Cleveland Clinic

RESPIRATORY EXCHANGE

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THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH TO PRONE POSITIONING IN ARDS

– p. 12

At the Respiratory Institute, specialists in pulmonology, allergy and immunology, infectious disease, and critical care medicine work in close collaboration to diagnose and manage the full spectrum of pulmonary and allergic disorders, serving more than 200,000 patients annually. The institute is part of Cleveland Clinic, a nonprofit, multispecialty academic medical center integrating outpatient and hospital care with research and education for better patient outcomes and experience. More than 4,500 staff physicians and researchers provide services through 11 patient-centered institutes. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*.

INSIDE

ON THE COVER — Prone positioning ventilation is one intervention that has been shown to significantly improve mortality among patients with acute respiratory distress syndrome.

DEAR COLLEAGUES,

Welcome to our second 2023 issue of *Respiratory Exchange*. This issue explores a wide range of topics from obstructive sleep apnea (OSA) to the components of a successful lung cancer screening program. You'll hear from several providers in our institute as they describe their approach to overcoming some of the challenges that we all face in our specialty.

Traditional treatment for OSA remains a challenge due to low patient adherence. But hypoglossal nerve stimulation (HNS) has emerged as an innovative therapeutic surgical approach for patients with severe OSA who are intolerant of the standard continuous positive airway pressure therapy. Two of our sleep specialists, Dr. Sunjeet Kaur and Dr. Reena Mehra, describe their experience with HNS in the article on page 6.

Although the number of students enrolled in respiratory therapy programs has declined in recent years, the demand for respiratory therapists continues to rise. The consequences of the shortage are dire, with patients potentially not receiving the level of care they need. When our caregivers noted that respiratory therapy programs are available but were inaccessible to those currently employed at Cleveland Clinic, the idea to inaugurate a respiratory therapy program at Cleveland Clinic was born. Dr. Umur Hatipoğlu and Karla Balasko discuss the new program and its conception on page 11.

As profiled on page 4, chronic cough can be one of the most frustrating conditions for patients and providers alike. The condition can severely affect a patient's quality of life, and the diagnostic process can be tedious. Dr. Michael Ghobrial explains how Cleveland Clinic is approaching this challenging condition and helping patients find relief.

While newer cancer treatments have led to increased survival, some of them come with severe complications. This has required more focused care by the ICU team. On page 16, Dr. Simon Mucha, Dr. Humberto Choi, physician assistant Elisha Fleig, pharmacist Heather Torbic and nursing manager Tiffany Lang show how Cleveland Clinic's new medical oncology ICU team is improving patient outcomes.

Similar to respiratory programs across the world, we are still working to fully understand the long-term impacts of COVID-19 on our patients. Dyspnea, like many of the associated conditions, presents a diagnostic and therapeutic challenge. Dr. Don Decoy and Dr. Rachel Taliercio discuss the importance of a multidisciplinary approach to care for patients suffering from dyspnea following a COVID-19 infection, on page 14.

When it comes to lung cancer screening, finding the balance point between benefit and harm is fundamental. On page 8, Dr. Peter Mazzone outlines 10 elements that make a successful lung cancer screening program and how these elements are incorporated into the program at Cleveland Clinic.

Finally, our cover story on page 12 reports on the benefits of prone positioning for patients with severe acute respiratory distress syndrome. While Cleveland Clinic has been advocating for prone positioning since the early 2000s, caregiver experiences during COVID-19 helped improve and expand application rates. Dr. Abhijit Duggal explains why having experienced nurses and taking a multidisciplinary approach to prone positioning are so critical.

I am grateful for the opportunity to share a portion of the work we do here in Cleveland Clinic Respiratory Institute. As always, we welcome the opportunity to connect and collaborate with you. Please be sure to take a look at the expanded list of clinical studies near the end of this issue and consider offering your patients the opportunity to participate in our research as we work to offer the highest level of respiratory care to all patients. I am exceedingly proud of what our team has accomplished as we take care of the patients of today and prepare to care for the patients of tomorrow.

I look forward to sharing more with you in future publications and hearing your thoughts and feedback.

Sincerely,

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E. Tom and Erika Meyer Professor and Chair
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THE CHRONIC COUGH CONUNDRUM

Diagnosing the cause of a chronic cough can be challenging and time-consuming, but multidisciplinary collaboration and the development of new treatments are improving the process

KEY POINTS

Chronic cough can have a significant impact on a patient's quality of life — and on their family and friends' quality of life.

Because there are so many causes of chronic cough, it's important to take a multidisciplinary approach in testing and evaluating patients.

Breakthrough therapies to treat chronic cough could be available soon, and the Chronic Cough Clinic has been enrolling patients for several trials of these therapies.

For patients with chronic cough — a cough that has been present for more than eight weeks — finding an answer to the simple question of "Why am I coughing?" can be a frustrating challenge. Often, the journey involves bouncing among several different specialists trying to pinpoint a cause.

Chronic cough can be related to several different conditions, so a multidisciplinary approach to diagnosis and treatment and strong communication between specialists are critical. At Cleveland Clinic, specialists work closely across the entire care path to accurately diagnose the cause of a patient's chronic cough.

"Determining the cause is the biggest challenge with chronic cough because there are so many conditions that could cause chronic coughing," explains Michael Ghobrial, MD, a pulmonologist and Director of the Chronic Cough Program. "For example, a patient could be experiencing chronic cough because of bronchial asthma, or maybe the cough is caused by undiagnosed gastroesophageal reflux disease or maybe it's secondary to postnasal drip. Other causes of chronic cough may be related to chronic interstitial lung diseases, chronic bronchitis, nonasthmatic eosinophilic bronchitis, allergic reactions, etc..," says Dr. Ghobrial, adding, " Less common is cough related to chronic upper airway hypersensitivity syndrome, often referred to as sensory neuropathic cough. While determining the cause of chronic cough is often challenging for caregivers, it's also frustrating for patients and their families."

IMPACT ON A PATIENT AND OTHERS

In addition to the challenges of diagnosis and treatment, the chronic cough itself has a significant impact on a patient's daily life … and on the daily lives of others.

"Recently, a patient with a chronic cough lasting over 20 years and his wife came in for a consultation," recounts Dr. Ghobrial. "When I asked him to tell me more about his cough, his wife interrupted and said, 'No, it's not his cough; it's our cough.' Chronic cough is not something that only affects the patient, but it has many indirect effects on the patient's family and friends too. This has become even more evident with the COVID-19 pandemic and patients who experience chronic cough as a result of long COVID."

Besides being a disturbance and the obvious pulmonary impact, chronic cough can impact other body systems as well. During a cough, the intra-abdominal pressure increases and some patients can develop urine incontinence or urethral, rectal and/or vaginal prolapse. Some patients have suffered recurrent hernias that fail surgical management because of chronic cough. These patients often are referred by their surgeons for evaluation and management prior to considering another surgery.

"While interference with daily living is the most common complaint I hear from patients with chronic cough, it's important to remember that chronic cough has some very disabling symptoms and can lead to significant risks," says Dr. Ghobrial.

THE DIAGNOSIS PROCESS

Most patients who see Dr. Ghobrial are referred by other pulmonologists, primary care physicians or other specialists. Dr. Ghobrial explains that the first step when consulting a new patient is to obtain a comprehensive history about their health, onset of the cough and its pattern. It's imperative to review the full workup that was completed by other physicians before patients

come to the Cleveland Clinic Chronic Cough Clinic. Evaluation often includes performing pulmonary function tests to uncover conditions like asthma or chronic obstructive pulmonary disease and a simple chest X-ray to look for any gross structural changes in the chest.

Further testing may be performed after the initial evaluation to help answer additional questions, such as blood work, more detailed imaging studies like a CT scan of the chest, and possible bronchoscopy. Depending on a patient's history, this could be followed with a gastrointestinal workup including pH monitoring, an upper endoscopy and and a Bravo™ reflux test. Patients usually will have a consultation with the Department of Allergy and Clinical Immunology, with possible allergy testing; and an ear, nose and throat exam with possible referral for speech evaluation for upper airway and vocal cord evaluation with a flexible laryngoscope.

TREATMENT

Dr. Ghobrial notes that depending on what the patient's history and physical exam indicate, he might talk to patients about undergoing empiric treatments for acid reflux, chronic rhinitis and postnasal drip before embarking on any advanced testing.

For certain patients who have sensory neuropathic cough, which is a disorder of the cough reflex, and who lack any other etiologies, neuromodulators may be an option. This type of therapy helps suppress or readjust the dysregulated cough reflex. Sometimes patients are referred for superior laryngeal nerve block to help control this type of cough when it is refractory to all medical therapy.

Dr. Ghobrial explains, "Our otolaryngology colleagues can perform these injections to help calm the cough reflex." Ultimately, though, Dr. Ghobrial notes that it's important to remember that coughing by itself isn't a disease — it is when it becomes dysregulated that it's a problem. "This is the problem that we need to work on, and it's through multidisciplinary collaboration, research, and individualized patient care and treatment that we can address this often frustrating condition," he says.

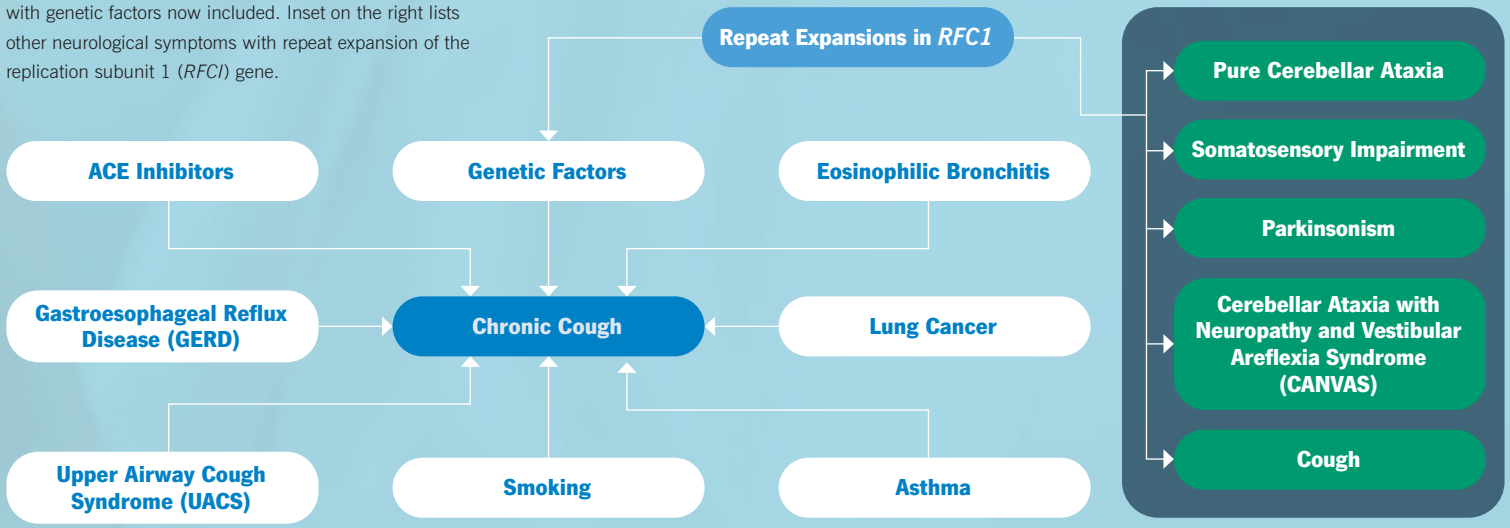
EXCITING NEWS FOR PATIENTS WITH CHRONIC COUGH

No new medications have been approved in the U.S. for the treatment of chronic cough since the approval of benzonatate in 1958. But new breakthrough therapies are in the final stages of development for the treatment of chronic cough. These include P2X3 receptor antagonists (gefapixant and camlipixant), a voltage-gated sodium channel antagonist (NTX-1175) and a transient receptor potential melastatin 8 agonist (AX-8). "We expect these medications to improve the quality of life for patients with refractory and unexplained chronic cough. Not only do they seem to be very effective treatments, but they also seem to be safe and well tolerated," says Dr. Ghobrial.

The Chronic Cough Clinic at Cleveland Clinic has been enrolling patients for several trials with these medications and will provide access to these medications as soon as Food and Drug Administration approval is fully granted.

Michael Ghobrial, MD

FIGURE. Flow diagram depicting causes of chronic cough, with genetic factors now included. Inset on the right lists other neurological symptoms with repeat expansion of the replication subunit 1 (*RFC1*) gene.



UPPER AIRWAY NEUROSTIMULATION DEVICE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

For patients with moderate to severe OSA who are intolerant of traditional CPAP therapy, HNS may provide a welcome improvement to quality of life

Written by Sunjeet Kaur, MD, and Reena Mehra, MD, MS

Obstructive sleep apnea (OSA), characterized by partial or complete airway obstruction during sleep reflecting apneas and hypopneas, respectively, afflicts nearly 1 billion individuals worldwide.[1] The standard treatment for OSA is continuous positive airway pressure (CPAP) therapy, which serves as a pneumatic splint to achieve airway patency. Although CPAP adherence is improving (range: 50%-70%), adherence remains a challenge for a variety of reasons, including mask interface issues, pressure intolerance, claustrophobia and nasal congestion.[2] Hypoglossal nerve stimulation (HNS) is an innovative therapeutic surgical approach that is increasingly being used for patients with severe OSA who are intolerant of CPAP therapy.

FIGURE 1. Depiction of hypoglossal nerve stimulator showing three implanted elements: a respiratory sensor, a small implanted electrical impulse generator and a hypoglossal nerve stimulation lead.

The Cleveland Clinic Sleep Disorders Center has been identified as a Center of Excellence for placement of the current commercially available HNS system (Inspire Medical Systems), leveraging cross-disciplinary collaborations involving Otolaryngology, Pulmonary and Neurology. The center has conducted 194 implantations (2015-2022).

UNDERSTANDING THE DEVICE AND THE SURGERY

The surgery for implantation is performed as an outpatient procedure and is done under general anesthesia. The device comprises three implanted elements: a respiratory sensor, a small implanted electrical impulse generator and an HNS lead (Figure 1). The system is activated by a hand-held remote control device for nightly use. Unilateral electrical stimulation of the hypoglossal nerve synchronized to respiration produces tongue protrusion. The genioglossus muscle innervated by the hypoglossal nerve is the primary tongue protrusion muscle and dilator of the upper airway. Electrical stimulation of the hypoglossal nerve leads to an increase in the genioglossal muscle tone and a slight protrusion of the tongue. The forward tongue movement and its increased muscle tone along with coupled movement of the soft palate results in an opening of the upper airway, thereby preventing the airway's collapse through stabilization.

BEST CANDIDATES AND RESPONSE

Effectiveness of and adherence with the device are well documented. However, selecting the most suitable patients and therapeutic tongue stimulation parameters is crucial for producing the best therapeutic outcomes. Criteria for candidacy include unsuccessful use of CPAP, apnea-hypopnea index (AHI) score between 15 and 65, at least 22

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years of age and a body mass index (BMI) < 35 kg/m^2. In the international ADHERE registry, we identified that increased age, reduced BMI and female sex were predictors of HNS response, defined by reduction in AHI.[3] Anatomical evaluation via drug-induced sleep endoscopy examination is also an essential step to assess candidacy, i.e., to establish absence of complete velopharyngeal concentric collapse.

Clinical use of HNS was evaluated in a multicenter, prospective cohort with 126 participants with mean age of 54.5 years, 83% male, mean BMI 28.4 kg/m^2 and mean baseline AHI of 34. HNS resulted in significant improvements in median AHI at 12 months: a 68% reduction, from 29.3 to 9.0 events per hour ($P < 0.001$).[4] In the randomization phase, 46 consecutive participants with adequate response to therapy were enrolled. The 23 participants randomized to the therapy-maintenance group at one-week did not have a significant change in AHI compared with a significantly higher AHI observed in the therapy-withdrawal group (25.8 events versus 7.6, respectively, at one-week follow-up, $P < 0.001$). Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire scores also improved. The only complication specific to the mechanism of the device was transient tongue weakness, which occurred in 17% of study participants. HNS therapy adherence, defined as daily use, remained high (81%).

Our group has shown that HNS also improves Insomnia Severity Index scores at one year, with results comparable to those for CPAP therapy.[5] We have also found that compared with CPAP therapy, HNS had less impact on blood pressure improvement and greater improvement of sleepiness symptoms.[5] The percentage of nonwhite patients receiving HNS implants is low, underscoring the need to identify barriers and expand access to the nonwhite patient population.[6]

HNS is approved for moderate to severe OSA in CPAP-intolerant patients without concentric collapse of the soft palate, and this option should be included in routine discussions of alternative therapies for OSA in cases of unsuccessful CPAP use. In the available outcomes data, HNS therapy is effective in reducing the severity of OSA and improving patient-reported outcomes of daytime sleepiness and quality of life.

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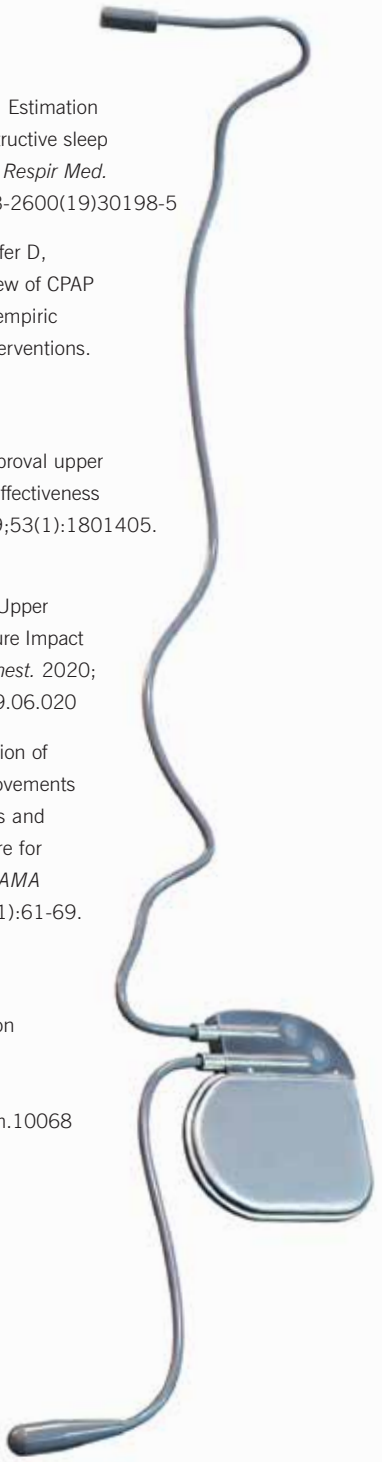

10 COMPONENTS OF A HIGH-QUALITY LUNG CANCER SCREENING PROGRAM

Finding the balance point between benefit and harm is critical for a successful lung cancer screening program, and these 10 elements can help centers optimize care

Written by Peter Mazzone, MD, MPH

The goal of screening is to detect a disease of serious consequence before it manifests clinical symptoms and to improve the likelihood of a cure. What makes a screening program successful is balance — the outcome of a successful screening program is reduced deaths from a disease without causing substantial harm to the population being screened. The benefit-harm balance for screening is different from that for diagnostic testing.

While diagnostic tests are used to evaluate individuals with symptoms or signs of a disease, we are testing asymptomatic individuals in screening. Only a minority of these individuals will benefit from screening, and the magnitudes of the benefit and the most common harms are not equal. But implementation of screening through the development of high-quality programs can optimize this balance.

Two large controlled trials have shown that lung cancer screening with a low radiation dose chest computed tomography (LDCT) scan reduces lung cancer mortality in a population at high risk for developing lung cancer.[1,2] These and other studies have also informed us about the potential harms of screening. Most commonly, harm can occur during the performance of the screening test (e.g., radiation exposure) or from the management of screen-detected findings (e.g., biopsy or surgery for screen-detected benign lung nodules, overtreatment of cancer). Thoughtful planning of the components of a lung cancer screening program can maximize the benefit and minimize the harm.

10 components of a high-quality screening program:

1 **Program structure:** At the extremes, a program can be centralized or decentralized. In a centralized program, individuals who are screen eligible are referred to the program and the program is responsible for their care. In a decentralized program, the care of individuals who are screen eligible is owned by the provider ordering the test. In between these extremes exists a hybrid option where the program elements are shared by the provider and the program. There is some evidence to suggest that the quality of centralized programs is highest, but all program structures can be successful if attention is paid to the remaining components.[3]

2 **Who to enroll in a lung cancer screening program:** Guidance from the United States Preventive Services Task Force has contributed to policy from the Centers for Medicare & Medicaid Services and other payers regarding who should be screened. Additional considerations at a program level include ensuring equity in access to care and the selection of individuals who are otherwise well enough to tolerate the evaluation of screen-detected findings and who would benefit from treatment of a screen-detected early stage lung cancer.

3 **How to identify and schedule screen-eligible individuals:** Uptake of lung cancer screening has been slow, with many screen-eligible individuals and providers either being unaware of their eligibility or choosing not to be screened. Educating individuals and providers, easing access to screening sites, and using reminders and automated communication within electronic health records can help increase uptake (Figure 1).

4 **Shared decision making:** The fulcrum of the balance between benefit and harm shifts based on individual values. Successful shared decision making (SDM) integrates available evidence with patient values — often incorporating a tool such as a decision aid — to help an individual make a decision that is in line with their values. A screening program should plan for SDM conducted by the central team or should support and share related tools with ordering providers.

5 **Performance and reporting of the LDCT:** A strong partnership with radiology is critical to high-quality screening. Key program elements are monitoring the radiation dose delivered, the quality of the images produced, the accuracy of the image interpretation and the delivery of the interpretation through a structured radiology report.

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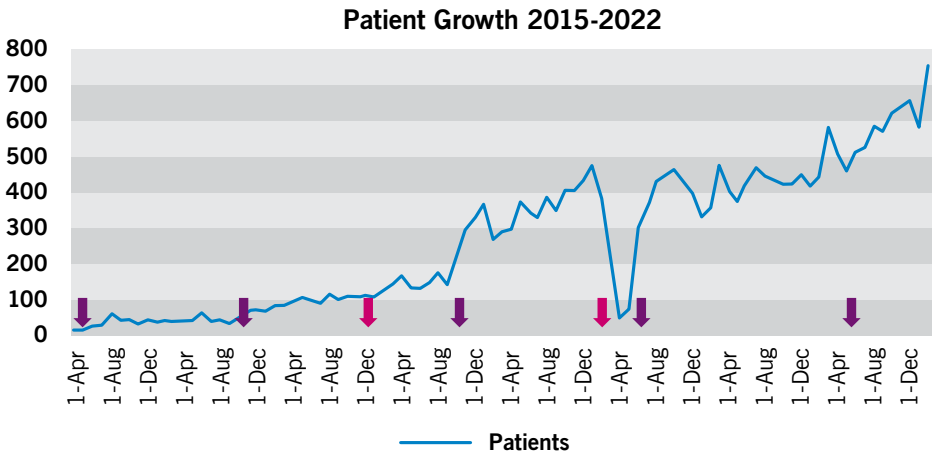

FIGURE 1. Cleveland Clinic health system Lung Cancer Screening Program growth. First purple arrow (4/2015), start of centralized program on main campus only, plateau at 40 patients per month; second purple arrow (10/2016), additional sites added, an additional nurse practitioner added, plateau at 100 patients per month; first red arrow (12/2017), best-practice advisory went live, referrals quadrupled, had to shut down the best-practice advisory; third purple arrow (10/2018), additional sites and personnel added, best-practice advisory restarted; second red arrow (3/2020), COVID-19 led to shutdown of program to new and annual visits; fourth purple arrow (6/2020), program reopened with more virtual visit shared decision making, growth in sites and personnel; fifth purple arrow (6/2022), increased direct electronic health record outreach, increase in sites and personnel. x-axis = date, y-axis = screening visits per month

6 **Lung nodule evaluation:** To expedite care of a screen- detected lung cancer and minimize harms from the evaluation of benign lung nodules, each program should have experts in lung nodule evaluation and management algorithms for small solid, larger solid and subsolid lung nodules. A common approach is to use the Lung CT Screening Reporting & Data System (Lung-RADS®) in the structured reports to guide the frequency of monitoring lower-risk lung nodules.[4] Review of the management of higher-risk lung nodules at a lung nodule tumor board may help the program meet the goals outlined.

7 **Non-lung nodule findings:** LDCT images often uncover other findings in the chest, such as parenchymal lung disease, coronary artery calcification, aortic aneurysms, and thyroid and adrenal nodules. These findings should be described in a standard fashion in a structured radiology report, and a screening program should develop an approach to supporting their management in partnership with specialists in these areas and in accordance with available guidelines.

8 **Screening adherence:** Adherence with annual screening and nodule follow-up has been reported to be quite low yet is critical to the success of a screening program. Systems should be put in place to allow for patient tracking and communication in order to maximize adherence.

9 **Smoking cessation:** Individuals who smoke should be offered smoking cessation guidance as part of the screening program, delivered by program personnel, through referral to central resources or by supporting the referring provider.

10 **Quality improvement:** Quality indicators have been developed in relation to the selection of screen-eligible individuals, the provision of smoking cessation guidance, adherence with annual screening and timely evaluation of lung nodules. Each program should be able to collect data that allows it to assess performance on these and other measures. This data should be tied to improvement projects. Program managers and population management software systems can be critical to these efforts.

LUNG CANCER SCREENING AT CLEVELAND CLINIC

Cleveland Clinic's lung cancer screening program is a centralized program. Providers across the health system refer eligible individuals to one of the program's providers at a local site. The program team engages each individual in an SDM visit that includes a review of eligibility, education about the benefits and harms of screening, use of a decision aid, an overview of likely findings, the need for annual screening, and smoking cessation counseling if needed. An LDCT is performed based on standardized protocols, with radiation dose monitoring and tracking. Trained thoracic imaging radiologists interpret the LDCT and report the findings in a structured report. Lung-RADS is used as the basis for the report and the management of low-risk lung nodules.

Cleveland Clinic also has several systems in place to ensure that each case is reviewed carefully and that patients follow their care team's recommendations. A multidisciplinary lung nodule tumor board reviews the management of all concerning lung nodules. Adherence with follow-up and annual screening is tracked using a population management software program. Algorithms and partnerships have been developed for the management of non-lung nodule findings. The program developed objectives and tracks key results by attaching action plans to areas in need of improvement.

By designing a lung cancer screening program with attention to these 10 components, screening programs can achieve the goal of optimizing the benefits and minimizing the harms of lung cancer screening.

Peter Mazzone, MD, MPH

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CLEVELAND CLINIC'S RESPIRATORY THERAPY TRAINING PROGRAM

Although the number of respiratory therapy training program enrollees has been declining, the demand for respiratory therapists continues to rise

Written by Umur Hatipoğlu, MD, MBA, and Karla Balasko, RRT, MBA

Over 440 respiratory care training programs are responsible for educating respiratory therapist candidates across the United States. The schools are accredited through a meticulous process overseen by the Commission on Accreditation for Respiratory Care (CoARC). Respiratory therapists are registered and credentialed by the National Board of Respiratory Care.

During recent years, however, a significant decline has been noted in the number of students enrolled in respiratory therapy training programs. In 2019, only 7,819 respiratory care program slots were filled of the available 12,394 slots. Conversely, according to the Bureau of Labor Statistics, the demand for respiratory therapists across the country will continue to rise until 2030, averaging 10,100 per year.

The current staffing shortage in Ohio is approximately 17% of budgeted respiratory therapist full-time equivalents. This number fluctuates widely among hospitals, though, sometimes exceeding 30%. The consequences of the shortage are dire and amplify in a vicious cycle — respiratory patients may not receive optimal care in those hospitals with critical staffing levels, and respiratory therapists are not able to function at the top of their license since they are bogged down with excessive scheduled work such as nebulized bronchodilator treatments.

This results in frustration for all involved: patients, respiratory therapists and attending clinicians. Unfortunately, burnout, retirement and simply leaving the profession have become commonplace in the respiratory therapy profession. As a result, hospitals pay enormous sums to staffing agencies to provide essential respiratory care services. The current status quo is not sustainable.

CREATION OF THE PROGRAM

Enterprise Respiratory Therapy at Cleveland Clinic includes 18 hospitals within the Cleveland Clinic health system in Ohio and Florida. While particularly exacerbated during the pandemic, staffing shortage was on the agenda for several years prior to the pandemic. During an internal recruitment event, Cleveland Clinic caregivers suggested that respiratory therapy programs are available but not accessible to those who are currently employed at Cleveland Clinic. The idea to inaugurate a respiratory therapy program at Cleveland Clinic main campus originated that day from caregiver suggestions.

Respiratory therapy programs can only exist under the auspices of accredited educational institutions. Hence, enterprise management began inquiry with local respiratory therapy schools on their interest in collaborating with Cleveland Clinic to start a satellite program in downtown Cleveland.

PARTNERSHIP WITH KENT STATE UNIVERSITY

After several productive meetings with Kent State University (KSU), a memorandum of understanding was produced between the institutions to start a respiratory therapy training program at Cleveland Clinic main campus. The program's curriculum would be jointly prepared by Cleveland Clinic and KSU. The satellite program would have a designated medical director and campus director, and Cleveland Clinic's advanced simulation center would provide hands-on education for the respiratory therapist candidates. All clinical rotations would take place at Cleveland Clinic facilities. The program would accommodate nine students.

The program was approved by the CoARC, and after extensive planning and recruitment efforts, the Cleveland Clinic–KSU respiratory therapy program welcomed its first nine students, an all-female class, on Jan. 17, 2023. The students are all currently employed in other Cleveland Clinic positions. Each has a unique story, either personal or concerning a loved one, that inspired them to become a respiratory therapist, but they all shared a strong desire to help the sick.

Umur Hatipoğlu, MD, MBA

Karla Balasko, RRT, MBA

THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH TO PRONE POSITIONING IN ARDS

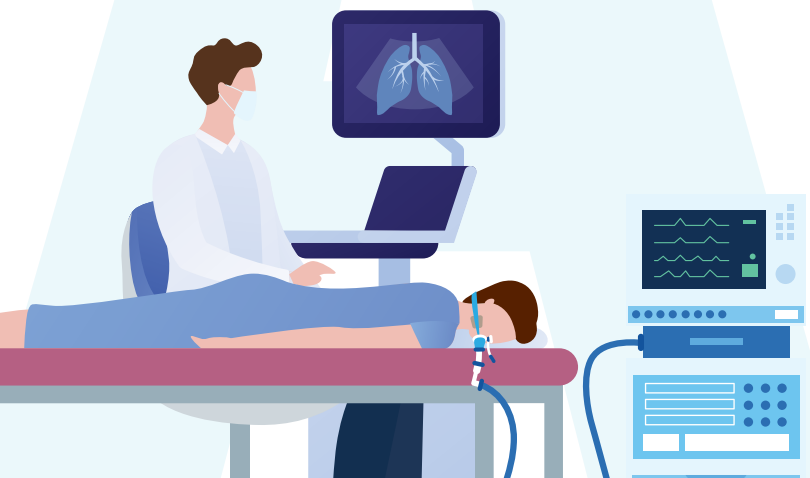
Cleveland Clinic pulmonologists share a framework for how to implement effective clinical protocols to standardize evaluation and management of complex acute respiratory distress syndrome

For patients with severe acute respiratory distress syndrome (ARDS), prone position ventilation (PPV) is one care intervention that has been shown to improve mortality significantly. The Prone Positioning in Severe Acute Respiratory Distress Syndrome (PROSEVA) trial in 2013 indicated that PPV can reduce a patient's absolute mortality risk by 16%.[1] However, one of the primary issues with PPV has been application of prone position in clinical practice. Following the publication of the 2013 study, two large international observational studies, Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure (LUNG SAFE) and ARDS Prone Position Network (APRONET), indicated that just 16%-33% of patients with severe ARDS underwent PPV.[2,3]

To improve PPV application rates, a recent study in the *Journal of Intensive Care Medicine* created a framework for multidisciplinary collaboration that helps identify patients who would benefit from PPV.[4] "Our study discusses our overall experience over the last decade with how we developed this protocol, and it also outlines the primer for other places to understand the main factors to consider as they institute prone position ventilation in patients with severe ARDS," says Abhijit Duggal, MD, a staff intensivist in Cleveland Clinic's Respiratory Institute and corresponding author of the article.

CLEVELAND CLINIC'S HISTORY WITH PPV

Cleveland Clinic's first PPV protocol was developed in the early 2000s as a nursing protocol to provide instruction for how to place patients in PP and provide care. PPV at this time was used inconsistently and for a duration of eight to 10 hours per day. But in 2009, when the H1N1 influenza pandemic occurred, the spike in severe ARDS patients led to increased usage of PPV and helped establish it as routine adjunct therapy at Cleveland Clinic's Medical Intensive Care Unit (MICU). This spike also led to two realizations about PPV: (1) Almost 60% of these patients were experiencing PP-associated pressure injuries, and (2) PPV was still being utilized inconsistently.



"We felt that the original PPV protocol was likely the culprit for these findings," says Dr. Duggal. "Since the protocol was primarily designed to help nurses care for patients already determined to be good candidates for PPV, it lacked specific instruction on patient selection, contraindications to PPV, or guidance on how to assess response to therapy and how long PPV should be utilized."

He continues: "The protocol was updated to address some of these issues, but because of the lack of high-quality evidence from large trials at the time, the protocol did not include specific guidance on patient selection and management until after the PROSEVA trial in 2013. In 2014, we updated it again and moved away from mechanical PP beds to manual prone positioning as well as including prone wedges, pillows and padding after we noticed pressure injuries and airway complications associated with the mechanical beds."

The MICU group reviewed data from 70 patients with ARDS after the application of these changes and found that while the number of pressure-induced skin injuries decreased dramatically, mortality was still high. This was attributed to patients being treated with PPV who fell outside the inclusion criteria established in the PROSEVA trial. The team also found that PPV was being incorporated into treatment as a rescue therapy late during persistent severe refractory hypoxemia or in the setting of marked hemodynamic instability.

When the team looked at the subgroup of "appropriately" selected patients, data showed that pateints derived significant benefits from PPV. The protocol was subsequently revised to stress the initiation of PPV as an early adjunct therapy in line with its use in the PROSEVA trial and highlight selection criteria for patients most likely to benefit from PPV.

Several additional revisions were made, including:

1. Introducing a hypoxemia checklist designed to help caregivers identify patients with moderate-to-severe ARDS and prompt caregivers to consider PPV for patient who meet the inclusion criteria.

2. Designing a nursing checklist to standardize pre- and post-PPV nursing care.

3. Designing a respiratory therapy checklist to enssure optimal maintenance of the endotracheal tube during and after PPV and standardize monitoring of ventilator mechanics in PPV.

4. Developing a new electronic medical record order set around the PPV protocol.

5. Implementing extensive educational seminars, webinars and hands-on simulation for physicians, trainees, nurses and respiratory therapists to improve training.

IMPACT OF COVID-19

The initial protocol was developed, modified and consistently implemented across five MICUs at just one hospital. But when the COVID-19 pandemic hit, the training and implementation accelerated dramatically.

"We implemented a train-the-trainer approach, which helped us maintain an adequate number of available instructors to make sure there was constant, uninterrupted education in target hospitals," explains Dr. Duggal. "This approach helped rapidly expand capacity and provide educational outreach to help meet local needs during the COVID surges. This also meant that some of the earliest trained caregivers became some of the earliest champions of PPV and content experts in their respective hospitals, where they could promote PPV implementation."

Between March and April 2020, more than 300 caregivers were trained in PPV to prepare for COVID-19, and this was in addition to the 456 caregivers who were trained prior to the pandemic. Dr. Duggal notes of the team's major takeaways was the importance of engaging with nursing leadership.

"When we are introducing a therapy, such as proning, one of the most critical aspects of the equation is having experienced nurses who understand how to move forward with this," says Dr. Duggal. "You can have nursing champions who really teach others, and everyone can be a part of the team to help prone these patients. But all of this requires teaching and proper implementation; otherwise you can cause harm because you won't understand what's the wrong way or the potential risk of doing something like this."

LOOKING AHEAD

Dr. Duggal notes that while education is a primary piece of PPV implementation, the team identified four other aspects of a successful PPV program. These include:

- **Patient factors:** Understanding the indications and contraindications for PPV.
- **Resources:** Identifying and incorporating necessary tools to ensure the PPV program runs smoothly, including injury prevention resources, educational resources and human resources.
- **Team culture:** Incorporating a multidisciplinary approach to care and empowering leaders to be champions of PPV and communicate any best-practice ideas.
- **Alternative therapies:** Understanding the role of different therapies for ARDS and knowing how to tailor them to patients correctly and timely.

Dr. Duggal notes that while implementation of the PPV framework in the Cleveland Clinic health system was successful, challenges still remain. "One thing that we are very interested in looking at is how to maintain the behavior of proning people and not go back to how it was," he says. "Presently, we are doing a lot of interventions in both teaching and training to identify potential barriers for patients with ARDS and see why providers might be at risk of going back to their previous behavior."

Abhijit Duggal, MD

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PERSISTENT DYSPNEA AFTER COVID-19 INFECTION: EVALUATION AND MANAGEMENT

Because of the associated symptoms, a multidisciplinary approach to care is essential

Written by Don Decoy, MD, and Rachel Taliercio, DO

KEY POINTS

Many patients who survive severe COVID-19 infection often experience pulmonary complications.

Patients with persistent dyspnea following a COVID-19 illness should undergo pulmonary testing and high-resolution chest imaging.

Patients with post-COVID-19 dyspnea will continue to present diagnostic and therapeutic challenges in both the near and distant future.

Post-COVID syndrome (PCS) includes a variety of conditions and symptoms, and the incidence of explicit signs and symptoms may vary according to the severity, duration and nature of the acute infections. Fatigue represents the most common concern in patients with PCS, and 17% to 72% of critically ill patients with COVID-19 present with the symptom. Respiratory symptoms are common in patients with PCS, and dyspnea is considered the most prevalent.

Pulmonary complications have been reported in SARS-CoV-2 survivors following acute pneumonia, with most patients experiencing mild to moderate respiratory complications, and approximately 5% of patients develop acute respiratory distress syndrome (ARDS).[1] Breathlessness and cough are noted in a substantial proportion of patients with long COVID-19 and may or may not correlate with prior COVID-19 severity. Other lung-related manifestations can include prolonged need for supplemental oxygen and difficulty liberating patients from mechanical ventilation.

ASSOCIATED SYMPTOMS

A majority of patients who survive severe COVID-19 illness have persistent symptoms. Physiologic abnormalities are common as well. In one survivor study, 42% of patients evaluated in clinic three months after hospital discharge had a significant reduction in diffusion capacity of the lung on pulmonary function testing, and this finding is the most commonly reported physiological lung impairment after acute COVID-19.[2] Decreased diffusion capacity appears to be related to the severity of acute illness and can also be detected in patients with moderate illness and normal lung function. Roughly half of COVID-19 survivors have persistent pulmonary and radiographic changes for up to six months following the acute illness. The radiographic abnormalities include ground-glass opacities; signs of reticulation, including coarse fibrous bands; bronchiectasis; and pulmonary fibrosis, and the abnormalities appear to be related to a more severe acute COVID-19 infection.[3,4]

Chronic cough can accompany dyspnea in patients with PCS. While radiographic changes, including lung fibrosis, can cause chronic cough and dyspnea, respiratory symptoms may persist in the absence of radiographic abnormalities and lung function impairment. Results from a cohort prospective study in the U.K. in 2020 revealed that respiratory symptoms may persist in patients with PCS even with improvement and normalization of pulmonary function and resolution of radiographic abnormalities.[5] This suggests that other pathophysiologic mechanisms might be responsible for dyspnea in patients with PCS.

TESTING AND MANAGEMENT

All patients with persistent dyspnea following a COVID-19 illness should undergo pulmonary function testing and high-resolution chest imaging.[6] Evidence of variable or fixed airflow obstruction can be managed with a trial of inhaled steroid and long-acting bronchodilator therapy. If patients do not have a clinical response to inhaled controller therapy, systemic steroids can be prescribed. It is important to minimize the morbidity of therapy with systemic steroids by prescribing lower doses and shorter courses.[7] Echocardiogram and ventilation/perfusion lung scanning can be ordered in the evaluation of persistent dyspnea, particularly if the pulmonary evaluation is unrevealing. Invasive cardiopulmonary exercise testing can be performed if the pulmonary and cardiac evaluations are unremarkable. For unexplained dyspnea following COVID-19 illness, we recommend referral to pulmonary rehabilitation. Patients can also be referred to speech language pathologists for the evaluation of dysfunctional breathing patterns. This condition can be successfully managed with respiratory retraining therapy.

After the patient is evaluated for ongoing dyspnea, cardiopulmonary exercise testing may identify the etiology of symptoms and those who may benefit from pulmonary or physical rehabilitation and functional medicine evaluation (e.g., patients with deconditioning, submaximal heart rate or dysfunctional breathing). This test is often helpful for classifying disease severity for treatment decisions and in the differential diagnosis of exercise intolerance and symptoms of dyspnea and fatigue.[8] The cause can be ventilatory, cardiac, pulmonary vascular, metabolic or deconditioning. Pulmonary rehabilitation may benefit those patients with mild symptoms (patients without an oxygen requirement and no cardiac etiology) as well as those with moderate to severe symptoms having persistent desaturations of less than 92%, a new requirement for supplemental oxygen or other concerning respiratory symptoms.

Patients with post-COVID-19 dyspnea require a multidisciplinary team approach to ascertain the cause of their symptoms, and the pulmonary evaluation is critical to establishing a diagnosis and treatment plan. Despite the downward trend of COVID-19 infections, patients with post-COVID dyspnea will continue to present diagnostic and therapeutic challenges for months and years to come.

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Don Decoy, MD

Rachel Taliercio, DO

HOW CLEVELAND CLINIC'S MEDICAL ONCOLOGY INTENSIVE CARE UNIT IMPROVES OUTCOMES

An interdisciplinary team of specialists improves outcomes with effective collaboration, communication, and identifying and implementing best practices

Written by Simon Mucha, MD; Humberto Choi, MD; Elisha Fleig, PA; Heather Torbic, PharmD; and Tiffany Lang

Approximately 5% of patients with cancer will require ICU care for management of acute life-threatening conditions often due to complications from the underlying cancer or toxicity from cancer-directed therapies. In Cleveland Clinic's Medical ICU (MICU), 20% of patients have a diagnosis of cancer that is being actively managed. We expect these numbers to further increase as progress in cancer treatment leads to increased survival.

KEY POINTS

As progress in cancer treatment leads to increased survival, the role of the Medical Oncology ICU becomes even greater.

Cleveland Clinic's Medical Oncology ICU includes medical intensivists, critical care pharmacists, advanced practice providers and an experienced nursing team.

Effective collaboration and communication between ICU and oncology teams is imperative.

Resource utilization, morbidity and mortality of critically ill patients with cancer remain high.[1,2,3] The complexity of their underlying illness, rapidly evolving oncologic therapies and distinct treatment-related toxicities make the ICU management needs of critically ill patients with cancer uniquely challenging. Therefore, Cleveland Clinic's main campus MICU developed a dedicated Medical Oncology ICU team to best meet these complex care needs. This team has been operational since February 2023.

A DEDICATED TEAM COMMITTED TO ONCOLOGY ICU CARE

The Medical Oncology ICU is an interdisciplinary team led by core medical intensivists with expertise in the care of critically ill patients with oncologic and hematologic disorders, dedicated critical care pharmacists, experienced advanced practice providers (nurse practitioners and physician assistants), and a nursing team cross-trained in oncology and critical care. The Medical Oncology ICU team works in close collaboration with the Cleveland Clinic Lymphoma, Myeloma, Leukemia, Bone Marrow Transplant and Solid Tumor Oncology inpatient services as well as Infectious Disease, Nephrology, Palliative Care Medicine and other specialty consulting services as needed.

ORGANIZATIONAL FACTORS IMPROVE OUTCOMES

Recent studies have shown that ICU length of stay is shorter among centers with greater experience providing cancer-specific treatment within the ICU, standardized practices and interprofessional care delivery models.[4,5,6] On the other hand, poor outcomes, including increased

This dedicated ICU team aims to address these issues by facilitating **effective collaboration** and communication between the ICU and oncology teams, standardizing the interdisciplinary ICU workflow, and **implementing protocols and best practices**.

IMAGE CAPTION: Medical Oncology ICU leadership (from left to right): Humberto Choi, MD (Associate Oncology ICU Director), Tiffany Lang (G62 MICU Nurse Manager), Simon Mucha, MD (Oncology ICU Medical Director), Deepa Jagadeesh, MD (Hematology Champion), Elisha Fleig, PA (APRN/PA Manager)

duration of ICU and hospital lengths of stay, have been shown to be associated with delayed ICU admission due to uncertainty about therapeutic benefit in the setting of limited ICU experience and poor communication between intensivist and oncologist.[7,8] Additionally, increased medication regimen complexity is associated with increased risk of medication errors and mortality.[9] Pharmacy interventions have been associated with reductions in adverse events, medication errors and resource utilization.[10]

This dedicated ICU team aims to address these issues by facilitating effective collaboration and communication between the ICU and oncology teams, standardizing the interdisciplinary ICU workflow, and implementing protocols and best practices. The Medical Oncology ICU conducts a daily team huddle, which allows for care coordination of our ICU patients and identification of patients admitted in regular floor oncology services who are at risk for decompensation and may need early ICU evaluation.

Simon Mucha, MD

Humberto Choi, MD

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SELECTED CLINICAL STUDIES

Consider offering your patients enrollment in a leading-edge clinical research trial at our Respiratory Institute. Contact the study coordinator or principal investigator for more information.

AIRWAY DISEASES

ALPHA1 ANTITRYPSIN DEFICIENCY (AATD)

A Multi-center, Single-Dose and Repeat-Dose over Eight Weeks, Sequential Cohort Study to Evaluate Safety and Tolerability as well as Pharmacokinetics of Two Different Doses of Alpha1-Proteinase Inhibitor Subcutaneous (Human) 15% Administered Subcutaneously in Subjects with Alpha1-Antitrypsin Deficiency

PRINCIPAL INVESTIGATOR: Vickram Tejwani, MD
STUDY COORDINATOR: Shauna Jo Hendershot | 216.554.6088

BRONCHIECTASIS

A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Center Study to Assess the Efficacy, Safety, and Tolerability of INS1007 Administered Once Daily for 52 Weeks in Subjects with Non-Cystic Fibrosis Bronchiectasis (ASPEN)

PRINCIPAL INVESTIGATOR: Lauryn Benninger, DO
STUDY COORDINATOR: Sheffa Almahd, RRT | 216.287.0906

CHRONIC COUGH

Observational Study of Chronic Refractory Cough and Associated Medical Sequela

PRINCIPAL INVESTIGATOR: Rachel Taliercio, DO
STUDY COORDINATOR: JoAnne Baran-Smiley, RN | 216.469.2855

COPD

Roflumilast or Azithromycin to prevent COPD Exacerbations (RELIANCE)

PRINCIPAL INVESTIGATOR: Umur Hatipoğlu, MD
STUDY COORDINATOR: Shauna Jo Hendershot | 216.554.6088

myAirvo 3 (High Flow Nasal Therapy; HFNT) for COPD patients in the home — a multi-centered randomized controlled trial

PRINCIPAL INVESTIGATOR: Vickram Tejwani, MD
STUDY COORDINATOR: Shauna Jo Hendershot | 216.554.6088

Video Telehealth Pulmonary Rehabilitation to Reduce Hospital Readmission in Chronic Obstructive Pulmonary Disease (TeleCOPD)

PRINCIPAL INVESTIGATOR: Umur Hatipoğlu, MD
STUDY COORDINATOR: Shauna Jo Hendershot | 216.554.6088

CYSTIC FIBROSIS

Cystic Fibrosis Foundation (CFF) Care Center and Patient Registry

PRINCIPAL INVESTIGATOR: Elliott Dasenbrook, MD
STUDY COORDINATOR: Cassie Best | 216.630.5281

A Prospective Study Evaluating Maternal and FetaL Outcomes in the ERa of ModulatorS (MAYFLOWERS)

PRINCIPAL INVESTIGATOR: Elliott Dasenbrook, MD
STUDY COORDINATOR: Cassie Best | 216.630.5281

Self-Sample Accuracy and Benefit Implementation Trial: S2wABIT

PRINCIPAL INVESTIGATOR: Lauryn Benninger, DO
STUDY COORDINATOR: Donna Lach, RN | 216.218.4997

ALLERGY

Food Allergy Center of Excellence Registry

PRINCIPAL INVESTIGATOR: Sandra Hong, MD
STUDY COORDINATOR: Sheffa Almahd, RRT | 216.287.0906

A Phase I clinical trial to evaluate the safety and tolerability of VLP Peanut (microcrystalline tyrosine [MCT]) in healthy subjects and subjects with peanut allergy and to explore preliminary signals of its efficacy (PROTECT)

PRINCIPAL INVESTIGATOR: Sandra Hong, MD
STUDY COORDINATOR: Sheffa Almahd, RRT | 216.287.0906

CRITICAL CARE MEDICINE

Cooling to Help Injured Lungs (CHILL) Phase IIb Randomized Control Trial of Therapeutic Hypothermia in Patients with ARDS

PRINCIPAL INVESTIGATOR: Rachel Scheraga, MD
STUDY COORDINATOR: Margaret Jeng | 216.219.4679

Center for Sepsis Driven Immunodeficiency

PRINCIPAL INVESTIGATORS: Rachel Scheraga, MD, and Vidula Vachharajani, MD
STUDY COORDINATOR: Margaret Jeng | 216.219.4679

INSPiRE-ICU: Isoflurane for ICU Sedation

PRINCIPAL INVESTIGATOR: Eduardo Mireles-Cabodevila, MD
STUDY COORDINATOR: Kiran Ashok | 216.538.9139

A Multicenter, Adaptive, Randomized, Controlled Trial Platform to Evaluate Safety and Efficacy of Strategies and Treatments for Hospitalized Patients with Respiratory Infections (STRIVE)

PRINCIPAL INVESTIGATOR: Abhijit Duggal, MD
STUDY COORDINATOR: Kiran Ashok | 216.538.9139

Ganciclovir to Prevent Reactivation of Cytomegalovirus in Patients with Acute Respiratory Failure and Sepsis (GRAIL-3)

PRINCIPAL INVESTIGATOR: Abhijit Duggal, MD
STUDY COORDINATOR: Caleb Chang, RN | 216.554.2792

Influenza and other Viruses in the Acutely Ill (IVY): Adult Inpatient SARS-CoV-2 Vaccine Effectiveness Surveillance

PRINCIPAL INVESTIGATOR: Abhijit Duggal, MD
STUDY COORDINATOR: Salem Stacey | 216.905.3491

DIFFUSE PARENCHYMAL LUNG DISEASE

A Multicenter Trial to Evaluate the Efficacy, Safety and Tolerability of HZN-825 in Subjects with Idiopathic Pulmonary Fibrosis

PRINCIPAL INVESTIGATOR: Leslie Tolle, MD
STUDY COORDINATOR: Sue Gole, RRT | 216.445.5836

A double blind, randomized, placebo-controlled trial evaluating the efficacy and safety of BI 1015550 over at least 52 weeks in patients with Idiopathic Pulmonary Fibrosis or with Progressive Fibrosing Interstitial Lung Diseases (PF-ILDs)

PRINCIPAL INVESTIGATOR: Leslie Tolle, MD
STUDY COORDINATOR: Sue Gole, RRT | 216.445.5836

A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of the Efficacy and Safety of Inhaled Treprostinil in Subjects with Idiopathic Pulmonary Fibrosis (TETON)

PRINCIPAL INVESTIGATOR: Joe Parambil, MD
STUDY COORDINATOR: Ron Wehrmann, RRT | 216.445.0574

Chronic Fibrosing Interstitial Lung Disease with Progressive Phenotype Prospective Outcomes (ILD-PRO) Registry

PRINCIPAL INVESTIGATOR: Daniel Culver, DO
STUDY COORDINATOR: Sue Gole, RRT | 216.401.5257

A Phase 1b Randomized, Double-Blind, Placebo-Controlled, Multiple-Ascending Dose Study to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of ACE-1334 Plus Standard of Care in Participants with Systemic Sclerosis (A1334-02)

PRINCIPAL INVESTIGATOR: Kristin Highland, MD
STUDY COORDINATOR: Ron Wehrmann, RRT | 216.445.0574

SARCOIDOSIS

Efficacy and Safety of Intravenous Efzofitimod in Patients with Pulmonary Sarcoidosis (ATYR1923-C-004)

PRINCIPAL INVESTIGATOR: Daniel Culver, DO
STUDY COORDINATOR: Shweta Josh | 216.445.7291

A Study to Assess the Efficacy and Safety of Namilumab in Participants with Chronic Pulmonary Sarcoidosis (RESOLVE-Lung)

PRINCIPAL INVESTIGATOR: Manuel Ribeiro, MD
STUDY COORDINATOR: Shweta Josh | 216.445.7291

Prospective Registry of Outcomes in Myocardial Sarcoidosis (PROMyS)

PRINCIPAL INVESTIGATOR: Daniel Culver, DO
STUDY COORDINATOR: Shweta Josh | 216.445.7291

Improving Black Sarcoidosis Patients' Care with a Collaboratively Developed, Patient Centered Program

PRINCIPAL INVESTIGATOR: Logan Harper, MD
STUDY COORDINATOR: Rhonda Jenkins | 216.444.0059

INFECTIOUS DISEASE

Prospective Observational Study of Human Immunodeficiency Virus (HIV) Positive Deceased Donor Renal Transplantation for HIV-Positive Recipients

PRINCIPAL INVESTIGATOR: Christine Koval, MD
STUDY COORDINATOR: Kiran Ashok | 216.538.9139

Breath Analysis to Detect Lung Disease (COVID Breath Study)

PRINCIPAL INVESTIGATOR: Nabin Shrestha, MD
STUDY COORDINATOR: Julie Sikora | 216.538.9571

INTERVENTIONAL PULMONOLOGY

A Sham Controlled Prospective Randomized Clinical Trial of the RejuvenAir® System for the Treatment of Moderate to Severe Chronic Obstructive Pulmonary Disease with Chronic Bronchitis (SPRAY-CB)

PRINCIPAL INVESTIGATOR: Tom Gildea, MD
STUDY COORDINATOR: Yvonne Meli, RN, BC, CCRP | 216.445.4215

A Prospective Multicenter Study of Transbronchial Microwave Ablation Using Robotic-Assisted Bronchoscopy in Patients with Oligometastatic Tumors in the Lung (POWER)

PRINCIPAL INVESTIGATOR: Michael Machuzak, MD
STUDY COORDINATOR: Yvonne Meli, RN, BC, CCRP | 216.445.4215

LUNG CANCER

DECAMP 1 PLUS: Prediction of Lung Cancer Using Noninvasive Biomarkers

PRINCIPAL INVESTIGATOR: Peter Mazzone, MD
STUDY COORDINATOR: Tiana Powell | powellt@ccf.org

Cascade-Lung: Cancer Screening Assay using Delfi; A Clinical Validation Study in Lung Cancer

PRINCIPAL INVESTIGATOR: Peter Mazzone, MD
STUDY COORDINATOR: Jax Rezakhani | 216.554.1669

Determination and Validation of Lung EpiCheck®: A Multianalyte Assay for Lung Cancer Prediction

PRINCIPAL INVESTIGATOR: Peter Mazzone, MD
STUDY COORDINATOR: Susan Charme | 216.318.5687

CFMEDIP-SEQ Assay Multicenter Prospective Observational Validation for Early Cancer Detection, Minimal Residual Disease, and Relapse (CAMPERR)

PRINCIPAL INVESTIGATOR: Peter Mazzone, MD
STUDY COORDINATOR: Cara Pannell | 216.308.6864

Detecting cancers Earlier Through Elective plasma-based CancerSEEK Testing – Ascertaining Serial Cancer patients to Enable New Diagnostic II (DETECT-ASCEND 2)

PRINCIPAL INVESTIGATOR: Peter Mazzone, MD
STUDY COORDINATOR: Patrick O'Rourke | 216.904.7198

LUNG TRANSPLANT

A Phase 3, Open-label, Randomized, Standard of Care-controlled, Parallel Study Arm Study to Demonstrate Efficacy and Safety of ARINA-1 in the Prevention of Bronchiolitis Obliterans Syndrome (BOS) Progression in Participants with a Bilateral Lung Transplant

PRINCIPAL INVESTIGATOR: Marie Budev, DO
STUDY COORDINATOR: Rijuta Singh | 216.894.3826

Cystic Fibrosis Lung Transplant Consortium (CFLTC) Biorepository and Registry (CLAD-PRO)

PRINCIPAL INVESTIGATOR: Maryam Valapour, MD
STUDY COORDINATOR: Erin McNamee | 216.210.8616

Cleveland Clinic Lung Transplant Biorepository

PRINCIPAL INVESTIGATOR: Maryam Valapour, MD
STUDY COORDINATOR: Katie Ross | 216.554.2597

PULMONARY HYPERTENSION

A Study to Evaluate Efficacy and Safety of Macitentan 75 mg in Inoperable or Persistent/Recurrent Chronic Thromboembolic Pulmonary Hypertension (MACiTEPH)

PRINCIPAL INVESTIGATOR: Gustavo Heresi, MD
STUDY COORDINATOR: Hailey Ryszka | 216.213.5993

A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate Sotatercept When Added to Background Pulmonary Arterial Hypertension (PAH) Therapy in Newly Diagnosed Intermediate- and High-risk PAH Patients (HYPERION)

PRINCIPAL INVESTIGATOR: Kristin Highland, MD
STUDY COORDINATOR: Natalie Taylor | 216.903.4705

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate Sotatercept When Added to Maximum Tolerated Background Therapy in Participants with Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Functional Class (FC) III or FC IV at High Risk of Mortality (ZENITH)

PRINCIPAL INVESTIGATOR: Kristin Highland, MD
STUDY COORDINATOR: Natalie Taylor | 216.903.4705

A Phase 2, Double-blind, Randomized, Placebo-controlled Study to Evaluate the Effects of Sotatercept versus Placebo for the Treatment of Combined Postcapillary and Precapillary Pulmonary Hypertension (Cpc-PH) due to Heart Failure with Preserved Ejection Fraction (HFpEF) (CADENCE)

PRINCIPAL INVESTIGATOR: Sanjeeb Bhattacharya, MD
STUDY COORDINATOR: Hailey Ryszka | 216.213.5993

Initial Evaluation of the Pulmonary Hypertension Functional Class Self Report

PRINCIPAL INVESTIGATOR: Kristin Highland, MD
STUDY COORDINATOR: Natalie Taylor | 216.903.4705

T32 SMARRT PROGRAM

With its T32 training grant award from the National Institutes of Health, Cleveland Clinic's Respiratory Institute, in collaboration with Lerner Research Institute, developed a program to accelerate the education of postdoctoral trainees with a research training curriculum.

The program, Supporting Multidisciplinary Achievement in Respiratory Research Training (SMARRT), is specifically tailored for MD, PhD or equivalent degrees in the areas of pulmonary, allergy or critical care medicine, and supports research in heart, lung, blood and sleep related disorders. The program is proud to graduate its inaugural class, both of whom will be joining Cleveland Clinic as staff physicians.

The hope is that the participants in this program will have the knowledge and skills to recognize the importance of different research paradigms, ranging from molecular medicine to public health sciences, and translate scientific discoveries into better clinical diagnostics and therapeutics.

For inquiries about the T32 SMARRT program, please contact to **dweikr@ccf.org** or **tsuangw@ccf.org**.

T32 SMARRT PROGRAM INAUGURAL CLASS

Erica Orsini, MD

Catherine Heinzinger, DO

RESPIRATORY EXCHANGE PODCAST

A Cleveland Clinic podcast for healthcare professionals exploring timely and timeless clinical and leadership topics in the disciplines of pulmonary medicine, critical care medicine, allergy/immunology, infectious disease and related areas.

Hosted by
Raed Dweik, MD, MBA | Chair, Cleveland Clinic Respiratory Institute, E. Tom and Erika Meyer Professor and Chair

2023 EPISODES

ATS LIVE! Interviews from the 2023 American Thoracic Society Conference (Part 1)

Host: Amy Attaway, MD
Guests and topics:
Dr. Elizabeth Regan: COPDGene study.
Drs. Onder Yildirim and Thom Conlon: COPD iNET.
Dr. Roger Kim: AI radio mix tool. Racial disparities in lung cancer screening.
Dr. Raed Dweik: Career Reflections and Becoming 2025 President of ATS

ATS LIVE! Interviews from the 2023 American Thoracic Society Conference (Part 2)

Host: Amy Attaway, MD
Guests and topics:
Dr. Anna May: Medication use before starting on positive airway pressure.
Dr. Neha Solanki: Platelets association with severe asthma.
Dr. Peng Zhang: Repurposing medications to decrease asthma inflammation.
Dr. Uddalak Majumdar: Mechanical ventilation and obstructive airway diseases.

Highlights from the 2023 American Thoracic Society Conference (ATS)

Host: Daniel Culver, DO
Chair, Cleveland Clinic Department of Pulmonary Medicine
Guest: Rachel Scheraga, MD
Department of Critical Care Medicine
Guest: Brian Southern, MD
Department of Pulmonary Medicine

Mistaken Identity: The Case for Early, Correct Identification of Fibrosing Mediastinitis

Host: Daniel Culver, DO
Chair, Cleveland Clinic Department of Pulmonary Medicine
Guest: Francisco Almeida, MD
Head, Fibrosing Mediastinitis Program
Guest: Atul Mehta, MD
Section Head, General Pulmonary Medicine

On the Job: Identifying Occupational Lung Disease

Guest: Mauve MacMurdo, MBChB
Director, Occupational Lung Disease Program

Where Lung Transplant and Health Policy Meet

Host: Sumita Khatri, MD
Guest: Maryam Valapour, MD
Director, Lung Transplant Outcomes Research

Where Are They? Patients with Alpha-1 Antitrypsin Deficiency

Guest: James Stoller, MD
Chairman, Education Institute

Burn Pit Exposure

Guest: Mauve MacMurdo, MBChB
Director, Occupational Lung Disease Program
Guest: Neha Solanki, MD
Department of Pulmonary Medicine

More episodes are available at **clevelandclinic.org/respiratoryexchangepodcast.**

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ART THERAPY AS A WAY TO HONOR ICU CAREGIVERS AND PROCESS COVID-19

As part of a collective way to heal and process the experienced grief and trauma of COVID-19, caregivers in each of our eight Ohio COVID-19 ICUs partnered with Art Therapy to create therapeutic works of art. The artwork and messages behind the art were shared at a Celebration Art reception, where people from different ICUs gathered and spoke from the heart about their teams' experiences throughout the COVID-19 pandemic.

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  clevelandclinic.org/criticalcaretransport
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ABOUT CLEVELAND CLINIC

Cleveland Clinic is a nonprofit, multispecialty academic medical center integrating outpatient and hospital care with research and education for better patient outcomes and experience. More than 4,500 staff physicians and researchers provide services through 20 patient-centered institutes. Cleveland Clinic is a 6,026-bed healthcare system with a main campus in Cleveland, 18 hospitals and over 220 outpatient locations. The health system includes five hospitals in Southeast Florida with more than 1,000 beds, a medical center for brain health in Las Vegas, a sports and executive health center in Toronto, a 364-bed hospital in Abu Dhabi, and a 184-bed hospital in London. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*.

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Cleveland Clinic

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STANDARDIZED EDUCATION IN VENTILATOR ASSISTANCE (SEVA) VENTROUNDS

SEVA VentRounds offers free, live, online training in using ventilator settings to evaluate the effectiveness of a patient's mechanical ventilation.

Held every other week on Tuesdays, 2-3 p.m. ET, each SEVA VentRounds session includes analysis of ventilator waveforms by course instructors using standardized methods and interactive discussion with participants.

This educational forum has been designed to benefit medical professionals who are (or have the equivalent medical education of) respiratory physicians, fellows or therapists.

INSTRUCTORS

› Eduardo Mireles-Cabodevila, MD
› Robert L. Chatburn, MHHS, RRT-NPS, FAARC

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