COVID-19 breakthrough infections twice as likely to be asymptomatic

BY JALEESA BAULKMAN
MDedge News

People with breakthrough COVID-19 infections are two times more likely to be completely asymptomatic and are about two-thirds less likely to be hospitalized, compared with those who are unvaccinated, according to a new observational study.

Individuals infected with COVID-19 after receiving their first or second dose of either the Pfizer, Moderna, or AstraZeneca vaccine experienced a lower number of symptoms in the first week of infection, compared with those who did not receive a COVID-19 vaccine, reported the authors of the report in The Lancet Infectious Diseases (2021 Sep 1. doi: 10.1016/S1473-3099(21)00460-6). These patients also had a reduced need for hospitalization, compared with unvaccinated peers. Those who received both doses of a vaccine were less likely to experience prolonged COVID – defined as at least 28 days of symptoms in this paper – compared with unvaccinated individuals.

“We are at a critical point in the pandemic as we see cases rising worldwide due to the Delta variant,” study co–lead author Claire S. J. Steves, MD, said in a statement. “Breakthrough infections are expected and don’t diminish the fact that these vaccines are doing exactly what they were designed to do – save lives and prevent serious illness.”

Children with obesity, asthma resistant to ICS

BY NEIL OSTERWEIL
MDedge News

Obese or overweight children with asthma could be using inhaled corticosteroids (ICS) to no avail, combined results from observational studies suggest.

Using Mendelian randomization, a method for reducing bias in observational studies, investigators from the University of Amsterdam Medical Center performed an analysis of data from four cross-sectional studies and one cohort study on a total of 1,511 children with asthma.

They showed that every 1-unit increase in the body mass index z score was associated with a more than twofold higher odds ratio for exacerbation, reported Cristina Longo, PhD, a former postdoctoral fellow at AMC, and assistant professor of medicine at the University of Montreal.

“In this large, multicenter Mendelian randomization study, our findings support current evidence that children with higher BMI status respond inadequately to inhaled corticosteroids, and that this association is likely not explained by measured confounding or reverse causation,” she said in an oral abstract presentation during the European Respiratory Society International Congress.

ASTHMA // continued on page 4
Unmeasured confounding
The obese-asthma phenotype in children is characterized by reduced lung function, high symptom expression, poor response to ICS, and high health care utilization. "While most observational studies suggest that weight status is associated with asthma exacerbations, despite using inhaled corticosteroids, it's unclear whether these associations may be due to unmeasured confounding or reverse causation, which captures the idea that perhaps obesity is a consequence rather than a cause of uncontrolled severe asthma," she said. Traditional observational studies of the obesity-asthma link rely on comparing data on asthma in a target population and comparing non-obese patients with obese patients. The problem with this method, Dr. Longo contended, is that the exposure assignment – weight status – is not random, and could lead to bias from potential imbalance of confounders, leading to unintentionally biased results.

In contrast, Mendelian randomization uses genetic data to approximate random assignment...
of exposures, using a risk score for BMI based on genetic susceptibility. The score is based on the accumulation of genetic variants (single-nucleotide polymorphisms, or SNPs) that predispose individuals to obesity, with higher numbers of variants results in a higher risk score.

The scores are then used to determine the comparison groups for evaluating the obesity-asthma association.

**Alphabet soup**

Dr. Longo and colleagues analyzed data on a total 1,511 children enrolled in four observational studies (PACMAN, PAGES, HPR, CLARA) and one cohort study (ALSPAC).

They included children with an asthma diagnosis who used ICS and had available information on both BMI and genetics.

The Mendelian randomization analysis was based on a weighted allele score based on 97 SNPs predictive of BMI based on large-scale genomewide association studies. The exposure for the analysis was age- and sex-adjusted BMI z scores based on World Health Organization growth charts designed for children.

They found that using the Mendelian randomization approach, for each standard deviation increase in BMI, the odds ratio for any parent-reported asthma exacerbations, including urgent care visits or use of oral corticosteroids, was 2.31 (95% confidence interval, 1.26-4.25).

In contrast, if the traditional observational model had been used, the OR would be a nonsignificant 1.10 (95% CI, 0.99-1.22).

“Treatment guidelines recommend steroids for children with asthma who have a higher-than-normal BMI,” Dr. Longo said in a statement. “Our research group felt that the one-size fits all approach to treating children with asthma with inhaled steroids as their first-line treatment, particularly those with excess weight, warrants revision. At the very least, research identifying potential alternative treatments should be encouraged and prioritized, especially since 30% of children with asthma are also obese. With the childhood obesity epidemic rising, we expect this percentage to increase meaning this problem of poor control will be seen more frequently in routine clinical practice.”

Christopher E. Brightling, PhD, professor of respiratory medicine at the University of Leicester (England), commented that “this is very good and fascinating research with findings that are important and novel.

“It sheds light on the complex interplay between genes, weight, and response to inhaled corticosteroids, underscoring the need to combine drug treatments with lifestyle and diet modifications. Policy makers, health care providers and families need to do much more to tackle the growing obesity epidemic in young people,” he said.

Dr. Brightling was not involved in the study.

The study was supported by the ERS and the European Union’s H2020 research and innovation program. Dr. Longo was a Horizon 2020 Marie-Sklodowska Cure Respire-3 fellow. Dr. Brightling reported no relevant disclosures.
Breakthrough infections

For the community-based, case-control study, Dr. Steves, who is a clinical senior lecturer at King’s College London, and her colleagues analyzed and presented self-reported data on demographics, geographical location, health risk factors, COVID-19 test results, symptoms, and vaccinations from more than 1.2 million UK-based adults through the COVID Symptom Study mobile phone app.

They found that, of the 1.2 million adults who received at least one dose of either the Pfizer, Moderna, or AstraZeneca vaccine, fewer than 0.5% tested positive for COVID-19 14 days after their first dose. Of those who received a second dose of a COVID-19 vaccine, 0.2% acquired the infection more than 7 days post vaccination.

Likelihood of severe symptoms dropped after one dose

After just one COVID-19 vaccine dose, the likelihood of experiencing severe symptoms from a COVID-19 infection dropped by a quarter. The odds of their infection being asymptomatic increased by 94% after the second dose.

Researchers also found that vaccinated participants in the study were more likely to be completely asymptomatic, especially if they were 60 years or older.

Furthermore, the odds of those with breakthrough infections experiencing severe disease – which is characterized by having five or more symptoms within the first week of becoming ill – dropped by approximately one-third.

When evaluating risk factors, the researchers found that those most vulnerable to a breakthrough infection after receiving a first dose of Pfizer, Moderna, or AstraZeneca COVID-19 vaccine were older adults (ages 60 years or older) who are either frail or live with underlying conditions such as asthma, lung disease, and obesity.

The findings provide substantial evidence that there are benefits after just one dose of the vaccine, said Diego Hijano, MD, MSc, pediatric infectious disease specialist at St. Jude’s Children’s Research Hospital, Memphis. However, the report also supports caution around becoming lax on protective COVID-19 measures such as physical distancing and wearing masks, especially around vulnerable groups, he said.

Findings may have implications for health policies

“It’s also important for people who are fully vaccinated to understand that these infections are expected and are happening, especially now with the Delta variant,” Dr. Hijano said.

“While the outcomes are favorable, you need to still protect yourself to also protect your loved ones. You want to be very mindful that, if you are vaccinated and you get infected, you can pass it on to somebody that actually has not been vaccinated or has some of these risk factors.”

The authors of the new research paper believe their findings may have implications for health policies regarding the timing between vaccine doses, for COVID-19 booster shots, and for continuing personal protective measures.

The authors of the paper and Dr. Hijano disclosed no conflicts.
Refined heart rate cutoffs may improve prognostics

BY ANDREW D. BOWSER
MEDedge News

FROM THE JOURNAL CHEST • In patients with acute pulmonary embolism, using cutoff values other than 110 beats per minute (bpm) might improve the prognostic value of heart rate (HR) at admission, a recent observational study suggests.

For identifying low-risk patients, a cutoff of 80 bpm increased the sensitivity of the simplified Pulmonary Embolism Severity Index (sPESI) from about 94% to nearly 99% among nonhypotensive patients with acute symptomatic pulmonary embolism (PE), according to results of the large, registry-based study. Similarly, using a 140-bpm cutoff increased the specificity of the Bova score for identifying intermediate–high–risk patients from about 93% to 98% in the study, which was recently published in the journal CHEST (2021. doi: 10.1016/j.chest.2021.08.059).

“Although standard dichotomization of HR [i.e., HR less than 110 vs. greater than 110 bpm] may be useful for guideline recommendations, our results will allow for more accuracy regarding clinical decision-making,” wrote lead author Ana Jaureguízar, MD, of the University of Alcalá in Madrid, on behalf of the RIETE (Registro Informatizado de la Enfermedad TromboEmbolica) investigators.

Findings inform future research

These observational findings are intuitive and do at least have the potential to inform the design of future randomized clinical trials, according to Albert J. Polito, MD, chief of the division of pulmonary medicine and medical director for the lung center at Mercy Medical Center in Baltimore.

“In medicine, there is a spectrum of risk,” Dr. Polito said in an interview. “While we love our cutoffs, which in this case has traditionally always been that 110 beats per minute for heart rate, it makes sense that there would be some range of risks of bad outcomes.”

Building on the observations of this study, subsequent prospective randomized studies could potentially aim to determine, for example, when thrombolytic therapy should be considered in nonhypotensive patients with acute PE and higher heart rates.

“It would not be easy to design, but it’s a straightforward question to ask whether patients with the highest heart rates are the ones who potentially might benefit the most from thrombolytic therapy,” Dr. Polito said.

Value of alternative HR cutoffs

Heart rate is a simple and easily available vital sign that is clearly linked to prognosis in patients with pulmonary embolism, authors of the RIETE registry study say in their report. Accordingly, a heart rate threshold of 110 bpm has made its way into scoring systems that seek to identify low-risk patients, such as the sPESI, and those focused on identifying higher-risk patients, such as the Bova score.

However, it has not been clear whether alternative HR cutoffs would improve upon the 110-bpm threshold, they added. At the low-risk end, more accurate scoring systems could optimize the selection of patients for home treatment, while at the intermediate-high–risk end, they could better select patients for close monitoring or advanced PE treatments.

Better granularity on risks?

To better define the prognostic value of different heart rate thresholds, investigators analyzed data from RIETE, a large, ongoing, multinational prospective registry including patients with objectively confirmed acute venous thromboembolism. For 44,331 consecutive nonhypotensive symptomatic PEs, the overall rate of 30-day all-cause mortality was 5.1%, and the 30-day PE-related mortality was 1.9%, the authors report.

Significantly poorer outcomes were seen in patients with higher heart rates as compared to patients in the 80-99 bpm range, they also found. As compared to that reference range, odds ratios for 30-day all-cause death ranged from 1.5 for heart rates of 100-109, up to 2.4 for those with heart rates of 140 bpm or greater.

Likewise, patients with higher heart rates had a 1.7- to 2.4-fold greater risk of 30-day PE-related death as compared to the 80- to 99-bpm reference range, while patients with lower heart rates had lesser risk, the data published in CHEST show.

Refinement of scoring

Next, investigators sought to refine the prognostic scoring systems for low-risk PE (sPESI) and intermediate–high–risk PE (Bova).

For sPESI, they found that dropping the cutoff value from 110 to 100 bpm increased the sensitivity of the score from 93.4% to 95.3%. Going down even further to 80 bpm increased sensitivity to 98.8%, according to the report.

By going down from 110 to 80 bpm, the proportion of patients defined as low-risk dropped from 35% to 12%, according to the investigators.

For the Bova score, increasing the cutoff value from 110 to 120 bpm likewise increased specificity from 93.2% to 95%, while going up even further to 140 bpm increased specificity to 98.0%, the report shows.

In sensitivity analyses, the findings were not impacted by excluding younger patients, those who received reperfusion therapies, or those with atrial fibrillation, according to the study findings.

Potential implications

Taken together, these findings could serve as a resource to inform discussions regarding PE management that include whether home therapy or use of thrombolytic therapy is appropriate, investigators said in their report.

For instance, among low-risk sPESI patients, those with borderline tachycardia [i.e., a heart rate between 100-109 bpm] might benefit from initial hospital observation for trending,” they wrote.

Dr. Jaureguízar reported no disclosures. One coinvestigator reported funding support from the Institute of Health Carlos III (ISCIII) and the European Development Regional Fund (ERDF). One coinvestigator reported consulting in litigation involving two models of inferior vena cava filters. Dr. Polito reported no disclosures.

Poor lung function linked to risk for sudden cardiac death

BY NEIL OSTERWEIL

Poor lung function appears to be a stronger marker of risk for sudden cardiac death than for a survivable first coronary event, results of a prospective population-based study suggest.

Among 28,584 adults with no history of acute coronary events who were followed over 4 decades, every standard-deviation decrease in forced expiratory volume in 1 second (FEV1) was associated with a 23% increase in risk for sudden cardiac death, reported Suneela Zaigham, PhD, a cardiovascular epidemiology fellow at the University of Lund, Sweden, and colleagues.

“Our main findings and subsequent conclusions are that low FEV1 is associated with both sudden cardiac death and nonfatal coronary events but is consistently more strongly associated with future sudden cardiac death,” Dr. Zaigham said in a narrated poster presented at the European Respiratory Society (ERS) 2021 International Congress, which was held online.

“We propose that measurement with spirometry in early life could aid in the risk stratification of future sudden cardiac death, and our results support the use of spirometry for cardiovascular risk assessment,” she said.

Marc Humbert, MD, PhD, professor of respiratory medicine at Université Paris–Saclay, who was not involved in the study, said that “this is something we can measure fairly easily, meaning that lung function could be used as part of a screening tool.

“We need to do more research to understand the links between lung function and sudden cardiac death and to investigate whether we can use lung function tests to help prevent deaths in the future,” he said.

It is well known that poor lung function is a
COVID-clogged ICUs ‘terrify’ those with chronic or emergency illness

BY MARCIA FRELLICK

Jessica Gosnell, MD, 41, from Portland, Oreg., lives daily with the knowledge that her rare disease – a form of hereditary angioedema – could cause a sudden, severe swelling in her throat that could require quick intubation and land her in an intensive care unit (ICU) for days.

“I’ve been hospitalized for throat swells three times in the last year,” she said in an interview.

Dr. Gosnell no longer practices medicine because of a combination of illnesses, but lives with her husband, Andrew, and two young children, and said they are all “terrified” she will have to go to the hospital amid a COVID-19 surge that

had shrunk the number of available ICU beds to 152 from 780 in Oregon as of Aug. 30. Thirty percent of the beds are in use for patients with COVID-19.

She said her life depends on being near hospitals that have ICUs and having access to highly specialized medications, one of which can cost up to $50,000 for the rescue dose.

Her fear has her “literally living bedbound.”

In addition to hereditary angioedema, she has Ehlers-Danlos syndrome, which weakens connective tissue. She wears a cervical collar 24/7 to keep from tearing tissues, as any tissue injury can trigger a swell.

Patients worry there won’t be room

As ICU beds in most states are filling with COVID-19 patients as the Delta variant spreads, patients worry there won’t be room.

At the end of 2019, 22% of respondents reported visiting an emergency department in the past year. That dropped to 17% by the end of 2020, and was at 17.7% in the first 3 months of 2021.

As of Aug. 30, in the United States, 79% of ICU beds nationally were in use, 30% of them for COVID-19 patients, according to the U.S. Department of Health & Human Services.

In individual states, the picture is dire. Alabama has fewer than 10% of its ICU beds open across the entire state. In Florida, 93% of ICU beds are filled, 53% of them with COVID patients. In Louisiana, 87% of beds were already in use, 45% of them with COVID patients, just as category 4 hurricane Ida smashed into the coastline on Aug. 29.

News reports have told of people transported and airlifted as hospitals reach capacity.

In Bellville, Tex., U.S. Army veteran Daniel Wilkinson needed advanced care for gallstone pancreatitis that normally would take 30 minutes to treat, his Bellville doctor, Hasan Kakli, MD, told CBS News.

Mr. Wilkinson’s house was three doors from Bellville Hospital, but the hospital was not equipped to treat the condition. Calls to other hospitals found the same answer: no empty ICU beds. After a 7-hour wait on a stretcher, he was airlifted to a Veterans Affairs hospital in Houston, but it was too late. He died on Aug. 22 at age 46.

Dr. Kakli said, “I’ve never lost a patient with this diagnosis. Ever. I’m scared that the next patient I treat is someone that I can’t get to where they need to get to. We are playing musical chairs with 100 people and 10 chairs. When the music stops, what happens?”

Also in Texas in August, Joe Valdez, who was shot six times as an unlucky bystander in a domestic dispute, waited for more than a week for surgery at Ben Taub Hospital in Houston, which was over capacity with COVID patients, the Washington Post reported.

Others with chronic diseases fear needing emergency services or even entering a hospital for regular care with the COVID surge.

Nicole Seefeldt, 44, from Easton, Penn., who had a double-lung transplant in 2016, said that she hasn’t been able to see her lung transplant specialists in Philadelphia – an hour-and-a-half drive – for almost 2 years because of fear of contracting COVID. Before the pandemic, she made the trip almost weekly.

“I protect my lungs like they’re children,” she said.

Continued on following page

VIEW ON THE NEWS

Daniel Ouellette, MD, FCCP, comments: It was the fall of 2020, and I was rounding in the ICU. Detroit was in the middle of a COVID-19 “surge.” All of my patients – all of them – had COVID-19 pneumonia. I reflected on the last 15 years of practice in the ICU at my hospital and considered that there had never been a time when the ICU wasn’t full. We always had a “bed crunch.” I knew that the type of patients previously being cared for were delaying their care, being cared for somewhere else, or worst of all not receiving needed care.

My experiences in my clinic confirmed my fears. My patients preferred video visits to office visits because they were scared of coming to the hospital. Patients with sarcoidosis and severe asthma chose not to come to the infusion center or clinic to receive biologic agents but sought other alternatives.

A patient dying of cancer had her therapy delayed because of the constraints caused by the epidemic, her fears of COVID-19, and hospital system access.

As physicians, we seek to treat our patients compassionately and well. It has been a shock to us to see how quickly this epidemic has led us to a state of resource limitation and poorer care for our patients.

I hope that we learn from this experience so that we can do better with the next epidemic.

She relies on her local hospital for care, but has put off some needed care, such as a colonoscopy, and has relied on telemedicine because she wants to limit her hospital exposure.

Ms. Seefeldt now faces an eventual kidney transplant.

Continued from previous page

strong predictor of future coronary events, but it was unknown whether patterns of lung impairment differ in their ability to predict future nonfatal coronary events or sudden cardiac death, Dr. Zaigham said.

To see whether measurable differences in lung function could predict risk for both fatal and nonfatal coronary events, the investigators studied 28,584 middle-aged residents of Malmö, Sweden. Baseline spirometry test results were available for all study participants.

Patients were followed for approximately 40 years for sudden cardiac death, defined as death on the day of a coronary event, or nonfatal events, defined as survival for at least 24 hours after an event. Dr. Zaigham and colleagues used a modified version of Lunn McNeill’s competing risks method to create Cox regression models.

Results of an analysis that was adjusted for potential confounding factors indicated that one standard deviation reduction in FEV₁ was associated with a hazard ratio for sudden cardiac death of 1.23 (95% confidence interval, 1.15-1.31). In contrast, one standard deviation in FEV₁ was associated with a lower but still significant risk for nonfatal events, with an HR of 1.08 (95% CI, 1.04-1.13; P for equal associations = .002).

The results remained significant among participants who had never smoked, with an HR for sudden cardiac death of 1.34 (95% CI, 1.15-1.55) and for nonfatal events of 1.11 (95% CI, 1.02-1.21; P for equal associations = .038).

“This study suggests a link between lung health and sudden cardiac death. It shows a higher risk of fatal than nonfatal coronary events even in people whose lung function is moderately lower but may still be within a normal range,” Dr. Humbert said.

Dr. Zaigham and Dr. Humbert reported having no relevant financial relationships.
plant, as her kidney function has been reduced to 20%. In the meantime, she worries she will need emergency care for her lungs or kidneys.

“For those of us who are chronically ill or disabled, what if we have an emergency that is not COVID related? Are we going to be able to get a bed? Are we going to be able to get treatment? It’s not just COVID patients who come to the [emergency room],” she said.

A pandemic problem

Paul E. Casey, MD, MBA, at Rush University Medical Center in Chicago, said that high vaccination rates in Chicago have helped Rush continue to accommodate both non-COVID and COVID patients in the emergency department.

Though the hospital treated a large volume of COVID patients, “The vast majority of people we see and did see through the pandemic were non-COVID patients,” he said. Dr. Casey said that in the first wave the hospital noticed a concerning drop in patients coming in for strokes and heart attacks – “things we knew hadn’t gone away.”

And the data backs it up. Over the course of the pandemic, the Centers for Disease Control and Prevention’s National Health Interview Survey found that the percentage of Americans who reported seeing a doctor or health professional fell from 85% at the end of 2019 to about 80% in the first 3 months of 2021. The survey did not differentiate between in-person visits and telehealth appointments.

Medical practices and patients themselves postponed elective procedures and delayed routine visits during the early months of the crisis. Patients also reported staying away from hospitals’ emergency departments throughout the pandemic. At the end of 2019, 22% of respondents reported visiting an emergency department in the past year. That dropped to 17% by the end of 2020, and was at 17.7% in the first 3 months of 2021.

Dr. Casey said that, in his hospital’s case, clear messaging became very important to assure patients it was safe to come back. And the message is still critical.

“We want to be loud and clear that patients should continue to seek care for those conditions,” Dr. Casey said. “Deferring health care only comes with the long-term sequelae of disease left untreated so we want people to be as proactive in seeking care as they always would be.”

In some cases, fears of entering emergency rooms because of excess patients and risk for infection are keeping some patients from seeking necessary care for minor injuries. Jim Rickert, MD, an orthopedic surgeon with Indiana University Health in Bloomington, said some of his patients expressed fears of coming into the hospital for fractures.

Some patients, particularly elderly patients, he said, are having falls and fractures and wearing slings or braces at home rather than going into the hospital for injuries that need immediate attention.

Bones start healing incorrectly, Dr. Rickert said, and the correction becomes much more difficult.

Dr. Gosnell made a plea for people to get COVID vaccinations. “It seems to me it’s easy for other people who are not in bodies like mine to take health for granted,” she said. “But there are a lot of us who live in very fragile bodies and our entire life is at the intersection of us and getting health care treatment. Small complications to getting treatment can be life altering.”

Dr. Gosnell, Ms. Seefeldt, Dr. Casey, and Dr. Rickert reported no relevant financial relationships.
LUNG CANCER

‘Urgent’ need to understand NSCLC immunotherapy

BY LIAM DAVENPORT

A growing body of research suggests there may be an optimal duration of immunotherapy for patients with non–small cell lung cancer (NSCLC), after which it can be de-escalated or discontinued to minimize toxicity and costs while maintaining long-term efficacy.

However, the research to date does not provide a clear picture of which patients will achieve this “exceptional and durable response” and at which point patients can safely reduce or withdraw from treatment, according to Yasushi Goto, MD, PhD, a staff doctor in the Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo.

Dr. Goto presented the latest evidence and explored the current unknowns surrounding immunotherapy de-escalation in NSCLC in a session this week at the virtual World Conference on Lung Cancer.

In addition to a toxicity and quality-of-life benefit for patients, immunotherapy de-escalation could have a significant impact on the costs of care, Dr. Goto stressed. The rising cost of new cancer treatments represents a “crisis” in terms of the affordability of health care, he said, and reducing these costs represents an “urgent global issue.”

Evidence for discontinuing

Dr. Goto began by emphasizing how immunotherapy has enhanced outcomes for patients with NSCLC and other cancers. This success has brought a pressing question to the forefront: How long should we treat patients with immunotherapy?

“The question arose over 10 years ago when ipilimumab (Yervoy) was granted FDA approval for patients with metastatic melanoma, but only for a total of four doses because of the drug’s toxicity,” Dr. Goto said. “However, some patients had very lasting efficacy with the drug, even after discontinuation,” Dr. Goto said, which raised the exciting prospect that patients could achieve a functional cure with immunotherapy.

Evidence highlighting this lasting effect among patients with NSCLC soon emerged as well. A 2015 study, for instance, indicated that, despite toxicities, 50% of patients receiving nivolumab (Opdivo) continued to have a treatment effect more than 9 months after their last dose.

A 2021 analysis of patients receiving pembrolizumab (Keytruda) found that 48% of patients were disease-free after 5 years, despite having discontinued treatment after 2 years.

Dr. Goto noted that there are also ongoing randomized studies examining the optimal duration of immunotherapy in advanced melanoma. One that he is involved in, the SAVE study, is enrolling patients with advanced NSCLC who have responded to anti–PD-1 agents for over a year and will compare overall survival in those who stop therapy versus those who continue. In addition, given the “growing importance” of biomarkers as a prediction tool, Dr. Goto plans to integrate circulating tumor DNA testing to help identify patients more likely to benefit from therapy discontinuation. If successful, such approaches could “disruptively decrease prescribing costs,” by lowering doses or dose frequency, by shortening the treatment duration, or by substituting therapies with fewer adverse effects, Dr. Goto said.

Discussing de-escalation

During the discussion period after his talk, session cochairs Loretta Erhumwuese, MD, City of Hope Comprehensive Cancer Center, Duarte, Calif., asked Dr. Goto what his current practice is in regard to de-escalation.

He replied that, in Japan, physicians are allowed to continue immunotherapy beyond 2 years, but “many patients stop their immune checkpoint inhibitor due to toxicity,” even if it is minor.

Exploring evidence surrounding the optimal duration of therapy, session cochair Bishal Gyawali, MD, PhD, Queen’s University, Kingston, Ont., pointed to collaborative studies in colon cancer that looked at chemotherapy duration, for example looking at 3 versus 6 months of treatment.

Dr. Gyawali wondered whether the same could be achieved in lung cancer to test the noninferiority of shorter duration of immunotherapy versus continuing treatment until disease progression.

Dr. Goto noted that the biggest difference in the current context of NSCLC is the toxicity incurred by both the adjuvant chemotherapy and the immunotherapy, making the overall benefit to the patient “very difficult to show.” Consequently, patients may not be willing to join a randomized trial in which they could experience additional toxicity for uncertain benefit.

No funding for this study was declared. Dr. Goto disclosed relationships with AbbVie, AstraZeneca, and a number of other biotechnology/pharmaceutical companies.
Air pollution – second-leading cause of lung cancer

BY LIAM DAVENPORT

Air pollution is the second-leading cause of lung cancer in the world, after smoking, results of a novel analysis suggest. The researchers call for concerted action.

The new data show that the rate of lung cancer deaths attributable to air pollution varies widely between countries. Serbia, Poland, China, Mongolia, and Turkey are among the worst affected.

The analysis shows that there is an association between deaths from lung cancer and the proportion of national energy that is produced from coal.

“Both smoking and air pollution are important causes of lung cancer ... both need to be eliminated to help prevent lung cancer and save lives. As lung cancer professionals, we can mitigate the effects of air pollution on causing lung cancer by speaking out for clean-energy standards.”

“Both smoking and air pollution are important causes of lung cancer,” said study presenter Christine D. Berg, MD, former codirector of the National Lung Screening Trial, and “both need to be eliminated to help prevent lung cancer and save lives.”

“As lung cancer professionals, we can mitigate the effects of air pollution on causing lung cancer by speaking out for clean-energy standards,” she said.

Dr. Berg presented the new analysis on Sept. 9 at the 2021 World Conference on Lung Cancer, which was organized by the International Association for the Study of Lung Cancer.

She welcomed the recent statement issued by the IASLC in support of the International Day of Clean Air for Blue Skies, which took place on Sept. 7. It was a call for action that emphasized the need for further efforts to improve air quality to protect human health.

The findings from the new analysis are “depressing,” commented Joachim G.J.V. Aerts, MD, PhD, department of pulmonary diseases, Erasmus University Medical Center, Rotterdam, the Netherlands. It is now clear that air pollution has an impact not only on the incidence of lung cancer but also on its outcome, he added.

Indeed, previous research showed that each 10-mcg/m³ increase in particulate matter of 2.5 mcg in size was associated with a 15%-27% increase in lung cancer mortality (Am J Respir Crit Care Med. 2011 Dec 15;184[12]:1374-81). There was no difference in rates between women and men.

A key question, Dr. Aerts said, is whether reducing air pollution would be beneficial.

Efforts to reduce air pollution over recent decades in the United Kingdom have not led to a reduction in lung cancer deaths. This is because of the increase in life expectancy – individuals have been exposed to pollution for longer, albeit at lower levels, Dr. Aerts pointed out.

Because of lockdowns during the COVID pandemic, travel has been greatly reduced.

This has resulted in a dramatic reduction in air pollution, “and this led to a decrease in the number of children born with low birth weight,” said Dr. Aerts. Hopefully, that benefit will also be seen regarding other diseases, he added.

The call to action to reduce air pollution is of the “utmost importance,” he said. He noted that the focus should be on global, national, local, and personal preventive measures.

“It is time to join forces,” he added, “to clean the air.” Dr. Berg's presentation was warmly received on social media.

It was "fabulous," commented Eric H. Bernicker, MD, director of medical thoracic oncology at Houston Methodist Cancer Center.

"Thoracic oncologists need to add air pollution to things they advocate about; we have an important voice here," he added.

It is “so important to understand that air pollution is a human carcinogen,” commented Iyf Elkins, a lung cancer survivor and advocate and co-founder of the EGFR Resisters Lung Cancer Patient Group. “All you need are lungs to get lung cancer!”

**Contribution of air pollution to lung cancer**

In her presentation, Dr. Berg emphasized that lung cancer is the leading cause of cancer death worldwide, although the distribution between countries “depends on historical and current smoking patterns and the demographics of the population.”

Overall, data from GLOBOCAN 2018 indicate that annually there are approximately 2.1 million incident cases of lung cancer and almost 1.8 million lung cancer deaths around the globe (CA Cancer J Clin. 2018 Nov;68[6]:394-424).

A recent study estimated that, worldwide, 14.1% of all lung cancer deaths, including in never-smokers, are directly linked to air pollution.

Synthesizing various estimates on global burden of disease, Dr. Berg and colleagues calculated that in 2019 the rate of lung cancer deaths attributable to particulate matter in people aged 50-69 years was highest in Serbia, at 36.88 attributable deaths per 100,000.

Next was Poland, with a rate of 27.97 per 100,000, followed by China at 24.63 per 100,000, Mongolia at 19.71 per 100,000, and Turkey at 19.2 per 100,000.

The major sources of air pollution in the most affected countries were transportation, indoor cooking, and energy sources, she said.

In Serbia, 70% of energy production was from coal. It was 74% in Poland, 65% in China, 80% in Mongolia, 35% in Turkey, and 19% in the United States.

At the time of the analysis, only 17.3% of U.S. adults were smokers, and the air concentration of particulate matter of 2.5 mcg/m³ was 9.6 mcg/m³. Both of these rates are far below those seen in more severely affected countries.

“But 40% of our energy now comes from natural gas,” noted Dr. Berg, “which is still a pollutant and a source of methane. It’s a very potent greenhouse gas.”

No funding for the study has been reported.

Dr. Berg has relationships with Amphiara, AstraZeneca, Bayer, BIOCAD, Bristol-Myers Squibb, Eli Lilly, and Roche.
**Pandemic strategies to boost trial enrollment should remain in place, survey suggests**

*BY LIAM DAVENPORT*

Although enrollment into lung cancer clinical trials fell during the early months of the COVID-19 pandemic, it increased after a number of mitigation strategies were introduced.

These strategies should now be maintained, say experts, in order to improve enrollment and access to trials and to ensure that trials are more pragmatic and streamlined.

These were the findings from a survey sent to 173 sites of clinical trials in 45 countries around the world. The findings were presented recently at the 2021 World Conference on Lung Cancer. The meeting and the survey were organized by the International Association for the Study of Lung Cancer (IASLC).

Responses to the survey revealed that enrollment into lung cancer trials fell by 43% during the early months of the pandemic. Patients stopped attending clinics, and some trials were suspended.

Patients were less willing to visit clinical trial sites, and lockdown restrictions made travel difficult.

Organizers of clinical trials responded by implementing mitigation strategies, such as changing monitoring requirements, increasing use of telehealth, and using local non–study facilities for laboratory and radiology services.

These measures led to an increase in trial enrollment toward the end of 2020, the survey results show. “The COVID-19 pandemic created many challenges [that led to] reductions in lung cancer clinical trial enrollment,” commented study presenter Matthew P. Smeltzer, PhD, from the Division of Epidemiology, Biostatistics, and Environmental Health, University of Memphis.

The employment of mitigation strategies allowed the removal of “barriers,” and although the pandemic “worsened, trial enrollment began to improve due in part to these strategies,” Dr. Smeltzer said.

Many of these measures were successful and should be maintained, he suggested. Strategies include allowing telehealth visits, performing testing at local laboratories, using local radiology services, mailing experimental agents “where possible,” and allowing flexibility in trial schedules.

This is a “very important” study, commented Marina Garassino, MD, professor of medicine, hematology, and oncology, the University of Chicago Medicine, in her discussion of the abstract.

Irrespective of the pandemic, the regulation and the bureaucracy of clinical trials hinder participation by patients and physicians, she said.

Many of the mitigation strategies highlighted by the survey were similar to recommendations on the conduct of clinical trials published by the American Society of Clinical Oncology during the pandemic. Those recommendations emphasize the use of telehealth and offsite strategies to help with patient monitoring, she noted.

The findings from the survey show that it is possible to conduct more “streamlined and pragmatic trials,” she said.

“More flexible approaches should be approved by the sponsors of clinical trials and global regulatory bodies,” she added.

However, she expressed concern that “with the telehealth visits, we can create some disparities.”

“We have to remember that lung cancer patients are sometimes a very old population, and they are not digitally evolved,” she commented.

Commenting on Twitter, Jennifer C. King, PhD, chief scientific officer at the GO2 Foundation for Lung Cancer, in Washington, D.C., agreed that many of the mitigation strategies identified in the study “are good for patients all of the time, not just during a pandemic.”

**Impact on lung cancer clinical trials**

The survey, which included 64 questions, was intended to assess the impact of the COVID pandemic on lung cancer clinical trials.

Most of the survey responses came from sites in Europe (37.6%); 21.4% came from Asia; 13.3% came from the United States; and 7.5% came from Canada.

The team found that enrollment into lung cancer trials declined by 43% in 2020 compared to 2019, at an incidence rate ratio of 0.57 (P = .0115).

The largest decreases in enrollment were between April and August 2020, Dr. Smeltzer noted. However, in the last quarter of 2020 (October to December), the differences in enrollment were significantly smaller (P = .0160), despite a marked increase in global COVID-19 cases per month, he added.

The most common challenges faced by clinical trial sites during the pandemic were the following: There were fewer eligible patients (cited by 67% of respondents); compliance protocol was worse (61%); trials were suspended (60%); there was a lack of research staff (48%); and there were institutional closures (39%).

Regarding patient-related challenges, 67% of sites cited less willingness to visit the site. Other challenges included less ability to travel (cited by 60%), reduced access to the trial site (52%), quarantining because of exposure to COVID-19 (40%), and SARS-CoV-2 infection (26%).

Concerns of patients included the following: fear of SARS-CoV-2 infection, which was cited by 83%; travel restrictions (47%); securing transportation (38%); and access to the laboratory/radiology services (14%).

“Patient willingness to visit the site was a consistent barrier reported across Europe, the U.S., and Canada,” said Dr. Smeltzer, although the effect was smaller in North America, he added.

Regarding mitigation strategies that were employed during the pandemic to combat the challenges and concerns, the team found that the most common measure was the modification of monitoring requirements, used by 44% of sites.

This was followed by the use of telehealth visits (43% sites), the use of laboratories at non–study facilities (27%), and alterations to the number of required visits (25%).

Other mitigation strategies included use of mail-order medications (24%), using radiology services at a non-study site (20%), and altering the trial schedules (19%).

The most effective mitigation strategies according to those surveyed were felt to be those that allowed patients to have flexibility with respect to location. These measures included use of remote monitoring, remote diagnostics, telehealth visits, and modified symptom monitoring.

Effective strategies that increased flexibility in time were delayed visits, delayed assessments, and changes to the Institutional Review Board.

The study was funded by the IASLC, which received industry support to conduct the project.

Dr. Smeltzer reported no relevant financial relationships.

Dr. Garassino has relationships with AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly, Ignyta, Incyte, MedImmune, Mirati, MSD International, Novartis, Pfizer, Regeneron, Roche, Takeda, and Seattle Genetics.
Post-Intensive Care.

Some patients who spend three or more days in an intensive or critical care unit need extended recovery time in an acute-level setting before transitioning home.

These post-intensive care patients can benefit from specialized care provided by clinicians with expertise in treating critically ill and medically complex patients.

Our interdisciplinary care features daily physician oversight, ICU/CCU-level staffing and specially trained caregivers who seek to improve outcomes and reduce costly readmissions for difficult-to-treat patients.

To learn more about how patients who have spent multiple days in the ICU can benefit from our care, contact us at recoveratkindred.com.

Daily Physician Oversight • ICU/CCU-Level Staffing Reduced Readmissions • Disease-Specific Certification from The Joint Commission
Lung transplantation for patients with severe COVID-19

BY QUINN HALVERSON, MD; AND AMIT BANGA, MD, FCCP

As of September 2021, over 222 million people worldwide (WHO, 2021) and 40 million Americans (CDC, 2021) have been infected with the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The total number of infections in the United States began climbing again this summer with the persistence of vaccine reluctance among a significant proportion of the population and the emergence of the much more infectious B.1.617.2 (Delta) variant. While the clinical illness caused by the SARS-CoV-2 virus, referred to as the Coronavirus disease 2019 (COVID-19), is mostly mild, approximately 10% of cases develop acute respiratory distress syndrome (ARDS) (Remuzzi A, et al. Lancet. 2020;395[10231]:1225-8). A small but substantial proportion of patients with COVID-19 ARDS fails to respond to the various supportive measures and requires extracorporeal membrane oxygenation (ECMO) support. The overarching goal of ECMO has the theoretical advantage for the lungs to ‘rest’ as the oxygenation and ventilation needs are met in an extracorporeal fashion. Regardless, this timeline is not always predictive enough pulmonary function to allow them to be weaned from the various respiratory support strategies.

For patients with irreversible lung injury, lung transplantation (LT) is a potential consideration. Earlier in the pandemic, older patients with significant comorbid illnesses were more vulnerable to severe COVID-19, often precluding consideration for transplantation. However, the emergence of the Delta variant may have altered this dynamic via a substantial increase in the incidence of COVID-19 ARDS among younger and healthier patients. A handful of patients with COVID-19 ARDS have already had successful transplantation. However, the overall number is still small (Bharat A, et al. Sci Transl Med. 2020 Dec 16;12[574]:eabe4282. doi: 10.1126/scitranslmed.abe4282. Epub 2020 Nov 30; and Hawkins R, et al. Transplantation. 2021;106(13):1381-7), and there is a lack of long-term outcomes data among these patients.

Given that the SARS-CoV-2 virus is a novel pathogen that leads to an illness that is unique from other forms of viral pneumonia, specific considerations regarding LT should be made among these patients.

The different support strategies, including ECMO, is to provide time for the lungs to recover from ARDS. ECMO has the theoretical advantage over other strategies in facilitating recovery by allowing the injured lungs to ‘rest’ as the oxygenation and ventilation needs are met in an extracorporeal fashion. Regardless, a small number of patients with COVID-19 ARDS will not recover enough pulmonary function to allow them to be weaned from the various respiratory support strategies.

For patients with irreversible lung injury, lung transplantation (LT) is a potential consideration. Earlier in the pandemic, older patients with significant comorbid illnesses were more vulnerable to severe COVID-19, often precluding consideration for transplantation. However, the emergence of the Delta variant may have altered this dynamic via a substantial increase in the incidence of COVID-19 ARDS among younger and healthier patients. A handful of patients with COVID-19 ARDS have already had successful transplantation. However, the overall number is still small (Bharat A, et al. Sci Transl Med. 2020 Dec 16;12[574]:eabe4282. doi: 10.1126/scitranslmed.abe4282. Epub 2020 Nov 30; and Hawkins R, et al. Transplantation. 2021;106(13):1381-7), and there is a lack of long-term outcomes data among these patients.

There is currently little guidance regarding criteria for patient selection and consideration for LT among patients with COVID-19 ARDS. Given that the SARS-CoV-2 virus is a novel pathogen that leads to an illness that is unique from other forms of viral pneumonia, specific considerations regarding LT should be made among these patients. In the current article, we discuss some of the pertinent issues related to the consideration of LT among patients with COVID-19 ARDS.

The timing for considering LT is one of the most important aspects. First, patients with COVID-19 ARDS must not be actively infected at the time of transplantation consideration. It has been suggested that LT should only be considered in patients with two separate negative polymerase chain reaction (PCR) test results for SARS-CoV-2 from bronchoalveolar lavage fluid 24 hours apart and at least 4 weeks after the onset of COVID-19 symptoms (Bharat A, et al. Sci Transl Med. 2020 Dec 16;12[574]:eabe4282. doi: 10.1126/scitranslmed.abe4282. Epub 2020 Nov 30). Among patients with persistently positive SARS-CoV-2 PCR 4 to 6 weeks after symptom onset, a negative viral culture from a bronchoalveolar lavage (BAL) can be used to confirm viral inactivity (Lang C, et al. Lancet Respir Med. 2020;8[10]:1057-60).

Despite the sparse data in this domain, there seems to be a consensus in the literature that LT could be considered once 4 to 6 weeks have elapsed since the onset of the respiratory failure (Cygel M, et al. Lancet Respir Med. 2020;8[10]:944-6). This timeline is felt to be long enough to alleviate the concerns regarding ongoing inflammatory processes that may be reversible while not so long to risk the development of irreversible ARDS.

Differentiating the extent of irreversibility, may not be sensitive enough. The standard of care in such situations remains serial assessments, often weekly, by a dedicated multidisciplinary group. We have found it useful to augment the imaging data with pulmonary physiologic assessments, including the extent of ventilator and ECMO support as well as dynamic and static compliance trends. Improvement in

In the absence of systemic studies and lack of longitudinal outcomes data, there is an emergent need to establish consensus guidelines regarding the approach to LT consideration in these patients.

References:


Is the end near for surgical and transbronchial biopsies? Challenges in the pediatric workforce. Cascade testing in PAH. And more ...

Interventional chest/diagnostic procedures

Endobronchial optical coherence tomography and interstitial lung diseases: Is the end near for surgical and transbronchial lung biopsies?

The early diagnosis of interstitial lung diseases (ILD) is paramount to initiating appropriate treatment and preventing irreversible pulmonary damage. Specific ILD subtypes may be diagnosed based on clinical evaluation, high resolution chest CT (HRCT) patterns, and serologic testing, but many patients require invasive procedures for histopathologic confirmation of lung tissue. Current modalities for obtaining tissue include transbronchial lung cryobiopsy (TBLC) and surgical lung biopsy (SLB), both of which carry a risk of potential complications (Troy LK, et al. Lancet Respir Med. 2020;8:171-81; Hutchinson JR, et al. Am J Respir Crit Care Med. 2016;193(10):1161-7). Recently, genomic classifiers applied to transbronchial biopsies have been proposed to facilitate the diagnosis of usual interstitial pneumonia (UIP), but the limited information provided still does not obviate the need for tissue diagnosis when needed (Raghu G, et al. Lancet Respir Med. 2019;7(6):487-96). It is in this context that endobronchial optical coherence tomography (EB-OCT) was proposed as a real-time, in vivo, optical biopsy method for ILD. EB-OCT uses near infrared light to generate large volumes of in-vivo three-dimensional tissue imaging with microscopic resolution (Goorsenberg A, et al. Respiration. 2020;99:190-205; Nandy S, et al. Am J Respir Crit Care Med. 2021;article in press). The OCT catheter is advanced through the bronchoscope working channel and can be used during outpatient procedures under conscious sedation. Available data suggests that minimal training is necessary, both for proceduralists and interpreting pathologists, but this will need to be confirmed in larger studies and various practice settings. Early studies suggest that OCT can identify microscopic honeycombing and other abnormalities even before they are evident on HRCT scans (Goorsenberg A, et al. Respiration. 2020;99:190-205). Newer research comparing ILD diagnosis and transbronchial biopsies.

continued from previous page

Physiologic data often precedes radiologic improvement. Nonetheless, an important area of future research is to identify objective markers for determining reversibility, which could include novel biomarkers in serum or bronchoalveolar lavage fluid.

When a determination is made regarding the irreversibility of pulmonary impairment, the LT evaluation should begin promptly. Pre-transplant deconditioning and debility is associated with worse post-transplant outcomes. In this regard, patients managed using an ambulatory ECMO strategy may have superior rehabilitation potential. Furthermore, an attempt should be made during the evaluation to wean sedation in order to facilitate discussions regarding the rigors of LT with the patient alongside present family members. An additional consideration, given the use of immunomodulatory medications for COVID-19 and prolonged intubation, is the dramatically increased risk of multi-drug resistant infections in this population; these must be aggressively managed for patients to remain eligible for LT.

The degree of pulmonary impairment and frequent colonization of the airways will likely dictate bilateral LT as the preferred strategy, although surgical feasibility may, at times, be the overriding determinant. Regardless of the type of transplant, certain unique aspects should be anticipated. The inflammatory responses during COVID-19 that often spill outside the confines of the pulmonary parenchyma, along with potentially frequent thoracic interventions prior to transplant, create significant technical challenges during the operation. Native pneumonectomy can take longer than usual leading to prolonged ischemic time, increased need for intra-operative blood products, and raised risk for primary graft dysfunction. All of these factors have a significant impact on early and late outcomes. Finally, the long-term immunologic consequences of severe infection from a novel virus remain unknown, and it is unclear if COVID-19 ARDS patients bridged to transplant will enjoy comparable survival. It is pertinent to acknowledge that the high-risk nature of such transplants is substantially accentuated due to several unique characteristics of the illness related to COVID-19.

The emergence of the COVID-19 pandemic has led to an increase in the number of urgent inpatient lung transplant consultations for refractory ARDS. While the basic principles of LT candidate selection should continue to guide us, the unique characteristics of this illness merit using a customized approach. There are few validated predictors to guide decision-making, and longitudinal assessments by a dedicated multidisciplinary group remain the best strategy. Finally, in the absence of systemic studies and lack of longitudinal outcomes data, there is an emergent need to establish consensus guidelines regarding the approach to LT consideration in these patients.

Dr. Halverson and Dr. Banga are with the Lung Transplant Program, Divisions of Pulmonary and Critical Care Medicine, University of Texas Southwestern Medical Center, Dallas.
As our field addresses the critical need to recruit more trainees in light of the unfilled fellowship positions and the increasing average age of members of the field, we should not underestimate the prevalence of systemic racism and bias in medicine.

“We should not underestimate the prevalence of systemic racism and bias in medicine.”

Dr. Sahay

Dr. Coates

Pediatric chest medicine Challenges in the pediatric pulmonary workforce

The future of the pediatric workforce has been the source of extensive discussion within the pediatric community and resulted in a considerable body of medical literature (Vinci RJ. Pediatrics. 2021; 147[6]: e2020013292). In pediatric pulmonology, there is growing concern that current trends will lead to a workforce shortage resulting in patients having difficulty accessing subspecialty care (Harris C, et al. Pediatric Pulmonol. 2019;54[4]:444-50).

The etiology of this shortage is multifactorial. Duration of fellowship training and subsequent financial implications are reported potential barriers to pursuing a fellowship (Nelson BA, et al. Pediatric Pulmonol. 2020;1-7). Discrepancies between pediatric and adult compensation may be another barrier. Insightful recruitment strategies based on the results of a recent study included maximizing resident interaction with pulmonary faculty, early identification and support of interested trainees, and consideration of flexible training models (Nelson BA, et al. ATS Sch. 2020;1:372-83).

Lifestyle has also been a factor that contributes to a trainee’s decision to go into pediatric pulmonology (Freed GL, et al. Pediatrics. 2009;123(suppl 1):S31-S37).

As our field addresses the critical need to recruit more trainees in light of the unfilled fellowship positions and the increasing average age of members of the field, we should not underestimate the prevalence of systemic racism and bias in medicine (Chiel L, et al. ATS Sch. 2020;1[4]:337-39) nor gender discrimination. Instead, we should seize the opportunity to understand and knock down barriers that trainees who are underrepresented in medicine face in pursuing pediatric subspecialty careers and build upon the excellent recent body of literature in this field to help recruit, support, and grow a robust, diverse workforce to provide the best pediatric care to all.

Anne C. Coates, MD: Steering Committee Member

Pulmonary vascular disease Cascade testing in PAH: Is there a role?

Pediatric guidelines for pulmonary arterial hypertension (PAH) recommends genetic screening as a part of the evaluation for the newly diagnosed, with expansion to first-degree relatives as indicated. Currently, this is not mandated, and implementation is variable. In adults, genetic screening is not routinely offered, and family screening is rare. This reflects a lack of definitive guidelines (Abman SH, et al. Circulation. 2015;24;132[21]:2037-99). However, it is intuitive that if carriers are not identified by screening, they will come to attention after pulmonary vascular disease burden causes symptoms and affects outcomes.

Cascade testing is a screening methodology that is used in heritable cancers (George RM, et al. Genet Couns. 2015;24[3]:388-99). In cascade testing, identification of systemic racism and bias in medicine.
an index case prompts screening of at-risk family members. If these relatives are positive for mutations, the cycle is repeated (cascaded) to their immediate relatives, allowing for targeted screening. This approach is especially effective in genetic mutations that are inherited in an autosomal dominant fashion, such as in BMPR2 gene mutation. Cascade testing is an effective way to capture relatives who would otherwise be overlooked.

Unfortunately, in the United States, the cost of genetic testing is a significant obstacle to universal implementation. A new diagnosis of heritable pulmonary arterial hypertension (HPAH) is often followed by a multigene panel with costs exceeding $1000 and may prompt subsequent targeted testing resulting in additional expense (Chung WK, et al. Can J Cardiol. 2015;31[4]:544-47). Furthermore, a positive mutation detected on screening is not definitively associated with disease due to variable penetrance (Morrell NW, et al. Eur Respir J. 2019;53[1]:1801899). As such, mass screening strategies are not recommended. The recent DELPHI-2 study (Montani D, et al. Eur Respir J. 2021;58[1]:2004229) have demonstrated that genetic screening is impactful in families with HPAH. A genetic screening algorithm should be considered, and cascade testing could be a cost-effective targeted approach.

Sandeep Sahay, MD, MSc, FCCP: Steering Committee Member
Jean M. Elwing, MD, FCCP: Chair

Pulmonary physiology, function, and rehabilitation
Physiological benefits of awake proning: Its role and relevance in the COVID-19 pandemic
The advent of the COVID-19 pandemic has put a significant strain on the health care systems and critical care services across several countries, including the United States. Amidst this, several concerted efforts to reduce the need for mechanical ventilation has resulted in the emergence of awake proning as a strategy to improve oxygenation, which has been instituted in critical care units, in-patient settings, as well as in EDs.

Although the evidence on this strategy has been vastly limited to case series and observational studies, several societies have incorporated awake proning as an initial management strategy in hypoxemic respiratory failure within their clinical guidelines (Chalmers JD, et al. Eur Respir J. 2021;57:2100048; Koeckerling D, et al. Thorax. 2020;75:833-4) and consensus statements (Nasa P, et al. Crit Care. 2021;25:106).

Physiological benefits of awake proning include improvement in ventilation-perfusion matching secondary to relative increase in ventilation in dorsal nondependent areas in the setting of higher density of perfusion within these units, thus reducing shunt and, hence, improving oxygenation. Other physiological mechanisms include homogenization of transpulmonary pressures, reduction of ventilator-induced lung injury (VILI) or patient self-inflicted lung injury (P-SILI), and possibly lung injury from pendelluft (Teilias I, et al. JAMA. 2020;323[22]:2265-67).

“Several questions remain—which patients would benefit the most? Can it be applied within general wards safely?”

A recent meta-trial involving randomized controlled trials done across six countries compared prone positioning with standard care in patients with hypoxemic respiratory failure (defined as SpO2/FiO2 < 315 and on high flow oxygen therapy) showed a reduced incidence of treatment failure and need for intubation without any signal of harm; although no mortality benefit was reported (Ehrmann S, et al. Lancet Respir Med. 2021 Aug 20;S2213-2600(21)00356-8).

The number needed to treat to prevent one intubation was 14. While promising and reinforcing the safety of this relatively easy maneuver, several questions remain—which patients would benefit the most? Can it be applied within general wards safely? Does institution of awake proning delay intubation rates with consequent worse outcomes? Several ongoing (NCT 04402879) and completed studies (NCT 04383613 and NCT 04350723) may shed light on these important questions (Weatherald J, et al. Lancet Respir Med. 2021 Aug 20;S2213-2600(21)00368-4).

Sujith Cherian, MD, FCCP: Steering Committee Member

When You Attend an Event, You Tend to Our Mission.

Every time you register for an event, what you’re really doing is funding our initiatives—programs that enable patients to get access to the care they need. Help us fulfill our mission by joining an event in honor of the CHEST Foundation 25th Anniversary:

- 2021 Irv Feldman Virtual Fall Poker Tournament
- Viva La Vino Wine Tasting
- 25th Anniversary CHEST Foundation Celebration

Our events are fun. Our work is serious.

Register today at chestfoundation.org
nimal and human models of the effects of therapeutic hypothermia, now called therapeutic hypothermia (TTM), began to surface in the late 1980s. The first randomized clinical trial employing TTM as a neuroprotective strategy following cardiac arrest did not appear until the early 2000s. When compared with normothermia, the HACA trial (Holzer M, et al. N Engl J Med. 2002;346[8]:549-56) demonstrated a 14% reduction in mortality and improved neurologic outcomes following out of hospital cardiac arrest (OHCA) due to ventricular fibrillation (VF) or ventricular tachycardia (VT) when maintaining body temperature between 32°C and 34°C post-arrest. Following the results of this trial, TTM in comatose patients following cardiac arrest was recommended by international guidelines and became the standard of care. It was not until the publication of the TTM1 trial (Nielsen N, et al. N Engl J Med. 2013;369[23]:2197-206) about a decade later, that serious questions regarding the efficacy of TTM were raised. The TTM1 trial showed no difference in mortality or neurologic outcomes when comparing TTM at 33°C vs 36°C for OHCA. The results of this trial heralded widespread practice change, with many abandoning deep cooling, and often active cooling measures, in favor of fever avoidance. The HYPERION trial (Lascarrou J, et al. N Engl J Med. 2019;381:2327-37) came next, comparing TTM at 33°C to normothermia (<37.5°C) for cardiac arrest with non-tachycardia (VT) when maintaining body temperature between 32°C and 36°C for at least 24 hours, followed by avoidance of fever (>37.7°C) for at least 72 hours after ROSC in patients who remain comatose. While it will be interesting to see what future iterations of the guidelines recommend, the results from the TTM1 and TTM2 trials support a shift in clinical practice away from TTM and toward more active fever avoidance.

The results of the TTM1 and TTM2 trials support a shift in clinical practice away from TTM and toward more active fever avoidance.

is the most recent trial to address the question of TTM post-cardiac arrest. The TTM2 trial was an international, randomized controlled superiority trial of TTM at 33°C vs normothermia (≤37.8°C) for patients with coma following OHCA with any initial rhythm. It was conducted by the same group as the TTM1 trial and, to date, represents the largest (N=1,850) and most robust trial conducted in this area. The trial spanned 61 institutions across 14 countries and had nearly complete follow-up at 6 months. Once again, there was no significant difference in all-cause mortality at 6 months in the TTM group compared with the normothermia group. Equally important, there were no differences observed in secondary outcomes, including functional neurologic status and health-related quality of life at 6 months. With the results of the TTM1 and TTM2 trials failing to show any neurologic or mortality benefit to TTM, we are left wondering, is there anything therapeutic about “therapeutic hypothermia”? Both the 2020 American Heart Association (AHA) and 2021 European Resuscitation Council (ERC) guidelines pre-date this trial; they recommend cooling any OHCA or in-hospital cardiac arrest (IHCA) patient who remains unresponsive after return of spontaneous circulation (ROSC) regardless of initial rhythm. They further suggest maintaining a target temperature between 32°C and 36°C for at least 24 hours, followed by avoidance of fever (>37.7°C) for at least 72 hours after ROSC in patients who remain comatose. While it will be interesting to see what future iterations of the guidelines recommend, the results from the TTM1 and TTM2 trials support a shift in clinical practice away from TTM and toward more active fever avoidance. Additionally, careful review of adverse events in the TTM2 trial suggests that induced hypothermia is not without risk of harm. When compared with the normothermia group in the TTM2 trial, the hypothermia group experienced higher rates of arrhythmias with hemodynamic instability (16% vs 24%), increased exposure to sedation, increased use of neuromuscular blockade, and increased duration of mechanical ventilation.

While the results of the TTM2 trial move the needle away from therapeutic hypothermia for OHCA patients, there is some nuance that warrants further discussion. First, the initial HACA trial, upon which the standard of TTM was based, included only patients with an initial shockable rhythm (VT/VF). Inherently, the etiology of these arrests is likely to be cardiac and more reversible in nature. Most subsequent landmark trials on TTM, including the TTM2 trial, have included OHCA patients with both shockable and nonshockable initial rhythms. Still, the majority of patients in the TTM2 trial had an initial shockable rhythm on presentation (72% hypothermia vs 75% normothermia). This may limit broad generalizability of study findings as an increasing number of OHCA patients are presenting with nonshockable initial rhythms. Next, it is well known that bystander CPR improves outcomes following OHCA. Impressively, over 75% of patients in both groups in the TTM2 trial received bystander CPR compared with an average of 46% of arrest patients in the US according to AHA data. Finally, like most of its predecessors, the TTM2 trial only included OHCA patients meaning no real conclusions can be drawn regarding application of TTM to IHCA patients. Of the major trials to date, only the HYPERION trial included IHCA patients – representing about 25% of the study population. Thus, the utility of TTM in the setting of IHCA remains largely unknown.

Taken in summation, recent trials, including TTM2, suggest that fever-avoidance post-cardiac arrest is likely the best option for improving mortality and neurologic outcomes while mitigating risk to the patient. We must remain vigilant in our enforcement of normothermia though as worse neurologic outcomes have been observed with hypothermia in the early post-arrest period (Zeiner A, et al. Arch Intern Med. 2001;161[16]:2007-12). A key takeaway from recent trials is that maintaining normothermia without active temperature control measures is likely to be difficult to achieve. A criticism of the HYPERION trial was that a “substantial proportion” of patients in the normothermia group had temperatures above 38°C. Similarly, 10% to 15% of patients in the TTM2 trial had body temperatures above 37.7°C, 40 to 72 hours after randomization and, ultimately, 46% of patients in the normothermia group required cooling with a temperature management device. Thus, we can conclude that maintenance of strict normothermia will likely continue to require active control with a temperature management device.

Despite an increasing number of well conducted studies in this area, there are several questions that remain unanswered. The first is whether cooling patients even earlier post-arrest is felt to increase the likelihood of survival with improved neurologic outcomes. Like HACA and HYPERION, the rate of cooling in the TTM2 trial was relatively quick with a time to randomization after onset of cardiac arrest of about 2 hours in both groups and a median time from intervention until reaching target temperature of 3 hours. While some retrospective data suggest ultra-early cooling may be beneficial, neither induction of therapeutic hypothermia during OHCA using a rapid infusion of...
Thoughts on becoming CHEST President

BY DAVID A. SCHULMAN, MD, MPH, FCCP
CHEST President – 2022

I am honored to have the privilege of serving as the 84th President of the American College of Chest Physicians. When I attended my first CHEST meeting, I sat in the opening plenary session with thousands of other members, never imagining that I would have the opportunity to lead the organization just two decades later. And while I don’t recall many sessions from that meeting, I vividly remember the way it made an emotional impact. I never felt like one of a drove of nameless learners; both faculty and staff made it a collegial experience, much like attending pulmonary grand rounds at my own institution. Speakers would stay after their presentations to answer questions from even the most junior members. Leadership made themselves available over coffee or in the hallways between sessions. And that experience was the first of a great many memorable interactions I have had with CHEST.

CHEST has meant a great deal to me personally; it served as my first professional home away from home. I had the opportunity to grow in a number of different areas through my service to CHEST, in ways that I would not have been able to do easily at my own institution. I’ve worked with incredible staff and volunteers in my service on a number of our committees, including the Council of NetWorks, the Training and Transitions Committee, the Education Committee, and the Program Committee, to name a few. While I’ve had a chance to learn what role each of these component parts of the College serves during my tenure on those committees, it wasn’t until far more recently that I better understood the role of the President.

Before I get into what I’d like to achieve during my year as President, I’d like to briefly review what that role entails.

Contrary to popular belief, the President does not set the organizational goals for CHEST; those are set by the Board of Regents. While I will have the privilege of running the Board meetings, it is the 17 incredibly talented folks who serve as voting members of the Board that set the College’s direction. Once the organizational goals are set, it is our committees that take charge of designing and implementing plans to work toward those goals. Concomitantly, Dr. Robert Musacchio (CHEST Chief Executive Officer and Executive Vice President) meets with his own executive leadership team to design a structure that lets the CHEST staff work, both on their own and in tandem with our members, to achieve these goals. One of the President’s main roles, as I see it, is to serve as a liaison. When the Board makes decisions that affect the membership, it will be my job to communicate changes and why they are being made. When our members have challenges that the College might be able to help solve, it is my role to work with the Board and the CEO to see what we can do about them. And when there is need to interface with other organizations, the President (or their designee) can speak on behalf of the College in those interactions.

In the context of those duties, what are the things that I would like to accomplish during my tenure as CHEST President? First, I want to spend more time with our committee members and you, our members. CHEST is a member-focused organization; I believe that this is the main thing that sets our professional society apart from its sister societies. I have always found CHEST to be very collegial and welcoming. But I am aware that some of our members haven’t always found it accessible. And I get that; our structure is complex. That’s the reason I provided a description of my role, and the reason that I intend to spend time making CHEST more accessible to all of you.

I’ve already developed dedicated social media channels for a number of our NetWorks in order to make you all more aware of their activities. In the coming year, I’ll provide regular updates to membership about ongoing CHEST activities. I’ll work to provide more member awareness of what role each of our committees plays in forwarding the College’s goals. And I’ll provide you with more information about the type of qualifications that each committee seeks in its nominees, in an effort to encourage you to run for a leadership position that best suits your interests and skill set.

While improving our members’ understanding of the inner workings at CHEST will help each of you better see how the College can meet your needs, my hope is that this increase in organizational accessibility will motivate each of you to engage more actively with us. This is my second goal as President. For some of you, that engagement may take the form of joining our Twitter chats; for others, it could mean attending one of our live learning courses in Chicago for the first time. But I hope that some of you will consider submitting session proposals to our annual meeting for the first time, or running for an available leadership position within the College when nominations open in the Spring.

As our organization grows (now almost twenty thousand members strong!), I want to provide a second home for all our members, spanning the range from medical students to full professors, from lifelong academic physicians to those just starting out in community practices, from busy clinicians to physician scientists, and including all members of the health care team. Although the makeup of our volunteer leadership is becoming more representative of the full breadth of our membership, we are not fully there yet. Until we get to that intended target, I would like to ask each of you to reach out to me with any thoughts about how CHEST can better meet your professional needs.

Creating greater access to leadership to let each of your opinions be heard is my third goal as President of CHEST. I’ll provide more details about how I’m hoping to achieve this in the coming months.

The world has been a crazy place over the last 18 months, filled with challenges that we could never have foreseen even a year prior. Our members have been on the front lines of the pandemic; in addition to the professional stresses related to caring for innumerable critically ill patients, many of us have suffered personal losses. Although none of us knows what 2022 holds, I look forward to a brighter future, knowing that regardless of what the coming year brings, we will face it together.

Continued from previous page

cold saline (Bernard SA, et al. Circulation. 2016;134[11]:797-805) nor transnasal evaporative cooling in the pre-hospital setting (Nordeberg P, et al. 2019;321[17]:1677-85) has shown improvement in survival with good neurologic outcomes. Next, if we are going to continue TTM, the TTM2 trial does not provide guidance on optimal duration of cooling. Although the current guidelines are to cool for at least 24 hours after ROSC, it is unclear for how long strict temperature control should be continued. The currently enrolling ICECAP study (https://clinicaltrials.gov/ct2/show/NCT04217551) aims to further elucidate the optimal duration of TTM for OHCA patients with both shockable and non-shockable initial rhythms.

Post-cardiac arrest management continues to be a significant area of interest in clinical research and for good reason. Although steady improvement has occurred with regards to survival and neurologic function for IHCA, of the approximately 350,000 nontraumatic OHCA that occur in a year in the United States, only about 10.2% of those patients will survive their initial hospitalization, and only about 8.2% of those who will survive will have good functional status (American Heart Association. Circulation. 2020;142(suppl 2):S366-S468). There remains much room for continued study and improvement.

Dr. Capp is a Pulmonary and Critical Care Fellow; and Dr. Pendleton is Assistant Professor of Medicine; Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine; University of Minnesota, Minneapolis, Minnesota.
COVID-19

Moderna vaccine more effective re: hospitalizations
BY RALPH ELLIS

A nationwide study of more than 3,600 adults found the Moderna vaccine does a better job at preventing COVID-19 hospitalizations than the two other vaccines being used in the United States, the Centers for Disease Control and Prevention has said.

"Among U.S. adults without immunocompromising conditions, vaccine effectiveness against COVID-19 hospitalization during March 11–Aug. 15, 2021, was higher for the Moderna vaccine (93%) than the Pfizer-BioNTech vaccine (88%) and the Janssen vaccine (71%)," the agency's Morbidity and Mortality Weekly Report said (2021 Sep 17. doi: 10.15585/mmwr.mm7038e1). Janssen refers to the Johnson & Johnson vaccine.

The CDC said the data could help people make informed decisions.

"Understanding differences in VE [vaccine effectiveness] by vaccine product can guide individual choices and policy recommendations regarding vaccine boosters. All Food and Drug Administration–approved or authorized COVID-19 vaccines provide substantial protection against COVID-19 hospitalization," the report said.

The study also broke down effectiveness for longer periods. Moderna came out on top again.

After 120 days, the Moderna vaccine provided 92% effectiveness against hospitalization, whereas the Pfizer vaccine's effectiveness dropped to 77%, the CDC said.

Weekly Report said (2021 Sep 17. doi: 10.15585/mmwr.mm7038e1).

Pfizer-BioNTech vaccine might be due to higher mRNA content in the Moderna vaccine, differences in timing between doses (3 weeks for Pfizer-BioNTech vs. 4 weeks for Moderna), or possible differences between groups that received each vaccine that were not accounted for in the analysis," the report said.

The CDC noted limitations in the findings. Children, immunocompromised adults, and vaccine effectiveness against COVID-19 that did not result in hospitalization were not studied.

Other studies have shown all three U.S. vaccines provide a high rate of protection against coronavirus.
COVID-19

Nurses ‘at the breaking point,’ many consider quitting

BY AVERY HURT

In the best of times, critical care nurses have one of the most difficult and stressful jobs in health care. The COVID-19 pandemic has made that immeasurably worse. As hospitals have been flooded with critically ill patients, nurses have been overwhelmed. “What we’re hearing from our nurses is really shocking,” Amanda Bettencourt, PhD, APRN, CCRN-K, president-elect of the American Association of Critical-Care Nurses (AACN), said in an interview. “They’re saying they’re at the breaking point.”

Between Aug. 26 and Aug. 30, the AACN surveyed more than 6,000 critical care nurses, zeroing in on four key questions regarding the pandemic and its impact on nurses.

Continued on following page
Continued from previous page

ing. The results were alarming – not only with regard to individual nurses but also for the nursing profession and the future of health care.

A full 66% of those surveyed said their experiences during the pandemic have caused them to consider leaving nursing. The respondents’ take on their colleagues was even more concerning.

Ninety-two percent agreed with the following two statements: “I believe the pandemic has depleted nurses at my hospital. Their careers will be shorter than they intended.”

“This puts the entire health care system at risk,” says Dr. Betten-court, assistant professor in the department of family and communiity health at the University of Pennsylvania School of Nursing, Philadelphia. Intensive care unit nurses are highly trained and are skilled in caring for critically ill patients with complex medical needs. “It’s not easy to replace a critical care nurse when one leaves,” she said.

And when nurses leave, patients suffer, said Beth Wathen, MSN, RN, CCRN-K, president of the ACCN and frontline nurse at Children’s Hospital Colorado, in Aurora.

“Hospitals can have all the beds and all the rooms and all the equipment they want, but without nurses and others at the front lines to provide that essential care, none of it really matters,
whether we're talking about caring for COVID patients or caring for patients with other health ailments.”

**Heartbreak of the unvaccinated**

The problem is not just overwork because of the flood of COVID-19 patients. The emotional strain is enormous as well. “What's demoralizing for us is not that patients are sick and that it's physically exhausting to take care of sick patients. We're used to that,” said Dr. Bettencourt.

But few nurses have experienced the sheer magnitude of patients caused by this pandemic. “The past 18 months have been grueling,” says Ms. Wathen. “The burden on frontline caregivers and our nurses at the front line has been immense.”

The situation is made worse by how unnecessary much of the suffering is at this point. Seventy-six percent of the survey's respondents agreed with the following statement: “People who hold out on getting vaccinated undermine nurses' physical and mental well-being.”

“That 9 out of 10 of the people we're seeing in ICU right now are unvaccinated just adds to the sense of heartbreak and frustration,” says Ms. Wathen.

“These deaths don't have to be happening right now. And that's hard to bear witness to.”

The politicization of public health has also taken a toll. “That's been the... Continued on following page
Continued from previous page

hard part of this entire pandemic,” says Ms. Wathen. “This really isn’t at all about politics. This is about your health; this is about my health. This is about our collective health as a community and as a country.”

Like the rest of the world, nurses are also concerned about their own loved ones.

The survey statement, “I fear taking care of patients with COVID puts my family’s health at risk,” garnered 67% agreement. Ms. Wathen points out that nurses take the appropriate precautions but still worry about taking infection home to their families.

“This disease is a tricky one,” she says. She points out that, until this pandemic is over, in addition to being vaccinated, nurses and the public still need to be vigilant about wearing masks, social distancing, and taking other precautions to ensure the safety of us all.

“Our individual decisions don’t just affect ourselves. They affect our family, the people in our circle, and the people in our community,” according to Ms. Wathen.

“COVID kills, and it’s a really difficult, tragic, and lonely death,” said Ms. Wathen. “We’ve witnessed hundreds of thousands of those deaths. But now we have a way to stop it. If many more people get vaccinated, we can stop this pandemic. And hopefully that will stop this current trend of nurses leaving.”
COVID-19

U.S. seniors’ pandemic care worst in wealthy nations?

BY MARCIA FRELLICK

Older adults in the United States — particularly among Black and Latino/Hispanic populations — experienced worse access to health care for chronic conditions during the pandemic than older adults in 10 other wealthy countries, according to findings from The Commonwealth Fund’s 2021 International Health Policy Survey of Older Adults released today.

David Blumenthal, MD, president of The Commonwealth Fund, said during a press briefing that surveying the senior population in the United States is particularly insightful because it is the only group with the universal coverage of Medicare, which offers a more direct comparison with other countries’ universal health care coverage.

Continued on following page
More than one-third (37%) of older U.S. adults with multiple chronic conditions reported pandemic-related disruptions in their care – higher than rates in Canada, the Netherlands, and U.K. In Germany, only 11% had canceled or postponed appointments.

The survey was conducted between March and June 2021 and included responses from 18,477 adults age 65 and older in Australia, Canada, France, Germany, the Netherlands, New Zealand, Norway, Sweden, Switzerland, and U.K., and U.S. adults age 60 and older.

Among older adults who need help with daily activities, those in the United States, Canada, U.K., and Australia were the most likely to say they did not receive needed services from professionals or family members.

In the United States, 23% of people who said they needed help with activities such as housework, meal preparation, and medication management experienced a disruption in care because services were canceled or very limited during the pandemic. For comparison, only 8% of seniors in Germany and 11% of seniors in the Netherlands did not receive help with basic daily activities.

Many U.S. seniors used up savings

“Nearly one in five older adults report that they used up their savings or lost their main source of income because of the pandemic. We see much lower rates in other countries like Germany, Switzerland, the Netherlands, and Sweden,” Reginald D. Williams, vice president for international health policy and practice innovations at The Commonwealth Fund, said during a briefing.

Older U.S. adults reported economic difficulties related to the pandemic at a rate of up to six times that of other countries, he said.

“The differences by race were stark. While 19% of U.S. seniors overall experienced financial hardships related to the pandemic, 32% of Black seniors and 39% of Latino/Hispanic seniors in the United States experienced hardships. Germany had the lowest rate, at 3% overall.

“As the COVID-19 pandemic in the United States continues to evolve,” Mr. Williams said, “finding ways to reduce care barriers – affordability and connecting adults to usual sources of primary care, enhancing access to economic supports and social services – can help narrow the gaps.”

Dr. Blumenthal said that, even though “Medicare is a critical life-line,” it has flaws.

“Medicare plans have significant gaps that leave beneficiaries vulnerable to sizable out-of-pocket expenses,” he said.

Placing caps on out-of-pocket costs and covering more health services, such as dental, vision, and hearing care, could help make the population less vulnerable, Dr. Blumenthal said. “The chronic lack of security facing U.S. seniors, especially those who are Black or Hispanic, is exacerbating the pandemic’s devastating toll,” he added.

Dr. Blumenthal and Mr. Williams have reported no relevant financial relationships.
PULMONARY MEDICINE

Should magnesium be used for COPD exacerbations?

BY AARON B. HOLLEY, MD

acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are a major driver of disease-related morbidity. Their prevention and treatment are a focus of COPD management. Antibiotics, corticosteroids, and nebulized bronchodilators are all given to patients with AECOPD, and while the supporting data aren’t perfect, there’s little debate surrounding their use. These medications are well known to most physicians; we’re comfortable with their efficacy and aware of their side effects. They are nothing if not familiar.

What about magnesium (Mg), though? Apparently, in the emergency room it is part of the standard AECOPD cocktail. I would argue that Mg is familiar to most too; every internal medicine trainee in the United States is taught to infuse 2 g of Mg intravenously for any inpatient (ICU or otherwise) with a serum level <2.0 mg/dL. In fact, “electrolyte protocols” are part of the order sets at most hospitals where I’ve worked. Mg is infused reflexively when it drops below certain levels.

I’m less familiar with using Mg in the setting of an AECOPD, though. A recent online post by an academic ER physician (Richard Pescatore, DO) urged caution in this setting. He argues that too many in the ER are embracing the “Dutch Hypothesis” and treating asthma and COPD as the same disease. Dr. Pescatore believes that Mg works for asthma exacerbations because asthma is a disease of smooth muscle and large airways, while COPD is not. COPD, he says, is a disease of the small airways, largely resulting from parenchymal distortions due to emphysema. Therefore, Mg, which is thought to act on the smooth muscle surrounding the large airways, won’t be beneficial for AECOPD and may even cause harm.

Data are lacking

What data exist for using Mg for AECOPD? The best randomized controlled trial I could find was published in 1995 and is cited in the reader’s rebuttal. The trial found a significant improvement in peak expiratory flow rate (PEFR) with Mg and a nonsignificant reduction in hospitalizations.

A poorly done systematic review of RCTs using Mg for AECOPD was published in 2014, and in 2020 the Agency for Healthcare Research and Quality (AHRQ) included Mg in its well-executed meta-analysis of pharmacologic treatments for AECOPD. Data across the four to five Mg RCTs included in each of the reviews (study inclusion criteria were slightly different) could not be combined. All RCTs were small, and only soft outcomes like PEFR and forced expiratory volume in 1 second (FEV1) seemed to improve with Mg. No adverse events were noted, but this should be interpreted with caution given that many studies did not report on adverse events at all.

A small RCT published this year (after both systematic reviews were completed) showed that using intravenous magnesium sulfate had no significant effect on FEV1, vital signs, or symptoms.

In summary, the data aren’t great. Mg doesn’t show up at all as a treatment option in the Global Initiative for Chronic Obstructive Lung Disease Report on COPD, and the authors of the AHRQ review concluded that large, high-quality RCTs are needed to assess the impact of Mg in AECOPD. Although I didn’t do an extensive review of Mg for asthma exacerbations, it’s not clear that the data here are much better. Mg gets an honorable mention (add for severe exacerbations when there’s inadequate response to standard treatments) in both the 2007 National Heart, Lung, and Blood Institute guideline and the 2019 Global Initiative for Asthma guide.

The 2020 update to the 2007 NHLBI guideline is more targeted in its review and does not cover Mg as a treatment option. On the basis of my anecdotal clinical experience and on networking with other experts, I do think Mg is used more often for asthma than for AECOPD.

Final thoughts on using Mg for AECOPD

All that being said, is it reasonable to use Mg for AECOPD? I think so. I’d stick to using it for severe cases where conventional treatments have failed, just like the NHLBI and GINA advise for asthma. I’d also limit it to 2-3 g, which is the dosing range employed by several of the existing AECOPD RCTs. The assertion that Mg may be harmful in AECOPD because COPD affects the small airways, and asthma does not, is misguided. Both affect the small airways. Furthermore, none of our inhaled therapies reach the small airways, so one can’t argue against using Mg because it only targets larger airways without abandoning albuterol and ipratropium as well. I don’t think anyone would advise that. Given what we now know about asthma and COPD phenotypes and asthma-COPD overlap, I’d caution against pediatric theories about response to therapies.

FDA blocks some vape products, delays action on others

BY AARON GOULD SHEININ

The Food and Drug Administration has ordered millions of e-cigarette products off the public market while saying it needs more time to review vape products sold by leading retailers like Juul, the country’s largest e-cigarette maker.

The agency had a court-ordered deadline of Sept. 9 to review more than 6.5 million applications for approval of what are considered new tobacco products – the vast majority of which are e-cigarettes and liquids, none of which has gone through FDA review before. The FDA reviewed 93% of those applications in the past year, acting FDA Commissioner Janet Woodcock, MD, and Mitch Zeller, director of the FDA’s Center for Tobacco Products, said in a statement.

Of those reviewed, the agency rejected more than 946,000 flavored vape products, “because their applications lacked sufficient evidence that they have a benefit to adult smokers sufficient to overcome the public health threat posed by the well-documented, alarming levels of youth use of such products,” Dr. Woodcock and Mr. Zeller said.

No e-cigarette product has been given official FDA approval to be sold, meaning all e-cigarette products technically are on the market illegally, the agency said in 2020, but federal officials decided to begin enforcing rules only against flavored products, which surveys show are more often used by children. Tobacco-flavored and menthol e-cigarette products – which some adults use to quit smoking cigarettes – were exempted.

The American Cancer Society and other advocacy groups slammed the FDA’s decision to withhold action on major e-cigarette manufacturers, including Juul.

“The FDA’s failure today to act on applications by Juul, the manufacturer with the single biggest e-cigarette market share, is extremely disappointing and will allow the industry to further endanger public health and hook more kids on their highly addictive products,” Lisa Lacasse, president of ACS CAN, said in a statement, according to CNN.

“The FDA has had ample time to review the applications and allowing additional delays is unconscionable. There is overwhelming data to demonstrate the negative impact these kinds of flavored products have had on public health and their role in the youth e-cigarette epidemic. The time to act is now,” Ms. Lacasse added.
How quickly can we complete TB prophylaxis in people with HIV?

BY JUDY STONE, MD

A 3-month, 12-dose regimen of rifapentine and isoniazid (INH) was less toxic, had better compliance, and showed similar efficacy as 6 months of INH alone in preventing tuberculosis (TB) in people with HIV, according to the results of a clinical trial reported in Annals of Internal Medicine (2021 Aug 24. doi: 10.7326/M20-7577).

The study, a randomized pragmatic trial in South Africa, Ethiopia, and Mozambique, was called WHIP3TB (Weekly High Dose Isoniazid and Rifapentine [P] Periodic Prophylaxis for TB).

Investigators randomized patients to three groups, comparing a 3-month course of weekly rifapentine-INH, given either once or repeated in a year, with daily isoniazid for 6 months. At 1 year, 90% of the rifapentine-INH groups (3HP) were still on therapy, compared with only 50.5% in the INH group.

In the study, patients were initially assessed for TB using the World Health Organization four-symptom screen, but the sensitivity in HIV patients on antiretrovirals (ARVs) was only 53%. In addition to symptoms, screening at 12 months included a chest x-ray and sputum culture.

Of the 30 patients at month 12 who had confirmed TB, 26 were asymptomatic, suggesting physicians should do further evaluation prior to initiating preventive TB treatment (which was not part of the WHO recommendation when the study was initiated).

Another unexpected finding was that 10.2% of the TB cases detected in the combined 3HP groups in South Africa, and in 18% of the cases in Mozambique, had rifampin resistance.

Investigator Gavin Churchyard, MBCh, PhD, CEO of the Aurum Institute in Johannesburg, South Africa, said in an interview: “It appeared that taking this potent short course regimen – they’re just taking a single course – provided the same level of protection as taking repeat courses of the antibiotics. So that’s good news.” He noted, too, that TB transmission rates have been declining in sub-Saharan Africa because of ARV, and “so it may just be that a single course is now adequate because the risk of exposure and reinfection” is decreasing.

But Madhu Pai, MD, PhD, associate director, McGill International TB Centre, Montreal, who was not involved in the study, shared a more cautious interpretation. He said in an interview that the 2020 WHO Consolidated Guidelines on Tuberculosis state: “In settings with high TB transmission, adults and adolescents living with HIV ... should receive at least 36 months of daily isoniazid preventive therapy (IPT) ... whether or not the person is on ART.” The problem is that almost no one can tolerate prolonged therapy with INH because of side effects, as has been shown in numerous studies.

For successful TB treatment, Dr. Pai said, “Even 3HP is not going to cut it; they’re going to get reinfected again. So that shortening of that 36 months is what this trial is really all about, in terms of new information ... and they were not successful.” But because this is still the most practical course, Dr. Pai suggests that follow-up monitoring for reinfection will be the most likely path forward.

Dr. Churchyard concluded: “If we wanted to end the global TB epidemic, we need to continue to find ways to further reduce the risk of TB overall at a population level, and then amongst high-risk groups such as people with HIV, including those on ARVs, and who have had a course of preventive therapy. ... We need to look for other strategies to further reduce that risk. Part of those strategies may be doing a more intensive screen. But also, it may be adding another intervention, particularly TB vaccines. ... No single intervention by itself will adequately address the risk of TB in people with HIV in these high TB transmission settings.”

Dr. Pai reported no relevant financial relationships. Dr. Churchyard has reported participation in a Sanofi advisory committee on the prevention of TB.

Dr. Stone is an infectious disease specialist and author of “Resilience: One Family’s Story of Hope and Triumph Over Evil” and of “Conducting Clinical Research.”
**Children’s airways primed to combat SARS-CoV-2**

**BY MEGAN BROOKS**

Epithelial and immune cells of the upper airways of children are preactivated and primed to detect SARS-CoV-2 infection, which may contribute to stronger early innate immune responses to SARS-CoV-2 infection than adults, new research suggests.

The findings may help to explain why children have a lower risk of developing severe COVID-19 illness or becoming infected with SARS-CoV-2 in the first place, the researchers say.

The study was published online in Nature Biotechnology (202. doi: 10.1038/s41587-021-01037-9).

**Primed for action**

Children appear to be better able than adults to control SARS-CoV-2 infection, but, until now, the exact molecular mechanisms have been unclear.

A team of investigators from Germany did an in-depth analysis of nasal swab samples obtained from 24 children and 21 adults who tested positive for SARS-CoV-2, as well as a control group of 18 children and 23 adults who tested negative for SARS-CoV-2.

“We wanted to understand why viral defense appears to work so much better in children than in adults,” Irina Lehmann, PhD, head of the molecular epidemiology unit at the Berlin Institute of Health Charité – Universitätsmedizin Berlin, explained in a news release.

Single-cell sequencing showed that children had higher baseline levels of certain RNA-sensing receptors that are relevant to SARS-CoV-2 detection, such as MDA5 and RIG-I, in the epithelial and immune cells of their noses.

This differential expression led to stronger early immune responses to SARS-CoV-2 infection in children than in adults.

Children were also more likely than adults to have distinct immune cell subpopulations, including KLRC1+ cytotoxic T cells, involved in fighting infection, and memory CD8+ T cells, associated with the development of long-lasting immunity.

**‘Clear evidence’**

The study provides “clear evidence” that upper-airway immune cells of children are “primed for virus sensing, resulting in a stronger early innate antiviral response to SARS-CoV-2 infection than in adults,” the investigators say.

Primed virus sensing and a preactivated innate immune response in children leads to efficient early production of interferons (IFNs) in the infected airways, likely mediating substantial antiviral effects, they note.

Ultimately, this may lead to lower viral replication and faster clearance in children. In fact, several studies have already shown that children eliminate the virus more quickly than adults, consistent with the concept that they shut down viral replication earlier, the study team says.

Weighing in on the findings for this news organization, John Wherry, PhD, director of the Institute for Immunology at the University of Pennsylvania, Philadelphia, said this “interesting study highlights potential differences in innate immunity and possibly geographic immunity in the upper respiratory tract in children versus adults.”

“We know there are differences in innate immunity over a lifespan, but exactly how these differences might relate to viral infection remains unclear,” said Dr. Wherry, who was not involved in the study.

“Children, of course, often have more respiratory infections than adults [but] whether this is due to exposure [i.e., daycare, schools, etc.] or susceptibility [lack of accumulated adaptive immunity over a greater number of years of exposure] is unclear,” Dr. Wherry noted.

“These data may help reveal what kinds of innate immune responses in the upper respiratory tract might help restrain SARS-CoV-2 and [perhaps partially] explain why children typically have milder COVID-19 disease,” he added.

The study was supported by the Berlin Institute of Health COVID-19 research program and fightCOVID@DKFZ initiative, European Commission, German Federal Ministry for Education and Research (BMBF), and German Research Foundation. Dr. Lehmann and Dr. Wherry have reported no relevant financial relationships.

**Vaccine appears safe, effective for children aged 5-11**

**BY BRENDA GOODMAN**

With record numbers of COVID-19 cases being recorded in kids, Pfizer and its partner BioNTech have announced that their mRNA vaccine for COVID-19 is safe and appears to generate a robust immune response in children as young as 5 years. The companies have been testing a lower dose of the vaccine – just 10 mg – in children between the ages of 5 and 11. That’s one-third the dose given to adults.

In a clinical trial that included more than 2,200 children, Pfizer says two doses of the vaccines given 3 weeks apart generated a high level of neutralizing antibodies, comparable to the level seen in older children who get a higher dose of the vaccine.

Rather than testing whether the vaccines are preventing COVID-19 illness in children, as they did in adults, the pharmaceutical companies that make the COVID-19 vaccines are looking at the antibody levels generated by the vaccines instead. The Food and Drug Administration has approved the approach in hopes of speeding vaccines to children, who are now back in school full time in most parts of the United States.

The company says side effects seen in the trial are comparable to those seen in older children. Pfizer says they plan to send their data to the FDA as soon as possible.

“We are pleased to be able to submit data to regulatory authorities for this group of school-aged children before the start of the winter season,” Ugur Sahin, MD, CEO and co-founder of BioNTech, said in a news release.

“The safety profile and immunogenicity data in children aged 5-11 years vaccinated at a lower dose are consistent with those we have observed with our vaccine in other older populations at a higher dose.”

**VIEW ON THE NEWS**

Mary Cataletto, MD, FCCP, comments: The scientific community has focused substantial efforts to elucidate the mechanisms underlying the distinct clinical course and outcomes of SARS-CoV-2 between adults and children.

Building on the finding of an impaired interferon response in pediatric COVID-19, researchers identified distinct subpopulations of immune cells with a memory phenotype found primarily in children and found that SARS-CoV-2–infected children had higher expression of relevant pattern-recognition receptors in the upper airways. Together these findings led them to conclude that preactivation of immune cells in the upper airway cells of children is associated with a stronger innate antiviral response to SARS-CoV-2 infection in this age group. As researchers continue to explore effective strategies to prevent pediatric SARS-CoV-2 infection this study provides important data that may translate into a targeted therapeutic approach for children.
This advertisement is not available for the digital edition.

CHEST Physician
THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS
Three ‘bad news’ payment changes coming soon for physicians

BY ELIZABETH WOODCOCK, MBA, CPC

Physicians are bracing for upcoming changes in reimbursement that may start within a few months. As doctors gear up for another wave of COVID, payment trends may not be the top priority, but some “uh oh” announcements in the fall of 2021 could have far-reaching implications that could affect your future.

The Centers for Medicare & Medicaid Services issued a proposed rule in the summer covering key aspects of physician payment. Although the rule contained some small bright lights, the most important changes proposed were far from welcome.

Here’s what could be in store:

1. The highly anticipated Medicare Physician Fee Schedule ruling confirmed a sweeping payment cut. The drive to maintain budget neutrality forced the federal agency to reduce Medicare payments, on average, by nearly 4%. Many physicians are outraged at the proposed cut.

2. More bad news for 2022: Sequestration will be back. Sequestration is the mandatory, pesky, negative 2% adjustment on all Medicare payments. It had been put on hold and is set to return at the beginning of 2022.

3. Down to a nail-biter: The final ruling is expected in early November. The situation smacks of earlier days when physicians clung to a precipice, waiting in anticipation for a legislative body to save them from the dreaded income plunge. Indeed, we are slipping back to the decade-long period when Congress kept coming to the rescue simply to maintain the status quo.

Many anticipate a last-minute Congressional intervention to save the day, particularly in the midst of another COVID spike. The promises of a stable reimbursement system made possible by the Medicare Access and CHIP Reauthorization Act have been far from realized, and there are signs that the payment landscape is in the midst of a fundamental transformation.

Other changes proposed in the 1,747-page ruling include:

Positive:
• More telehealth services will be covered by Medicare, including home visits.

Continued on following page
Tele–mental health services got a big boost; many restrictions were removed so that now the patient’s home is considered a permissible originating site. It also allows for audio-only (no visual required) encounters; the audio-only allowance will extend to opioid use disorder treatment services. Phone treatment is covered.

Permanent adoption of G2252: The 11- to 20-minute virtual check-in code wasn’t just a one-time payment but will be reimbursed in perpetuity.

Boosts in reimbursement for chronic care and principal care management codes, which range on the basis of service but indicate a commitment to pay for care coordination.

Clarification of roles and billing opportunities for shared visits, which occur if a physician and advanced practice provider see the same patient on a particular day. Prepare for new coding rules to include a modifier. Previously, the rules for billing were muddled, so transparency helps guide payment opportunities.

Delay of the appropriate use criteria for advanced imaging for 1 (more) year, a welcome postponement of the ruling that carries a significant administrative burden.

Physician assistants will be able to bill Medicare directly, and referrals to be made to medical nutrition therapy by a nontreating physician.

A new approach to patient cost-sharing for colorectal cancer screenings will be phased in. This area has caused problems in the past when the physician identifies need for additional services (for example, polyp removal by a gastroenterologist during routine colonoscopy).

Not positive:

• Which specialties benefit and which get zapped? The anticipated impact by specialty ranges from hits to interventional radiologists (−9%) and vascular surgeons (−8%), to increases for family practitioners, hand surgeons, endocrinologists, and geriatricians, each estimated to gain a modest 2%. (The exception is portable x-ray supplier, with an estimated increase of 10%.) All other specialties fall in between.

• The proposed conversion factor for 2022 is $33.58, a 3.75% drop from the 2021 conversion factor of $34.89. The proposed ruling also covered the Quality Payment Program, the overarching program of which the Merit-Based Incentive Payment System (MIPS) is the main track for participation. The proposal incorporates additional episode-based cost measures as well as updates to quality indicators and improvement activities.

MIPS penalties. The stakes are higher now, with 9% penalties on the table for nonparticipants. The government offers physicians the ability to officially get out of the program in 2021 because of the COVID-19 pandemic, thereby staying off the steep penalty. The option, which is available through the end of the year, requires a simple application that can be completed on behalf of the entire practice. If you want out, now is the time to find and fill out that application.

Exempt from technology requirements. If the proposal is accepted, small practices – defined by CMS as 15 eligible clinicians or fewer – won’t have to file an annual application to reweight the “promoting interoperability” portion of the program. If acknowledged, small practices will automatically be exempt from the program’s technology section.

That’s a big plus, as one of the many chief complaints from small practices is the onus of meeting the technology requirements, which include a security risk analysis, bi-directional health information exchange, public health reporting, and patient access to health information. Meeting the requirements is no small feat. That will only affect future years, so be sure to apply in 2021 if applicable for your practice.

Changes in MIPS. MIPS Value Pathways (MVPs) are anticipated for 2023, with the government releasing details about proposed models for heart disease, rheumatology, joint repair, and more. The MVPs are slated to take over the traditional MIPS by 2027. The program will shift to 30% of your score coming from the “cost” category, which is based on the government’s analysis of a physician’s claims – and, if attributed, the claims of the patients for whom you care. This area is tricky to manage, but recognize that the costs under scrutiny are the expenses paid by Medicare on behalf of its patients. In essence, Medicare is measuring the cost of your patients as compared with your colleagues’ costs (in the form of specialty-based benchmarks). Therefore, if you’re referring, or ordering, a more costly set of diagnostic tests, assessments, or interventions than your peers, you’ll be dinged.

However, physicians are more likely this year to flat out reject participation in the federal payment program. Payouts have been paltry and dismal to date, and the buzz is that physicians just don’t consider it worth the effort. Of course, clearing the threshold (which is proposed at 70 points next year) is a must to avoid the penalty, but don’t go crazy to get a perfect score as it won’t count for much: 2022 is the final year that there are any monies for exceptional performance.

Considering that the payouts for exceptional performance have been less than 2% for several years now, it’s hard to justify dedicating resources to achieve perfection. Experts believe that even exceptional performance will only be worth pennies in bonus payments.

The fear of the stick, therefore, may be the only motivation. And that is subjective, as physicians weigh the effort required versus just taking the hit on the penalty. But the penalty is substantial, and so even without the incentive, it’s important to participate at least at the threshold.

Fewer cost-sharing waivers. While the federal government’s payment policies have a major impact on reimbursement, other forces may have broader implications. Commercial payers have rolled back cost-sharing waivers, bringing to light the significant financial responsibility that patients have for their health care in the form of deductibles, coinsurance, and so forth.

More than a third of Americans had trouble paying their health care bills before the pandemic; as patients catch up with services that were postponed or delayed because of the pandemic, this may expose challenges for you. Patients with unpaid bills translate into your financial burden.

Virtual-first health plans. Patients may be seeking alternatives to avoid the frustrating cycle of unpaid medical bills. This may be a factor propelling another trend: Lower-cost virtual-first health plans such as Alignment Health have taken hold in the market. As the name implies, insurance coverage features telehealth that extends to in-person services if necessary.

These disruptors may have their hands at least somewhat tied, however. The market may not be able to fully embrace telemedicine until state licensure is addressed. Despite the federal regulatory relaxations, states still control the distribution of medical care through licensure requirements. Many are rolling back their pandemic-based emergency orders and only allowing licensed physicians to see patients in their state, even over telemedicine.

While seemingly frustrating for physicians who want to see patients over state lines, the delays imposed by states may actually have a welcome effect. If licensure migrates to the federal level, there are many implications. For the purposes of this article, the competitive landscape will become incredibly aggressive. You will need to compete with Amazon Care, Walmart, Cigna, and many other well-funded national players that would love nothing more than to launch a campaign to target the entire nation. Investors are eager to capture part of the nearly quarter-trillion-dollar market, with telemedicine at 38 times prepandemic levels and no signs of abating.

Increased competition. While the proposed drop in Medicare reimbursement is frustrating, keep a pulse on the fact that your patients may soon be lured by vendors like Amazon and others eager to gain access to physician payments. Instead of analyzing Federal Registers in the future, we may be assessing stock prices.

Consider, therefore, how to ensure that your digital front door is at least available, if not wide open, in the meantime. The nature of physician payments is surely changing.

Ms. Woodcock is president of Woodcock & Associates, Atlanta. She has disclosed no relevant financial relationships.
‘Empathy fatigue’ rises with latest COVID-19 wave

BY EMILY SOHN

Hedi Erickson, MD, is tired. As a pulmonary and critical care physician at Hennepin Health-care in Minneapolis, she has been providing care for patients with COVID-19 since the start of the pandemic. It was exhausting from the beginning, as she and her colleagues scrambled to understand how to deal with this new disease. But lately, she has noticed a different kind of exhaustion arising from the knowledge that, with vaccines widely available, the latest surge was preventable.

Her intensive care unit is currently as full as it has ever been with COVID-19 patients, many of them young adults and most of them unvaccinated. After the recent death of one patient, an unvaccinated man with teenage children, she had to face his family’s questions about why ivermectin, an antiparasitic medication that was falsely promoted as a COVID-19 treatment, was not administered.

“I’m fatigued because I’m working more than ever, but more people don’t have to die,” Dr. Erickson said in an interview. “It’s been very hard physically, mentally, emotionally.”

Amid yet another surge in COVID-19 cases around the United States, clinicians are speaking out about their growing frustration with this preventable crisis.

Some are using the terms “empathy fatigue” and “compassion fatigue” – a sense that they are losing empathy for unvaccinated individuals who are fueling the pandemic.

Dr. Erickson says she is frustrated not by individual patients but by a system that has allowed disinformation to proliferate. Experts say these types of feelings fit into a widespread pattern of physician burnout that has taken a new turn at this stage of the pandemic. Empathy is a cornerstone of what clinicians do, and the ability to understand and share a patient’s feelings is an essential skill for providing effective care, says Kaz Nelson, MD, a psychiatrist at the University of Minnesota, Minneapolis.

Practitioners face paradoxical situations all the time, she notes. These include individuals who break bones and go skydiving again, people who have high cholesterol but continue to eat fried foods, and those with advanced lung cancer who continue to smoke.

To treat patients with compassion, practitioners learn to set aside judgment by acknowledging the complexity of human behavior. They may lament the addictive nature of nicotine and advertising that targets children, for example, while still listening and caring.

Empathy requires high-level brain function, but as stress levels rise, brain function that drives empathy tends to shut down. It’s a survival mechanism, Dr. Nelson says.

When health care workers feel overwhelmed, trapped, or threatened by patients demanding unproven treatments or by ICUs with more patients than ventilators, they may experience a fight-or-flight response that makes them defensive, frustrated, angry, or uncaring, notes Mona Masood, DO, a Philadelphia-area psychiatrist and founder of Physician Support Line, a free mental health hotline for doctors.

Clinicians see a disconnect between what is and what could be, Dr. Nelson notes. “Prior to vaccines, there weren’t other options, and so we had toxic stress and we had fatigue, but we could still maintain little bits of empathy by saying, ‘You know, people didn’t choose to get infected, and we are in a pandemic.’ We could kind of hate the virus. Now with access to vaccines, that last connection to empathy is removed for many people,” she says.

Practitioners may also feel as if they are just going through the motions of their job, or they might disassociate, ceasing to feel that their patients are human. Plenty of doctors and nurses have cried in their cars after shifts and have posted tearful videos on social media.

Early in the pandemic, Dr. Masood says, physicians who called the support hotline expressed sadness and grief. Now, she and her colleagues hear frustration and anger, along with guilt and shame for having feelings they believe they shouldn’t be having, especially toward patients. They may feel unprofessional or worse – unworthy of being physicians, she says.

An emergency department physician told Dr. Masood about a young child who had arrived at the hospital with COVID-19 symptoms.

When asked whether the family had been exposed to anyone with COVID-19, the child’s parent lied so that they could be triaged faster.

The physician, who needed to step away from the situation, reached out to Dr. Masood to express her frustration so that she wouldn’t “let it out” on the patient.

“It’s hard to have empathy for people who, for all intents and purposes, are very self-centered,” Dr. Masood says.

To help practitioners cope, Dr. Masood offers words that describe what they’re experiencing. She often hears clinicians say things such as, “This is a type of burnout that I feel to my bones,” or “This makes me want to quit,” or “I feel like I’m at the end of my rope.”

She encourages them to consider the terms “empathy fatigue,” and “moral injury” in order to reconcile how their sense of responsibility to take care of people is compromised by factors outside of their control.

Being frustrated with a patient doesn’t make someone a bad doctor, and admitting those emotions is the first step toward dealing with them, she says.

“We’re trained to just go, go, go and sometimes not pause and check in,” she says. Clinicians who open up are likely to find they are not the only ones feeling tired or frustrated right now, she adds.

“Connect with peers and colleagues, because chances are, they can relate,” Dr. Nelson says.

INDEX OF ADVERTISERS

Actelion
Biodex
Boehringer Ingelheim
Pharmaceuticals, Inc.
Genentech USA, Inc.
GSK
Koninklijke Philips N.V.
Kindred Healthcare, LLC

By Emily Sohn

“Empathy fatigue” rises with latest COVID-19 wave

Hedi Erickson, MD, is tired. As a pulmonary and critical care physician at Hennepin Health-care in Minneapolis, she has been providing care for patients with COVID-19 since the start of the pandemic. It was exhausting from the beginning, as she and her colleagues scrambled to understand how to deal with this new disease. But lately, she has noticed a different kind of exhaustion arising from the knowledge that, with vaccines widely available, the latest surge was preventable.

Her intensive care unit is currently as full as it has ever been with COVID-19 patients, many of them young adults and most of them unvaccinated. After the recent death of one patient, an unvaccinated man with teenage children, she had to face his family’s questions about why ivermectin, an antiparasitic medication that was falsely promoted as a COVID-19 treatment, was not administered.

“I’m fatigued because I’m working more than ever, but more people don’t have to die,” Dr. Erickson said in an interview. “It’s been very hard physically, mentally, emotionally.”

Amid yet another surge in COVID-19 cases around the United States, clinicians are speaking out about their growing frustration with this preventable crisis.

Some are using the terms “empathy fatigue” and “compassion fatigue” – a sense that they are losing empathy for unvaccinated individuals who are fueling the pandemic.

Dr. Erickson says she is frustrated not by individual patients but by a system that has allowed disinformation to proliferate. Experts say these types of feelings fit into a widespread pattern of physician burnout that has taken a new turn at this stage of the pandemic.

Empathy is a cornerstone of what clinicians do, and the ability to understand and share a patient’s feelings is an essential skill for providing effective care, says Kaz Nelson, MD, a psychiatrist at the University of Minnesota, Minneapolis.

Practitioners face paradoxical situations all the time, she notes. These include individuals who break bones and go skydiving again, people who have high cholesterol but continue to eat fried foods, and those with advanced lung cancer who continue to smoke.

To treat patients with compassion, practitioners learn to set aside judgment by acknowledging the complexity of human behavior. They may lament the addictive nature of nicotine and advertising that targets children, for example, while still listening and caring.

Empathy requires high-level brain function, but as stress levels rise, brain function that drives empathy tends to shut down. It’s a survival mechanism, Dr. Nelson says.

When health care workers feel overwhelmed, trapped, or threatened by patients demanding unproven treatments or by ICUs with more patients than ventilators, they may experience a fight-or-flight response that makes them defensive, frustrated, angry, or uncaring, notes Mona Masood, DO, a Philadelphia-area psychiatrist and founder of Physician Support Line, a free mental health hotline for doctors.

Clinicians see a disconnect between what is and what could be, Dr. Nelson notes. “Prior to vaccines, there weren’t other options, and so we had toxic stress and we had fatigue, but we could still maintain little bits of empathy by saying, ‘You know, people didn’t choose to get infected, and we are in a pandemic.’ We could kind of hate the virus. Now with access to vaccines, that last connection to empathy is removed for many people,” she says.

Practitioners may also feel as if they are just going through the motions of their job, or they might disassociate, ceasing to feel that their patients are human. Plenty of doctors and nurses have cried in their cars after shifts and have posted tearful videos on social media.

Early in the pandemic, Dr. Masood says, physicians who called the support hotline expressed sadness and grief. Now, she and her colleagues hear frustration and anger, along with guilt and shame for having feelings they believe they shouldn’t be having, especially toward patients. They may feel unprofessional or worse – unworthy of being physicians, she says.

An emergency department physician told Dr. Masood about a young child who had arrived at the hospital with COVID-19 symptoms.

When asked whether the family had been exposed to anyone with COVID-19, the child’s parent lied so that they could be triaged faster.

The physician, who needed to step away from the situation, reached out to Dr. Masood to express her frustration so that she wouldn’t “let it out” on the patient.

“It’s hard to have empathy for people who, for all intents and purposes, are very self-centered,” Dr. Masood says.

To help practitioners cope, Dr. Masood offers words that describe what they’re experiencing. She often hears clinicians say things such as, “This is a type of burnout that I feel to my bones,” or “This makes me want to quit,” or “I feel like I’m at the end of my rope.”

She encourages them to consider the terms “empathy fatigue,” and “moral injury” in order to reconcile how their sense of responsibility to take care of people is compromised by factors outside of their control.

Being frustrated with a patient doesn’t make someone a bad doctor, and admitting those emotions is the first step toward dealing with them, she says.

“We’re trained to just go, go, go and sometimes not pause and check in,” she says. Clinicians who open up are likely to find they are not the only ones feeling tired or frustrated right now, she adds.

“Connect with peers and colleagues, because chances are, they can relate,” Dr. Nelson says.
This advertisement is not available for the digital edition.