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Climate change is leading to new diseases and exacerbations and increases in chronic illnesses such as asthma and COPD.

The breathtaking effects of climate change

BY NEIL OSTERWEIL

To see the harmful effects of climate change firsthand, you need look no farther than the nearest pulmonary clinic.

The causes and effects are unmistakable: pollen storms leading to allergy sufferers flooding into allergists' offices; rising air pollution levels increasing risk for obstructive airway diseases, cardiopulmonary complications, and non-small cell lung cancer; melting snowpacks and atmospheric rivers inundating neighborhoods and leaving moldy debris and incipient fungal infections in their wake.

"The reason why we think climate change is going to change the type of disease patterns and

the severity of illness that we see in patients with respiratory diseases is that it changes a lot of the environment as well as the exposures," said Bathmapriya Balakrishnan, BMedSci, BMBS, from the section of Pulmonary, Critical Care, and Sleep Medicine in the department of medicine at West Virginia University, Morgantown.

"What we're going to see is not just new diseases but also exacerbation of chronic diseases, things like asthma [and] COPD. And there's also concern that patients who are otherwise healthy, because they now have more exposures that are due to climate change, can then develop these diseases," she said in an interview.

Ms. Balakrishnan is the lead author of a

CLIMATE CHANGE // continued on page 7

Perioperative durvalumab for NSCLC: Practice changing?

BY NEIL OSTERWEIL

Systemic therapy prior to surgery has been slow to catch on in the treatment of patients with resectable non-small cell lung cancer (NSCLC), primarily out of concern that neoadjuvant therapy could delay surgery or render patients ineligible for resection.

That may change, however, in light of new data from the phase 3 AEGEAN trial.

AEGEAN showed that neoadjuvant immunotherapy with durvalumab (Imfinzi) and chemotherapy followed by adjuvant durvalumab was associated with significant improvements in pathologic complete response rates and event-free survival, compared with neoadjuvant placebo plus chemotherapy followed by adjuvant placebo, and it did not affect patients' ability to undergo surgery.

The event-free survival benefit among patients who received durvalumab translated to a 32% reduction in the risk of recurrence, recurrence precluding definitive surgery, or death, according to John V. Heymach, MD, who reported in an oral abstract session at the annual meeting of

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INSIDE HIGHLIGHT



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the American Association for Cancer Research.

“Perioperative durvalumab plus neoadjuvant chemotherapy is a potential new treatment for patients with resectable non-small cell lung cancer,” said Dr. Heymach, chair of thoracic/head and neck medical oncology at the University of Texas MD Anderson Cancer Center in Houston.

The AEGEAN findings confirm the benefits of neoadjuvant immunotherapy that were first seen on a large scale in the Checkmate 816 study, which was reported at last year’s AACR annual meeting.

In CHECKMATE 816, adding the immune checkpoint inhibitor nivolumab along with chemotherapy in the neoadjuvant setting resulted in significantly longer event-free survival and a 14-fold greater likelihood of a pathologic complete response compared with chemotherapy alone.

“I’m impressed by the fact that we now have a second study that shows the benefits of immunotherapy in the neoadjuvant setting, along with several adjuvant studies,” the invited discussant, Roy S. Herbst, MD, PhD, deputy director of the Yale Cancer Center, New Haven, Conn., said in an interview.

“There’s no doubt that in early lung cancer – resectable disease – immunotherapy is part of the equation,” he added.

For the current study, Dr. Heymach and colleagues recruited 802 patients from 222 sites in North and South America, Europe, and

Asia. The patients had NSCLC and were treatment-naive, regardless of programmed cell death–ligand-1 (PD-L1) expression.

After excluding patients with targetable EGFR/ALK alterations, the team randomly allocated 740 patients who had good performance status (ECOG 0 or 1) to receive either neoadjuvant chemotherapy plus adjuvant immunotherapy or neoadjuvant chemotherapy alone. Overall, 77.6% of patients in the treatment arm and 76.7% of patients in the placebo arm underwent surgery following neoadjuvant therapy.

At the trial’s first planned interim analysis, for patients assigned to preoperative durvalumab plus platinum-based chemotherapy and postoperative durvalumab, the 12-month event-free survival rate was 73.4%, compared with 64.5% for patients who received chemotherapy alone before and placebo after surgery (stratified $P = .003902$).

The other endpoint, pathologic complete response, was observed in 17.2% of patients in the durvalumab arm, vs. 4.3% in the control arm – a 13% difference ($P = .000036$). Major pathologic responses, a secondary efficacy endpoint, were seen in 33.3% and 12.3% of patients, respectively.

The benefits of durvalumab were consistent across all subgroups, including those based on age at randomization, sex, performance status, race, smoking, histology (squamous

DURVALUMAB continued on following page

“There’s no doubt that in early lung cancer – resectable disease – immunotherapy is part of the equation.”

Russell Miller, MD, comments: The preliminary results from the AEGEAN trial are indeed a promising development for those involved in cancer care. After the groundbreaking results from the CHECKMATE 816 study, there might have been some doubt due to the extraordinary outcomes being observed in just one trial.

However, the AEGEAN trial, which replaced nivolumab with durvalumab, strengthens the belief that immunotherapy, when combined appropriately with conventional chemotherapy, can have a significant effect on the treatment of high-risk, potentially operable lung cancers.

The repeated positive results from both trials provide additional evidence of the potential advantages of using neoadjuvant immunotherapy in the battle against lung cancer.

Dr. Miller is a member of the CHEST Physician Editorial Board.



CRITICAL CARE COMMENTARY

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comprehensive, evidence-based review focused on the effects of climate change and air pollution across the spectrum of pulmonary disorders. The review is published online ahead of print in the journal *Chest* (2023 Apr 10. doi: 10.1016/j.chest.2023.04.009).

“As pulmonologists, understanding and improving awareness of the adverse effects of climate change and air pollution are crucial steps. To inform health care providers of evidence-based methods and improve patient counseling, further research regarding measures that limit exposure is needed. Empowering patients with resources to monitor air quality and minimize exposure is a key preventative measure for decreasing morbidity and mortality while improving quality of life,” Ms. Balakrishnan and colleagues write.

Similarly, in a statement on the effects of climate change on respiratory health, the American Public Health Association succinctly summarized

“Empowering patients with resources to monitor air quality daily, in inclement weather, and during disasters would help minimize exposure and thus improve overall health.”

the problem: “Warmer temperatures lead to an increase in pollutants and allergens. Poor air quality leads to reduced lung function, increased risk of asthma complications, heart attacks, heart failure, and death. Air pollution and allergens are the main exposures affecting lung and heart health in this changing climate.”

Early spring

Stanley Fineman, MD, MBA, a past president of the American College of Allergy, Asthma, & Immunology and an allergist in private practice in Atlanta, has seen firsthand how global warming and an earlier start to spring allergy season is affecting his patients.

“The season, at least in our area metro Atlanta, started earlier and has been lasting longer. The pollen counts are very high,” he told this news organization.

“In February we started seeing pollen counts over 1,000 [grams per cubic meter], which is unheard of, and in March about half the days we counted levels that were over 1,000, which is also unheard of. In April it was over 1,000 almost half the days.”

Dr. Fineman and colleagues both in Atlanta and across the country have reported sharp increases in the proportion of new adult patients and in existing patients who have experienced exacerbation of previously mild disease.

“Probably what’s happened is that they may have had some allergic sensitivity that resulted in milder manifestations, but this year they’re getting major manifestations,” Dr. Fineman said.

In a 2014 article in the journal *European Respiratory Review* (Jun;23[132]:161-9), Gennaro D’Amato, MD, from High Speciality Hospital Antonio Cardarelli, Naples, Italy, and colleagues outlined the main effects of climate on pollen levels: “1) an increase in plant growth and faster plant growth; 2) an increase in the amount of pollen produced by each plant; 3) an increase in the amount of allergenic proteins contained in pollen; 4) an increase in the start time of plant growth and, therefore, the start of pollen production; 5) an earlier and longer pollen season; 6) change in the geospatial distribution of pollen, that is plant ranges and long-distance atmospheric transport moving polewards,” they write.

Bad air

In addition to pollen, the ambient air in many places is increasingly becoming saturated with bioallergenic proteins such as bacteria, viruses, animal dander, insects, molds, and plant species, Ms. Balakrishnan and colleagues noted. Adding that “atmospheric levels of carbon dioxide have also been found to increase pollen productivity. These changes result in greater over-the-counter medication use, emergency department visits, and outpatient visits for respiratory illnesses.”

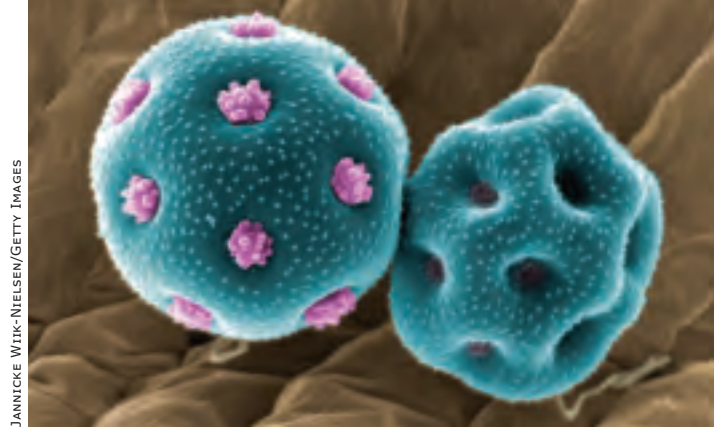
The rash of violent storms that has washed over much of the United States in recent months is also likely to increase the incidence of so-called “thunderstorm asthma,” caused when large quantities of respirable particulate matter are released before or during a thunderstorm.

Air pollution from the burning of carbon-based fuels and from wildfires sparked by hotter and drier conditions increase airborne particulate matter that can seriously exacerbate asthma, COPD, and other obstructive airway conditions.

In addition, exposure to particulate matter has been implicated as a possible cause of non-small cell lung cancer in persons who have never smoked.

Critical care challenges

Among the myriad other effects of climate change postulated in evidence enumerated by Ms. Balakrishnan and colleagues are chest infections and pleural diseases, such as aspergillosis infections that occur after catastrophic flooding;



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Image shows hydrated and de-hydrated pollen grains (*Stellaria graminea*), a common allergen.

increased incidence of *Mycobacterium avium* complex infections and hypersensitivity pneumonitis; increased demands on critical care specialists from natural disasters; pollution-induced cardiac arrest; and heat prostration and heat stroke from increasingly prevalent heat waves.

The reviewers also examined evidence suggesting links between climate change and pulmonary hypertension, interstitial lung disease, sleep disorders, and occupational pulmonary disorders.

Power to the patients

“Pulmonologists should counsel patients on ways to minimize outdoor and indoor pollution, using tight-fitting respirators and home air-purifying systems without encroaching on patients’ beliefs and choices,” the authors advise.

“Empowering patients with resources to monitor air quality daily, in inclement weather, and during disasters would help minimize exposure and thus improve overall health. The pulmonologist can play an important role in emphasizing the impact of climate change on pulmonary disorders during patient care encounters,” they write.

Ms. Balakrishnan adds that another important mitigation measure that can be taken today is education.

“In medical school we don’t really learn about the impact of climate change – at least in my generation of physicians, climate change or global warming weren’t part of the medical curriculum – but now I think that there’s a lot of advocacy work being done by medical students who actually want more education on climate change and its effects on pulmonary diseases,” she said.

The study by Ms. Balakrishnan and colleagues was unfunded. Ms. Balakrishnan reports no relevant financial relationships. Co-author Mary-Beth Scholand, MD, has received personal fees from serving on advisory boards and speakers bureaus for Genentech, Boehringer Ingelheim, VeracYTE, and United Therapeutics. Co-author Sean Callahan, MD, has received personal fees for serving on advisory boards for Gilead and Boehringer Ingelheim. Dr. Fineman reports no relevant financial relationships. ■

DURVALUMAB continued from previous page

vs. nonsquamous), disease stage, baseline PD-L1 expression, and planned neoadjuvant agent.

The safety profile of durvalumab plus chemotherapy was manageable, and the addition of durvalumab did not affect patients’ ability to complete four cycles of neoadjuvant chemotherapy, Dr. Heymach said.

Are these data practice changing? Dr. Herbst gave a “resounding ‘Yes.’”

But while the AEGEAN protocol represents a new standard of care, it can’t yet be labeled the standard of care, Dr. Herbst explained.

Dr. Herbst emphasized that, because this regimen was not compared against the current standard

of care, it’s “impossible to determine” whether this is indeed the new standard.

“The data are early, and additional maturity is needed to better understand the benefit of the extra adjuvant therapy, and we’ll await the survival results,” he said.

It will also be important to analyze why some patients have only

minor responses with the addition of durvalumab and whether there are resistance mechanisms at play for these patients. That would be a great setting “to start to test new therapies in a personalized way,” Dr. Herbst said.

Dr. Heymach and Dr. Herbst disclosed ties to AstraZeneca, which funded the study. ■

Fatigue is a monster for patients with pulmonary disease

BY AARON B. HOLLEY, MD, FCCP

If you're looking for it, you'll find fatigue almost everywhere. It's so common that it hides in plain sight, never dealt with because it's present for good reason: the inevitable consequence of age, whatever disease you're treating, poor lifestyle choices, and the daily grind of 21st-century life. Its impact is so ubiquitous and pernicious that it's considered acceptable.

Is it though? After all, fatigue can be debilitating. Not every symptom is worthy of a chronic syndrome bearing its name. Furthermore, what if its relationship to the disease you're treating is bidirectional? What if we actually paid attention, asked about it, and expended energy trying to relieve it? Could we improve quality of life and other outcomes too?

Outside of sleep medicine, I see little focus on fatigue among pulmonologists. This despite the existing data on fatigue related to sarcoidosis, chronic obstructive pulmonary disease (COPD), and interstitial lung disease. Even when we do pay it lip service, "addressing" fatigue or sleep is essentially a euphemism for ordering a sleep study.

As with fatigue, if you look for obstructive sleep apnea, it'll be there, although with OSA, it's related to the incredibly low, nonevidence-based threshold the American Academy of Sleep Medicine has established for making the diagnosis. With continuous positive airway pressure (CPAP) in hand, the patient has a new disease to worry about and a difficult behavioral change (wearing, cleaning, and resupplying their CPAP equipment) to make. Too often, the CPAP isn't used – or is – and the fatigue persists. But it's okay, because we

Sleep, exercise, and nutrition require time for counseling and a behavior change for the physician and patient. Both are in short supply, and commitment is always ephemeral.

followed somebody's guideline.

The American Thoracic Society just published a research statement on cancer-related fatigue. It is comprehensive and highlights the high prevalence and poor recognition of cancer-related fatigue. The authors note that, among cancers, those of the lung are associated with a higher comorbid disease burden, older age, and cigarette smoking. All these factors make patients with lung cancer particularly prone to fatigue. Interactions between these factors, lung cancer histology, and specific chemotherapy regimens are poorly understood. True to its title, the "research statement" serves more as a call to action than an evidence-based blueprint for diagnosis and management.

The cancer-related fatigue data that do exist suggest treatment starts with recognition followed by a focus on sleep, exercise, and nutrition. This should surprise no one. The data on fatigue in general (not specific to cancer-related fatigue) show that, although fatigue is not synonymous with poor quality or insufficient sleep, sleep is usually a major factor. The cancer-related conditions affecting sleep include anxiety, depression, insufficient sleep, insomnia, medication side effects, and OSA. The intersecting web is complex, but across underlying conditions (cancer or otherwise), the quickest most efficient method for mitigating fatigue is optimizing sleep.

Exercise and nutrition are also important. Again, across disease processes (interstitial lung disease, COPD, lung cancer, and so on), no drug comes close to aerobic exercise for reducing symptoms, including fatigue. If an exercise prescription could be delivered in pill-form, it'd be a blockbuster. But it can't be, and the ATS lung



Dr. Holley is professor of medicine at Uniformed Services University, Bethesda, Md., and a pulmonary/sleep and critical care medicine physician at MedStar Washington Hospital Center in Washington. He disclosed ties with Metapharm, CHEST, and WebMD.

cancer-related fatigue research statement nicely outlines the evidence for increased activity levels and the barriers to obtaining support and compliance. As is the case with exercise, support for improving nutrition is limited by cost, access, and patient education.

Perhaps most importantly, sleep, exercise, and nutrition require time for counseling and a behavior change for the physician and patient. Both are in short supply, and commitment is always ephemeral. Incentivization could perhaps be re-structured, but the ATS document notes this will be challenging. With respect to pulmonary rehabilitation (about 50% of patients with lung cancer have comorbid COPD), for example, reimbursement is poor, which serves as a disincentive. Their suggestions? Early integration and repeated introduction to rehabilitation and exercise concepts. Sounds great.

In summary, in my opinion, fatigue doesn't receive the attention level commensurate with its impact. It's easy to understand why, but I'm glad the ATS is highlighting the problem. Unbeknownst to me, multiple cancer guidelines already recommend screening for fatigue. The recent sarcoidosis treatment guideline published by the European Respiratory Society dedicated a PICO (Patients, Intervention, Comparison, Outcomes) to the topic and recommended exercise (pulmonary rehabilitation). That said, consensus statements on COPD mention it only in passing in relation to severe disease and end-of-life care, and idiopathic pulmonary fibrosis guidelines ignore it entirely. So, recognition is improving, but we've got ways to go. ■

PULMONOLOGY

General, abdominal obesity linked to respiratory disease

BY TERRY L. KAMPS, PHD

A recent Swedish study found that both abdominal and general obesity were independently associated with respiratory illnesses, including asthma and self-reported chronic obstructive pulmonary disease.

Relationships between respiratory conditions with characterized obesity types in adults were assessed using self-report surveys from participants originally enrolled in the European Community Respiratory Health Survey (ECRHS) investigating asthma, allergy, and risk factors. The Respiratory Health in Northern

Europe (RHINE) III provides a second follow-up substudy of ECRHS focused on two forms of obesity associated with respiratory illnesses.

Obesity is a characteristic risk factor linked to respiratory ailments such as asthma and COPD. High body mass index (BMI) and waist circumference (WC) provide quantitative measurements for defining conditions of comprehensive general and abdominal obesity, respectively.

Although both types of obesity have been associated with asthma incidence, studies on their independent impact on this disease have been limited. Previous reports on abdominal obesity associated with

asthma have been inconsistent when considering sexes in the analysis. Additionally, COPD and related outcomes differed between abdominal and general obesity, indicating a need to discover whether self-reported WC abdominal obesity and BMI-based general obesity are independently associated with respiratory symptoms, early- and late-onset asthma, COPD, chronic bronchitis, rhinitis, and sex, Marta A. Kisiel, MD, PhD, of the department of environmental and occupational medicine, Uppsala University, Sweden, and colleagues write.

In a prospective study published in the journal *Respiratory Medicine*

(2023 Mar 16. doi: 10.1016/j.rmed.2023.107213). the researchers report on a cross-sectional investigation of responses to a questionnaire similar to one utilized 10 years earlier in the RHINE II study. Questions required simple yes/no responses that covered asthma, respiratory symptoms, allergic rhinitis, chronic bronchitis, and COPD. Additional requested information included age of asthma onset, potential confounding variables of age, smoking, physical activity, and highest education level, weight and height for BMI calculation, and WC measurement

OBESITY continued on following page

Asthma tied to increased risk for multiple cancers

BY MEGAN BROOKS

People with asthma have an elevated risk for a variety of cancers other than lung cancer, including melanoma as well as blood, kidney, and ovarian cancers, new research suggests.

But, the authors found, treatment with an inhaled steroid may lower that risk, perhaps by keeping inflammation in check.

“Using real-world data, our study is the first to provide evidence of a positive association between asthma and cancer risk in United States

patients,” Yi Guo, PhD, with the University of Florida, Gainesville, said in a news release.

The study was published online in *Cancer Medicine* (2023 Mar 31. doi: 10.1002/cam4.5875).

The relationship between chronic inflammation and cancer remains a key area of exploration in cancer etiology. Data show that the risk for developing cancer is higher in patients with chronic inflammatory diseases, and patients with asthma have complex and chronic inflammation. However, prior studies exploring a possible link between asthma and cancer have yielded mixed results.

To investigate further, Dr. Guo

and colleagues analyzed electronic health records and claims data in the OneFlorida+ clinical research network for roughly 90,000 adults with asthma and a matched cohort of about 270,000 adults without asthma.

Multivariable analysis revealed that adults with asthma were more likely to develop cancer, compared with peers without asthma (hazard ratio, 1.36), the investigators found.

Adults with asthma had an elevated cancer risk for 5 of the 13 cancers assessed, including melanoma (HR, 1.98), ovarian cancer (HR, 1.88), lung cancer (HR, 1.56), kidney cancer (HR, 1.48), and blood cancer (HR, 1.26).

Compared with adults without asthma, those with asthma who did not treat it with an inhaled steroid had a more pronounced overall cancer risk, compared with those who were on an inhaled steroid (HR, 1.60 vs. 1.11).

For specific cancer types, the risk was elevated for 9 of 13 cancers in patients with asthma not taking an inhaled steroid: prostate (HR, 1.50), lung (HR, 1.74), colorectal (HR, 1.51), blood (HR, 1.44), melanoma (HR, 2.05), corpus uteri (HR, 1.76), kidney (HR, 1.52), ovarian (HR,

2.31), and cervical (HR, 1.46).

In contrast, in patients with asthma who did use an inhaled steroid, an elevated cancer risk was observed for only two cancers, lung cancer (HR, 1.39) and melanoma (HR, 1.92), suggesting a potential protective effect of inhaled steroid use on cancer, the researchers said.

Although prior studies have shown a protective effect of inhaled steroid use on some cancers, potentially by reducing inflammation, the “speculative nature of chronic inflammation (asthma as a common example) as a driver for pan-cancer development requires more investigation,” Dr. Guo and colleagues cautioned.

And because of the observational nature of the current study, Dr. Guo’s team stressed that these findings do not prove the presence of a causal relationship between asthma and cancer.

“More in-depth studies using real-world data are needed to further explore the causal mechanisms of asthma on cancer risk,” the researchers concluded.

Funding for the study was

The risk was elevated for 9 of 13 cancers in patients with asthma not taking an inhaled steroid: prostate, lung, colorectal, blood, melanoma, corpus uteri, kidney, ovarian, and cervical.



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provided in part by grants to the researchers from the National Institutes of Health, National Cancer Institute, National Institute on Aging, and the Centers for Disease Control and Prevention.

This project was supported by the Cancer Informatics Shared Resource in the University of Florida Health Cancer Center. The authors have disclosed no conflicts of interest. ■

OBESITY continued from previous page

with instructions and a provided tape measure.

The population of the RHINE III study conducted from 2010 to 2012 was composed of 12,290 participants (53% response frequency) obtained from a total of seven research centers located in five northern European countries.

Obesity categorization classified 1,837 (6.7%) participants as generally obese based on a high BMI ≥ 30 kg/m² and 4,261 (34.7%) as abdominally obese by WC measurements of ≥ 102 cm for men and ≥ 88 cm for women. Of the 4,261 total participants, 1,669 met both general and abdominal obesity criteria. Mean age was in the low 50s range and the obese population consisted of more women than men.

Simple linear regression revealed that BMI and WC were highly correlated, and both were associated with tested respiratory conditions when adjusted for confounding variables. Differences with respect to WC and BMI were independently

associated with most of the examined respiratory conditions when WC was adjusted for BMI and vice versa. Neither early-onset asthma nor allergic rhinitis were associated with WC, BMI, or abdominal or general obesity.

A significantly high proportion of individuals with general and abdominal obesity experienced a variety of defined respiratory symptoms, and asthma, chronic bronchitis, or COPD. An independent association of abdominal obesity (with or without general obesity) was found to occur with respiratory symptoms, asthma, late-onset asthma, and chronic bronchitis.

After adjusting for abdominal obesity, general obesity showed an independent and significant association with respiratory symptoms, asthma, adult-onset asthma, and COPD. An analysis stratified by sex indicated a significant association of abdominal and general obesity with asthma in women presented as an odds ratio of 1.56 (95% confidence interval,

1.30-1.87) and 1.95 (95% CI, 1.56-2.43), respectively, compared with men, with an OR of 1.22 (95% CI, 0.97-3.17) and 1.28 (95% CI, 0.97-1.68), respectively. The association of abdominal and general obesity with COPD was also stronger in women, compared with men.

The researchers conclude that “both general and abdominal obesity [were], independent of each other, associated with respiratory symptoms in adults.” There is also a distinct difference between women and men for the association of self-reported asthma and COPD with abdominal and general obesity.

The large randomly selected sample size of participants from research centers located in five northern European countries was considered a major strength of this study as it permitted simultaneous adjustment for multiple potential confounders. Several limitations were acknowledged, including absence of data on obstructive respiratory disease severity, WC measurements not being performed by trained staff, and self-reported height and weight measurements.

The authors have disclosed no relevant financial relationships. ■

An independent association of abdominal obesity (with or without general obesity) was found to occur with respiratory symptoms, asthma, late-onset asthma, and chronic bronchitis.

Improved swallowing may mitigate chronic obstructive pulmonary disease exacerbations

BY HEIDI SPLETE

Dysphagia treatment may be a way to reduce risk for chronic obstructive pulmonary disease (COPD) exacerbations, according to Yoshitaka Oku, MD, of Hyogo Medical University, Nishinomiya, Japan.

Gastroesophageal reflux disease (GERD) is known to be associated with exacerbations in COPD, but previous studies have shown little impact of standard GERD therapy on COPD exacerbations. However, additional research indicates that delayed swallowing contributes to COPD exacerbations, as reported in a research review.

In an article published in *Respiratory Physiology & Neurobiology* (doi:10.1016/j.resp.2023.104061), Dr. Oku hypothesized that swallowing abnormalities are a confounding factor in the association between GERD and COPD exacerbation, and that counteracting swallowing disorders may reduce COPD exacerbations.

Swallowing disorder (dysphagia) is a common comorbidity in patients with COPD and has been reported at a 17%-20% greater prevalence in those with COPD, compared with controls, the researchers said.

Patients with COPD have altered swallowing behavior because of several factors,

including decreased maximal laryngeal elevation, Dr. Oku said. Individuals with COPD “are also prone to laryngeal penetration and aspiration when swallowing large volumes of liquid and tend to follow an inspiratory-swallow-expiratory (I-SW-E) pattern when swallowing large volumes,” he explained.

Dr. Oku conducted prospective studies to investigate the impact of breathing-swallowing discoordination on COPD exacerbation. He found that discoordination in swallowing patterns and the inability to produce airway protective mechanism (such as the I-SW-E pattern) may contribute to more frequent aspirations and more frequent exacerbations.

Dr. Oku also examined whether CPAP and bilevel positive airway pressure (BiPAP) might affect breathing-swallowing coordination in healthy controls and patients with COPD. He found a decrease in breathing-swallowing coordination with CPAP, but not BiPAP, in both controls and stable COPD patients.

“During BiPAP, a brief negative flow associated with relaxation of the pharyngeal constrictor

muscle triggers inspiratory support, which results in the SW-I pattern,” Dr. Oku noted.

Dr. Oku also wrote that interferential current (IFC) has been used to stimulate muscles. Studies of transcutaneous electrical sensory stimulation using IFC (IFC-TESS) as an intervention to improve swallowing have shown some success, and also may improve airway protection.

“However, its safety and efficacy in patients with COPD remains unknown,” he wrote. Dr. Oku conducted a study of stable COPD patients and found that repeated salivary swallow

test (RSST) scores improved significantly after an IFC-TESS intervention.

Breathing-swallowing discoordination may be an early indicator of swallowing disorder in COPD, and interventions can improve these disorders, Dr. Oku added. However, more research is needed to explore whether interventions to improve dysphagia reduce the frequency of exacerbations in COPD patients, he concluded.

The study was supported by a grant from JSPS KAKENHI. Dr. Oku serves as a senior managing director at EuSense Medical. ■

Swallowing disorder (dysphagia) is a common comorbidity in patients with COPD and has been reported at a 17%-20% greater prevalence in those with COPD, compared with controls.

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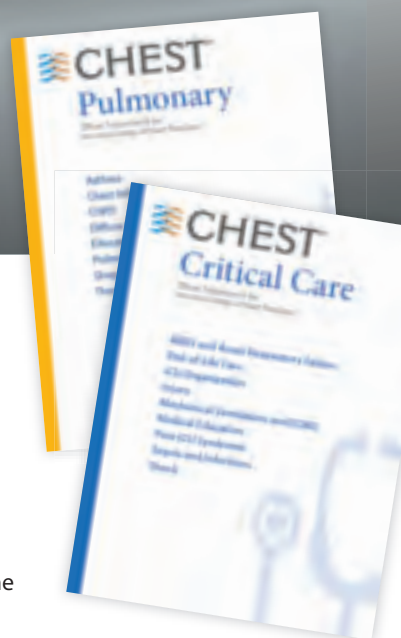
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New clues to how air pollution fuels the development of lung cancer in nonsmokers

BY MEGAN BROOKS

Air pollution may promote the growth of lung cancer in people who have never smoked by activating normally inactive cells in the lung that harbor cancer-causing mutations, new research indicates.

“This work adds to our understanding of the mechanism by which air pollutants promote the earliest stages of lung cancer, particularly in people who have never smoked,” William Hill, PhD, co-first author and postdoctoral researcher at the Francis Crick Institute, London, told this news organization.

The study, which assessed human lung samples and mouse cancer models, was published online in *Nature* (2023 Apr 5. doi: 10.1038/s41586-023-05874-3).

Although smoking remains the chief risk factor for lung cancer, outdoor air pollution causes roughly 1 in 10 cases of lung cancer in the United Kingdom, according to Cancer Research UK. In 2019, about 300,000 lung cancer deaths around the world were attributed to exposure to ambient particulate matter measuring ≤ 2.5 μm ($\text{PM}_{2.5}$).

While the link between air pollution and lung cancer is well known, the mechanism that explains this link has been harder to pinpoint.

One theory is that environmental carcinogens such as tobacco smoke and UV light cause mutations by damaging DNA directly. However, recent data have hinted that that may not be the case.

In the current study, Dr. Hill and colleagues proposed that, rather than act on DNA directly, air pollutants might promote inflammatory



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changes in the lung tissue that wake up inactive cancer-causing mutations, which accumulate naturally in these cells as people age. This idea lines up with a decades-old theory of cancer promotion, according to which tumorigenesis is a two-step process: The initial step induces mutations in healthy cells, after which a promoter step triggers cancer development.

The study team focused on epidermal growth factor receptor (EGFR)-driven lung cancer, which is more common in never-smokers and light smokers, and on environmental particulate matter measuring ≤ 2.5 μm ($\text{PM}_{2.5}$), which is fine enough to travel into the lungs and is associated with lung cancer risk.

Dr. Hill and colleagues analyzed data from over 400,000 people in three countries. They compared rates of EGFR-mutant lung cancer cases in areas with different levels of $\text{PM}_{2.5}$ pollution. The team found a significant association between $\text{PM}_{2.5}$ levels and the incidence of lung cancer for 32,957 EGFR-driven lung cancer cases in England, South

Korea, and Taiwan. The researchers then studied genetically engineered mouse models of lung adenocarcinoma to determine whether particulate matter exposure could trigger the development of lung tumors. In these functional mouse models, air pollutants led to an influx of macrophages in the lung and the release of interleukin-1beta, a key mediator of the inflammatory response.

This process ultimately “fuels tumorigenesis,” the study team concluded. The team also found that treatment with an anti-interleukin-1beta antibody during $\text{PM}_{2.5}$ exposure reduced lung cancer promotion by air pollutants.

A detailed mutational profiling of histologically normal lung tissue from 295 individuals revealed oncogenic EGFR and KRAS-driver mutations in 18% and 53% of healthy tissue samples, respectively. Overall, “our data suggest a mechanistic and causative link between air pollutants and lung cancer,” the team wrote.

The study demonstrates that air pollution rouses cells in the lung that carry cancer-causing mutations,

“encouraging them to grow and potentially form tumors,” Dr. Hill said. “Understanding the biology could help identify high-risk individuals and, in the future, may open avenues to prevent cancer caused by breathing polluted air.”

In a related article in *Nature Genet.* (doi:10.1038/s41588-020-00727-5), Allan Balmain, PhD, of the University of California, San Francisco, said these results have “major implications for how to think about cancer prevention.”

“There is presently nothing that can be done to remove the mutated cells that accumulate in normal tissues, but if there is a promotion stage that influences the rate of cancer development, then inhibition of this stage might be an effective way to prevent cancer,” Dr. Balmain said.

Another prevention option, Dr. Hill noted, is to reduce the levels of air pollution. “Our study provides a mandate for the reduction of $\text{PM}_{2.5}$ emissions globally,” he said.

Dr. Hill also believes the findings may extend beyond lung cancer.

“It’s possible that this inflammatory pathway could be involved in other types of cancer and that it could be triggered by other environmental carcinogens,” he said. “But further research is needed to find out which other environmental carcinogens might trigger this pathway, as well as which other parts of the body this may occur in.”

Funding for the study was provided by Cancer Research UK, the European Research Council, and other noncommercial entities. A list of author disclosures is available with the original article. Dr. Balmain disclosed no financial conflicts. ■

ASTHMA

Mucus plugging phenotype associated with adverse features

BY WALTER ALEXANDER

In a study aimed at determining phenotypic associations of mucus plugging in moderate to severe asthma patients, those with mucus plugging had worse lung function, more frequent severe exacerbations needing oral corticosteroids, and higher T2 biomarkers.

Rory Chan, MBChB, of the University of Dundee (Scotland) and colleagues also found that the presence of these features was associated with an increased likelihood of mucus plugging (*J Allergy Clin Immunol Pract.* 2023;11:195-9).

Mucus plugging contributes significantly to airway obstruction and death in acute asthma, the investigators stated, noting further that the understanding of mucus plugging’s role in chronic asthma is increasing.

Their retrospective cohort study included 126 patients with respiratory physician-diagnosed moderate to severe asthma who attended their clinic (January 2016–March 2022) and were receiving daily doses of inhaled corticosteroid (ICS) (≥ 800 mcg) and a second-line controller. All had prior high-resolution CT (HRCT) scans with mucus plugs identified by an experienced

thoracic radiologist. Prior to the start of biologic therapy, a mucus plug score (MPS) signifying the number of affected lung segments (0-20) was calculated and considered along with pulmonary function testing, T2 inflammatory markers, asthma control data, and measures of peripheral blood eosinophils (PBE), as well as total IgG and IgE antibodies to *Apergillus fumigatus*.

The analysis showed that reduced forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio (OR, 3.01), two or more exacerbations per year (OR, 5.00), raised PBE

MUCUS continued on following page

Number of cancer survivors with functional limitations doubled in 20 years

MARCIA FRELICK

The number of cancer survivors who report functional limitation has more than doubled in 20 years, according to a research letter published in JAMA Oncology (doi:10.1001/jamaoncol.2023.1180).

Vishal Patel, BS, a student at the Dell Medical School at the University of Texas at Austin, and colleagues identified 51,258 cancer survivors from the National Health Interview Survey, representing a weighted population of approximately 178.8 million from 1999 to 2018.

Most survivors were women (60.2%) and were at least 65 years old (55.4%). In 1999, 3.6 million weighted survivors reported functional limitation. In 2018, the number increased to 8.2 million, a 2.25-fold increase.

The number of survivors who reported no limitations also increased, but not by as much. That group grew 1.34-fold during the study period.

For context, “the 70% prevalence of functional limitation among survivors in 2018 is nearly twice that of the general population,” the authors wrote.

Patients surveyed on function

Functional limitation was defined as “self-reported difficulty performing any of 12 routine physical or social activities without assistance.” Examples of the activities included difficulty sitting for more than 2 hours, difficulty participating in social activities or difficulty pushing or pulling an object the size of a living room chair.

Over the 2 decades analyzed, the adjusted prevalence of functional limitation was highest among survivors of pancreatic cancer (80.3%) and lung cancer (76.5%). Prevalence was lowest for survivors of melanoma (62.2%), breast (61.8%) and prostate (59.5%) cancers.

Not just a result of living longer

Mr. Patel told this publication that one assumption people might make when they read these results is that people are just living longer with cancer and losing functional ability accordingly.

“But, in fact, we found that the youngest [those less than 65 years] actually contributed to this trend more than the oldest people, which means it’s not just [happening], because people are getting older,” he said.

Hispanic and Black individuals had disproportionately higher increases in functional

limitation; percentage point increases over the 2 decades were 19.5 for Black people, 25.1 for Hispanic people, and 12.5 for White people. There may be a couple of reasons for that, Mr. Patel noted.

Those who are Black or Hispanic tend to have less access to cancer survivorship care for reasons including insurance status and historic health care inequities, he noted.

“The other potential reason is that they have had less access to cancer care historically. And if, 20 years ago Black and Hispanic individuals didn’t have access to some chemotherapies, and now they do, maybe it’s the increased access to care that’s causing these functional limitations. Because

chemotherapy can sometimes be very toxic. It may be sort of a catch-up toxicity,” he said.

Quality of life beyond survivorship

Mr. Patel said the results seem to call for building on improved survival rates by tracking and improving function.

“It’s good to celebrate that there are more survivors. But now that we can keep people alive longer, maybe we can shift gears to improving their quality of life,” he said.

The more-than-doubling of functional limitations over 2 decades “is a very sobering trend,” he noted, while pointing out that the functional limitations applied to 8 million people in the United States – people whose needs are not being met.

There’s no sign of the trend stopping, he continued. “We saw no downward trend, only an upward trend.” Increasingly, including functionality as an endpoint in cancer trials, in addition to improvements in mortality, is one place to start, he added.

“Our findings suggest an urgent need for care teams to understand and address function, for researchers to evaluate function as a core outcome in trials, and for health systems and policy makers to reimagine survivorship care, recognizing the burden of cancer and its treatment on physical, psychosocial, and cognitive function,” the authors wrote in their paper.

Limitations of the study include the potential for recall bias, lack of cancer staging or treatment information, and the subjective perception of function.

A coauthor reported personal fees from Astellas, AstraZeneca, AAA, Blue Earth, and a variety of other pharm companies, as well as grants from Pfizer and Bayer during the conduct of the study. No other disclosures were reported. ■

The more-than-doubling of functional limitations over 2 decades “is a very sobering trend There’s no sign of the trend stopping. We saw no downward trend, only an upward trend.”

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(OR, 3.23), raised total IgE (OR, 3.20), and *Aspergillus fumigatus* IgE titers (OR, 9.37) all conferred significantly higher likelihood of the presence of mucus plugging. Highest prevalence of mucus plugs was in the right and left lower lung lobes (about 26% vs. about 10% and 14% in the middle and upper lobes).

Adjusted ORs in patients with impaired FEV₁/FVC showed the likelihood of mucus plugging to be 67% higher. In those with frequent exacerbations, they were 80% higher, and in those with raised PBE and IgE, 69% higher. Patients without mucus plugging had preserved FEV₁ and FEV₁/FVC.

Asthma patients with mucus plugging in the study exhibited higher levels of routinely measured T2 biomarkers, including blood eosinophils, FeNO, and total IgE,

with median values all exceeding traditionally accepted cut points. Although patients with mucus plugging were receiving significantly higher ICS doses, and despite the suppressive effect of ICS on FeNO, they still had higher FeNO levels. “We therefore postulate that asthma patients with the MP phenotype might potentially experience greater treatment response to biologics targeting the underlying inflammatory endotype,” the investigators stated, adding that “the presence of mucus plugging should be recognized as a treatable trait for patients with severe asthma in terms of targeting therapy with biologics.”

They wrote that, “in a real-life clinic setting, the presence of mucus plugging detected on HRCT was associated with more severe exacerbations, more severe airflow obstruction, and greater T2

inflammation. This, in turn, suggests that imaging should be part of the routine workup of patients with poorly controlled severe asthma.”

In an accompanying editorial (J Allergy Clin Immunol Pract. 2023 Feb;11[2]:527-8), Jorge Cedano, MD, Jiwoong Choi, PhD, and Mario Castro, MD, MPH, of the University of Kansas, Kansas City, said that the contribution of mucus plugging in the morbidity of uncontrolled asthma is much greater than appreciated. They focused particularly on the suggestion that, even after adjusting for confounders, molds such as *Aspergillus* may play a causal role, along with blood eosinophils, fractional exhaled nitric oxide, and total IgE, in T2 inflammation.

While current biologic therapies targeting the T2 phenotype have not yet been shown to reverse the progressive loss of lung function or

lung remodeling process, the editorialists referenced a recent post hoc analysis of the CASCADE study showing mucus plugging reduction with the biologic tezepelumab versus placebo correlated with lung function improvement. “At least 20% of patients with moderate to severe asthma will experience progressive decline in lung function, more exacerbations, and worse asthma control despite the use of controller therapies. If physicians could identify the MP phenotype using computed tomography, then potentially earlier treatment with biologic therapy may improve asthma control and prevent future decline in lung function.”

Study authors cited numerous conflicts of interest with pharmaceutical companies. Dr. Castro reported affiliation or involvement in multiple entities with a financial interest in the subject discussed. ■

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NETWORKS

RSV future directions; BMPR2-based therapies for PAH; beating jet lag at CHEST 2023; and more...

CHEST INFECTIONS & DISASTER RESPONSE NETWORK

Chest Infections Section RSV: Current patterns and future directions

Respiratory syncytial virus (RSV) is an underappreciated cause of hospital admission in adult patients, especially among those who have underlying cardiopulmonary comorbidities (Branche AR, et al. *Clin Infect Dis.* 2022;74[6]:1004). A meta-analysis estimated an annual incidence rate of 37.6 per 1000 persons per year with a hospital case fatality rate of 11.7% (5.8%-23.4%) in industrialized countries (Shi T, et al. *J Infect Dis.* 2022;226 [suppl 1]).

Recent work showed RSV to be quite pathogenic in adults (Begley KM, et al. *Clin Infect Dis.* 2023:ciad031). In 10,311 hospitalized adults with an acute respiratory illness, 6% tested positive for RSV and 18.8% for influenza virus. Compared with influenza virus, patients infected with RSV were more likely to have COPD or CHF and had longer admission and more requirements for mechanical ventilation.

There have been new advances in the prevention of RSV-associated illness. Nirsevimab, an IgG1 monoclonal antibody that locks the RSV F protein in prefusion stage, had an efficacy of 74.5% in preventing RSV-associated lower respiratory tract infection (LRTI) in infants up to 150 days, which is an improvement over palivizumab (Bergeron HC, et al. *Expert Opin Investig Drugs.* 2022;31 [No. 1]: 23). The FDA advisory committee just approved two RSV vaccines, both of which target prefusion F protein, for elderly adults. The RSVpreF3OA had 82.6% efficacy against LRTI in adults over 60 years of age (Papi A, et al. *N Engl J Med.* 2023;388:595) and Ad26.RSV.preF-RSV preF protein vaccine had 80% efficacy in adults over 65 years of age (Falsey AR, et al. *N Engl J Med.* 2023;388:609).

Shekhar Ghamande, MD, MBBS, FCCP – Section Member-at-Large
Paige Marty, MD – Section Fellow-in-Training

PULMONARY VASCULAR & CARDIOVASCULAR NETWORK

Pulmonary Vascular Disease Section

The STELLAR Travel to BMPR2-based therapies for pulmonary

arterial hypertension: Insights from bench to bedside

The recently published STELLAR trial was a phase 3, multicenter, double-blind, randomized, placebo-controlled study designed to evaluate patients with PAH receiving stable vasodilator therapy after treatment with sotatercept, a first-in-class recombinant fusion protein with parts of the activin receptor type IIA, a member of the BMPR2/TGF- β superfamily of receptors and ligands (Hoepfer. *N Engl J Med.* 2023;388:1478).

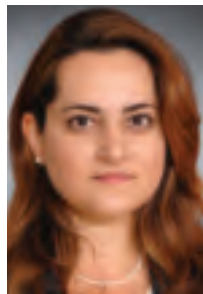


Dr. Gomez-Arroyo

Sotatercept improved 6-minute walk distance, the primary endpoint of the trial at 24-weeks, as well as eight of the trial's nine secondary endpoints including changes in PVR, NT-ProBNP levels, functional class, French risk score, and time-to-clinical worsening when compared with placebo. However, many questions remain about the mechanisms whereby sotatercept achieved its clinical endpoints, the answers to which may lie within its basic molecular biology.

The focus on BMPR2/TGF- β cell signaling pathways originated from the identification of loss-of-function mutations in the BMPR2 gene in patients with heritable and idiopathic PAH (Morrell, NW. *Eur Respir J.* 2019;53[3]: 1900078). An imbalance in BMPR2/TGF- β signaling (low BMPR2/high TGF- β function) has been proposed as a central mechanism in the development of PAH. Specifically, researchers have shown increased levels of Activin A, one of 33 ligands that can bind either BMPR2 or TGF- β receptors, within vascular lesions in the lungs of patients with PAH. It has been thus hypothesized that reducing the amount of circulating Activin A could treat PAH by rebalancing BMPR2/TGF- β signaling in lung vascular cells. In preclinical experimental models of PAH with elevated Activin A levels, sotatercept has been shown to reduce distal small vessel medial thickness/muscularization and increase the number of patent small vessels (Yung, LM. *Sci Transl Med.* 2020;12).

The exact mechanism by which sotatercept improves hemodynamics and outcomes remains unclear.



Dr. Kay

Indeed, whether de-remodeling of the lung vasculature or new vessel formation occurs in humans is unknown. The results from STELLAR mark a new era in the development of potential “disease-modifying agents” for PAH; however, the question is: what exactly are we modifying?

Jose Gomez-Arroyo, MD, PhD – Section Fellow-in-Training
Dana Kay, DO – Section Member-at-Large

SLEEP MEDICINE NETWORK

Non-Respiratory Sleep Section

Beating jet lag at CHEST 2023

Want to feel your best when enjoying CHEST 2023 sessions, games, vendors, networking events, and much more on the island paradise of Hawai'i? It's time to start making plans to align your circadian rhythm with Hawai'i Standard Time (HST).



Dr. Chung

Dr. Sabra Abbott, a circadian rhythm expert and the Director of the Circadian Medicine Clinic at Northwestern University, recommends “to best adapt to the time zone change, you can take advantage of the time-of-day specific phase shifting properties of light and melatonin.”

Before heading west to the meeting, Dr. Abbott recommends mainland USA travelers to get extra light exposure in the evening. On arrival in Hawai'i, morning bright-light exposure should be limited. Luckily, afternoon/early evening light exposure is encouraged, which will help get some extra hours on the beach! Don't forget your sunglasses to help with blocking light in the morning.

Once the meeting has concluded, attendees from mainland USA will need to advance their internal clocks

earlier as they travel east back home. This can be achieved by taking melatonin 0.5 mg around bedtime and seeking bright-light during the mid-to-late morning.

To develop a personalized sleep prescription based on your time zone and preferred sleep times, you can use an online jet lag calculator, such as Jet Lag Rooster (jetlag.sleepopolis.com; no affiliations with authors or Dr. Abbott).

To learn more about circadian rhythm alignment when working and traveling, we'll see you at the CHEST 2023 session “Shifting to Hawai'i – Jet Lag, Shift Workers, and Sleep for Health Care Providers” (10/8/2023 at 0815-HST).

Paul Chung, DO – Section Fellow-in-Training
Lisa Wolfe, MD – Section Member-at-Large
William Healy, MD – Section Member-at-Large

THORACIC ONCOLOGY & CHEST IMAGING NETWORK

Pleural Disease Section

Lobar vs. sublobar resection in stage 1 lung cancer

Lobectomy with intrathoracic nodal dissection remains the standard of care for early stage (tumor size ≤ 3.0 cm) peripheral non-small cell lung cancer (NSCLC). This practice is primarily influenced by data from the mid-1990s associating limited resection (segmentectomy or wedge resection) with increased recurrence rate and mortality compared with lobectomy



Dr. Yurosko

(Ginsberg, et al. *Ann Thorac Surg.* 1995;60:615). Recent advances in video and robotic-assisted thoracic surgery, as well as the implementation of lung cancer screening, improvement in minimally invasive diagnostic modalities, and neoadjuvant therapies have driven the medical community to revisit the role of sublobar lung resection.

Two newly published large randomized control multicenter multinational trials (Saji, et al. *Lancet.* 2022; 399:1670 and Altorki, et al. *N Engl J Med.* 2023;388:489) have

NETWORKS continued on following page

Respiratory management of patients with neuromuscular weakness: The latest CHEST guideline

BY KINSLEY HUBEL, MD, AND AKRAM KHAN, MD

Patients with neuromuscular diseases (NMD) face an increased risk of respiratory muscle weakness, which can contribute to various health problems. These include chronic respiratory failure, sleep-related breathing disorders, sialorrhea, and reduced cough effectiveness. In collaboration with AASM, AARC, and ATS, CHEST has developed guidelines to help clinicians manage patients with NMD.

Through a systematic review of 128 studies related to this topic, the expert panel developed 15 graded recommendations, a good practice statement, and a consensus-based statement using the population, intervention, comparator, and outcome (PICO) format using the GRADE (Grading of Recommendations, Assessment, Development,

and Evaluations) methodology.

A few of the key recommendations are as follows:

1. Addressing the use and timing of pulmonary function tests (PFT), the panel suggests measuring vital capacity (FVC or SVC), MIP/MEP, SNIP, or PCF in patients with NMD every 6 months.

2. For the detection of respiratory failure and sleep-related breathing disorders in symptomatic patients with NMD who have normal PFT and overnight oximetry (ONO), the panel suggested that clinicians consider polysomnography (PSG) to assess whether noninvasive ventilation (NIV) would be beneficial. Adult patients do not have to have PSG to manage NMD if the PFT or ONO criteria support using NIV.

3. The panel recommends the use of NIV for the treatment of respiratory failure. To guide the initiation

GUIDELINE *continued on following page*



COURTESY CHEST

NETWORKS *continued from previous page*

challenged our well-established practices. They compared overall and disease-free survival sublobar to lobar resection of early stage NSCLC (tumor size ≤ 2.0 cm and negative intraoperative nodal disease) and demonstrated noninferiority of sublobar resection with respect to overall survival and disease-free survival. While the sublobar resection in the Saji et al trial consisted strictly of segmentectomy, the majority of sublobar resections in the Altorki et al trial were wedge resections. Interestingly, both trials chose lower cut-offs for

tumor size (≤ 2.0 cm) compared with the Ginsberg trial (≤ 3.0 cm), which could arguably have accounted for this difference in outcomes. In summary, these emerging data are here to tell us a new story by supporting more limited anatomical lung resection options for our patients with early stage NSCLC.





Christopher Yurosko, DO – Section Fellow-in-Training
Melissa Rosas, MD – Section Member-at-Large
Labib Debiane, MD – Section Member-at-Large



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Hot topics you won't want to miss at CHEST 2023

The CHEST Annual Meeting offers hundreds of top-notch educational sessions every year—and narrowing down your choices can be a tall order. As we look forward to CHEST 2023 in Honolulu, Hawai'i, October 8 to 11, we're highlighting key sessions recommended by members of the CHEST Scientific Program Committee.

To see what else is in store, browse the full educational program at chestmeeting.chestnet.org. Sessions are categorized by clinical topic so that you can easily find the ones that interest you.

"If you've never been to a CHEST Annual Meeting before, you're in for a treat," said Sleep Medicine Curriculum Group Chair, Carolyn D'Ambrosio, MD, FCCP. "The sessions are robust in that they provide scientific information, but they're also applicable to your day-to-day practice."

Airways disease

Muhammad Adrish, MD, MBA, FCCP, Chair of the Airways Disease Curriculum Group, is excited about the breadth of the curriculum his group has planned this year.

"We're going to have sessions on asthma, COPD, bronchiectasis, bronchiolitis, cystic fibrosis, and more," he said. "It really is such a wide spectrum of diseases in the airway curriculum."

A few sessions he can't wait to attend include Controversies in Asthma-COPD Overlap - A Pro-Con Debate, Maximizing Oxygen Efficacy in the Ambulatory Setting, and Hands-on Training on Airway Clearance Techniques and Devices.

Dr. Adrish noted that one of the major advantages of the CHEST Annual Meeting is the opportunity to be in the same room as other clinicians specializing in airways.

"It's always stirring to hear the dialogue of those with tremendous experience, especially when it's in a field that you love," he added.

Read more of Dr. Adrish's top picks by scanning the QR code.



Critical care

Organizers of the CHEST 2023 critical care curriculum made a concerted effort to cover more advanced topics this year, said Critical Care Curriculum Group Chair, Christopher Carroll, MD, FCCP.

"We have some excellent sessions on advanced ventilator physiology and leveraging technology to improve patient management," he explained. "We also have some great sessions on waveform analysis that dive into respiratory and cardiac physiology in a way that we haven't really done before. It's going to be an exciting meeting."

Sessions he's looking forward to include:

- Advanced Ventilator Management: Where Technology Meets Physiology
- Cardiac Waveforms in the ICU
- Case-Based Ventilator Graphics: Using Ventilator Graphics to Optimize Patient Management
- A Systematic Approach to Undifferentiated Shock: From POCUS to PACs!

Dr. Carroll has been attending CHEST Annual Meetings since 2003 and believes that, over the years, the educational sessions presented keep getting better. Sessions have adapted to focus on education both for people who are early in their careers, as well as those who have been out of fellowship for years and are wanting to explore more advanced topics,

including literature reviews.

Read more of Dr. Carroll's top picks by scanning the QR code.



Sleep medicine

Dr. D'Ambrosio said CHEST 2023 will have a lot to offer sleep medicine specialists.

"We're a fun, tight-knit group," she said. "There's great networking, as well as a lot of collegiality."

Sessions that she's highlighted will address some of the most pertinent topics affecting the field. For example, in light of recent device recalls, a highly anticipated session will compare the applications of specific noninvasive ventilation and home mechanical ventilation devices and modes.

"This session will explore what to do now with all the different devices that are on the market. Despite the recall of some devices, there are many options, and this session will help you determine the best one for your patient," Dr. D'Ambrosio said.

She's also looking forward to a session that will provide an update on sleep disorders in women, including sleep-disordered breathing, insomnia, restless legs syndrome, and other diseases.

"We will talk about sleep in women because I do believe that there are differences in the sexes and genders," she said. "And for many, many years – particularly for obstructive sleep apnea – it's been thought of as a disease for men only. I think we need to keep going with that. What's the latest research? Where are we going forward with therapeutics?"

Read more of Dr. D'Ambrosio's top picks by scanning the QR code.

Join Dr. Adrish, Dr. Carroll, and Dr. D'Ambrosio in Hawai'i by registering to attend now before prices increase on July 1. Visit chestmeeting.chestnet.org for details. ■



GUIDELINE *continued from previous page*

of NIV, clinicians can use any fall in FVC to <80% of predicted with symptoms or FVC to <50% of predicted without symptoms or SNIP/MIP to < -40 cm H₂O or hypercapnia. The panel recommended individualizing treatment.

4. The panel suggested mouth piece ventilation (MPV) for daytime ventilatory support in patients with preserved bulbar function. Its desirable effects include delaying or avoiding tracheostomy and improving speech, cough effectiveness, and coordination of breathing and swallowing.

5. Invasive home mechanical ventilation (MV) by tracheostomy was identified as an acceptable option for patients with progressive respiratory failure, particularly those who were unable to clear secretions. Because of the high costs and caregiver burden, the guideline highlights the need to consider patient preferences, tolerability, the ability to maintain mouthpiece ventilation, and the availability of resources when choosing an appropriate treatment option.

6. The panel suggested practicing clinicians address the management of sialorrhea and airway clearance techniques in patients with NMD, as they face the risk of aspiration and pneumonia. For sialorrhea, the panel suggests starting with a trial of anticholinergic agents, as they are inexpensive and readily available. The panel also provided advice on botulinum toxin therapy and radiation therapy, which have limited data and should be reserved for experienced centers.

7. The panel reviewed data on airway clearance techniques, including glossopharyngeal breathing (GPB), mechanical insufflation-exsufflation (MI-E), also commonly known as cough-assist device, manually assisted cough, lung volume recruitment (LVR) by air stacking, and high-frequency chest wall oscillation (HFCWO). The panel suggested using airway clearance techniques based on local resources, expertise, and shared decision-making with patients.

The panel stressed the importance of respect

for patient preferences, treatment goals, and quality of life considerations. The panel emphasized the need to modernize and improve access to ventilatory support for patients with NMD and the role of shared decision-making in improving quality of life and long-term outcomes. The panel also suggests that randomized controlled trials in patients with NMD would help establish a higher grade of evidence. ■

Dr. Hubel and Dr. Khan are from the Division of Pulmonary Allergy and Critical Care Medicine, Oregon Health and Science University, Portland, OR.

Reference

Khan A, Frazer-Green L, Amin R, et al. Respiratory Management of Patients With Neuromuscular Weakness: An American College of Chest Physicians Clinical Practice Guideline and Expert Panel Report [published online ahead of print, 2023 Mar 13]. *Chest*. 2023;S0012-3692(23)00353-7. doi:10.1016/j.chest.2023.03.011

CRITICAL CARE COMMENTARY

Fluids or vasopressors: Is sepsis management that simple?

BY H. BRYANT NGUYEN, MD

In recent months, we have seen the results of the much awaited Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis (CLOVERS) trial showing that a restrictive fluid and early vasopressor strategy initiated on arrival of patients with sepsis and hypotension in the ED did not result in decreased mortality compared with a liberal fluid approach (PETAL Network. *N Engl J Med.* 2023;388[6]:499). The March 2023 issue of *CHEST Physician* provided a synopsis of the trial highlighting several limitations (Splete H. *CHEST Physician.* 2023;18[3]:1). Last year in 2022, the Conservative versus Liberal Approach to Fluid Therapy in Septic Shock (CLASSIC) trial also showed no difference in mortality with restrictive fluid compared with standard fluid in patients with septic shock in the ICU already receiving vasopressor therapy (Meyhoff TS, et al. *N Engl J Med.* 2022;386[26]:2459). Did CLOVERS and CLASSIC resolve the ongoing debate about the timing and quantity of fluid resuscitation in sepsis? Did their results suggest a “you can do what you want” approach? Is the management of sepsis and septic shock limited to fluids vs vasopressors? Hopefully, the ongoing studies ARISE FLUIDS (NCT04569942), EVIS (NCT05179499), FRESHLY (NCT05453565), 1BED (NCT05273034), and REDUCE (NCT04931485) will further address these questions.

In the meantime, I continue to admit and care for patients with sepsis in the ICU. One example was a 72-year-old woman with a history of stroke, coronary artery disease, diabetes, and chronic kidney disease presenting with 3 days of progressive cough and dyspnea. In the ED, temperature was 38.2°C, heart rate 120 beats per min, respiratory rate 28/min, blood pressure 82/48 mm Hg, and weight 92 kg. She had audible crackles in the left lower lung. Her laboratory and imaging results supported a diagnosis of sepsis due to severe community-acquired pneumonia, including the following values: white blood cell 18.2 million/mm³; lactate 3.8 mmol/L; and creatinine 4.3 mg/dL.

While in the ED, the patient received 1 liter of crystalloid fluids and appropriate broad spectrum antibiotics. Repeat lactate value was 2.8 mmol/L. Patient’s blood pressure then decreased to 85/42 mm Hg. Norepinephrine was started peripherally and titrated to 6 mcg/min to achieve blood pressure 104/56 mm Hg. No further fluid administration was given, and the patient was admitted to the medical ICU. On admission, a repeat lactate had increased to 3.4 mmol/L with blood pressure of 80/45 mm Hg.

Instead of further escalating vasopressor administration, she received 2 L of fluid and continued at 150 mL/h. Shortly after, norepinephrine was titrated off. Fluid resuscitation was then deescalated. We transferred the patient to the general ward within 12 hours of ICU admission.

Could we have avoided ICU admission and critical care resource utilization if the patient had received more optimal fluid resuscitation in the ED?

While our fear of fluids (or hydrophobia) may be unwarranted, the management of this patient was a common example of fluid restriction in sepsis (Jaehne AK, et al. *Crit Care Med.* 2016;44[12]:2263). By clinical criteria, she was in septic shock (requiring vasopressor) and appropriately required ICU admission. But, I would posit that the patient had severe sepsis based on pre-Sepsis 3 criteria. Optimal initial fluid resuscitation would have prevented her from requiring vasopressor and progressing to septic shock with ICU admission. Unfortunately, the patient’s care reflected the objective of CLOVERS and its results. Other than the lack of decreased mortality, decreased ventilator use, decreased renal

replacement therapy, and decreased hospital length of stay, restricting fluids resulted in an increase of 8.1% (95% confidence interval 3.3 to 12.8) ICU utilization. Furthermore, the data and safety monitoring committee halted the trial for futility at two-thirds of enrollment. One must wonder if CLOVERS had completed its intended enrollment of 2,320 patients, negative outcomes would have occurred.

Should an astute clinician interpret the results of the CLOVERS and CLASSIC trials as “Fluids, it doesn’t matter, so I can do what I want?” Absolutely not! The literature is abundant with studies showing that increasing dose and/or number of vasopressors is associated with higher mortality in septic shock. One example is a recent multicenter prospective cohort study examining the association of vasopressor dosing during the first 24 hours and 30-day mortality in septic shock over 33 hospitals (Roberts RJ, et al. *Crit Care Med.* 2020;48[10]:1445).

Six hundred and sixteen patients were enrolled with 31% 30-day mortality. In 24 hours after shock diagnosis, patients received a median of 3.4 (1.9-5.3) L of fluids and 8.5 mcg/min norepinephrine equivalent. During the first 6 hours, increasing vasopressor dosing was associated with increased odds of mortality. Every 10 mcg/min increase in norepinephrine over the 24-hour period was associated with a 33% increased odds of mortality. Patients who received no fluids but 35 mcg/min norepinephrine in 6 hours had the highest mortality of 50%. As fluid volume increased, the association



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Did CLOVERS and CLASSIC resolve the ongoing debate about the timing and quantity of fluid resuscitation in sepsis?

between vasopressor dosing and mortality decreased, such that at least 2 L of fluid during the first 6 hours was required for this association to become nonsignificant. Based on these results and a number of past studies, we should be cautious in believing that a resuscitation strategy favoring vasopressors would result in a better outcome.

Shock resuscitation is complex, and there is no one-size-fits-all approach. With the present climate, the success of resuscitation has been simplified to assessing fluid responsiveness. Trainees learn to identify the inferior vena cava and lung B-lines by ultrasound. With more advanced technology, stroke volume variation is considered. And, let us not forget the passive leg raise. Rarely can our fellows and residents recite the components of oxygen delivery as targets of shock resuscitation: preload, afterload, contractility, hemoglobin, and oxygen saturation. Another patient example comes to mind when fluid responsiveness alone is inadequate.

Our patient was a 46-year-old man now day 4 in the ICU with Klebsiella bacteremia and acute cholecystitis undergoing medical management. His comorbidities included diabetes, obesity, hypertension, and cardiomyopathy with ejection fraction 35%. He was supported with mechanical ventilation, norepinephrine 20 mcg/min, and receiving appropriate antibiotics. For hemodynamic monitoring, a central venous and arterial catheter have been placed. The patient had a heart rate 92 beats per min, mean arterial pressure (MAP) 57 mm Hg, central venous pressure (CVP) 26 mm Hg, stroke volume variation (SVV) 9%, cardiac output (CO) 2.5 L/min, and central venous oxygen saturation (ScvO₂) 42%.

Based on these parameters, we initiated dobutamine at 2.5 mcg/kg/min, which was then titrated to 20 mcg/kg/min over 2 hours to achieve ScvO₂ 72%. Interestingly, CVP had decreased to 18 mm Hg, SVV increased to 16%, with CO 4.5 L/min. MAP also increased to 68 mm Hg. We then administered 1-L fluid bolus with the elevated SVV. Given the patient’s underlying cardiomyopathy, CVP < 20 mm Hg appeared to indicate a state of fluid responsiveness. After our fluid administration,

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BY PETER J. MAZZONE, MD,
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Editor in Chief

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heart rate 98 beats per min, MAP 70 mm Hg, CVP increased to 21 mm Hg, SVV 12%, CO 4.7 L/min, and ScvO₂ 74%. In acknowledging a mixed hypovolemic, cardiogenic, and septic shock, we had optimized his hemodynamic state. Importantly, during this exercise of hemodynamic manipulation, we were able to decrease norepinephrine to 8 mcg/min, maintaining dobutamine at 20 mcg/kg/min.

The above case illustrates that the hemodynamic perturbations in sepsis and septic shock are not simple. Patients do not present with a single shock state. An infection progressing to shock often is confounded by hypovolemia and underlying comorbidities, such as cardiac dysfunction. Without considering the complex physiology, our desire to continue the debate of fluids vs vasopressors is on the brink of taking us back several decades when the management of sepsis was to start a fluid bolus, administer “Rocephin,” and initiate dopamine. But I remind myself that we have made advances – now it’s 1 L lactated Ringer’s, administer “vanco and zosyn,” and initiate norepinephrine. ■

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Cardiopulmonary exercise testing for unexplained dyspnea

BY CRAIG P. COOK, MD, AND
MATTHEW J. HEGEWALD, MD,
FCCP

Unexplained dyspnea is a common complaint among patients seen in pulmonary clinics, and can be difficult to define, quantify, and determine the etiology. The ATS official statement defined dyspnea as “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity” (*Am J Respir Crit Care Med.* 2012; 185:435). A myriad of diseases can cause dyspnea, including cardiac, pulmonary, neuromuscular, psychological, and hematologic disorders; obesity, deconditioning, and the normal aging process may also contribute to dyspnea. Adding further diagnostic confusion, multiple causes may exist in a given patient.

Finding the cause or causes of dyspnea can be difficult and may require extensive testing, time, and cost. Initially, a history and physical exam are performed with more focused testing undertaken depending on most likely causes. For most patients, initial evaluation includes a CBC, TSH, pulmonary function tests, chest radiograph, and, often, a transthoracic echocardiogram. If these tests are unrevealing, or if clinical suspicion is high, more costly, invasive, and time-consuming tests are obtained. These may include bronchoprovocation testing, cardiac stress tests, chest CT scan, and, if warranted, right- and/or left-sided heart catheterization. Ideally, these tests are utilized appropriately based on the patient’s clinical presentation and the results of initial evaluation. In addition to high cost, invasive testing risks injury.

Cardiopulmonary exercise testing (CPET) has been called the “gold standard” test for evaluation of unexplained dyspnea (Palange P, et al. *Eur Respir J.* 2007;29:185).

Symptom-limited CPET measures multiple physiological variables during stress, potentially identifying the cause of dyspnea that is not evident by measurements made at rest. CPET may also differentiate the limiting factor in patients with multiple diseases that each could be contributing to dyspnea. CPET provides an objective measurement

of cardiorespiratory fitness and may provide prognostic information. CPET typically consists of a symptom-limited maximal incremental exercise test using either a treadmill or cycle ergometer. The primary measurements include oxygen uptake (Vo_2), carbon dioxide output (Vco_2), minute ventilation (VE), ECG, blood pressure, oxygen saturation (Spo_2) and, depending on the indication, arterial blood

In some patients, CPET wasn't able to accurately differentiate cardiac disease from deconditioning.

gases at rest and peak exercise. An invasive CPET includes the above measurements and the addition of a pulmonary artery catheter and radial artery catheter allowing the assessment of ventricular filling pressures, pulmonary arterial pressures, cardiac output, and measures of oxygen transport. Invasive CPET is less commonly performed in clinical practice due to cost, high resource utilization, and greater risk of complications.

What is the evidence that CPET is the gold standard for evaluating dyspnea? Limited evidence supports this claim. Martinez and colleagues (*Chest.* 1994;105[1]:168) evaluated 50 patients presenting with unexplained dyspnea with normal CBC, thyroid studies, chest radiograph, and spirometry with no-invasive CPET. CPET was used to make an initial diagnosis, and this was compared with a definitive diagnosis based on additional testing guided by CPET findings and response to targeted therapy. Most patients (68%) eventually received a diagnosis of normal, deconditioned, hyperactive airway disease, or a psychogenic cause of dyspnea. The important findings from this study include: (1) CPET was able to identify cardiac or pulmonary disease, if present; (2) A normal CPET excluded significant cardiac or pulmonary disease in most patients suggesting that a normal CPET is useful in limiting subsequent testing; (3) In some patients, CPET wasn't able to accurately

differentiate cardiac disease from deconditioning as both exhibited an abnormal CPET pattern including low peak Vo_2 , low Vo_2 at anaerobic threshold, decreased O_2 pulse, and often low peak heart rate. In more than 75% of patients, the CPET, and focused testing based on CPET findings, confidently identified the cause of dyspnea not explained by routine testing.

There is evidence that invasive CPET may provide diagnostic information when the cause of dyspnea is not identified using noninvasive testing. Huang and colleagues (*Eur J Prev Cardiol.* 2017;24[11]:1190) investigated the use of invasive CPET in 530 patients who had undergone extensive evaluation for dyspnea, including noninvasive CPET in 30% of patients, and the diagnosis remained unclear. The cause of dyspnea was determined in all patients and included: exercise-induced pulmonary arterial hypertension (17%), heart failure with preserved ejection fraction (18%), dysautonomia or preload failure (21%), oxidative myopathy (25%), primary hyperventilation (8%), and various other conditions (11%). Most patients had been undergoing work up for unexplained dyspnea for a median of 511 days before evaluation in the dyspnea clinic. Huang et al's study demonstrates some of the limitations of noninvasive CPET, including distinguishing cardiac limitation from dysautonomia or preload failure, deconditioning, oxidative myopathies, and mild pulmonary vascular disease. This study didn't answer how many patients having noninvasive CPET would need an invasive study to get their diagnosis.

A limitation of both the Martinez et al and Huang et al studies is that they were conducted at subspecialty dyspnea clinics located in large referral centers and may not be representative of patients seen in general pulmonary clinics for the evaluation of dyspnea. This may result in over-representation of less common diseases, such as oxidative myopathies and dysautonomia or preload failure. Even with this limitation, these two studies showed that CPETs have the potential to expedite diagnoses and treatment in patients with unexplained dyspnea.

More investigation is needed to understand the clinical utility, and potential cost savings, of CPET for patients referred to general pulmonary clinics with unexplained dyspnea. We retrospectively reviewed 89 patients who underwent CPET for unexplained dyspnea from 2017 to 2019 at Intermountain Medical Center (Cook CP. *Eur Respir J.* 2022; 60: Suppl. 66, 1939). Nearly 50% of the patients undergoing CPET were diagnosed with obesity, deconditioning, or normal. In patients under the age of 60 years, 64% were diagnosed with obesity, deconditioning, or a normal study. Conversely, 70% of patients over the age of 60 years had an abnormal cardiac or pulmonary limitation.

We also evaluated whether CPET affected diagnostic testing patterns in the 6 months following testing. We determined that potentially inappropriate testing was performed in only 13% of patients after obtaining a CPET diagnosis. These data suggest that CPET results affect ordering provider behavior. Also, in younger patients, in whom initial evaluation is unrevealing of cardiopulmonary disease, a CPET could be performed early in the evaluation process. This may result in decreased health care cost and time to diagnosis. At our institution, CPET is less expensive than a transthoracic echocardiogram.

So, is CPET worthy of its status as the gold standard for determining the etiology of unexplained dyspnea? The answer for noninvasive CPET is a definite “maybe.” There is evidence that some CPET patterns support a specific diagnosis. However, referring providers may be disappointed by CPET reports that do not provide a definitive cause for a patient's dyspnea. An abnormal cardiac limitation may be caused by systolic or diastolic dysfunction, myocardial ischemia, preload failure or dysautonomia, deconditioning, and oxidative myopathy. Even in these situations, a specific CPET pattern may limit the differential diagnosis and facilitate a more focused and cost-effective evaluation. A normal CPET provides reassurance that significant disease is not causing the patient's dyspnea and prevent further unnecessary and costly evaluation. ■

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DIVERSITY IN MEDICINE

Momentum gains to ban legacy admissions

BY STEPH WEBER

Leaders of medical student groups and legislators in a few states are trying to convince medical schools to end a century-old practice of legacy admissions, which they say offer preferential treatment to applicants based on their association with donors or alumni. An estimated 25% of public colleges and universities still use legacy admissions, but a growing list of top medical schools have moved away from the practice.

Legacy admissions contradict schools' more inclusive policies, Senila Yasmin, MPH, a second-year medical student at Tufts University, said in an interview. While Tufts maintains legacy admissions for its undergraduate applicants, the medical school stopped the practice in 2021, said Ms. Yasmin.

As a member of the American Medical Association (AMA) Medical Student Section, she coauthored a resolution stating that legacy admissions go against the AMA's strategic plan to advance racial justice and health equity. The Student Section passed the resolution in November, and in June, the AMA House of Delegates will vote on whether to adopt the policy.

Along with a Supreme Court decision that could strike down race-conscious college admissions, an AMA policy could convince medical schools to rethink legacy admissions and how to maintain diverse student bodies.

In June, the court is expected to issue a decision in the Students for Fair Admissions lawsuit against Harvard University, Cambridge, Mass., and the University of North Carolina, Chapel Hill, which alleges that considering race in holistic admissions constitutes racial discrimination and violates the Equal Protection Clause.

Opponents of legacy admissions, like Ms. Yasmin, say such practices penalize students from racial minorities and lower socioeconomic backgrounds.

Some schools, such as Morehouse School of Medicine, Atlanta, the University of Virginia School of Medicine, Charlottesville, and the University of Arizona College of Medicine, Tucson, perform a thorough review of candidates while offering admissions practices

designed specifically for legacy applicants. The schools assert that legacy designation doesn't factor into the student's likelihood of acceptance.

Legislation may end legacies

In December, Ms. Yasmin and a group of Massachusetts Medical Society student-members presented another resolution to the state medical society, which adopted it. The society's new policy opposes the use of legacy status in medical school admissions and supports mechanisms to eliminate its inclusion from the application process, according to Theodore Calianos II, MD, FACS, president of the Massachusetts Medical Society, in an interview. "Legacy preferences limit racial and socioeconomic diversity on campuses, so we asked, 'What can we do so that everyone has equal access to medical education?' It is exciting to see the students and young physicians – the future of medicine – become involved in policymaking."

Proposed laws may hasten the end of legacy admissions. Last year, the U.S. Senate began considering a bill prohibiting colleges receiving federal financial aid from giving preferential treatment to students based on their relations to donors or alumni. However, the bill allows the Department of Education to make exceptions for institutions serving historically underrepresented groups.

The New York State Senate and the New York State Assembly also are reviewing bills that ban legacy and early admissions policies at public and private universities. Connecticut announced similar legislation last year. Massachusetts legislators are considering two bills: one that would ban the practice at the state's public universities and another that would require all schools using legacy status to pay a "public service fee" equal to a percentage of its endowment.

At schools like Harvard, whose endowment surpasses \$50 billion, the option to pay the penalty will make the law moot, Michael Walls, DO, MPH, president of the American Medical Student Association (AMSA), said in an interview. "Smaller schools wouldn't be able to afford the fine and are less likely to be doing [legacy admissions] anyway," he said. "The schools that want to continue doing it could just pay the fine." ■

NP-PA interactions: How the relationship can improve

BY BATYA SWIFT YASGUR, MA, LSW

Physician interactions with nurse practitioners (NPs) and physician assistants (PAs) are only going to increase in frequency. – The U.S. Bureau of Labor Statistics forecasts a 40% increase in the NP workforce by 2031, coupled with a 28% rise in PAs.

In recent reports on the quality of the relationships involving these health care professions, survey respondents mostly gave positive accounts of collaboration, using words such as like “comradery,” “teamwork,” “congenial,” and “cohesion.” But all was not perfect. Where and how could these important health care provider relationships improve?

PA: ‘Competition and collaboration’ with RNs

In a Medscape survey of more than 770 PAs about their working relationships with other health care professionals; 83% of them supported the idea of PAs and NPs practicing more independently from physicians, but sometimes it’s not easy to stay in their individual lanes.

One PA respondent complained that NPs get “more opportunities and preference,” another pointed to PA-NP “turf issues,” and a third griped about NPs’ “strong unions,” which have stoked more fighting about practice abilities and available settings.

Robert Blumm, MA, PA-C, a retired surgical and emergency medicine PA who regards himself as an advocate for both PAs and NPs, describes their interaction

as a “mixture of competition and collaboration.”

On one hand, the two groups typically “cooperate and do an excellent job, incurring patient errors similar to or less than physician colleagues or senior residents.” On the other hand, Mr. Blumm conceded, there is some jealousy among PAs over NPs’ advantage in staffing and hiring decisions, “since they don’t need [direct physician] supervision ... and there are limits on how many PAs can be supervised by one physician.”

Most PA-NP interactions are collaborative, although many people emphasize the relatively few conflicts, said Jennifer Orozco, DMSc, PA-C, president and chair of the American Academy of PAs.

“We see that a lot in this country,” she said. “People try to drive a wedge, but it’s often a misnomer that there’s a lot of arguing and infighting.”

NPs: Different backgrounds, same goal

The Medscape survey also included information from 750 NPs on working relationships; 93% of them favored nurses and PAs working more independently from doctors.

April Kapu, DNP, ARPN, has worked closely with PAs for more than 20 years. “In my experience ... they complement one another as health team members, although the education and training are somewhat different,” said Ms. Kapu, president of the American Association of Nurse Practitioners.

Some respondents noted the different educational trajectories for NPs and PAs. “Doctors and PAs are taught using the same model, but NPs are taught under the nursing

model,” wrote a family medicine PA.

In emergency departments where Mr. Blumm has worked, ICU NPs have an edge over PAs in terms of preparation, organization, and the tabulation of formulas. On the other hand, some of Mr. Blumm’s fellow PAs were also emergency medicine technicians or respiratory therapists, who had “2 years of classroom training, on par with that of medical students.”

Must these differences in training and education foment conflict between NPs and PAs? “We all bring something different to the table,” said Ms. Kapu, who also is associate dean for clinical and community partnerships at Vanderbilt University, Nashville, Tenn. “It is important to respect each person’s entry point, education, and training.”

Differing personalities and environments

Numerous PA respondents said that individual personalities and work environments are more likely to trigger issues with NPs than are differences in training.

“It depends on the team and situation and who the people are, not the letters behind their names,” an emergency medicine PA wrote. A surgical PA noted that “group dynamics and work culture differ from place to place,” while a third PA agreed that “it’s personality dependent, not title dependent.”

No single formula will resolve areas of NP-PA conflict, Ms. Orozco said. “What works in Chicago might not work in rural Colorado or Texas or California, but we do have to come together. The overall focus should be on greater flexibility for PAs and NPs. Patients will fare better.”

Corinne Young, MSN, FNP-C, FCCP, comments: It’s important to point out the vast consensus

of advanced practice practitioners were positive about working together. Focusing on the minority aims to drive a wedge between professions that serves no purpose other than to undermine the professions. The fact that 83% of PAs and 93% of NPs support working with each other should be commended and is not likely repeatable among other parallel work groups. Over the past 18 years of working in multiple hospitals and states with all varieties of health care professionals, I too have had the experience represented by the majority and have not witnessed the West Side Story-esk turf war the article implies. However, if singing and dancing is promised... I’m in!
Corrine Young is a member of the CHEST Physician Editorial Board.



Joint research, publishing could help

About a decade ago, Mr. Blumm joined with another PA and an NP to form the American College of Clinicians, the first joint PA-NP national professional organization. Although it disbanded after 6 years, owing to low membership, he hopes a similar collaboration will take off in the future.

“I also recommend that PAs and NPs publish articles together, with research as an excellent place to start,” he added. “PAs and NPs should stand together and be a source of healing for all our patients. Regardless of our titles, our responsibility is to bring healing together.” ■

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