Editor's Memo

Redefining the Window of Opportunity in Lung Transplantation

Our articles in this issue span the spectrum of treatment for severe pulmonary hypertension (PH), not only from a historical perspective through our profiling of the work of Joel Cooper, MD, a true pioneer in the surgical suite, but also in terms of the therapeutic options available, from medical therapy to lung transplantation. The discussion is particularly timely and relevant because the allocation system for donated lungs may soon be changed by the United Network of Organ Sharing.

Although the options for managing patients with right ventricular failure have expanded significantly through the use of prostanoids and with atrial septostomy, the paramount issue remains in those patients whose disease is no longer adequately responding to these measures: When is it the right time to proceed with transplantation or listing?

Our experts on the Pulmonary Hypertension Roundtable addressed a multitude of issues surrounding this question. Although outcomes have improved in the 20 years that lung transplantation has been available for PH, the observation of Dr Cooper—that this surgery remains among the most demanding and difficult largely because of postoperative considerations—remains true. Outcomes in general for lung transplantation for PH have been inferior to those for many other diseases, such as chronic obstructive pulmonary disease.

Because of strides made in medical management, however, we have been able to extend the window prior to lung transplantation in many patients. Ironically, this sometimes has proved to be a mixed blessing. The advent of continuous intravenous epoprostenol, a medication that has revolutionized the treatment of pulmonary arterial hypertension, thereby offering the potential to delay transplantation, may have resulted in a higher proportion of extremely sick, higher-risk patients presenting for transplantation.

The articles in this issue offer a comprehensive resource to address these questions as they delineate the practices and policies prevailing at centers of excellence throughout the country. Once again, I wish to congratulate my colleagues who contributed to this issue on a job well done.

Victor F. Tapson, MD
Editor-in-Chief

Joel D. Cooper, MD, the Physician Who Launched Lung Transplantation on Its Path to Successful Outcomes

Joel D. Cooper, MD

You might say that every patient with pulmonary hypertension whose life has been extended by a lung transplant continues to live and thrive in the long shadow cast by Joel D. Cooper, MD, the physician who performed the first successful lung transplant surgery in 1983. Not that Dr Cooper would seriously consider this metaphor, but there is no doubting the everlasting impact of his research in lung transplantation.

Dr Cooper no longer performs lung transplantation in PH, yet he remains a towering figure not only in this setting but in his other areas of clinical interest, including general thoracic surgery, lung volume reduction surgery for emphysema, myasthenia gravis, gastroesophageal reflux, and esophageal cancer. Although lung transplantation in PH has evolved significantly since the time when Dr Cooper pioneered the operation, the principles and precepts governing the technique when it was first performed offer insights into how far its evolution has progressed.

Currently Chief of the Division of Cardiothoracic Surgery, Washington University at Barnes-Jewish Hospital, St. Louis, Missouri, Dr Cooper recalls his years in residency at Massachusetts General Hospital where he served under the well-known thoracic surgeon Hermes Grillo, MD, whom he credits as the inspiration for later research on lung transplantation. Moving to the University of Toronto after completing his residency in Boston, Dr Cooper was further encouraged by his colleagues to pursue his interest, particularly by William Nelems, MD, who had studied with surgeons in Europe. By 1978, 38 lung transplant operations had been attempted worldwide, but with no success. "Most of them were deathbed rescue attempts, maybe one attempted every other year around the world," said Dr Cooper.

"We went back to the lab and we saw that most of these patients had died within 2 weeks and those who lived longer all had complications of the airway connection. We studied these issues in a dog model and came up with a better understanding." A combination of factors, including poor blood supply, posed obstacles to a successful outcome. "During surgery the bronchial arteries are severed and cannot be reconstructed. High doses of prednisone were also required to prevent rejection. We recognized that it was also sort of a wound-healing problem. Cyclosporin helped and finally we were able to improve the technique in a dog model." Not long afterward, in 1983, Dr Cooper and his associates performed the first successful lung transplant.

This first successful transplant occurred several years before additional attempts were made in patients with PH. "It was thought at the time that you needed to replace both the heart and the lung. We went back to the lab and working with a dog model we produced a model of right heart

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patients we have done a liver biopsy to make sure it is essentially a noncirrhotic liver, in order to be confident that we weren't going to have a problem in that way. For most PH patients we have found that if we treat them with enough inotropes and really treat them vigorously, we can usually control the ascites. If we couldn't control it, I would be quite worried and might consider liver biopsy in some situations. I have actually not encountered that yet, where I couldn't control the ascites with inotropes and diuretics in a primary PH patient.

Dr Tapson: Bob and John, I'd like to thank you both for taking the time to discuss these issues for *Advances in Pulmonary Hypertension*. I look forward to our future interactions.

Profiles

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strain. We did it by gradually constricting the pulmonary artery with a band, tightening it every week or two until the right heart failed just as it does in the clinical situation. Then we released the band, dropping the pressure to more normal in these dogs and we studied how quickly the right ventricle recovers if you take the load off of it. This was a prelude to considering lung transplant rather than heart-lung transplant and we found that in these dogs there could be very rapid recovery of function in the right ventricle."

This led Dr Cooper and colleagues to rethink their strategy, namely, that they did not need to perform both a heart and a lung transplant. This meant that many more organs would be available for additional patients. "You could do a lung transplant and the heart would recover. We found that the heart undergoes remodeling, the thickened right ventricle returns to a more normal shape and thickness." Dr Cooper recalls that a single lung transplant for PH was performed on November 21, 1989, in a woman who survived and lived for a number of years. "We do have good results for single lung transplant for PH even though a bilateral is done most of the time now. Fortunately, medical management of these patients has greatly improved, so the number of patients coming to transplant has diminished somewhat," he added.

"I've always felt that lung transplantation for PH is the most critical, most demanding surgery—not so much from a technical standpoint, although it does involve the use of cardiopulmonary bypass, but in terms of postoperative care of the patient. Therefore, the best results will be obtained by centers that are very experienced. The problem is, if you have too few centers of excellence, you are not accessible to the patient."

The program at Barnes Hospital, however, is exceptional in that the hospital assumes the responsibility for the patient while he or she is on the waiting list. "In the long term, successful outcomes for lung transplantation, particularly for PH, require an experienced team," said Dr Cooper.

In the Next Issue

Portopulmonary Hypertension

- Understanding the natural history and pathophysiology
- Screening and current diagnostic criteria
- Therapeutic options
- Liver transplant considerations and outcomes