 26-27 August 28-29	Ultrasonography: Essentials in Critical Care
September 3 September 4	Mechanical Ventilation: Critical Care Management
September 9-10 September 11-12	Difficult Airway Management
September 16-17 September 18-19	Comprehensive Bronchoscopy With Endobronchial Ultrasound
September 23-24 September 25-26	Advanced Critical Care Echocardiography
November 4-5 November 6-7	Ultrasonography: Essentials in Critical Care
November 12	Comprehensive Pleural Procedures With Cadavers
November 13	Advanced Airway Management With Cadavers
November 19 November 20 November 21	Critical Care Ultrasound: Integration Into Clinical Practice
December 2-3 December 4-5	Ultrasonography: Essentials in Critical Care
December 10 December 11	Extracorporeal Support for Respiratory and Cardiac Failure in Adults
December 7 December 14 December 16	LIVESTREAM 5 -7 PM Virtual Advanced Critical Care Echocardiography Board Review Exam Course

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

### **NETWORKS** continued from previous page **Transplant**

**Lung transplant for older patients** Over the past 20 years, there has been a dramatic increase in lung

transplantation

tients, with wide variability in age

in elderly pa-

limit amongst

transplant cen-

the age of 65

has risen from

6.9% in 2004 to

ters. The number

of recipients over



Dr. Lesko

29.6% in 2016 in the United States, and 2.6% to 17% internationally. There is a number of factors driving this increase; the prevalence of advanced lung disease with increasing age, advances in targeted therapies to treat cystic fibrosis, an increased willingness of centers to perform transplants in older patients, and the 2005 revision of the Lung Allocation Scoring System (Courtwright A, Cantu E. *J Thoracic Dis.* 2017:9[9]:3346-51).

In the past, outcomes posttransplant for elderly patients have been conflicting in single-center studies. More recently, Hayanga et al found no difference in survival up to 1 year between individuals 60-69 and those over 70 (J Heart Lung Transplant. 2015;34[2]:182-88). Mosher et al, however, found the median survival dropped from 4.64 years for patients aged 65-69 to 3.07 years for patients  $\geq$ 74 (*J* Heart Lung Transplant. 2021;40[1]:42-55). Notably, older recipients were more likely to be readmitted at 30 and 90 days, and more likely to be discharged to an inpatient rehabilitation facility following transplant (McCarthy et al. J Heart Lung Transplant. 2017;36:S115; Tang et al. Clin Transplant. 2015;29:581-587).

These transplants come with many concerns regarding neurocognitive status, frailty, and other comorbidities, all of which must be rigorously tested prior to consideration(Biswas R et al. *Ann Thorac Surg.* 2015;100:443-51). Recipient age, creatinine level, bilirubin level, steroid use at the time of transplant, and hospitalization at the time of transplant were associated with increased mortality (Mosher et al. *J Heart Lung Transplant.* 2021;40[1]:42-55). Further research is warranted.

> Melissa B. Lesko, DO Grant Turner, MD, MHA Steering Committee Members

### Women's lung health

Will the new pulmonary hypertension hemodynamic classification temper the PH 'sex-paradox'?

Older and contemporary PH registries have consistently shown that PH predominantly affects women ~2 to 3.5 times than men, with female patients having better survival compared with men (Kozu K et al. Heart Vessels. 2018;33[8]:93), a fact attributed to better RV function in female than male subjects. This PH sex-paradox denotes that while estrogen leads to increased susceptibility to PH, it appears to confer better outcomes after PH develops due to improved RV function, since RV dysfunction is a strong predictor of poor outcomes in PH. Multiple preclinical studies have described how estrogen provides protective effects on the RV (Cheng TC et al. Am J Physiol Heart Circ Physiol. 2020;319:H1459; Frump AL et al. Am J Physiol Lung Cell Mol Physiol. 2015;308:L873).

The recent recommended updates to the hemodynamic definition reflect acknowledgment of irrefutable evidence that even mildly elevated mPAP (between 19 and 24 mm Hg) is associated with increased morbidity and mortality based on consistent data from pulmonary arterial hypertension (PAH) as well as from other forms of PH [Simonneau G et al. Eur Respir J. 2019;(Jan 24);53(1):1801913). With incorporation of the updated definition that more accurately captures the disease state and its progression, an unaddressed question still remains as to how the new classification will change PH treatment algorithm and outcomes in women compared with men. Setting the definition of PH at a mPAP of 20 mm Hg not only better represents the typical patients with PH in practice, such as those with PH due to left-sided heart disease (Group 2) or PH associated with chronic lung disease (Group 3), but incorporates the preclinical pathologic disease state of PH, in which symptoms may not be evident (Maron BA, et al. Circu*lation*. 2016;133:1240). In adhering to the new PH definition, will earlier diagnosis across the spectrum of all individuals with PH before RV dysfunction has developed improve outcomes for all those afflicted with PH and equalize outcomes between men and women?

As future studies continue to investigate the direct effects of sex hormones on the RV and dissect the mechanisms leading to the sex differences in RV function in PH, a pre-clinical diagnosis in all PH patients, particularly male patients with Group 2/3 disease, may mitigate some of previously observed advantages of estrogen on outcomes in PH.

Lavannya Pandit, MD, FCCP, Steering Committee Member

### What's new, what's back, and what's better at CHEST 2021

here's never been a better year to attend this year's CHEST annual meeting. Whether it's your first time or your 20th, now is the time to come together again.

This is your chance to connect with colleagues, view the latest original research in hot-button topic areas, learn from leading faculty working in the trenches every day, engage in hands-on simulation sessions, and more. Most importantly, CHEST 2021 is the perfect opportunity to reconnect as a community in pulmonary, critical care, and sleep medicine.

Catch up on the latest education from the last year in topic areas like cultural diversity, disaster medicine, biotechnology, and more. COVID-19 will be at the forefront of some sessions, including Racism in Health Care: The Fuel That Lit the COVID-19 Fire, and You Think You Survived COVID-19: What's Next?

Simulation is back with 47 handson sessions in Orlando, seven of them being new, and more than 1,000 seats available for these unique training opportunities. There will also be nine on demand

### CHEST 2021 ANNUAL MEETING | OCTOBER 17-20

more than 100 hours of education available.

The new CHEST Studio will be unveiled at the meeting, allowing in-person attendees to take a peek behind the scenes with leadership. We'll be filming pre-, half-time, and post-show news style videos throughout the meeting.

These videos will also be livestreamed on the CHEST 2021 online platform.

This year, abstracts and case reports are getting a revamp. During the meeting, in lieu of physical posters, we're introducing rapid presentations in dedicated pods throughout the Exhibit Hall floor. This new format will allow for more live presentations in the form of three sessions featuring eight presentations each on October 18,

sessions closing out simulation, with 19, and 20. Learners will have the chance to showcase posters in the virtual platform.

> And back by popular demand, we're welcoming the return of some experiences first introduced during CHEST 2019. First is the Wellness Zone, an area created to help you relax and recharge during your busy week at CHEST.

This space features meditation, posture consultants, and bite-sized education for your personal wellness and professional productivity as we get into the next normal post-COVID-19 era. After the madness of the past year, you deserve a moment of calm.

We're also bringing back the complimentary professional headshot booth. Show off your new quarantine look - did you grow a mustache or decide your natural

hair color is perfect? This is your chance to update your professional social media accounts with your latest look.

If you're worried about attending CHEST 2021 with children, don't be! The Kiddie Corp childcare program ensures your children ages 6 months to 12 years are looked after while you attend education sessions.

Besides the meeting, don't miss out on great activities for the whole family in Orlando this October, including: The Walt Disney World 50th Anniversary Celebration, Boo Bash at Magic Kingdom in Walt Disney World, the Epcot International Food & Wine Festival at Walt Disney World in Bay Lake, Florida, and SeaWorld Spooktacular at Sea-World Orlando.

As an in-person attendee for CHEST 2021, you can purchase discounted tickets for Disney through our website at https://chestmeeting. chestnet.org/hotel-and-travel/. Please plan ahead for these events by purchasing tickets early, as they are likely to sell out.

While we can't wait to see you in Orlando, we know not everyone can travel. That's why this year's meeting will feature more than 200 live, in-person sessions that will also be livestreamed and more than 100 prerecorded lectures offered online.

Keep watching the CHEST 2021 meeting website at chestmeeting. chestnet.org for updates on programs and plans.

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### **NetWorks Compete to Combat Health Disparities**

ne way members get involved in CHEST's philanthropic efforts takes place each year with the start of the NetWorks Challenge. CHEST members compete through their NetWorks - special interest groups that focus on particular areas of chest medicine - to raise funds that support Foundation microgrants.

NetWorks Challenge 2021 kicked off in June with a special twist to celebrate the Foundation's 25th anniversary. Each NetWork is asked to complete a 25k virtual physical challenge. This can be done by walking, running, biking, swimming—or any other physical activity.

Through the challenge, members engage in friendly competition while supporting the goals of the Foundation.

This year, money raised will directly help the Foundation in addressing health disparities through



our microgrants program. In addition, the funds will support travel grants for doctors in training looking to attend CHEST 2021.

By participating in the NetWorks Challenge, members help fund grants that aim to lend a hand to those who need it the most. Expanding research capabilities, improving patient care, and giving access to medical equipment are just a few ways microgrants from the CHEST Foundation have been used in the past.

Inspired by the Listening Tour and the struggles experienced by underserved communities, money raised through the Network Challenge will go to a new pilot microgrant program called Rita's Fund.

The grants aim to supplement community-based projects that provide resources to individuals to help drastically change their quality of life. Funding will assist with coverage for medical equipment, transportation, and access to technology for those living with lung disease and other medical complications.

NetWork members are asked to encourage one another to join in this summer's race to 25k.

To learn more about this initiative and this year's NetWorks Challenge, visit chestfoundation.org/nwc21. And, don't miss the summer issue of Donor Spotlight.

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