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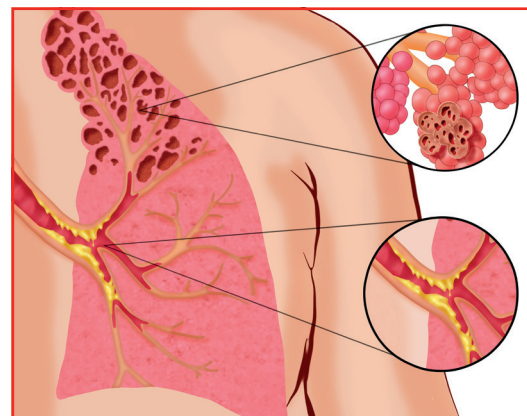
COPD: Converging Expertise on a Challenging Lung Disease

NewYork-Presbyterian has been pursuing advances in the diagnosis and treatment of lung disease and, in particular, chronic obstructive pulmonary disease (COPD), for a very long time, at a very high level. With major clinical programs in lung disease at Columbia and Weill Cornell, the Hospital covers the full spectrum of care for patients with COPD – from diagnostic expertise to innovative therapeutic studies and proven medical, surgical, and rehabilitation interventions. Most recently, NewYork-Presbyterian was ranked #1 for COPD in New York State and among the top in the country by *U.S. News & World Report*.

Byron M. Thomashow, MD, Medical Director of the Jo-Ann LeBuhn Center for Chest Disease at NewYork-Presbyterian/Columbia University Medical Center, and Medical Director of NewYork-Presbyterian's Lung Volume Reduction Program, and **Fernando J. Martinez, MD, MS**, who joined NewYork-Presbyterian/Weill Cornell Medical Center last year as Executive Vice Chairman of Medicine and who is a pulmonologist in the Division of Pulmonary and Critical Care Medicine, are long-time friends and collaborators in the field. Throughout their

The Changing Demographics of COPD

Some 16 million people in the United States have been diagnosed with chronic obstructive pulmonary disease according to data from the Behavioral Risk Factor Surveillance System, and the numbers continue to grow. Other data suggest that another 12 to 13 million have the disease but have gone undiagnosed. COPD is presently the third leading cause of death and second leading cause of disability. The cost of caring for COPD now stands at over \$50 billion a year.



Airways in chronic obstructive pulmonary disease

"The face of COPD is changing. It is increasingly a disease of the middle-aged and not the elderly, affecting more and more women, and 70 percent of people with COPD are now in the workplace."

— Dr. Byron M. Thomashow

careers, Dr. Thomashow, at Columbia, and Dr. Martinez, at the University of Michigan Medical Center and now at Weill Cornell, have been involved in a series of NIH studies that have been paradigm-changing for COPD. Today, with their medical, surgical, and scientific colleagues at NewYork-Presbyterian, they are making even greater progress in the understanding and care of this widespread and challenging lung disease.

"The face of COPD is changing," says Dr. Thomashow, a founder and current Board Chairman of the COPD Foundation, a non-profit organization established to improve the lives of people affected. "It is increasingly a disease of the middle-aged and not the elderly, affecting more and more women, and 70 percent of people with COPD are now in the workplace. Well over 40 percent have seen a doctor about their COPD over the last year; 17 to 18 percent have been hospitalized or in an emergency room because of it."

Dr. Thomashow notes that while the incidence of smoking in the U.S. has decreased to about 20 percent, in the COPD world the incidence remains close to 30 percent. "The damage from this disease takes so long to develop that even though more people are middle-aged, the impact continues for many years after they have stopped smoking."

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Dr. Byron M. Thomashow

But smoking, Dr. Thomashow reminds us, is only one of the causal factors of COPD. Environmental issues are at play as well. For example, worldwide, COPD is developing because of exposure to biomass fuels, which are used in many cooking stoves. “Over 3 billion people, half the world’s population, are exposed to these cooking stoves on a regular basis,” says Dr. Thomashow. “If you look at countries around the world, specifically in the Far East, where over 70 percent of men over the age of 16 are still smoking, not only do you have the smoking risk, but you also have terrible pollution in the cities and extensive use of biomass fuels in the rural areas. We’re only seeing the tip of the iceberg of this epidemic.”

A New Tool for COPD Screening

“COPD carries a huge burden and yet we still struggle with diagnosing it,” says Dr. Thomashow. “We face a number of challenges. There are issues of underdiagnosis and undertreatment, but also overdiagnosis and overtreatment. We need to find more of the 12 million who have the disease but are undiagnosed. We need to make sure that those who have already been diagnosed have been appropriately diagnosed.”

With a grant from the National Heart, Lung, and Blood Institute, NewYork-Presbyterian, led by Drs. Martinez and Thomashow, and five other clinical centers have been focused over the past three years on defining the optimal way of identifying COPD correctly in primary care settings. “This is a paradigm-changing project,” says Dr. Martinez. “The disease is diagnosed with a pulmonary function test, which is used infrequently in clinical practice in the United States. When we started this project, the goal was to develop a format that would allow primary care clinicians, in a very simple fashion, to identify individual patients who may be at risk for significant COPD requiring treatment. We asked our primary care collaborators how difficult they want the approach to be. They responded, ‘One question,’ but acquiesced to no more than five questions.”

The study investigators, through a very thorough process in concert with one of the world’s top groups in questionnaire development, were able to keep the patient questionnaire to five questions much to the surprise of all involved. “Some of the items were surprising but flowed directly from patient experience,” notes Dr. Martinez. “For example, you would think that an active smoking

history would be among them. But it did not make the final cut. In its place is a more general question querying about exposures: fume, dust, smoke. There are also items for breathlessness and whether you have missed school or work in the past year because of a respiratory condition. Another surprising one: Do you tire more easily than other people your own age? We have multiple ways of asking each of these questions, in English and in Spanish.”

“The results are really very impressive,” says Dr. Thomashow. “It’s most intriguing that the questionnaire does not ask, Have you smoked/are you smoking? This is potentially very important because data suggest that as many as 25 percent of people with COPD in this country never smoked at all. This would give us a completely new way of approaching the disease. When we started working with this process, not only were we able to find the people who were undiagnosed, we were also able to find the people who were overdiagnosed. So this method might actually revolutionize the way we deal with this disease, which is very exciting.”

Drs. Thomashow and Martinez are now in the process of establishing a follow-up study to test the validity of the questionnaire in up to 10,000 people in 50 different sites across the country.

Lessons Learned from NETT

In the late 1990s, Dr. Thomashow, at NewYork-Presbyterian/Columbia, and Dr. Martinez, who at the time was with the University of Michigan Medical Center, were the lead investigators in the top two centers in patient enrollment among the 17 centers to participate in the National Emphysema Treatment Trial (NETT) sponsored by the National Heart, Lung, and Blood Institute, the Centers for Medicare & Medicaid Services, and the Agency for Healthcare Research and Quality. NETT was the first multicenter clinical trial to investigate bilateral lung volume reduction surgery (LVRS) compared to medical therapy in the treatment of emphysema, with a secondary objective to develop criteria for identifying patients who are likely to benefit from the procedure. In LVRS diseased portions of the lung are removed, allowing for the expansion of remaining, still functional lung tissue.

“NETT was a sentinel study for many reasons. It clarified short-term and long-term risks and benefits of bilateral LVRS to treat severe emphysema and identified characteristics that help determine patients who are most likely to benefit and those at greater risk of death and complications from LVRS.”

— Dr. Fernando J. Martinez

“The study established the practice of LVRS globally,” says Dr. Martinez. “It was a sentinel study for many reasons. It clarified short-term and long-term risks and benefits of bilateral LVRS to treat severe emphysema and identified characteristics that help determine patients who are most likely to benefit and those at greater risk of death and complications from LVRS.” The results of NETT were published in 2003 in *The New England Journal of Medicine*.

“This was probably the largest trial ever performed for advanced COPD,” adds Dr. Thomashow, who also served on the study’s Steering Committee. “It was also the first time that Medicare had ever co-sponsored a program with the National



Dr. Fernando J. Martinez

Institutes of Health. Out of that trial, we found that there were individuals who should not have the procedure as it places them at high risk for mortality without any benefit. But we also found that a subset of patients – those with predominantly upper lobe emphysema – had improvements in quality of life, exercise capacity, and survival. It was the first treatment since oxygen, some 40 years earlier, to actually lead to improvement in survival of patients with this disease.”

Medicare reviewed the data and approved LVRS for people who met the criteria outlined in the National Emphysema Treatment Trial Centers of Excellence. NewYork-Presbyterian/Columbia was among those centers named. “Since that time we have been one of the most active centers in the country involved in this procedure,” says Dr. Thomashow. “But it’s interesting to note that although it was a procedure that obviously had potentially major benefits, it has been relatively underutilized – probably less than 800 cases since the trial was completed. Yet, before NETT, almost 2,000 cases had been performed around the country. The reason is almost certainly because the first paper that came out of that study that was published in *The New England Journal of Medicine*, and was front-page news, focused on the high risk group. I think that has influenced decisions going forward. Relatively few centers have continued to do this work.”

In April 2015, **Mark Ginsburg, MD**, Associate Director, General Thoracic Surgery, and Surgical Director, Center for Lung Failure at NewYork-Presbyterian/Columbia, presented 10-year data on LVRS at the 95th annual meeting of the American Association for Thoracic Surgery. Their results showed that LVRS produces durable benefits and should prompt wider adoption of LVRS in patients with severe emphysema.

The majority of patients underwent bilateral video-assisted thoracoscopic surgery. At one year patients’ lung function improved by a mean of 43 percent, and at five years after surgery, improvement was 44 percent, indicating that results of the surgery are durable. “Surgical LVRS remains the gold standard against which all other forms of lung volume reduction must be judged,” says Dr. Ginsburg. “Surgical LVRS should be more widely offered to patients with advanced emphysema who meet CMS selection criteria.”

“The results were really quite remarkable,” adds Dr. Thomashow. “There were no deaths six months post-surgery – down from an

8 to 12 percent mortality rate occurring in the earliest days of the NETT trial. Our one-year survival was 99 percent; three-year survival was 97 percent, and five-year survival 75 percent. Many of these patients had significant physiologic benefits and continue to be much better than they were before the surgery. When these results are presented at national meetings, the reaction is generally surprise as so few are doing this procedure.”

One area that Dr. Thomashow and his colleagues looked at more closely was ventilator efficiency – clearance of carbon dioxide and minute ventilation (VE). In comparing a select group of 55 subjects undergoing LVRS with 25 controls from NETT who received standard medical care, the researchers calculated VE/VCO₂ from cardiopulmonary exercise testing at baseline and at six months. “At six months, the patients undergoing surgery significantly increased their peak VO₂, work load, minute ventilation, VCO₂, and tidal volume while lowering peak and lowest VE/VCO₂ [improved ventilatory efficiency] and end-tidal carbon dioxide pressure. The control group did not display these changes. The changes were greatest in the surgery subjects who improved their exercise capacity after surgery and showed the most functional improvement, indicating an association of improved ventilation with improved functional outcome.”

Addressing Additional Treatment Questions

Dr. Martinez is also involved in the Long-term Option Treatment Trial (LOTT), another large study in COPD sponsored by the NHLBI and CMS. “The study, which began in 2006 and is now wrapping up, focused on another crucial question: What is the role of oxygen therapy in COPD?” says Dr. Martinez. “We’ll have an answer by the end of the year. It, too, is expected to transform care for COPD.”

NewYork-Presbyterian is also one of 14 research centers across the country participating in a large, multisite study funded by the Department of Defense – with the University of Alabama as the primary investigative center – that seeks to determine if beta blockers can reduce the acute exacerbations in patients with COPD without causing major side effects. The study will enroll approximately 1,100 patients. “Here we are taking an old, simple cardiology drug and applying it to a different population to see if it has a targeted benefit in that population,” says Dr. Martinez. “If this crucial study demonstrates that beta blockers are safe and effective, it will offer yet another treatment option with the potential to dramatically help patients who suffer with the debilitating effects of this chronic disease.”

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