

portant, Sobel suggested, is that a clear procedure be established that protects the privacy of the justice who is ill and assigns responsibility for ensuring competence to a group of that person's peers. According to Supreme Court spokeswoman Kathy Arberg, "The Court has an internal practice" for dealing with such situations.

When concerns arise in other settings about a person's competence to do an important job — be it driving a school bus, flying an airplane, or serving as a general in the military — an increasingly common strategy is to require a confidential examination by a forensic psychiatrist. This measure has periodically been used to assess the competence of sitting federal judges, and it could also be used in the case of a Supreme Court justice. If the current

justices have already agreed on such a policy, or have adopted some other procedure for responding to concerns about an individual justice's competence, they should share that decision with the American public.

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MEDICAL HISTORY

Transplantation — A Medical Miracle of the 20th Century

Peter J. Morris, F.R.S.

Fifty years ago, on December 23, 1954, a kidney was transplanted from one healthy identical twin to his twin who was dying of renal disease. The surgery was performed at the Peter Bent Brigham Hospital in Boston, and John Merrill, Joseph Murray, and Hartwell Harrison^{1,2} led the clinical team. The operation was successful, renal function was restored in the recipient (although he would later have both his own kidneys removed in order to control hypertension), and the donor suffered no ill effects. This was the first successful transplantation, performed against a background of failure. For this reason, it created enormous excitement, both in the media and among medical professionals, at a time when the pioneers of kidney transplantation were despondent about the possibility of any real clinical application.

This successful transplantation occurred some 50 years after Emerich Ullmann performed the first experimental transplantation of a kidney between dogs in Vienna in 1902. A few years later, in 1906, Mathieu Jaboulay, professor of surgery in Lyon, France, connected the renal vessels of a sheep and a pig kidney, respectively, to the brachial vessels of two patients who were dying of renal failure. Neither kidney worked, but these were the first transplants, albeit xenografts, that had been placed in humans.

The techniques used to join the vessels together were those developed and described by Alexis Carrel, who had been a young surgeon in Jaboulay's unit, and in fact, the techniques of vascular anastomosis described by Carrel are exactly those still used in renal transplantation today. By the time of Jaboulay's transplantations, Carrel had moved to Chicago to work with Charles Guthrie, studying experimental organ and even limb transplantation.

Carrel subsequently moved to the Rockefeller Institute in New York, but he continued his organ-transplantation work until the beginning of the First World War. Indeed, in a prescient lecture in 1914, he said that the technical problems of transplantation were essentially solved, but until some method was developed to prevent the reaction of the organism against the foreign tissue, there would be no clinical application of organ transplantation. Between the wars, experimental transplantations were occasionally performed, but there was no advance in knowledge. There was a serious clinical attempt by a Russian surgeon, Yu Yu Voronoy, who transplanted cadaveric kidneys into six human recipients, but without success.³

The modern era of clinical transplantation began in Paris and Boston after the Second World War, and one highlight of postwar efforts was the small



The First Successful Kidney Transplantation, by Joel Babb, 1996.

series of transplantations of cadaveric kidneys performed by David Hume at Peter Bent Brigham Hospital in Boston.²⁻⁴ No immunosuppression was used, but some kidneys did function for days or weeks, and one for several months — no doubt because of the immunosuppression resulting from the profound uremia in the recipients.⁴ Enormously encouraged by the successful transplantation between identical twins that had shown that renal failure could be reversed completely, those pursuing immunosuppression, in Boston and Europe, now directed all their efforts at total-body irradiation. Although such irradiation did achieve immunosuppression, however, it also produced profound marrow aplasia, which led to patients' deaths from overwhelming infections. By the early 1960s, it was clear that total-body irradiation was not the solution.

Gertrude Elion and George Hitchings of Burroughs Wellcome had, some years earlier, developed an anticancer agent called 6-mercaptopurine. This drug was shown by Robert Schwartz and William Dameshek of Boston to suppress the immune response to a foreign protein in rabbits and to prolong the survival of skin allografts. After their report, Roy Calne in England and Charles Zukoski and David Hume (now in Richmond, Va.) showed that 6-mercaptopurine prolonged the survival of kidney grafts in dogs. This agent was soon to be replaced by azathioprine, a derivative of 6-mercaptopurine that was perhaps less toxic. Corticosteroids, first

used to treat the inevitable rejection, were then added to azathioprine therapy for maintenance immunosuppression. Later, antilymphocyte globulins were introduced — first to treat corticosteroid-resistant acute rejection and then, by some, as part of an induction protocol. At last, there was a realistic alternative to dialysis for the treatment of end-stage renal failure.^{2,3,5}

The so-called azathioprine era lasted until the early 1980s and spawned early efforts at liver, heart, and pancreas transplantation. However, these early years of renal transplantation were marked by high mortality among patients — as high as 40 percent at one year after surgery, although survival rates of cadaveric grafts of about 60 percent were being achieved. But with the change to low-dose corticosteroids, patient survival at one year was greater than 90 percent by the end of the 1970s, although graft survival remained around 60 percent. In the early 1980s, cyclosporine, a calcineurin inhibitor, was introduced into the clinic and led to a marked reduction in the loss of kidneys from irreversible rejection, as well as a dramatic improvement in the outcome of liver and cardiac transplantation. In the last decade of the 20th century, other immunosuppressive drugs became available — tacrolimus, mycophenolate mofetil, and sirolimus, all with different profiles of safety and efficacy. The first monoclonal antibody directed against T lymphocytes (OKT3) was introduced into clinical practice in the early 1980s. Since then, many other monoclonal antibodies against lymphocyte targets have been developed, but only those directed at the interleukin-2 receptor are in widespread use.

I am not sure that the clinical team that carried out that first identical-twin transplantation in 1954 would have believed that transplantation would come as far as it has today. Today, transplantation clinicians have an armamentarium of immunosuppressive agents at their disposal, all of which are used in various combinations both for induction and maintenance immunosuppression. Loss of organs due to acute, irreversible rejection is now uncommon, and one-year graft-survival rates of 80 to 90 percent are the norm for all types of organ transplantation.

But many problems remain to be solved — for example, the insidious loss of grafts from chronic allograft failure; the various complications associated with immunosuppressive drugs, such as nephrotoxic effects, hypertension, hyperlipidemia, and diabetes; and with long-term immunosuppression,

an increased incidence of cancer. Furthermore, the gap between the number of organs available and the demand for organs increases every year, giving rise to serious ethical dilemmas of equity versus utility in the allocation of this increasingly valuable resource.

Without question, since that momentous occasion in 1954, clinical organ transplantation has remained an enormously exciting field, and transplantation can rightly be considered one of the medical miracles of the 20th century. Moreover, transplantation provided the initial stimulus for the definition of the major histocompatibility complex in humans at a time when its predominant role in the cellular reactions of the immune response was unknown. Indeed, a whole science of transplantation biology has arisen during the past 50 years. I would venture to suggest, however, that the next 50 years will be even more exciting and will see the translation of laboratory models of tolerance into

the clinic, the successful development of xenotransplantation, and the use of stem-cell technology to provide tissues for transplantation. And, I hope, we will see the prevention of many of the causes of end-stage organ failure for which transplantation is currently the most attractive, or indeed the only, therapeutic option.

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Affirmative Action, Cuban Style

Fitzhugh Mullan, M.D.

“I feel as if I’m standing on the backs of all my ancestors. This is a huge opportunity for me,” Teresa Glover, a 27-year-old medical student, told me during a recent visit to her medical school. “Nobody in my family has ever had the chance to be a doctor.” Glover’s mother is a teacher, and her father a dispatcher for the New York subway system. Her background is a mix of African American, Barbadian, and Cherokee. She graduated from the State University of New York at Plattsburgh. “I wanted to be a doctor, but I wasn’t sure how to get into medicine. I had decent grades, but I didn’t have any money, and even applying to medical school cost a lot.”

This young woman from the Bronx may be helping to rectify the long-standing problem of insufficient diversity in the medical profession in the United States. Twenty-five percent of the U.S. population is black, Hispanic, or Native American, whereas only 6.1 percent of the nation’s physicians come from these backgrounds.¹ Students from these minority groups simply don’t get into medical school as often as their majority peers, which results in a

scarcity of minority physicians. This inequity translates into suffering and death, as documented by the Institute of Medicine.² Poorer health outcomes in minority populations have been linked to lack of access to care, lower rates of therapeutic procedures, and language barriers. Since physicians from minority groups practice disproportionately in minority communities, they are an important part of the solution to the health-disparities quandary.

In her third year, Glover is negotiating the classic passage from the laboratory to the clinic. But her school isn’t in the United States. She is enrolled at the Latin American School of Medicine (ELAM, which is its Spanish acronym) in Havana — a school sponsored by the Cuban government and dedicated to training doctors to treat the poor of the Western hemisphere and Africa. Twenty-seven countries and 60 ethnic groups are represented among ELAM’s 8000 students.

Glover’s mother heard about ELAM from her congressman, Representative José Serrano (D-N.Y.). “Mom calls me. ‘I have news. There’s a chance for