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“Obesity completely changes lung health,” said Anne E. Dixon, MA, BM, BCh, director of the Vermont Lung Center, Burlington.

Obesity and lung disease: Much more than BMI

BY CHRISTINE KILGORE
MDedge News

The diverse effects of obesity on lung health and disease are increasingly being teased apart, with researchers honing in on the impact of metabolic dysfunction, circulating inflammatory factors produced by adipose tissue, lipid handling, and other factors – in addition to body mass index – that are associated with the obese state.

“The bird’s eye view is that obesity completely changes lung health. It’s something we’ve only recently begun to appreciate,” said Anne E. Dixon, MA, BM, BCh, director of the Vermont Lung Center at the University of Vermont,

Burlington, who is focused on the research field of obesity and lung disease.

Structural, mechanical effects of obesity on lung function are better known and appreciated. Accumulation of fat in the mediastinum and abdominal and thoracic cavities causes reductions in lung volume, in functional residual capacity, and in the compliance of the lungs, chest wall, and entire respiratory system, for instance.

Yet obesity is more than a state of increased BMI, and “what we’ve begun to understand is that [its impact on the lungs and respiratory health] is much more complicated than just a mechanical problem,” said Dr. Dixon, also

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Risk calculator may help predict death after COPD hospitalization

BY RICHARD MARK KIRKNER

Researchers in Scotland have developed a risk calculator using a large electronic health records database that has shown a high reliability in predicting the risk of death for patients hospitalized for chronic obstructive pulmonary disease (COPD), providing another potential tool for improving postdischarge survival in these patients.

In a study published online in the journal *Pharmacological Research* (2022 Apr 4. doi: 10.1016/j.phrs.2022.106199), Pierpalo Pellicori, MD, and colleagues reported that a few variables, including prescriptions and laboratory data in routine EHRs, could help predict a patient’s risk of dying within 90 days after a hospital stay for COPD. Dr. Pellicori is a clinical cardiologist and research fellow at the Robertson Center for Biostatistics at the University of Glasgow.

“Identification of patients at high risk is valuable information for multidisciplinary teams,”

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Dr. Pellicori said in a written comment. “It allows the most vulnerable patients to be highlighted and prioritized for consideration of optimized value-based care, and for anticipatory care plan discussions.”

The retrospective cohort study analyzed EHR records of 17,973 patients who had an unplanned hospitalization for COPD in the Glasgow area from 2011 to 2017. The risk calculator model achieved a potential accuracy of 80%.

The study also found a linear increase in mortality with serum sodium less than 140 mmol/L or serum chloride less than 105 mmol/L – but that higher concentrations of each were associated with a worse outcome.

“Interestingly,” Dr. Pellicori added, “social deprivation was not associated with mortality in this cohort.”

The final predictive model included age, sex, length of stay, and just nine other variables. “The

The final predictive model included age, sex, length of stay, and just nine other variables. “The model can be applied easily in clinical practice, even if electronic records are not available, because there are only 12 variables.”

The study noted that, while a number of models have been developed to calculate the risk of exacerbations, inpatient death and prognosis in patients hospitalized for COPD, most of those models were based on cohorts of 1,000 patients or less.

“Older age, male sex, and a longer hospital stay were important predictors of mortality in patients with COPD,” Dr. Pellicori said. “We also found that use of commonly prescribed medications such as digoxin identify patients with COPD more likely to die, perhaps because many have underlying heart failure, a highly prevalent but frequently missed diagnosis.”

He noted that heart failure and COPD share many risk factors, signs, and symptoms, such as smoking history, peripheral edema, and breathlessness. “Distinguishing between COPD and heart failure can be difficult, but is very important, as appropriate treatment for heart failure can improve a patient’s quality of life and survival substantially in many cases.”

The study also found that routinely collected and inexpensive blood markers – such as hemoglobin, neutrophil/lymphocyte ratio, serum chloride, urea, creatinine, and albumin – can also improve predictability of outcomes.

For example, the study found a linear increase in mortality of blood hemoglobin concentration less than 14 g/dL, but higher levels posed no greater risk. Higher white blood cell and neutrophil counts and lower lymphocyte and eosinophil counts were associated with a worse prognosis.

model can be applied easily in clinical practice, even if electronic records are not available, because there are only 12 variables,” Dr. Pellicori said. “These could easily be entered manually into the risk calculator that we provide.”

“What is notable about this risk calculator is that it uses some of the techniques of machine learning, although it’s not specifically machine learning,” Angel Coz, MD, at the Cleveland Clinic Respiratory Institute and Editor in Chief of *CHEST Physician*, said in an interview. “But it’s a retrospective data analysis, and actually by doing that it may catch some factors that we may not have necessarily paid attention to on a regular basis.”

While he called it a “well-done study,” Dr. Coz cautioned that “we have to be conservative in how to interpret and apply this because it is retrospective,” adding that future research should also use a prospective cohort.

Dr. Pellicori said that, while EHRs provide a “rich source” of data for such risk calculators, systems differ greatly across hospitals and health care systems and don’t link easily.

Future research would focus on validating the model in other large national datasets and seeing if machine learning can improve its predictability, Dr. Pellicori said. “Whether such models can provide a real-time, refined risk assessment for all patients in both primary or secondary care settings and improve the efficacy, efficiency, and quality of health care is our long-term goal.”

Dr. Pellicori and Dr. Coz disclosed no relevant financial relationships. ■

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Angel Coz, MD, FCCP, is Editor in Chief of *CHEST Physician*.

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CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Frontline Medical Communications Inc., 283-299 Market Street (2 Gateway Building), 4th Floor, Newark, NJ 07102. Subscription price is \$244.00 per year. Phone 973-206-3434, fax 973-206-9378.

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With obesity, adipose tissue changes not only in quantity, but in function, producing proinflammatory cytokines and hormones – such as tumor necrosis factor-alpha (TNF-alpha), leptin, and interleukin-6 – that can have direct effects on the lung. Insulin resistance, which is common with obesity, is also seemingly deleterious. And obesity-associated changes in immune function, lipid handling, diet, and the gut microbiome may also impact lung health and disease, she said.

Dr. Dixon, who wrote about these changes in a 2018 review article in the journal *CHEST* and another 2019 piece in *Expert Review of Respiratory Medicine*, has developed a research program focused on obesity and lung disease and has edited a book and organized international conferences on the topic. (*CHEST* 2018;153[3]:702-9 and *Exper Rev Respir Med*. 2018;12[9]:755-67.)

“The more I do, the more I realize that there are multiple obesity-associated changes involved, and that [our current high level of] obesity is like a huge population-level natural experiment ... on lung health,” she said in an interview.

Associations between lung disease and the metabolic and other disturbances of obesity are most established in asthma research and have taken hold in the realm of sleep-disordered breathing. But as the prevalence of obesity continues to grow, its role in other lung diseases such as chronic obstructive pulmonary disease (COPD) and, most recently, pulmonary arterial hypertension (PAH), is getting attention in academia.

And certainly, COVID-19 has highlighted an “urgent need” to better understand how obesity increases susceptibility to severe viral infections, Dr. Dixon added.

Here are some glimpses into current thinking and some examples of research that may have preventive and therapeutic implications in the future:

OSA and OHS

“With sleep apnea we tend to focus on anatomic considerations, but there may be relationships or interactions between obesity and neuromuscular function and neuroventilatory control,” Susheel P. Patil, MD, PhD, director of the sleep medicine program for University

Hospitals and assistant professor at Case Western Reserve University, Cleveland, said in an interview.

Some studies suggest, for instance, that TNF-alpha can increase obstructive sleep apnea (OSA) susceptibility and severity through



Dr. Patil

its neuroventilatory modulating properties during sleep. And the potential for additional proinflammatory cytokines produced by adipose tissue to similarly affect upper airway neuroventilatory control is an “intriguing line” of inquiry for researchers in the sleep apnea space, he said.

“Patients with OHS may have resistance to leptin at the central nervous system level – with leptin not reaching the sites of ventilatory control. This could explain why these patients do not augment their ventilation to maintain homeostasis, normal levels of CO₂.”

Leptin is of interest particularly in obesity hypoventilation syndrome (OHS), which is characterized by chronic daytime hypercapnia. Best known as a satiety hormone, leptin is produced by adipose tissue and suppresses appetite at the central nervous system level. But it has long been known that leptin also affects ventilation and the control of breathing.

When transported across the blood-brain barrier, leptin increases the hypercapnic ventilatory response, Babak Mokhlesi, MD, MSc, codirector of the Rush Lung Center and chief of pulmonary, critical care, and sleep medicine at Rush University Medical Center in Chicago, said in an interview.

Research suggests that patients with OHS may have resistance to leptin at the central nervous system level – with leptin not reaching the sites of ventilatory control. This is a “prevailing theory” and could explain why these patients “do not augment their ventilation to maintain homeostasis, normal levels of CO₂,” Dr. Mokhlesi said.

“Why some patients with severe obesity develop CO₂ retention while others do not is not fully understood,” he said, noting that patients with OHS can normalize their CO₂ quickly when instructed to take deep breaths. “What we know is that

“Visceral fat has a completely different cytokine-secretion profile than subcutaneous fat ... It is the more metabolically active fat that may secondarily impact upper airway function through a neuroinflammatory mechanism.”

the centers in the brain responsible for augmenting ventilation when CO₂ goes up are somehow blunted.”

In a study of obese mice led by Vsevolod Y. Polotsky, MD, PhD, of Johns Hopkins University, Baltimore – and highlighted by Dr. Mokhlesi as an example of important, recent research – leptin delivered intrana-



Dr. Mokhlesi

sally alleviated hypoventilation (and upper-airway obstruction), while intraperitoneally administered leptin did not, seemingly overcoming “central leptin deficiency.” (*Am J Respir Crit Care Med*. 2019;199[6]:773-83).

“This proved that there is some level of resistance in this animal model ... and has potential for therapeutics in the future,” Dr. Mokhlesi said.

Understanding the role of insulin resistance in OSA is another research focus. Some data suggest that insulin resistance, which is more common in obesity, is more prevalent in populations with OSA, Dr. Patil said. Researchers have discussed a bidirectional relationship for years, but it’s likely that insulin resistance is a precursor, he said.

In a mechanistic study published in 2016, Dr. Patil and his coinvestigators found that obese individuals with insulin resistance but without frank diabetes or sleep apnea demonstrated preclinical elevations in pharyngeal collapsibility during sleep. The findings suggest that insulin resistance could play a causal

role in OSA pathogenesis by “generating requisite elevations in pharyngeal collapsibility,” they wrote (*Eur. Respir J*. 2016;47[6]:1718-26).

More recently, Dr. Patil noted in the interview, there is increasing appreciation in academia that the type of fat may be important to predicting OSA. “Visceral fat has a completely different cytokine-secretion profile than subcutaneous fat ... It is the more metabolically active fat that may secondarily impact upper airway function through a neuroinflammatory mechanism,” he said. “That is one of the working hypotheses today.”

Asthma

Research has so roundly suggested that metabolic dysfunction contributes to severe, poorly controlled asthma that there’s recent and growing interest in targeting metabolic dysfunction as part of the treatment of obese asthma, said Dr. Dixon, whose own research in obesity and lung disease has focused on asthma.

Data from animal models and some epidemiologic studies have suggested that drugs used to treat type 2 diabetes mellitus, such as glucagon-like peptide receptor-1 (GLP-1) agonists and metformin, may help control asthma. In one recent study – cited by Dr. Dixon in a 2022 review of obesity and asthma – people with obesity and asthma who were prescribed GLP-1 agonists for diabetes had fewer asthma exacerbations compared with those who took other medications for diabetes (*Semin Respir Crit Care Med*. 2022 Feb 17. doi: 10.1055/s-0042-1742384).

There is also research interest in targeting the pro-inflammatory adipokine interleukin-6 (IL-6), since increased circulating levels of IL-6 correlate with asthma severity, and in addressing oxidative stress in asthma through treatment with a mitochondrially targeted antioxidant, she said. Oxidative stress is increased in the airways of people with obesity, and researchers believe it may contribute to the pathophysiology of obese asthma through effects on airway nitric oxide levels.

(Her own research work at the University of Vermont has found associations between poor asthma control and high levels of leptin, and similar associations involving low levels of adiponectin, an anti-inflammatory adipokine that has been shown to downregulate eosinophil recruitment in the airways.)

Weight loss has been shown in

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mostly small, single-center studies to improve asthma control, but short of weight loss, researchers are also investigating the role of poor dietary quality. Thus far, data suggest that it's the composition of the diet, and not just its contribution to weight gain, that could be impactful, Dr. Dixon said.

More basic research questions cited by Dr. Dixon include the extent to which adipose tissue inflammation causes inflammation in the lungs. "It's a little unclear whether all the metabolic dysfunction associated with poor asthma control is causing inflammation in the lungs," she said, though "we've done some work here that shows mediators produced by the adipose tissue could be impacting production of inflammatory mediators by the airway epithelium."

Overall, she said, "the big questions [in asthma] are, how does adipose tissue affect the airway? Is it through direct effects? Through effects on the immune system? And obesity is affected by diet and the gut microbiome – how can these be [impacting] the airway?"

Obesity "is associated with so many changes – the gut, the immune system, and metabolic dysfunction, in addition to airway mechanics," she said, "that I no longer think, as I did when I came to this, that it's just one thing. It's probably all of these things together."

In the meantime, questions about potential shared pathways for the development of obesity and asthma remain. "Obesity is a risk factor for developing asthma, but it's also entirely possible that asthma is a risk factor for developing obesity," she said. (Some data from pediatric populations, she noted, suggest that nonobese children with asthma are at increased risk of developing obesity.)

Also important, Dr. Dixon said, is "emerging literature in the last 5-10 years" that suggests that people with obesity are more susceptible to the effects of air pollution. Research involving inner-city schoolchildren with asthma, for instance, has shown that those with obesity had worse symptoms with air pollution exposure than did those who were not obese.

Pulmonary arterial hypertension

Some research has looked at adipose tissue-produced substances in PAH, but the most well-established association in obesity and PAH involves insulin resistance.

"I don't think we're certain as a

community that obesity [in general] is the problem – it's not itself considered a risk factor for PAH," Anna R. Hemnes, MD, associate professor of medicine at Vanderbilt University Medical Center in Nashville, Tenn., said in an interview. She noted that it's "hard to dissect obesity" apart.

Researchers are "more confident," she said, "that insulin resistance – one feature of obesity [in some people] – is associated with worse outcomes in PAH." Metabolic disease resembling insulin resistance is common in PAH and is believed to contribute to pulmonary vascular disease and right ventricular (RV) failure – the main cause of mortality in PAH – at least in part because of increased oxidative stress.

Dr. Hemnes led a mechanistic phase II clinical trial of metformin in PAH in which the drug was associated with improved RV fractional area change and reduced RV lipid deposition (*J Am Heart Assoc.* 2020;9[22]:e018349), and she's now leading a National Institutes of Health-funded multicenter trial looking at the impact of metformin and an exercise intervention on 6-minute walk distance and World Health Organization functional class in PAH.

At the Rush Lung Center, in the meantime, Dr. Mokhlesi is utilizing animal models of OSA and OHS to explore the effect of hypoxia and nighttime hypercapnia on the development of PAH. "I think the jury is still out as to whether obesity itself is a major risk factor, but if so, by what mechanism?" he said. "Is it worsening [sleep-disordered breathing], which then worsens PAH?"

COPD

The focus in COPD has traditionally been on underweight, but the relationship between obesity and COPD has increasingly been recognized in the last 10-15 years, said Frits M. E. Franssen, MD, PhD, of CIRO, a research institute in Horn, the Netherlands, that treats COPD and other chronic lung diseases, and of the department of respiratory medicine at Maastricht University.

Researchers like Dr. Franssen are trying, for one, to understand obesity's impact on COPD pathophysiology and to tease apart the impact of both conditions on disease severity and patient-related outcomes such as exercise capacity and exercise-related symptoms.

When Dr. Franssen's group compared responses to weight-bearing exercise (6-min. walk test) and weight-supported exercise (cycling) in obese and normal weight COPD

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BLVR may boost severe COPD survival, study shows

BY HEIDI SPLETE

MDedge News

Bronchoscopic lung volume reduction (BLVR) significantly increased survival in patients with severe chronic obstructive pulmonary disease, based on data from more than 1,400 individuals.

Previous studies have shown that patients with severe COPD can benefit from treatment with BLVR involving lung volume reduction coils or endobronchial valves (EBVs) in terms of improved pulmonary function, lung volume, exercise capacity, and quality of life.

However, data on the impact of the procedure on patient survival are limited, and most previous studies have been small, wrote Jorine E. Hartman, MD, of the University of Groningen, the Netherlands, and colleagues. In their study published in *Respiratory Medicine* (doi.org/10.1016/j.rmed.2022.106825), the researchers reviewed data from 1,471 patients with severe COPD who had consultations for BLVR at a single center between 2006 and 2019; 483 (33%) underwent a BLVR treatment.

The follow-up period ranged from

Loren Harris, MD, FCCP, comments: This study indicates great potential for the current version of the lung volume reduction procedure. The study shows an improvement in overall survival for patients with severe COPD over those who did not have the procedure in a concurrent group of patients treated over a 13-year period. The follow-up was excellent – up to almost 15 years. However, there were several issues with the data such as non-randomization, somewhat different populations of patients involved and no specific criteria for treatment. Therefore, like lung volume reduction surgery (LVRS) before, this technology has great potential to improve survival and functional status for patients with severe COPD when applied to the right population and thus, again like LVRS, it will require a well-designed prospective, randomized trial to identify those populations of patients who will best obtain those benefits.



633 days to 5,401 days. During this time, 531 patients died (35%); 165 of these (34%) were in the BLVR group.

Overall, the median survival of BLVR patients was significantly longer, compared with those who did not have the procedure, for a difference of approximately 1.7 years (3,133 days vs. 2,503 days, $P < .001$). No significant differences in survival were noted in BLVR patients treated with coils or EBVs.

The average age of the study population at baseline was 61 years, and 63% were women. Overall, patients treated with BLVR were more likely to be younger and female, with fewer COPD exacerbations but worse pulmonary function, as well as lower body mass index and more evidence of emphysema than the untreated patients, the researchers noted.

Patients treated with BLVR also

were more likely than untreated patients to have a history of myocardial infarction, percutaneous coronary intervention, or stroke.

However, BLVR was a significant independent predictor of survival after controlling for multiple variables, including age, sex, and disease severity, the researchers noted.

The current study supports existing literature on the value of BLVR for severe COPD but stands out from previous studies by comparing patients who underwent BLVR with those who did not, the researchers noted.

The study findings were limited by several factors, including the fact that the non-treated patients were not eligible for treatment for various reasons that might have impacted survival. However, the results were strengthened by the large sample size and long-term follow-up and suggest that “reducing lung volume in patients with COPD and severe hyperinflation and reduced life expectancy may lead to a survival benefit,” they concluded.

The study received no outside funding. Dr. Hartman had no financial conflicts to disclose. ■

OBSESITY continued from previous page

patients matched for age, gender, and degree of airflow limitation, the researchers found that walking capacity was significantly reduced while cycling capacity was preserved in the obese group (*Respirology*. 2016;21[3]:483-8).

Exercise-related symptoms (dyspnea and leg fatigue) were largely comparable between the obese and normal-weight COPD patients in both exercise modalities. However, in other studies, dyspnea ratings during cycling – at any given level of ventilation – have been lower in obese patients, indicating that “additional fat mass may have a beneficial effect on lung functioning [in non-weight-bearing exercise],” he said in an interview.

Dr. Franssen’s group also has assessed body composition in overweight and obese patients with COPD and found that a significant number have low muscle mass. These patients had worse lung function, exercise tolerance, and muscle strength compared to patients with comparable BMI and normal muscle mass (*Respir Res*. 2021 Mar 25. doi: 10.1186/s12931-021-01689-w).

“We’d always thought that obese

patients have normal muscle mass ... but now we know it can be dramatically low,” he said. In assessing obesity and formulating any weight loss plans, “we’re now interested not only in weight but in the distribution of fat mass and fat-free mass ... and in maintaining muscle mass in patients who are [prescribed dietary interventions].”

Paradoxically, in patients with severe COPD, obesity is associated with prolonged survival, while in patients with mild to moderate COPD, obesity is associated with increased mortality risk, he noted.

The impact of adipose tissue and the chronic inflammation and metabolic disturbances that characterize obesity are currently largely unexplored, he said. Researchers have not yet studied what optimal weights may be for patients with COPD. “And we’re interested in the questions, are body weight and body composition the result of the disease, or [are they] determining the type of COPD one will get?” Dr. Franssen said.

Patients with COPD who are obese have “more of the phenotype of chronic bronchitis,” he noted, “while typical emphysema patients are normally underweight.” ■

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Severe COVID-19 adds 20 years of cognitive aging

BY ROB HICKS, MBBS

Cognitive impairment from severe COVID-19 is equivalent to 20 years of aging, report scientists behind a new study, adding that the impairment is “equivalent to losing 10 IQ points.”

In their study, published in *eClinicalMedicine* (2022 Apr 28. doi: 10.1016/j.eclinm.2022.101417), a team of scientists from the University of Cambridge (England) and Imperial College London said there is growing evidence that COVID-19 can cause lasting cognitive and mental health problems. Patients report fatigue, “brain fog,” problems recalling words, sleep disturbances, anxiety, and even posttraumatic stress disorder months after infection.

The researchers analyzed data from 46 individuals who received critical care for COVID-19 at Addenbrooke’s Hospital between March and July 2020 (27 females, 19 males, mean age 51 years, 16 of whom had mechanical ventilation) and were recruited to the NIHR COVID-19 BioResource project.

At an average of 6 months after acute COVID-19 illness, the study participants underwent detailed computerized cognitive tests via the Cognitron platform, comprising eight tasks deployed on an iPad measuring mental function such as memory, attention, and reasoning. Also assessed were anxiety, depression, and posttraumatic stress disorder via standard mood, anxiety, and posttraumatic stress scales – specifically the Generalized Anxiety Disorder 7 (GAD-7), the Patient Health Questionnaire 9 (PHQ-9), and the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders 5 (PCL-5). Their data were compared against 460 controls – matched for age, sex, education, and first language – and the pattern of deficits across tasks was qualitatively compared with normal age-related decline and early-stage dementia.

Slower response times

The authors highlighted how this was the first time a “rigorous assessment and comparison” had been carried out in relation to the after-effects of severe COVID-19.

“Cognitive impairment is common to a wide range of neurological disorders, including dementia, and even routine aging, but the patterns we saw – the cognitive ‘fingerprint’ of COVID-19 – was distinct from all of these,” said David Menon, MD, the

study’s senior author.

The scientists found that COVID-19 survivors were less accurate and had slower response times than the control population, and added that survivors scored

particularly poorly on verbal analogical reasoning and showed slower processing speeds.

Critically, the scale of the cognitive deficits correlated with acute illness severity, but not fatigue or

mental health status at the time of cognitive assessment, said the authors. The effects were strongest for those with more severe acute illness, and who required mechanical ventilation, said the authors,

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who found that acute illness severity was “better at predicting the cognitive deficits.”

The authors pointed out how these deficits were still detectable when patients were followed up 6 months later, and that, although patients’ scores and reaction times began to improve over time, any

recovery was “at best gradual” and likely to be influenced by factors such as illness severity and its neurological or psychological impacts.

“We followed some patients up as late as 10 months after their acute infection, so were able to see a very slow improvement,” Dr. Menon said. This improvement was not

statistically significant, it was “at least heading in the right direction.”

However, he warned it is very possible that some of these individuals “will never fully recover.”

The cognitive deficits observed may be due to several factors in combination, said the authors, including inadequate oxygen or

blood supply to the brain, blockage of large or small blood vessels due to clotting, and microscopic bleeds.

They highlighted how the most important mechanism, however, may be “damage caused by the body’s own inflammatory response and immune system.” ■

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Long-COVID symptoms a serious challenge for elderly

BY BRIDGET M. KUEHN

Even mundane tasks such as making a meal can be exhausting for Louise Salant. Many older people who contract

COVID-19 experience prolonged symptoms of the disease. An analysis of Medicare Advantage claims data published in the BMJ (2022 Feb. doi: 10.1136/bmj-2021-068414) found that about one-third of

roughly 87,000 adults aged 65 in the database with a COVID-19 diagnosis sought care for persistent or new symptoms 21 or more days later.

That figure is about twice the rate of persistent COVID-19-related

symptoms seen in a cohort of adults younger than age 65 with commercial insurance analyzed by the same group of researchers in a separate BMJ study reported in 2021 (doi: 10.1136/bmj.n1098).

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Compared with a 2020 comparator group of patients in this age cohort, these patients had a greater likelihood of respiratory failure, fatigue, hypertension, memory problems, kidney injury, mental health conditions, hypercoagulability, and cardiac rhythm disorders.

“It became clear early in the pandemic that there is going to be a second pandemic related to all of the complications that we’ve seen related to COVID-19 infections,” said Ken Cohen, MD, who coauthored the BMJ studies.

The results are among a growing body of evidence suggesting that

older adults are at high risk of persistent post-COVID-19 symptoms.

Researchers in Rome, for example, found that 83% of 165 patients aged 65 or older who had been hospitalized for COVID-19 reported at least one lasting symptom – problems like fatigue, shortness of breath, joint pain, and coughing – in

the months after hospitalization (JAMDA 2021 Jul 18. doi: 10.1016/j.jamda.2021.07.003). One-third of those had two symptoms, and 46% had three or more.

A similar study in Norway found that two-thirds of patients aged 60 or older reported reduced

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health-related quality of life during follow-up visits 6 months after hospitalization for COVID-19 (BMC Geriatr. 2021 Mar 22. doi: 10.1186/s12877-021-02140-x). The most-reported impairments among those patients were the inability to perform the tasks of daily life, reduced mobility, and increased

pain and discomfort.

Mounting evidence indicates that COVID-19 may contribute to chronic cognitive impairment in older adults. A multisite U.S. study found that 28% of 817 adults presenting to emergency departments with COVID-19 had delirium and poorer outcomes (JAMA Netw Open. 2020. doi: 10.1001/

jamanetworkopen.2020.29540). A Chinese case-control study that enrolled 1,438 individuals hospitalized in Wuhan for COVID-19, along with 438 of their uninfected spouses, found that 12% of COVID-19 survivors experienced cognitive impairment a year after discharge (JAMA Neurol. 2022 Mar 8. doi: 10.1001/jamaneurol.2022.0461).

“Hospitalization and the acute illness itself accelerate cognitive decline,” said Jin Ho Han, MD, associate professor of emergency medicine at Vanderbilt University, Nashville, Tenn., and previous evidence links delirium with worsening cognition (JAMA Neurol. 2020;77[11]:1373-81). Dr. Han emphasized the importance

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of preventing COVID-19–related delirium through vaccines and other strategies to reduce exposure of older patients to the virus. “Once you have cognitive decline, there are no interventions to reverse it,” he said.

Alarm bells for long-term care

Experts expressed concern that the situation might be even worse

for people living in long-term care facilities.

“It’s common for long-term care facility residents to experience functional and cognitive decline, even after seemingly minor things, like a cold or a trip to the hospital,” said Karl Steinberg, MD, president of the Society for Post-Acute and Long-Term Care Medicine.

“It makes it a little harder to determine whether the declines we’ve been seeing post COVID in these residents are attributable to post COVID versus just an accelerated step in their overall expected decline.”

“During the many months where family visits were prohibited, we saw people – whether they had

COVID-19 or not – suffer major clinical, functional, cognitive declines or severe psychological symptoms,” Dr. Steinberg said.

He said the benefit of preventing lasting symptoms is often a strong motivator for family caregivers of people with dementia to get them vaccinated or boosted.

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Easing symptoms and offering support

As with long COVID generally, many questions remain about the causes of lasting symptoms of COVID-19 in older patients, and how best to treat them. Matteo Tosato, MD, PhD, who led the study of long-COVID patients in Rome,

is focusing on inflammation as a critical factor in the condition. He and colleagues across Europe hope to answer some of them by launching a multicenter study of lasting COVID-19 symptoms.

In the meantime, Dr. Steinberg and Dr. Tosato said they are doing their best to evaluate and treat patients empirically. “We pull from

our armamentarium to treat system-specific symptoms,” Dr. Steinberg said. “We want to improve the quality of life and help each day be the best it can.”

Physicians in long-term care facilities might use medications such as antidepressants or nonpharmacologic approaches for patients experiencing depression symptoms.

Families are also crucial in helping patients.

“We’ve seen with the return of families and loved ones visiting to some extent has alleviated some people’s symptoms, especially psychological ones,” Dr. Steinberg said.

Dr. Tosato said he and his colleagues start with an individualized, multidisciplinary assessment to determine what types of care may help. He noted that physicians might recommend medications or rehabilitative therapies depending on the patient’s needs.

“A personalized approach is key,” Dr. Tosato said. His study also found that the proportion of older patients experiencing symptoms declined over time – a glimmer of hope that many will recover.

Dr. Cohen emphasized the need for a multimodal rehabilitation, an evidence-based approach used to care for patients who survived hospitalization with severe COVID-19 – a group that has substantially higher rates of persistent symptoms. This approach includes cognitive rehabilitation, physical therapy, occupational therapy, and a graded exercise program.

Dr. Han and colleagues are studying potential therapies such as cognitive rehabilitation in adults who’ve experienced delirium. But until evidence-based treatments are available, they stress the role of support for patients with cognitive decline and their families.

“A lot of the work we do is teach patients and their families to compensate for newly acquired cognitive deficits from any illness, including COVID-19,” Dr. Han said.

Ms. Salant said she has experienced some improvement in her energy since her pulmonologist recommended a new inhaler based on her symptoms. Her sense of smell and taste, lost to the infection, returned after she received her first dose of a vaccine against COVID-19. She takes comfort in participating in Survivor Corps, a group of more than 170,000 COVID-19 survivors and their families who advocate for more scientific research on the disease.

She also expressed gratitude for the support she receives from her primary care physician, who she said has taken the time to learn more about the symptoms of long COVID, listens to her, and respects what she has to say.

“I have hope that I will keep getting better by baby steps,” Ms. Salant said.

Dr. Tosato, Dr. Steinberg, and Dr. Han have disclosed no relevant financial relationships. ■

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NETWORKS

Bronchiectasis, microplastics, and end of life

AIRWAYS DISORDERS NETWORK Bronchiectasis section

Phenotyping bronchiectasis: Focus on eosinophilic bronchiectasis

Bronchiectasis has been often linked to neutrophilic inflammation; however, 20% may have a predominantly eosinophilic inflammation.

Eosinophilic bronchiectasis has been associated with a distinct airway microbiome. Shoemark and colleagues showed in an analysis of 1,007 patients from five countries that 22.6% of patients had blood



Dr. Narendra



Dr. Ramesh

eosinophil counts (BEC) of >300 cells/ μ L. BEC of <100 cells/ μ L were associated with higher bronchiectasis severity and increased mortality (Shoemark et al. *Am J Respir Crit Care Med*. 2022;205[8]:894-902).

BEC of >300 cells/ μ L were correlated with *Streptococcus*- and *Pseudomonas*-dominated microbiome profiles. Compared with patients with BEC of <100 cells/ μ L, patients with 100-299 cells/ μ L (hazard ratio [HR], 2.38; 95% confidence interval, 1.33-4.25; $P = .003$) and those with >300 cells/ μ L (HR, 3.99; 95% confidence interval, 2.20-7.85; $P = .0001$) were associated with shorter time to exacerbation. Eosinophilic inflammation is a risk factor for exacerbations in patients with *P. aeruginosa* infection and may be considered as a treatable trait. Shoemark and colleagues' data show that quality of life was improved with inhaled corticosteroid treatment in patients with bronchiectasis who had BEC of >3%, and eosinophils contribute to bronchiectasis exacerbations.

Dharani Narendra, MD
Navitha Ramesh, MD, FCCP
Diego Maselli Caceres, MD, FCCP
Section Members-at-Large

DIFFUSE LUNG DISEASE AND LUNG TRANSPLANT NETWORK Occupational and environmental health section

A ubiquitous invasion: The rise of microplastics

About 6.3 billion tons of plastic waste were produced between 1950 and 2015.¹ Their degradation into submillimeter fragments of 1 μ m to 5 mm, is called microplastics (MP).² MP are vectors of pollutants, pathologic microorganisms, and chemical additives used in their fabrication.³ Exposure to MP is unavoidable as they are bio-persistent and ubiquitous, even indoors.⁴ MP have been detected in the snow of large metropolitan areas and in remote locations.⁵ Humans are exposed to MP via oral ingestion and inhalation.

A Brazilian study of human lung autopsy specimens revealed the presence of MP in 13 of 20 subjects.³ In vitro studies have suggested a causal role of polystyrene-MP in the development of chronic pulmonary disease through the formation of reactive oxygen species, inhibition of cell proliferation, and cellular morphology aberration.⁶ MP can cause local effects due to macrophage-induced inflammation, or alternatively, be transported distantly to the pleura and the systemic circulation.

In addition, MP may disrupt the endocrine pathway due to its estrogenic effects.⁷ Larger MPs of 8 to 10 μ m, like nylon, have been associated with interstitial lung disease.⁸ Lung biopsies from workers exposed to airborne synthetic fibers (acrylic, polyester, and terylene) have revealed different degrees of inflammation, granulomas, and interstitial fibrosis.⁹ Factory workers exposed to polyvinyl chloride dust have increased risk of exertional dyspnea and decreased pulmonary function.¹⁰ Due to the pervasive nature



Dr. Balakrishnan



Dr. Church

of MP, it is essential to establish the global burden of airborne MP and to determine its role in lung health.

Bathmapriya Balakrishnan, MD,
Member-at-Large

*Tyler Church, DO, Fellow-in-
Training Member

*Disclaimer: The views expressed in this article are those of the author(s) and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or U.S. Government.

References

- Rhodes CJ. Plastic pollution and potential solutions. *Sci Prog*. 2018;101(3):207-60.
- Danopoulos E et al. Microplastic contamination of drinking water: A systematic review. *PLoS One*. 2020;15(7):e0236838.
- Amato-Lourenço LF et al. Presence of airborne microplastics in human lung tissue. *J Hazard Mater*. 2021;416:126.
- Al Horr Y et al. Occupant productivity and office indoor environment quality: A review of the literature. *Building and Environment*. 2016;105:369-89.
- Bergmann M et al. White and wonderful? Microplastics prevail in snow from the Alps to the Arctic. *Sci Adv*. 2019;5:eaax1157.
- Dong CD et al. Polystyrene microplastic particles: In vitro pulmonary toxicity assessment. *J Hazard Mater*. 2020;385:121575.
- Amato-Lourenço LF et al. An emerging class of air pollutants: Potential effects of microplastics to respiratory human health. *Sci Total Environ*. 2020;749:141676.
- Kern DG et al. Flock worker's lung: Chronic interstitial lung disease in the nylon flocking industry. *Ann Intern Med*. 1998;129[4]:261-72. Erratum in: *Ann Intern Med*. 1999;130[3]:246.
- Pimentel JC et al. Respiratory disease caused by synthetic fibers: a new occupational disease. *Thorax*. 1975;30:204-19.
- Soutar CA et al. Epidemiological study of respiratory disease in workers exposed to polyvinyl chloride dust. *Thorax*. 1980;35:644-52.

CRITICAL CARE NETWORK Palliative and end-of-life section

Discussing code status with families of critically ill patients

Discussing code status with patients is complex and emotional, especially when critically ill. The complexity further increases when these conversations have to take place with family members.

Here are some practical tips to help have these conversations in a concise and compassionate manner.

Introduction

- Introduce yourself, and make sure to identify the correct decision-maker.
- Get to know the patient.
 - What kind of person are they?
 - What brings them joy?

- Find out what the family knows about the current clinical condition of their family member.
 - What have you been hearing from the medical team?
 - What are you worried about?



Dr. Mahmood



Dr. Kelemen

Update

- Fill in the gaps – update them on the clinical condition and ongoing management.
- Discuss how you think they will respond to current management and further management options.
- Allow them to process the information.

Provide a medical recommendation

- Example: We are worried he might die, and if his heart stops, interventions like CPR or intubation would not work, and we would not recommend them.
- Do not pressure for a decision right away. (You can say “We do not need a decision today, so please take time to process this information.”)

Respond to emotions

- I can't image how hard this must be.
- Offer chaplain services if that is important to them.

Things to avoid

- Aggressive language.
 - We will have to pound on their chest, break ribs.
 - They would be suffering.
- Blaming or judgmental language.
 - While this complex discussion requires individualization, these tips will help set a framework for goals of care conversations that lead to high quality care for patients that aligns with their goals.

Reference

Goldfish and Rosielle. Language for Routine Code Status Discussions, Fast Facts and Concepts #365, Palliative Care Network of Wisconsin (<https://tinyurl.com/52598573>).

Syed Nazeer Mahmood, MD
Fellow-in-Training Member
Anne Kelemen, LCSW
Member-at-Large

2022 billing and coding updates: Critical care services

HUMAYUN ANJUM, MD, FCCP
CHEST Physician Editorial Board Member

The principal idea behind this article is to summarize comprehensively yet concisely the 2022 CMS updates regarding the critical care services. I would encourage and urge all the members to read this section attentively to stay abreast with all the recent developments.

As a general reminder the two critical care services billing codes for the evaluation and management of the critically ill injured patients are:

99291: First 30-74 minutes

99292: Each additional 30 minutes

And, the five major changes for 2022 as proposed by the CMS for critical care services are:

1. It is allowed for the physicians and APPs in the same specialty to bill concurrent critical care services.

Previously, same specialty practitioners were required to bill and were paid as “one” when multiple practitioners provided services on the same date. Now, they can bill

for critical care services as subsequent care or as aggregate time, and they are highlighted below with examples:

Subsequent care

Initial visit by a provider for 65 minutes (bill as **99291** as the first claim)

Subsequent visit at a later time on the same day for 60 minutes (bill as **99292** x2 as the second claim)

Aggregate time

Time of multiple practitioners in the same specialty can be added to meet **99291** or **99292**. If Practitioner A spends 15 minutes of critical care, then **99291** cannot be billed; but, if Practitioner B spends 30 minutes of critical care, they can bill **99291** with a total time of 45 minutes as one claim

The prerequisites are that the visits are medically necessary, and each visit meets the definition of critical care.

2. Modifier FS needs to be used for split sharing of critical care services.

Previously, critical care services could not be split shared, but it can



Dr. Anjum

be done in 2022. The practitioner who provides the significant portion of the visit needs to bill. A significant or substantive portion is considered to be more than half the cumulative total time of both providers.

Example: The APP spends 20 minutes in critical care services and the physician spends 30 minutes. Total time spent is 50 minutes, and the physician may bill **99291**.

It is crucial to note that each provider needs to document a note for the medically necessary critical care that they personally performed and the time they spent. Additionally, upon review of the medical records, the two providers should be easily identifiable, and the medical record must be signed and dated by the provider who performed the substantive portion and billed.

Lastly, do not forget to submit the modifier FS.

3. Modifier 25 needs to be used to get paid for an ED visit or other E/M service on the same day as critical care.

Previously, hospital ED services were not paid on the same date as critical care by the same provider. But, in 2022, the practitioners may bill for ED visit at the hospital and also for other E/M services on the same day when there is supporting documentation. The practitioners will need to document that the E/M service was provided prior to the time when the patient did not require critical care, that the service was medically necessary, and that the service was separate and distinct with no duplication.

Of note, do not forget to submit the modifier 25.

4. Critical care visits will be separately billable from global surgery when unrelated with the use of modifier FT.

Previously pre- and postoperative critical care was included in the surgical package of many procedures with a global period of 10-90 days, and critical care visits would be paid

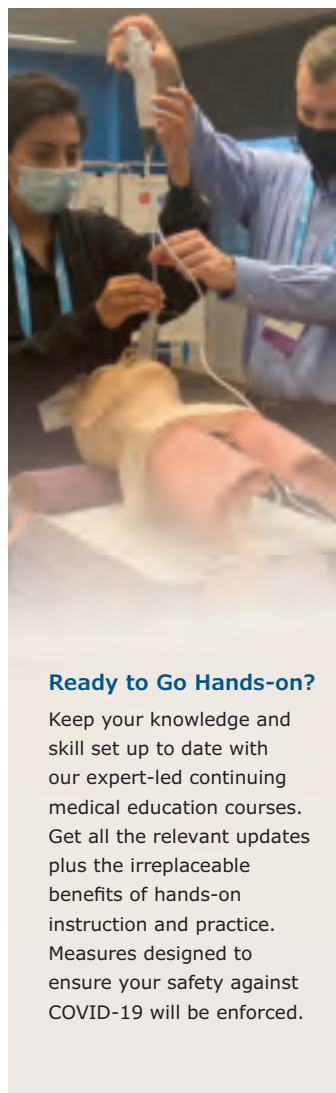
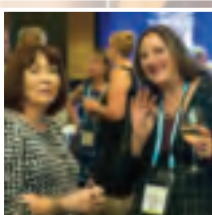
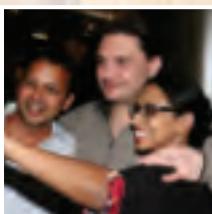


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only if the service was unrelated to the procedure. The concept remains the same in 2022 but, now, new modifier FT will need to be used to report critical care services unrelated to the procedure. Also, the service provided will need to meet the definition of critical care, which is usually above and beyond the procedure performed and should be unrelated to the specific injury or general surgical procedure performed.

5. There will be certain critical care medical record documentation requirements.

It is paramount that each practitioner must document the exact total critical care time and not a range or approximation of time. Additionally, it is equally as important for the documentation to indicate that the services provided were medically

reasonable and necessary. In the setting of split/shared billing, the role of each practitioner should be clearly identifiable (the condition for which each practitioner treated the patient, how the care was concurrent either subsequent or aggregate, and the total time of each practitioner).

Hopefully, this review will provide a good perception for our members in regards to major updates for 2022, help them navigate the regulatory rules, and avoid any unnecessary setbacks. In the upcoming months, we will try to cover some more topics on practice management and administration, such as Medicare Physician Fee Schedule Rule, Hospital Outpatient Prospective Payment Rule, and coding/billing for teaching physicians, telehealth, and pulmonary rehabilitation services. ■

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Editor in Chief

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By Dr. Rajat Suri et al.

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BRIDGING SPECIALTIES™

Timely diagnosis for patients with ILD

Experts in pulmonary and primary care medicine come together to reduce delays in diagnosing complex lung diseases.

Affecting around 400,000 people in the United States, interstitial lung diseases (ILD), like pulmonary fibrosis (PF), present with symptoms that are similar to other more common lung diseases, frequently resulting in misdiagnosis or delayed diagnosis. Some studies show that reaching a proper diagnosis for rarer lung diseases can take upwards of several years.

Despite scientific advancements and increased information available, timely and accurate diagnosis for PF remains a challenge. The course of the disease varies from person to person and can progress rapidly in some cases, increasing the necessity to have the condition diagnosed in its earliest stages. By the time patients learn they have PF, the condition may require reliance on oxygen use and hospitalizations, and it can lead to poor quality of life and a significantly shortened lifespan.

To address this issue, Three Lakes Foundation (TLF) and the American College of Chest Physicians (CHEST) recently announced their collaboration on a multiphase educational initiative led by a steering committee of medical experts aiming to reduce the time it takes to diagnose patients with ILDs like PF. Composed of pulmonologists, primary care physicians, and a nursing professional, the steering committee will work to create materials that will aid in identifying and diagnosing complex lung diseases quicker.

“As a catalyst for change in the PF community, Three Lakes Foundation spoke with patients, health care professionals, physicians, and advocacy groups to advance an understanding of the PF diagnostic experience,” said Dana Ball, executive director for Three Lakes Foundation. “We approached CHEST when it became apparent that primary care physicians could use specific tools to identify high-risk patients with pulmonary conditions. This collaboration is the result of our common need to increase awareness among health care professionals and to improve patient outcomes.”

Members of the expert steering committee include individuals from leading medical institutions, health systems, and organizations across the country:

- **Daniel F. Dilling, MD, FCCP**, Professor of Medicine, Division of Pulmonary and Critical Care, Loyola University Chicago, Stritch School of Medicine, Maywood, IL.
- **Andrew Duggan, MPH**, Patient Engagement and Innovation Leader representing Three Lakes Foundation, Boston, MA.
- **Jessica Glennie, APRN, MSN**, Nurse Practitioner, Interstitial Lung Disease Clinic, Cleveland Clinic, Cleveland, OH.
- **Timothy Hernandez, MD**, Family Medicine Physician, Chief Executive Officer of Entira Family Clinics, San Antonio, TX.
- **Corey D. Kershaw, MD, FCCP**, Associate Professor of Medicine, Division of Pulmonary and Critical Care Medicine, University of Texas Southwestern Medical Center, Dallas, TX.
- **Tejaswini Kulkarni, MD, MPH, FCCP**, Assistant Professor, Director, Interstitial Lung Disease Program, Division of Pulmonary, Allergy and Critical Care Medicine, The University of Alabama at Birmingham, Birmingham, AL.
- **William Lago, MD**, Family Medicine Physician, Wooster Family Health Center, Cleveland Clinic Foundation, Wooster, OH.
- **Andrew H. Limper, MD, FCCP**, Annenberg Professor of Pulmonary Medicine, Professor of Biochemistry and Molecular Biology, Director – Thoracic Disease Research Unit, Mayo Clinic College of Medicine, Rochester, MN.
- **Anoop M. Nambiar, MD, MS, FCCP**, Professor of Medicine, Founding Director of the UT Health San Antonio Center for Interstitial Lung Diseases, Division of Pulmonary and Critical Care Medicine, Department of Medicine, The University of Texas Health Science Center at San Antonio and South Texas Veterans Health Care System, San Antonio, TX.

- **Mary Beth Scholand, MD**, Associate Professor of Internal Medicine, Division of Pulmonary Diseases, Director, Interstitial Lung Program, University of Utah, Salt Lake City, UT

“While interstitial lung diseases do not affect a substantial amount of the population, those touched by the disease are impacted tremendously,” said steering committee member and pulmonologist, Dr. Andrew H. Limper. “Any delay in receiving a diagnosis is time that could be dedicated to finding a treatment therapy that can improve their quality of life. I look forward to the work of this committee helping to shape how patients with ILDs are diagnosed and treated in the future.”

Starting with data-gathering surveys sent to both primary care physicians and pulmonologists, the committee will evaluate the findings to develop tools that can be used to aid in diagnosing complex lung diseases.

“Having experts from both pulmonary and primary care medicine as members of the steering committee is critical,” said steering committee member and family medicine physician, Dr. William Lago. “Patients first see their family medicine or primary care clinicians and, all too often, the most complex lung diseases present in ways that are indistinguishable from more common conditions like asthma and COPD. Bringing together experts in both fields will yield the best results in creating a path to diagnosis.”

Three Lakes Foundation is providing the initial funding for CHEST to begin designing an educational intervention that addresses the gaps in knowledge and practice and will play an active role in overseeing the development of the program.

For more information on the Bridging Specialties™: Timely Diagnosis for Patients With ILD initiative and to sign up for updates, visit info.chestnet.org/bridging-specialties-timely-diagnosis-for-ild-patients. ■

Living and leading with lung disease

Fred Schick and Betsy Glaeser use their diagnoses to help others

Receiving a chronic disease diagnosis can be unHINGING, with a wide range of associated emotions. A patient’s family, physicians, and other health care professionals can provide a source of support, but, often, the strongest support comes from those who can empathize.

Someone who has lived with a diagnosis can provide guidance and empathy at a more personal level because, to them, it is just that – personal. Fred Schick and Betsy

Glaeser have done just that by taking their personal experiences and using them to help others navigate their diagnoses.

Improving patients’ lives is the core focus of the American College of Chest Physicians and the CHEST Foundation. Events like the Belmont Stakes Dinner and Auction provide an opportunity for us to recognize and celebrate powerful stories such as Fred and Betsy’s, while also raising funds to support important

initiatives that will improve patient care. Please consider joining the fight against lung disease by making a donation to the CHEST Foundation today at chestfoundation.org/donate.

Patient advocate – Fred Schick Increasing awareness of pulmonary fibrosis

Fred Schick of the Chicagoland area was diagnosed with idiopathic pulmonary fibrosis (IPF) in 2017 after

years of searching for the root cause of his worsening symptoms.

Fred started experiencing shortness of breath and labored breathing—once to the extent that he needed to be pulled out of the water on vacation despite being an active swimmer. Because Fred was a former cardiac patient, his doctors looked to his heart for a diagnosis.

It wasn’t until his primary care

LIVING *continued on following page*

LIVING *continued from previous page*

physician retired that he started seeing a new doctor who took a different look at his symptoms. In hearing about the strong changes in his exercise endurance, this particular doctor made the decision to refer Fred to a pulmonologist, which ultimately led Fred on the right path to his IPF diagnosis.

Helping others navigate the path

In his 5 years since being diagnosed with IPF, Fred uses his experience to advocate for others living with this illness. Active in support groups for those with IPF, he is especially focused on helping others navigate the first few months after receiving their diagnosis.

Fred knows from experience that receiving the IPF diagnosis is something to come to terms with but encourages others to look to him for an example of how to live with the illness.

“The first thing I say to someone who has been recently diagnosed with pulmonary fibrosis is, ‘Whatever you’ve read on the Internet, don’t believe it, because there are a lot of people who live well beyond the 3- to 5-year expectancy you’ll see in your Google search.’”

“I also encourage everyone to be their own health advocate – tell your doctor if anything in your life is abnormal because you know your body better than anyone.”

Like Fred, many living with IPF wait years for a diagnosis because of the commonality in the way the symptoms present, including shortness of breath, fatigue, difficulty breathing, and others. To address this delay, the American College of Chest Physicians, supported by the CHEST Foundation, partnered with the Three Lakes Foundation to create an initiative led by a steering committee of pulmonologists and primary care physicians to join together to shorten the time to diagnosis for interstitial lung diseases like IPF. Among other activities, the steering committee will work to create tools for physicians to use during patient intake that can more quickly bring IPF into the conversation when it is pertinent.

Patient advocate – Betsy Glaeser

Blazing the trail for NTM

Local to New York, Betsy Glaeser was diagnosed with pulmonary nontuberculous mycobacteria disease (NTM) more than 20 years ago.

Leading up to her diagnosis, Betsy was frequently short of breath with overwhelming fatigue and fevers. She was hospitalized multiple times for pneumonia and treated again and again with short-term standard antibiotics. At the time (1998), there were no clinical programs dedicated to NTM, and when her sputum was tested, it was only for pneumonia.

As a financial consultant required to travel 4 days per week for work, Betsy grew especially concerned about her illness when she developed hemoptysis and began coughing up blood. Lacking local resources, she sought care at the Mayo Clinic in Rochester, Minnesota, where she received her NTM diagnosis.

Based on the severity of her illness and her worsening symptoms, the recommendation of the Mayo Clinic was that she stop working. After 30 years of challenging jobs, quitting was very painful, but a Mayo doctor asked Betsy a very poignant question that resonated with her: “Are you planning to die for your employer?”

With that, she left her job and sought care for her illness. As her NTM developed a second, more resistant strain associated with her disease, requiring daily, constant treatment, Betsy was fortunate to be

accepted into the National Institutes of Health NTM protocol, which has directed her care, coordinated with NYU-Langone.

Despite the challenges of having NTM, Betsy maintains an active and enriching life.

Leading with experience

Betsy uses her diagnosis and her experience with NTM to help others who are hearing their diagnoses for the first time. She serves as a charter member and co-leader of a New York NTM patient support group and serves as a member of the NTM Info & Research (NTMir) Board of Directors.

Her goal is to ensure that no one living with NTM feels alone or frightened.

“Not so long ago – and now, too, even – there were doctors who did not know how to treat NTM,” says Betsy. “But, it has really gotten better – as I’ve progressed through all of my medications and lived with this disease, NTM has progressed as well. I hope I helped expand NTM knowledge with my lived experiences, but I’ve been so fortunate to receive medical care from those doctors who knew the most about NTM.” ■

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PULMONARY PERSPECTIVES®

Updates on eosinophilia in asthma

BY ERIN N. HABER, MD, AND DANIEL B. JAMIESON, MD

Our understanding of asthma endotypes and phenotypes has grown substantially in the last decade. Endotype-targeted therapy has become a foundation of management, and classification of patients during initial assessment is extremely important. The use of history, laboratory data, and pulmonary function testing together help to categorize our patients and help guide therapy. One lab test, that of sputum or blood eosinophils, facilitates categorization and has been evaluated for its ability to determine response to medications and predict exacerbations.

In particular, eosinophilia has been extensively studied in severe asthma and is associated with type 2 inflammation. The 2021 GINA guidelines describe type 2 inflammation as characterized by cytokines (especially IL-4, IL-5, and IL-13). “T2-high patients” tend to have elevated blood or sputum eosinophil counts and elevated fractional concentration of exhaled nitric oxide (FENO) and are more likely to respond to biologic therapy. (Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021).

However, what about patients with more mild-to-moderate asthma? Two recent studies have asked this question. In 2020, Pavord and colleagues performed a prespecified secondary subgroup analysis on an open-label randomized control trial comparing prn salbutamol alone to budesonide and as needed salbutamol to as needed budesonide-formoterol. The population was 675 adults with mild asthma receiving only as needed short acting beta-agonists (SABA) at baseline. The primary outcome was annual rate of asthma exacerbation, and whether it was different based on blood eosinophil count, FENO or a composite of both. They had several interesting findings. First, for patients only on an as needed SABA, the proportion having a severe exacerbation increased progressively with increasing blood eosinophil count. Second, inhaled corticosteroids (ICS) plus as needed SABA were more effective than SABA alone in patients

with a blood eosinophil count of ≥ 300 cells/ μL , both in terms of total exacerbations and severe exacerbations. The effects of budesonide-formoterol on exacerbations, however, was not associated with blood eosinophil count or FENO. This last point is particularly interesting in light of GINA guidelines that prioritize this combination (Pavord ID et al. *Lancet Respir Med*. 2020;8[7]:671-80).

More recently, a prespecified secondary analysis of the SIENA trial looked at 295 subjects with mild persistent asthma (237 adults aged 18+, and 58 adolescents aged 12-17). The primary outcome was a composite of asthma control (treatment failure, asthma control days, and FEV₁). They found that sputum eosinophil levels, blood eosinophil levels, and FENO all predicted response to ICS in adults; however, the area under the receiver operative characteristic curve (AUC) was less than 0.7 for each of these findings, which was below the threshold for acceptability. A blood eosinophil count of ≥ 100 cells/ μL offered 87% sensitivity and 17% specificity for response to ICS (Krishnan JA et al. *Ann Am Thorac Soc*. 2022;19[3]:372-80).

What does this tell us? Blood eosinophil count may help determine who will respond to ICS, and there remains utility in assessing blood eosinophil count in severe asthma for determining candidacy for biologic therapies. However, the overall utility of blood eosinophils in mild to moderate asthma is not as clear.

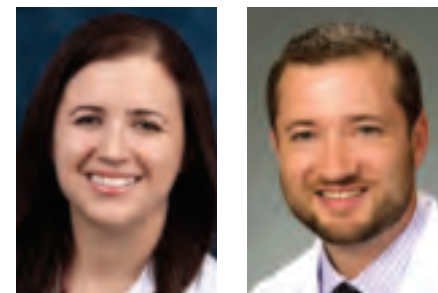
But, are we asking the right questions? Many studies look at a single blood eosinophil level, either at a single point in time, a baseline level, or a highest level over a specific time period. But do eosinophil counts vary over time?

A 2018 single-center study initially asked this question. The authors evaluated blood eosinophil levels in 219 adult patients at the NYU/Bellevue Hospital Asthma Clinic over a 5-year period. They found that individual patients had variable eosinophil levels. For example, only 6% (n=13) of patients had levels consistently above 300 cells/ μL , but nearly 50% (n=104) had at least one level above 300. The degree of variability was then assessed by K-mean clustering

yielding three clusters. Cluster 2 had the largest variability in blood eosinophil counts and a slightly higher absolute eosinophil level. While not significant, there was a suggestion of worse asthma control with more hospitalizations and more prescriptions for multiple controllers in this cluster with more variability. Clearly, this warranted further study (Rakowski E et al. *Clin Exp Allergy*. 2019;49[2]:163-70).

Variability was re-examined more recently in 2021. A post hoc analysis of two phase III clinical trials from the reslizumab BREATH program looked at eosinophil counts in the 476 patients randomized to receive placebo during the 52-week study. These patients did have eosinophilic asthma by definition and had to have an elevated eosinophil count >400 cells/ μL over the 4-week enrollment period to enter the study. However, 124 patients (26.1%) had an eosinophil level <400 cells/ μL immediately before the first dose of placebo. The primary outcome was variability in blood eosinophil count. Of patients who started with serum eosinophils <400 , 27% to 56% of patients shifted to the ≥ 400 cells/ μL category during the treatment period (this wide range is across three categories of low “baseline” blood eosinophil count; <150 , 150 to 300, and 300 to 400). On the contrary, patients who started with eosinophils ≥ 400 cells/ μL tended to stay at that level. The variability is reduced by taking two to three repeat measurements at baseline (Corren et al. *J Allergy Clin Immunol Pract*. 2021;9[3]:1224-31).

Does this variability have clinical significance? A recent retrospective cohort study looked at 10,059 stable adult patients with asthma from the MAJORICA cohort in Spain, compared with 8,557 control subjects. The primary outcome was total blood eosinophil count and an “eosinophil variability index” (EVI) where $\text{EVI} = (\text{Eosmax} - \text{Eosmin} / \text{Eosmax}) \times 100\%$. They found that an elevated EVI was associated with hospitalization, more so than maximum eosinophil count or any other eosinophil count variable, with an odds ratio of 3.18 by univariate regression (2.51 by multivariate). They also found that patients with an EVI $\geq 50\%$ were twice as



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likely to be hospitalized or visit the ED than those with a lower EVI (Toledo-Pons N et al. *Ann Am Thorac Soc*. 2022;19[3]:407-14). These results are very interesting and merit further research.

So, what to do with this information? We know that patients with peripheral eosinophilia and severe asthma symptoms are candidates for biologic therapy. They are also more likely to respond to steroids, although the utility of this assessment alone in mild to moderate asthma is less clear. It does seem that more variability in eosinophils over time may be linked to more difficult-to-treat asthma.

Should you check eosinophils in your patients with asthma? GINA 2021 guidelines say to consider it, and list blood eosinophilia as a risk factor for future exacerbation, even if patients have few asthma symptoms. They also say to repeat blood eosinophils in patients with severe asthma, if the level is low at first assessment, based on the studies discussed above. We would agree. We also see the blood eosinophil count as one part of a clinical assessment of a patient’s overall asthma control – even if the patient has mild symptoms.

More study on variability is welcome. ■

In memoriam

CHEST has been informed of the following deaths of CHEST members. We remember our colleagues and extend our sincere condolences.

Edward C. Rosenow III, MD, Master FCCP (Full obit in March 2022 issue)
Jack Stanko, MD, MS, FCCP
Arthur S. Turetsky, MD, FCCP

CRITICAL CARE COMMENTARY

Pneumothorax, pneumomediastinum, and subcutaneous emphysema: The many faces of COVID-19 ARDS

BY HAFSA ABDULLA, MD

I recall early in the pandemic being called to the bedside to examine an acutely decompensating patient with COVID-19. This was a 33-year-old, previously healthy woman, admitted to the medical ICU with hypoxemic respiratory failure requiring mechanical ventilation and undergoing treatment for severe acute respiratory distress syndrome (ARDS). I quickly realized she was seconds away from an arrest. As I examined her, one thing caught my eye. Her airway pressures had skyrocketed over the past few minutes. Could it be? I

Perhaps one of the main reasons patients with COVID-19 ARDS are at an increased risk for developing certain complications, such as pneumothorax, is inherent to the unique type of alveolar injury sustained.

thought to myself as I reached for the ultrasound that confirmed my suspicions, tension pneumothorax. One emergent needle decompression and chest tube later and she survived, only to die a week later from overwhelming hypoxemia.

As we reflect on these past 26 months, we recall that caring for the critically ill patient with COVID-19 has posed numerous challenges. One challenge was the overwhelming incidence of the so-called “barotrauma-related complications.” However, we also recall seeing many patients develop such complications while receiving supplemental noninvasive forms of respiratory support. Perhaps, this is in agreement with prior literature that specifically discusses the presence of air outside the tracheobronchial tree and how it does not always correlate with high airway pressure and high tidal volumes, refuting the argument that these complications always fall under the umbrella of barotrauma. We will discuss these complications and attempt to shed light on the

potential variables associated with their development.

The development of pneumothorax is a well-recognized complication associated with ventilator-dependent ARDS thought to be a form of barotrauma, with some reports indicating an incidence of 48.8% (Gattinoni L et al. *JAMA*. 1994;271[2]:1772-9) and a significantly increased mortality rate compared with postprocedural pneumothorax in the ICU (Chen K et al. *Chest*. 2002;122[2]:678-83). The incidence of such complications in COVID-19-related ARDS is significantly higher than in ARDS from other causes (Belletti A et al. *Crit Care Med*. 2022;50[3]:491-500), with a mortality rate approaching 100% (Chong WH et al. *Heart Lung*. 2021;50[5]:599-608).

So why are patients with COVID-19 developing these complications at a higher rate? When we examine the literature, we note that Leisman and colleagues (*Am J Respir Crit Care Med*. 2022;205[5]:507-19) describe higher baseline markers of alveolar damage, including RAGE (receptor for advanced glycation end-products) in mechanically ventilated patients with COVID-19 vs patients requiring mechanical ventilation for other causes. This poses a question that perhaps one of the main reasons patients with COVID-19 ARDS are at an increased risk for developing certain complications, such as pneumothorax, is inherent to the unique type of alveolar injury sustained with the infection. The authors also note that alveolar markers of injury had moderate to poor discrimination for invasive ventilation early in the disease and diminished over time in both ventilated patients receiving lung protective ventilation strategy and those spontaneously breathing. Likewise, this important finding suggests that the development of pneumothorax in patients with COVID-19 may not be entirely related to barotrauma.

Another phenomenon worth investigating is the development of pneumomediastinum and subcutaneous emphysema, with a reported seven-fold increased

risk of development in patients with COVID-19. Lemmers and colleagues (*ERJ Open Res*. 2020;6[4]:00385-2020) found no statistically significant difference in PEEP, plateau pressure, ratio of tidal volume to ideal body weight, or compliance between patients who developed this complication and those who did not, again, signifying that perhaps there is more to the story here.

Belletti and colleagues (*J Cardiothorac Vasc Anesth*. 2021;35[12]:3642-51) published an article examining the predictors of pneumothorax and pneumomediastinum in patients with COVID-19. The authors found that the time from symptom onset to intubation and the total bilirubin level were the only two significant predictors for the development of these complications. They explain that longer time

As we phase out of the pandemic and move into an epidemic, future research direction will likely focus on some of the more unusually common complications.

from symptom onset to intubation likely increased the risk for self-induced lung injury, inflammation, and fibrosis, contributing to the development of such complications. It is important to note that the authors did not find a significant difference in the ventilation parameters between patients who developed pneumothorax/pneumomediastinum and those who did not.

In our institute, we examined a total of 102 patients admitted to the ICU with COVID-19 ARDS over a 3-month period from March 2020 to May 2020. We identified a total of 36 patients who developed pneumothorax, pneumomediastinum, and/or subcutaneous emphysema. We compared these subjects to age- and gender-matched control subjects. Higher age was associated with an increased risk of development



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of these complications, whereas the presence of diabetes mellitus, hypertension, and chronic kidney disease at baseline was associated with lower risk. This translated into lower mSOFA scores in our subjects as opposed to the control subjects mainly due to higher creatinine levels at baseline in the control group, skewing our data and indicating that some predictive criteria may not reflect the underlying disease severity and risk for development of such complications. In analyzing our ventilator data and comparing the subjects to the control group, we found no differences in mode of ventilation, set tidal volumes, or PEEP levels between the two. The subjects had significantly higher peak airway pressures, lower compliance, and longer ventilator days. Intubation was needed significantly earlier in the subjects compared with the control group with a median of 2 days vs 6 days from admission. Our data are in concordance with prior published reports and are set to be presented in abstract form this May.

COVID-19 remains a challenging disease with the potential for morbid outcomes. As we phase out of the pandemic and move into an epidemic, future research direction will likely focus on some of the more unusually common complications, such as the ones presented here. ■

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