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Looking into the crystal ball: kidney transplantation in 2025

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Kidney transplantation is now the treatment of choice for end-stage renal disease. Since 1954, when the first successful kidney transplantation between identical twins was performed, tremendous advances have occurred in the science and clinical practice of transplantation surgery and medicine that have considerably improved the outcomes of the procedure. Indeed, kidney transplantation provides recipients with a survival advantage over dialysis. However, several challenges remain that limit the success of transplantation for chronic, irreversible, renal insufficiency.

The ultimate goal in transplantation is to have an unlimited number of organs available for all potential recipients; these individuals will develop immunologic tolerance and accept the organ with no acute or chronic rejection, and will maintain normal graft function without long-term maintenance immunosuppression. This tolerant state should prevent the complications of long-term immunosuppression, which include premature cardiovascular disease, metabolic disorders, infections and malignancy. With transplantation science continuing to advance at a rapid pace, how far will we have progressed toward achieving this idealistic goal by 2025?

The recent report describing successful induction of tolerance in four kidney transplant recipients by creation of transient mixed allogeneic chimerism (Kawai T *et al.* [2008] *N Engl J Med* 358: 353–361) is an encouraging first step towards achieving clinical tolerance. The Immune Tolerance Network (www.immunetolerance.org) is currently conducting several pilot tolerance trials in human kidney and liver transplant recipients. The challenge is to learn from the successes and failures of these trials and ultimately expand the pilot protocols into multicenter, randomized trials, to determine whether tolerance is truly achievable on a wide clinical scale.

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New immunosuppressive drugs will continue to be tested in clinical trials with the goal of minimizing overall immunosuppression and enhancing adherence. To this end, the long-term administration of biological agents such as monoclonal antibodies and fusion proteins could be a useful strategy (Vincenti F and Kirk AD [2008] *Am J Transplant* 8: 1972–1981). Looking into the crystal ball, it is not far-fetched to imagine, in the near future, kidney transplant recipients being maintained on a single immunosuppressive agent, and selected recipients needing no immunosuppressive drugs at all. Obviously, these individuals will require frequent and careful monitoring to detect incipient rejection and ensure a stable, tolerant state.

Solving the problem of organ shortage is likely to be difficult in the short term. However, improving the long-term survival of kidney transplants and developing the capability to induce and maintain tolerance will ease some of the burden of organ shortage, as retransplantation will no longer be required for those recipients whose transplants currently fail. More advances in the science of xenotransplantation and possibly some pilot clinical trials are likely in the next decade or two, but widespread transplantation of pig kidneys into humans is an unlikely prospect, at least in the foreseeable future. Cloning of fully functional and transplantable human organs is likely to lag behind xenotransplantation, but this idea is far from fantasy (Atala A [2008] *Curr Stem Cell Res Ther* 3: 21–31). Mesenchymal stem cell transplantation to prevent progressive organ damage through immunomodulation or regeneration (or both) is a promising strategy.

Clearly, the next two decades will see interesting and important advances in the field of organ transplantation. Only time will tell whether the above predictions will become clinical realities.

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