A Personal View on the History of Lung Transplantation

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Lung transplantation experienced a roller coaster of a ride during its clinical development, having experienced a difficult childhood and traumatic teens, and finally emerging as a gloriously successful treatment for advanced lung disease in adulthood. I am minded to compare it with the development of a Medoc premier cru classé in this respect!

The first successful attempt at isolated human lung transplantation was performed in the USA by James Hardy in 1963. I choose to use the word success with the same confidence as Humpty Dumpty in Lewis Carroll’s Alice through the looking glass who said “when I choose a word it means exactly what I choose it to mean.” I say this because some twenty more years later the Toronto group led by Joel Cooper claimed the first successful clinical examples of isolated lung transplantation and certainly their patients survived longer and left the hospital.... Nevertheless Hardy is usually credited with the important first clinical step, in an era when there was no concept of brain stem death so, unbeknownst to him, he was also the first to use a DCD donor of which more later. What we do know after Hardy’s “success” was that over the next 15 years the literature recorded 40 further attempts all of which failed, largely as a result of primary graft failure, bronchial anastomotic breakdown and multiorgan failure – problems which seemed insuperable. By the late 1970s interest in lung transplantation as a clinical prospect had waned, contrasting with major developments in renal, liver and cardiac transplantation.

The introduction of cyclosporine as a highly effective immunosuppressant heralded renewed interest in lung transplantation, notably at Stanford University. The combination of effective safe immunosuppression, the development of heart lung transplantation ensuring a viable blood supply with a tracheal anastomosis by coronary bronchial anastomoses and a meticulous and rigorous approach in the laboratory under Shumway’s direction led to clinical success.

In 1982 the Stanford group reported success in a small series of patients with advanced idiopathic pulmonary hypertension.

From these modest beginnings, lung transplantation has developed into a well-established treatment option for a wide range of respiratory conditions including COPD, lung fibrosis and, perhaps most notably, cystic fibrosis. Moreover, advances in surgical technique have permitted the re-introduction of isolated lung transplantation initially as single, then bilateral followed by lobar transplantation. Isolated lung transplantation, in particular bilateral transplantation, is now by far the most common surgical approach in the current era.
Success in long term, survival with a good life quality following single lung transplantations was first reported in 1986 by Joel Cooper and colleagues from Toronto and in 1987 the Newcastle team performed the first successful isolated lung transplantation in Europe on a 50-year-old lady suffering from advanced Langerhan’s Cell Histiocytosis who was a patient of mine both before and following transplantation.

As the early lung transplantation recipients aged, it was recognised that many began to develop progressive irreversible airflow obstruction which on lung biopsy was shown to be due to obliterative bronchiolitis. Initially thought to be a manifestation of chronic allograft rejection alone, it is now recognised to represent allograft dysfunction as a consequence of diverse insults including infections and gastro oesophageal reflux. It remains the most important barrier to improving long-term outcomes of lung transplantation and is a major focus of international research.

Recently, use of the macrolide antibiotic azithromycin, which also has anti-inflammatory properties, has been shown to be able to halt the progress of this condition and improve lung function in approximately 50% of patients.

It is a comforting fact that over the last 25 years we have witnessed huge improvements in survival following lung transplantation. In the late 1980’s a recipient only had a 50% chance of living one year whereas now 40-50% of recipients can expect to live over 10 years. Moreover, the quality of life gained is excellent with near normal restoration of exercise tolerance and the ability to fully participate in work and active recreations.

Many female recipients worldwide have now had successful pregnancies after lung transplantation.

The shortage of donor lungs remains a problem and despite increases in the number of potential donors joining national donor registries, the number of lungs from brainstem dead donors has not increased significantly in many countries. New approaches, including the use of lungs from non-heart beating donors (the DCD donor pool I spoke of when recalling Hardy’s exploits) have increased the donor pool. More recently, the size of the donor pool has further been boosted by the technique of reconditioning lungs that are not safe to use for primary lung transplantation during ex vivo perfusion and ventilation. It would be remiss of me not to note the work of Stig Steen from Lund and Shaf Keshavjee from Toronto in developing this approach.

The last 25 years have seen lung transplantation grow from a procedure associated with little success to an established therapeutic option for patients with advanced lung disease. It has brought hope on the basis of its success to many patients. It is truly a remarkable story of medical advancement in the field of respiratory medicine and I am proud to have played a small role.