

Lung Transplantation

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“He who would learn to fly one day must first learn to stand and walk and run and climb and dance; one cannot fly into flying.”

Nietzsche

“Education is the kindling of a flame, not the filling of a vessel.”

Socrates

The recent addition of a volume on lung transplantation (vol. 243) in the very successful “Lung biology in health and disease” series follows on from the preceding volume addressing Lung and Heart Transplantation (vol. 217) in 2006. This is testament to the continuing rapid growth in knowledge and practice in the field of lung transplantation and justifies the excellent panel of international experts that has been assembled to produce a state-of-the-art review with broad appeal. Each expert addresses a particular facet of lung transplantation along key thematic lines. Although this provides us with a clearly organised multidimensional review in which each individual piece is well researched and presented, the reader’s educational experience could have been further enhanced by more explicitly addressing the difficult but extremely important topic of the “integrated whole” at key junctions.

It is now just 30 years since technical advances in thoracic surgery and the use of cyclosporin enabled the first successful lung/heart transplant to be performed, ushering in the modern era of lung transplantation. Having learned from earlier failures, the initial pioneers were, appropriately, very cautious early on but what commenced as a hopeful endeavour has gradually now become the standard of care for selected patients with end-stage lung disease in many parts of the world. Over the past 7 years the tendency for lung transplantation to be regarded as “routine and expected” has accelerated even further. Although this review clearly outlines the major advances that continue to be made in this field, there is still along way to go before long-term results (survival and quality of life) match expectations for the majority of lung transplant recipients. In particular, we need to continue to invest in improving our understanding of individual alloresponses and tolerogenic pathways, better titrating immunosuppressant drugs according to specific pharmacodynamic effect, more effective control of the destabilising influence of infection on the allograft, better management of comorbidities and the impact of psychosocial factors on quality of life, improving service structures to keep up with present day needs, and strengthening the ethical framework required to navigate increasingly new and complex territory (younger patients, older patients, patients with increasingly severe comorbidities, bridging to transplant strategies, multiple organ transplants and re-transplantation); and all this in the current setting of increasing economic restraint, workflow restructuring and healthcare reform.

This volume successfully bridges much of the knowledge gap that has opened up over the past 7 years. After a short general section that serves as an introduction, there are six distinct subsections that address pre-transplant issues, donor management, the recipient operation, post-operative care, and early and late medical management in logical sequence. In general, the chapters follow a theme of introductory comments before launching into chapter-specific information for the most part, and then variably entertaining future possibilities. Overall, each section is well detailed and although there is a strong descriptive focus, the use of the best available evidence to support current practice is used whenever possible. As such, all important areas are covered and

the review is well balanced. A final section on future directions is appropriate but could have been further enhanced by succinctly expanding this section to cover key areas of controversy and a more holistic view (*e.g.* individual patient management decisions/ key trade-offs and healthcare systems support/societal wishes).

The general introduction, focusing on history, immunology, ethics and service structures, is accurate and provides useful pillars of background information. A brief overview of where lung transplantation sits in the broader context of solid organ transplantation, as well as key similarities/differences and variations in practice and long-term outcomes between the various solid organs currently being transplanted may well have been useful here to better orientate the reader.

The chapter on ethics is particularly well written and outlines unique ethical concerns for each group of patients, as well as general ones that relate to organ scarcity, availability, allocation and payment (equity, justice and utility). Similarly, the chapter on structure and support for success is thoroughly relevant in discussing key aspects of programmes and service that are often not addressed in other chapters.

The next three sections address: pre-transplant evaluation and management (part 2), donor management (part 3) and the recipient operation (part 4). Each of the chapters addressing the pre-transplant evaluation of specific patient groups and the issues relating to lung transplant decision making in part 2 is well thought out and written.

In part 3, the availability and suitability of donor organs are identified as major limiting factors for lung transplantation. In this setting the evolution of lung donor allocation score in the USA is described in detail and compared and contrasted with the practice in other countries. Lung donor selection criteria are clearly listed in this section and were appropriately conservative initially, but gradually relaxed, thereby helping to increase donor organ utilisation without necessarily decreasing short-term lung and patient outcomes.

In part 4, the specific surgical operations used for lung transplantation are practically outlined with a focus on appropriate technical aspects for single lung transplantation, bilateral sequential lung transplantation, heart–lung transplantation and lobar lung transplantation. These four chapters in the recipient operation section are coupled with two further chapters at either end of the spectrum regarding the transplant operation; namely, anaesthesia for lung transplantation and managing the sensitised patient.

Parts 5, 6 and 7 address post-operative care, early medical management and late medical management, respectively. The general principles of immediate post-operative support is detailed in the chapter on critical care management, with a specific focus on key problem areas including ventilatory support, haemodynamic/renal support, immunosuppression induction protocols and infection prophylaxis, as well as a broad range of other potential ICU-related complications. Primary graft dysfunction is, appropriately, the biggest focus in this section and its description, classification and risk factor profile are well detailed and lead directly to a more speculative discussion on pathobiology and to potential prevention and treatment considerations. Early surgical complications are also addressed in this section, with a major focus on technical and practical aspects such that common things are relatively well covered, although perhaps the long-term negative impact of phrenic nerve and vagal nerve injuries could have been emphasised more. This section appropriately finishes with a discussion on extracorporeal membrane oxygenation (ECMO) support. The use of both veno-venous and veno-arterial ECMO is outlined with a

particular focus on post-transplant care, although pre-transplant and intra-operative support is also addressed. Practical comments regarding specific indications, contraindications, advantages and disadvantages are variably made for each scenario and mode of support.

The section on early medical management begins with a chapter on maintenance immunosuppression which is classification based and very descriptive. This approach is very useful with respect to how these drugs work, their monitoring (if applicable) and their likely toxicities and drug interactions. However, it is relatively poor at addressing the principles of decision making relating to immunosuppressant drug use and the inevitable risk/benefit trade-offs that need to be made. Similarly, each of the individual chapters on infection post-lung transplantation (specifically fungal, viral and bacterial infections) cover the general area well but perhaps still underplay the ever-present trade-offs in decision making and management that result from diagnostic limitations in this area. The section on viruses covers DNA viral reactivation well, particularly CMV and the continuing diagnostic and management advances for what was once a major cause of morbidity and mortality post-transplantation (with specific mention also of both other herpes viruses and other DNA viruses). However, the focus on respiratory RNA viruses is relatively light, which is to be expected given the diagnostic difficulties here and the spasmodic use of newer molecular techniques to systematically diagnose these infections. Nevertheless, the potentially large negative impact of community respiratory viruses on long-term lung allograft outcomes is being increasingly appreciated. This section concludes with a chapter on post-transplant pathology that is largely descriptive and covers the histopathology of the various types of allograft rejection and certain infections in particular, but again the diagnostic limitations of histopathology in this setting are important to elucidate and the implications of this could have been more explicitly explained and discussed.

The section on late complications and medical management is appropriately focused on bronchiolitis obliterative syndrome (BOS), its known risk factors, and the likely pathobiological pathways that may lead to its development. The chapter on BOS diagnosis and management is clearly written but perhaps fails to adequately discuss the pros and cons of this label, and the alternative label of chronic lung allograft dysfunction, on conceptual thinking and research opportunities. As expected, risk factor modification and treatment options are described following the usual paradigms (and remain limited). Malignancy associated late complications are well covered. A review of non-allograft related chronic complications post-lung transplantation (including drug toxicities and the impact of co-morbidities), as well as psychosocial/socioeconomic and quality of life issues that apply to all patients completes this section.

The final section on future directions is appropriately far-reaching in delving into the potential opportunities that may be offered by broader proteomic/genomic approaches and “new inspirations” that may be associated with the development of an artificial lung.

Overall, this review of lung transplantation represents an excellent, up-to-date reference that addresses all aspects of this field and significantly builds on the previous edition. The editors and all those involved with this book should be congratulated on achieving their aims of giving all caregivers (specialist physicians, nurses, surgeons, intensivists, immunologists, pathologists, social workers and transplant coordinators) access to an increased understanding of the biological, medical and surgical basis of lung transplantation, as well as the psychosocial, ethical and healthcare system implications of this intervention. Finally, this review arguably provides both an extremely solid platform and the kindling spark for continual progress and improvement in the future in this complex but extremely rewarding area of medicine.

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