

ADVANCES IN CARDIOLOGY, INTERVENTIONAL CARDIOLOGY, AND CARDIOTHORACIC SURGERY

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NewYork-Presbyterian Cardiology and Heart Surgery ranks #4 in the nation.

Pursuing Progress in Pulmonary Hypertension

The Pulmonary Hypertension Centers of NewYork-Presbyterian are among the largest programs in the world for pulmonary hypertension, caring for patients with idiopathic and heritable pulmonary hypertension and those with medical conditions that predispose them to its development. Accredited by the Pulmonary Hypertension Association as Pulmonary Hypertension Centers of Comprehensive Care, the Heart Failure and Pulmonary Hypertension Services in the Perkin Center for Heart Failure of NewYork-Presbyterian/Weill Cornell Medical Center directed by Evelyn M. Horn, MD, and the Pulmonary Hypertension Comprehensive Care Center of NewYork-Presbyterian/Columbia University Irving Medical Center led by Erika S. Berman Rosenzweig, MD, manage some of the most complicated and sickest patients with this rare, progressive cardiopulmonary disease.

Pulmonary Hypertension and Heart Failure

In the Perkin Center for Heart Failure at Weill Cornell, physicians specialize in heart failure, pulmonary hypertension, and mechanical circulatory support. According to Dr. Evelyn Horn, pulmonary hypertension and right heart failure complicate the management of about one-third of the patients with heart failure. “Because we wear the hats for both pulmonary hypertension and heart failure, we provide best management strategies for all aspects of pulmonary hypertension. They could be idiopathic or hereditary; connective tissue disease; congenital heart disease associated PAH [WHO Group 1]; or a consequence of left-sided heart disease, such as heart failure reduced or preserve ejection fraction, cardiomyopathy or valvular heart disease; lung or hypoxic related; or chronic thromboembolic disease related pulmonary hypertension. All are a focus of our group and a strength at our institution,” says Dr. Horn.

“When we talk about pulmonary hypertension, that’s part of heart failure. It’s not a separate issue. The two are integrated,” continues Dr. Horn. “In many cases, right heart failure follows left heart failure, but management of difficult cases may require a special expertise and understanding of the interdependence of the right and the left ventricles. We cannot just extract what we know about left heart failure.”

Dr. Horn has particular expertise in right heart failure. In fact, historically, early on in her career,

which began at Columbia, she became known as the “right heart doctor” by colleagues seeking her expertise on cases complicated by secondary pulmonary hypertension or right heart failure. “The phenotype of heart failure has multiple etiologies, and not all heart failure behaves the same way,” says Dr. Horn. “Because of the nuances and subtleties involved in advanced heart failure, a multidisciplinary, collaborative center is of utmost importance.”

In particular, Dr. Horn points to the Center’s expertise in identifying the optimal timing of therapeutic interventions. “We also have fantastic technologies and therapies available, but these may not be appropriate for every patient. It is essential to understand when therapies will or will not work, and when one has to move on to mechanical assist devices, or heart transplantation for heart failure and lung transplantation for pulmonary hypertension if more conventional high risk cardiac surgery or catheter-based procedures are no longer possible. If we wait too long, we may have missed the opportunity to treat a patient, but no one wants to resort to devices or transplantation before a patient absolutely needs it. We were one of the first institutions to have an acute pulmonary embolus intervention program, which is a multi-discipline team. Most recently one of our cardiac surgeons has trained specifically at the University of California San Diego for pulmonary thromboendarterectomy.”

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Pursuing Progress in Pulmonary Hypertension *(continued from page 1)*



Dr. Evelyn M. Horn



Dr. Erika S. Berman Rosenzweig

Collaborations are Key

“Every one of our physicians is trained in both heart failure and pulmonary hypertension,” adds **Irina Sobol, MD**, who completed an advanced fellowship in Heart Failure and Pulmonary Hypertension at Weill Cornell and is now a full-time faculty member at the Perkin Center for Heart Failure and Director of the Advanced Heart Failure Fellowship Program. “Pulmonary hypertension is a very important focus of our group. It’s not a circumstance of ‘by the way, we do pulmonary hypertension.’ We treat all forms of PH and we have in-depth collaborations with designated providers that work closely with us.”

Dr. Sobol attributes the program’s successful outcomes to these collaborations with specialists and their own wealth of knowledge on pulmonary hypertension. “Our gastroenterologists are publishing discussions specifically on PH and gastroenterologic care in scientific journals. The team also has formal relationships with Weill Cornell’s renal group, which has formed a cardio-renal hemodynamics team within the renal department to support the PH and heart failure team. “They also come to our multidisciplinary rounds every Monday, where we discuss all of the PH and heart failure patients on our inpatient service,” notes Dr. Sobol.

Another strong and growing alliance is occurring with the oncology groups at Weill Cornell and Memorial Sloan Kettering Cancer Center. “We are seeing an increasing appreciation of aspects of pulmonary hypertension as sequela of not only the disease, but also, more importantly, of treatments of various malignancies,” says Dr. Sobol. “We collaborate very closely with oncologists on different aspects of evaluation and management of these patients.”

In addition, Dr. Sobol works closely with pulmonologists to explore possibilities for the treatment of pulmonary hypertension secondary to lung disease. “This is a population of patients who do not have very good treatment options outside of supportive care for their lung disease,” she says. “I’m currently serving as Principal Investigator on a multicenter clinical trial for patients with interstitial lung disease and pulmonary hypertension. This is a unique trial offering patients treatment with an inhaled pulmonary vasodilator, treprostinil, and evaluating efficacy of this drug in a patient population that has never been looked at before.”

Adds Dr. Horn, “We also have very strong collaborations with our imaging and our catheterization specialists to allow us to make

what I call ‘zebra diagnoses.’ We have a pulmonary hypertension anesthesia group and a critical care group. We also have a close relationship with the Rheumatology Division at Hospital for Special Surgery and see a lot of patients with rheumatological-based and inflammatory pulmonary, vascular, and cardiac disease, where the care presents something beyond the usual.”

“For example, many patients with scleroderma develop PH,” explains Dr. Sobol. “So, we have collaborated with rheumatologists not just in managing the care of these patients, but enrolling them in clinical trials as well. A current multicenter clinical trial sponsored by the National Institute of Allergy and Infectious Diseases is underway to evaluate the effectiveness of rituximab for scleroderma-associated pulmonary arterial hypertension [PAH].” The Phase 2 study, which includes investigators at Hospital for Special Surgery and Columbia, seeks to determine if rituximab changes the resistance in lung blood vessels in patients with systemic sclerosis (SSc) as measured by right heart catheterization after 24 weeks of treatment. A sub-study is evaluating the therapeutic effect of rituximab on the right ventricle of patients with SSc-PAH as determined by cardiac MRI.

“At times pulmonary hypertension is the primary condition and other times it is a marker of higher risk of another disease, which is why nuanced care and assessment for these patients is so critical,” continues Dr. Horn. “Because of our integration with other specialists, we can offer patient-specific, specialized care, approaching every patient in light of their unique characteristics. Whether it is a GI, pulmonary, rheumatological, or infectious disease complication, or otherwise complex disease management, we can all speak the same language. All of these different relationships and specialized groups mean that patients can be comprehensively approached and their specific conditions addressed.”

Covering All Bases of Care

The pulmonary hypertension program at NewYork-Presbyterian/Columbia was established more than 30 years ago, and today it is one of the largest adult and pediatric pulmonary hypertension programs for patients of all ages in the country. Researchers here have long been leaders in the field of genetic discovery in cardiovascular disease and, notably, pulmonary arterial hypertension, having reported the very first mutation associated with inherited forms of pulmonary hypertension.

Dr. Erika S. Berman Rosenzweig is the Director of the Pulmonary Hypertension Comprehensive Care Center and the CTEPH-PTE program at NewYork-Presbyterian/Columbia. A member of the Board of Trustees of the Pulmonary Hypertension Association and immediate past Chair of its Scientific Leadership Council, Dr. Berman Rosenzweig is an avid researcher pursuing genetic causes of and newer treatments for pulmonary hypertension, as well as novel approaches related to mechanical support for patients with end-stage pulmonary hypertension.

In Columbia's CTEPH-PTE program people can be treated for any form of clots in the lung that block or narrow the pulmonary vessels and disrupt circulation. "We have medication options, but we also have a team that is equipped to go in and surgically remove this chronic thromboembolic disease," says Dr. Berman Rosenzweig. "In fact, our program is one of the few in the country to perform pulmonary thromboendarterectomy, which can cure pulmonary hypertension."

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— Dr. Erika Berman Rosenzweig

"Evidence shows that surgery is the best treatment for CTEPH in extending a patient's survival," says **Koji Takeda, MD, PhD**, Surgical Director of the Pulmonary Thromboendarterectomy Program. "This complex and highly specialized surgery to remove chronic blood clots from arteries in the lung requires careful patient selection, a surgical skill set with this procedure, and a high level of postoperative medical care and management."

Columbia has also begun a balloon angioplasty program led by **Ajay Kirtane, MD**, who directs Columbia's cardiac catheterization laboratories, for patients with CTEPH who are inoperable. "This means that their disease is too far distal in the branches or other medical problems make them poor candidates for surgery," says Dr. Berman Rosenzweig. "So, we are able to provide the entire spectrum of treatment options in our toolbox, including medical, interventional, and surgical therapies."

Additionally, Dr. Berman Rosenzweig and her team participate in NewYork-Presbyterian's ECMO program, which has extensive experience providing mechanical support as a bridge to transplant or bridge to surgery specifically for patients with pulmonary hypertension. "Our ECMO program is highly respected in the field," she notes. "We can take patients who are at 'death's door' and offer them a temporary solution while we determine the optimal treatment plan. We have accomplished this with our surgical colleagues by using novel configurations of ECMO. These patients used to have sudden catastrophic pulmonary hypertensive crises, and now we can actually manage them safely through to transplant, if that's what they need. Mechanical support has enabled some of our patients with pulmonary hypertension to undergo elective surgeries such as hip replacement, as well as gall bladder and thyroid surgery. Our ECMO team also assisted in the management of a successful pregnancy, from delivery through recovery, of a patient with Eisenmenger's syndrome."

Columbia's medical and surgical team was one of the first to perform a palliative unidirectional valved Potts shunt in an adult with severe idiopathic pulmonary artery hypertension and has since performed the procedure in a teenager. "This is a novel procedure to decompress the lungs for pulmonary hypertension," explains Dr. Berman Rosenzweig. "We created a new type of one-way valve shunt as a palliative bridge in lieu of or before the patient would need a lung transplant."

"Essentially, the shunt provides a connection from the main pulmonary artery to the descending aorta," continues Dr. Berman Rosenzweig. "When the pulmonary artery or lung circulation is under high pressure the shunt enables the right heart to decompress, allows the right ventricle to function under less strain, and maintains fully oxygenated blood flow to the upper body, thereby improving exercise tolerance and reducing the risk of syncope and cardiovascular collapse. What we did that was novel was put in a one-way valve within this shunt so that the blood only goes from right to left and doesn't backflow into the lungs from left to right."

Columbia is one of only four centers in the country participating in the TROPHY 1-US (Treatment of Pulmonary Hypertension 1-US) clinical trial, which is evaluating pulmonary artery denervation using the Therapeutic Intra-Vascular UltraSound (TIVUS™) System. Performed in the catheterization lab by Dr. Kirtane, the approach seeks to improve functional capacity, hemodynamics, and overall effectiveness in patients with pulmonary arterial hypertension, notes Dr. Berman Rosenzweig, who serves as the Principal Investigator for the study at Columbia.

"There are currently 14 drugs that have been approved by the FDA for the treatment of patients with pulmonary hypertension. Our Center has participated in most of the pivotal clinical trials that prompted FDA approval for these agents. That's extremely rewarding for me because these patients have a disease that previously was universally fatal," says Dr. Berman Rosenzweig. "In conjunction with developing novel therapeutics, we are doing omics research with the hope of being able to uncover other causes of pulmonary hypertension that we can target differently and enable us to personalize treatment to the patient."

"Pulmonary hypertension can be a consequence of several diseases that are challenging in and of themselves. These include diseases of the connective tissue, congenital heart and left heart disease, and lung, hematological, oncologic, and renal and hepatic diseases," adds **Jennifer H. Haythe, MD**, Associate Medical Director, Adult Pulmonary Hypertension at Columbia. "We work closely with specialists in other fields, and in particular, rheumatology, pulmonology, congenital cardiology, and interventional cardiology, to help manage these patients. Patients suspected of having pulmonary hypertension should be referred to a pulmonary hypertension comprehensive care center that can offer this highly specialized expertise."

Redefining Pulmonary Vascular Disease

In 1973, pulmonary hypertension was classified into only two categories: primary pulmonary hypertension and idiopathic pulmonary hypertension. In 1998, the classification was expanded to five groups to incorporate more specific detail related to the underlying cause of the disease and has been updated approximately every five years to better reflect pathology, hemodynamics, how the disease is

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treated, and disease progression. However, as clinicians and scientists uncovered more understanding about pulmonary hypertension and its underlying complexities and many presentations, it became clear a few years ago that the current classification system put forth by the World Health Organization two decades ago, and albeit updated, was inadequate for current day clinical practice.

In 2014, the National Heart, Lung and Blood Institute launched the PVDOMICS (Redefining Pulmonary Hypertension through Pulmonary Vascular Disease Phenomics) program with additional funding from the Pulmonary Hypertension Association to augment the current pulmonary hypertension classification based on shared biological features of participants. Columbia and Weill Cornell, led by Dr. Berman Rosenzweig and Dr. Horn, respectively, were selected as two of the seven clinical centers across the country to carry out the study, which continues to recruit patients.

“Our pulmonary hypertension centers provide the broad expertise and the ability to carry out key novel testing that will enable us to help redefine pulmonary vascular disease in terms of pathobiologic substrates,” says Dr. Berman Rosenzweig. “By systemically characterizing pulmonary hypertension patients in the WHO groups utilizing clinical, biochemical, imaging, and physiological and pathological assessments, combined with genomic and RNA technology, we can improve our mechanistic and pathobiological understanding of the pulmonary vascular disease process, ultimately hoping to better target the right patient for the right therapeutic intervention.”

“As we take care of more and more patients with pulmonary hypertension, you realize that many overlap into more than one of the WHO groups,” says **Maria Karas, MD**, a cardiologist and faculty member of Weill Cornell’s Perkin Center for Heart Failure. “One of the important objectives of this project is to improve communication about the patient’s phenotype among healthcare providers. What it has brought to light is that every patient is

unique and there’s not just a ‘cookie cutter’ strategy that we can apply for all patients that are in one specific WHO group. There are different overlapping syndromes that are a challenge to treat.”

For example, describes Dr. Karas, “WHO Group I patients have precapillary hypertension. In some patients the underlying cause may be identified, such as autoimmune disease or familial genetic mutations, and in others the cause is unknown and classified as idiopathic. Sometimes it can be combined with lung disease, which falls under WHO Group III. And there may also be an overlap with left-sided heart disease, which is totally different and categorized within WHO Group II. How we describe these complex patients isn’t always easy.”

“The PVDOMICS study includes all spectrums – both traditional and non-traditional forms – of pulmonary hypertension, including those patients with heart failure and pulmonary hypertension, lung disease and pulmonary hypertension, and chronic thromboembolic pulmonary hypertension,” says Dr. Horn. “The group’s aim is to augment the current pulmonary hypertension classification based on shared biological features of 1,500 participants, including patients with all types of PH, patients with heart and lung diseases that place them at increased risk of developing PH, and 500 who serve as healthy comparators. The phenomic data generated is expected to be a rich resource to heart and lung disease investigators seeking to identify therapeutic targets.”

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