Overview: Future Approaches to Renal Replacement and Regeneration

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Improvements in surgical techniques and medical management of posttransplant complications, and recent development of novel immunosuppressive strategies have improved the outcome of organ transplantation and have made cell transplantation a front line therapy for replacement of pancreatic islets in recipients with autoimmune (type 1) diabetes. Indeed, organ replacement is presently considered the therapy of choice for end-stage failure of the heart, lungs, liver, and kidney. However, this therapy is not without challenges and risks.

The first and most important challenge in organ transplantation is the shortage of organs; simply put, there are not enough organs for potential candidates on transplant waiting lists or for patients with organ failure that have not even been listed for a transplant. Even when organs become available, this availability may only come after a lengthy wait, so that the patient with renal failure experiences the risks and complications of both dialysis and transplantation.

The second challenge is that recipients need to continue to take immunosuppressive drugs for the rest of their lives to prevent allograft rejection. These drugs engender the risk of side effects and toxicities, as well as general morbidities related to overall immunosuppression, including infections and malignancy. In addition, these drugs likely contribute to increased mortality from cardiovascular disease, the major cause of premature death in transplant recipients.

The third challenge is the problem of chronic rejection or allograft nephropathy. This problem arises in part because immunosuppressive strategies do not completely inhibit alloimmune responses, resulting in slow progressive deterioration in graft function.

The last challenge—but not the least—is the cost of transplantation, which places a burden on society and may limit application of some new technologies.

In this issue of “Frontiers in Nephrology,” a group of world-renowned experts in the field tackle recent advances and future technologies in the field of transplantation that may someday solve the issue of organ shortage. The theme of this “Frontier” is the research currently under way to address the long-term imbalance of organ supply and demand. The authors, by looking into the future, provide state-of-the-art reviews on five important topics.

Platt and coworkers reconsider the potential need for kidney transplantation, suggesting it may exceed current estimates by an order of magnitude, and they review new ways that xenotransplantation might be used to address that need. The novel approaches to xenotransplantation include the use of animals as an incubator for organogenesis and as a source of cells for regeneration. Hammerman presents an intriguing review of growing new organs in situ via xenotransplantation of developing primordia from animal embryos. He reviews results of studies exploring the therapeutic potential for renal organogenesis after transplantation of kidney primordia. Atala’s group focuses on tissue regeneration and engineering, which introduces the concepts of cloning and stem cells for regenerative medicine. The review by Piedrahita et al. specifically addresses the issue of somatic cell cloning as a way of developing histocompatible cells or complete organs that can be used for transplantation. They focus on the factors affecting cell differentiation and nuclear reprogramming. Strom’s group tackles the issue of stem cell transplantation and its use for organ and tissue repair.

Collectively, these reviews point the way to the future of organ, tissue, and cell transplantation. Some ideas may be ready to implement immediately as a novel form of renal replacement; others suggest ways to provide a platform for regeneration and tissue repair that could prevent organ failure altogether.