

# The Ultimate Gift: 50 Years of Organ Transplants



Courtesy of Brigham and Women's Hospital

The first successful organ transplant took place on Dec. 23, 1954, when Richard Herrick received a kidney from his healthy identical twin brother, Ronald. Richard survived for eight years until the original kidney disease struck again.



Steve Ruark for The New York Times

Robert Phillips has lived almost 42 years since a kidney transplant.

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By LAWRENCE K. ALTMAN

**W**hen Robert Phillips, a truck driver in Virginia, was dying of kidney failure in 1963, his younger sister, Ruth, read in a newspaper about a mother-to-son kidney transplant in Denver. Ms. Phillips picked up the phone and called the transplant doctors. Could she give one of her kidneys to her brother? she asked them. Blood tests revealed that the siblings' blood types did not match. But the doctors still agreed to bring Mr. Phillips, 37, to Denver for the highly experimental surgery, in the hope they could give him the "two good years" he wished for.

Forty-two years later, Mr. Phillips is the world's longest organ transplant survivor. He still has his sister's kidney. He retired in 2000, having never taken a sick day. Just before Thanksgiving, he underwent triple bypass surgery. But his kidney, he says, is just fine.

Thursday, Dec. 23, will be the 50th anniversary of the first successful organ transplant, a kidney transplant from a living donor performed in Boston in 1954. Mr. Phillips and a small number of other long-term survivors attest to how well organ transplants can work in the best cases.

Over the last five decades, surgeons have learned how to transplant virtually every vital organ in the human body. They have also branched out to transplant an array of nonvital body parts including, most recently, the hand. In the near future, face transplants, still a subject of controversy, are likely to become a reality: last month, the Cleveland Clinic became the first institution to receive approval for the operation. Since 1982, at least 416,457 people in the United States have received new kidneys, hearts, livers, lungs, pancreases and intestines to extend their lives and relieve their discomfort, according to the United Network for Organ Sharing in Richmond, Va., which tracks transplants in this country.

Advances in surgery, medicine, anesthesia and intensive care have extended patients' longevity and quality of life, and surgeons now give transplants even to patients with diseases like diabetes, who were rejected in earlier years. Scientists also have improved techniques to preserve organs from cadavers and have developed more effective anti-rejection drugs and antibiotics. And as doctors learned how to use older drugs more effectively, they reduced deaths from acute rejection to a rarity instead of a common problem.

"The growth of transplantation from ground zero to its present state seems like a fairy tale, a fantasy that became reality because of the courage of our patients," said Dr. Thomas E. Starzl, a pioneering transplant surgeon who led the team that performed Mr. Phillips's operation and now is at the University of Pittsburgh. "The truth is that none of us in the 1950's remotely envisioned the height to which transplantation would rise and the way it has changed the face of medicine. Transplants have had trickle down effects on all aspects of society like acceptance of criteria for brain death, passage of anatomical gift acts and the growth of biomedical ethics."

### **Frustration in Early Efforts**

The first successful organ transplant recipient was a 23-year-old man from Northboro, Mass., named Richard Herrick, who had just been discharged from the Coast Guard. On Dec. 23, 1954, he received a kidney from his healthy identical twin brother, Ronald, in an operation performed by Dr. Joseph E. Murray at what is now Brigham and Women's Hospital in Boston. Richard survived for eight years until the original kidney disease destroyed his new organ. Mr. Herrick's surgery was a victory long in coming. The very first transplants were blood transfusions, procedures that became much safer after the discovery of blood groups in 1900. In 1905, doctors performed the first corneal transplant, and then moved on to solid organs. But for many years, they had no real success. Beginning with the first attempted transplant of a human kidney in France in 1906, doctors performed about 40 kidney transplants, but all the patients died. In some early transplants, the donor kidney was placed not in the pelvis, as is now standard practice, but in areas like the arm or thigh.

In June 1950, a Chicago surgeon removed one of a woman's two failing cystic kidneys and gave her a healthy organ that functioned for at least 53 days. But the organ was rejected sometime in the next months. Still, the woman lived five more years, probably because the donor organ survived long enough to allow her damaged kidney to recover partial function, Dr. Nicholas L. Tilney, also of Brigham and Women's, wrote in "Transplant: From Myth to Reality." But Mr. Herrick's is considered the first successful transplant because experts defined success as survival of a graft for at least a year.

In their struggle to make transplants work, the pioneers had to overcome the objections of antivivisectionists to conduct the animal experiments needed to develop the techniques for human transplants. They also knew that a failed operation could set the field back by decades, Dr. Murray said. The radical nature of an operation to remove a healthy organ from a donor led Dr. Murray's team to seek support from religious, legal and community leaders. Nevertheless, critics accused the doctors of playing God. Dr. Starzl recalled how participants at scientific meetings lampooned his and other surgeons' first - and often disappointing - reports.

### **Main Obstacle Is Rejection**

Transplants are now performed almost routinely in many countries. "The expectation is that we'll always get good results," said Dr. John J. Fung, the chairman of general surgery at the Cleveland Clinic, "but we're not quite there yet." Over the years, the biggest obstacle facing patients and surgeons has been the rejection of transplanted organs. Several years after Mr. Herrick's surgery, doctors began using anti-rejection drugs like azathioprine and, later, cyclosporine.

In the early 1990's, Dr. Starzl and other transplant surgeons noticed that some patients who did not take their drugs regularly or at all were able to keep their donated organs. The observation taught the surgeons an important lesson: they had been prescribing too many immunosuppressive drugs at amounts that were too great and sometimes at the wrong time. In 1992, for example, Dr. Starzl took Mr. Phillips, the kidney transplant survivor, off his anti-rejection drug because he believed his patient could survive for without it.

Now some transplant doctors are working to determine whether they can safely wean patients off anti-rejection drugs as their immune systems stop trying to reject the new organ, a form of tolerance known as mixed chimerism. But lacking a test to determine who can safely stop the drugs, weaning is mainly a trial and error process that can have devastating effects if the graft is rejected.

Because anti-rejection drugs can have serious side effects, experts have been concerned about their effects on children born to transplant recipients. Women who have had transplants have delivered at least 11,000 babies - and possibly as many as 30,000 - proving that transplants can reverse the infertility from organ failure, said Dr. John M. Davison, emeritus professor of obstetrics at the University of Newcastle Upon Tyne in England. (It is not known how many babies have been fathered by transplant recipients.) The childbirth complications rate can be high. Medical journals have reported that up to half of the women delivered small, preterm babies. About 30 percent developed hypertension; 30 percent had infections.

Although doctors have not noted obvious serious defects among the babies born to organ recipients, some experts are concerned about the development of learning disabilities and other neurocognitive problems among the children. Also, some animal studies have suggested that such children may have a higher incidence of autoimmune disorders, said Dr. Dianne McKay, who directs transplantation medicine at Scripps Green Hospital in San Diego. The studies involve small numbers, she said, so their meaning is not yet clear. "There's a lot we don't know and a lot we really need to know," Dr. McKay added.

### **The Face Transplant Debate**

Perhaps the most disputed frontier in transplantation science is the face transplant, a procedure that surgeons say is now within their capabilities and that raises complex ethical questions extending even beyond identity and appearance. Ethics committees in England and France have rejected proposals to perform face transplants because of the unknown risks of long-term use of large doses of immunosuppressive drugs for a procedure that does not save lives. But in October, an institutional review board that oversees the safety of human experiments at the Cleveland Clinic became the first such group to approve a face transplant. The leader of the Cleveland team, Dr. Maria Siemionow, has spent years developing the technique on rats. Also, by working on five human cadavers, she has determined that doctors need about five hours to remove the facial tissue, a clinic spokeswoman said.

Meanwhile, doctors at the University of Louisville and at the University of Utrecht hope to perform a human face transplant in a joint venture in the Netherlands. The teams have continually refined their scientific blueprint after holding public and professional discussions, the latest in *The American Journal of Bioethics*. Dr. John H. Barker, who directs plastic surgery research at the University of Louisville, said the teams intended to submit a revised protocol soon for the necessary approval from institutional review boards at each center. The plans call for the surgeons to remove a face from a cadaver and sew it to an individual whose face has been grotesquely disfigured by injury, cancer, burns or a birth defect.

Proponents contend that recent experience with hand transplants, which involve skin, muscle, bone, blood vessels, tendons and cartilage, show that such transplants can be carried out safely. They argue that the benefits of such surgery would outweigh the risks among the thousands of people who have devastating facial disfigurement. Conventional reconstructive methods used today can require 100 or more operations, in a series, over a period of many years, Dr. Barker said. He contended that a successful facial transplant would require far fewer operations and would have fewer risks than standard reconstructive methods.

Trying to give someone a new face creates a number of practical problems, among other things the need to match the donor and recipient as closely as possible for sex, age, skin color and texture. Team members are working with organ procurement agencies to learn whom to approach as potential donors and how best to do it. Would a transplanted face look like the donor? Not likely, experts say. The new face presumably will look like a cross between that of the donor and the recipient, depending in part on how much facial muscle the recipient retains. A face transplant could also raise unrealistic hopes, experts say. No guarantee exists that the transplant recipient will look normal. The new face could worsen the appearance and reduce facial expression. A face transplant could be technically successful but leave the recipient and the family dissatisfied. At the same time, a successful transplant may send a message that disfigured people who do not choose to have transplants cannot have a high quality of life.

An overriding concern is making sure that the first face transplant recipient will be strong enough psychologically to deal with the emotional consequences - and the expected barrage of media coverage.

### **Recipients of New Hands**

Surgeons who favor face transplants have based their case largely on what they consider the success of transplants of the hand. Since 1998, surgeons have transplanted 24 hands and forearms in 18 male recipients, according to a registry from the hospitals that have performed them. Of these, six patients received two new hands. The longest survivor, Matthew Scott of Mays Landing, N.J., received one hand nearly six years ago at Jewish Hospital in Louisville.

Elsewhere, two recipients have had their donor hands removed. One was from the first patient, Clint Hallam from New Zealand, who failed to take his medications and attend rehabilitation sessions. The reason for removing the other hand, from a patient in Guangzhou, China, is unclear. Critics say that reports of other cases are incomplete. The most recent hand transplant was performed in April 2003 in Lyon, France, where the first was done.

The American Society for Surgery of the Hand says that transplant surgeons have achieved "acceptable functional and cosmetic outcomes" similar to those when a person's hand is reattached, but that recipients face unknown long-term risks because they must keep taking immunosuppressive drugs. The society says that the procedure is still experimental and that more research and progress in immunology are needed to reduce the need for lifelong anti-rejection drugs before hand transplants can be considered "consistently safe and efficacious." Dr. W. P. Andrew Lee, chief of plastic surgery at the University of Pittsburgh, has independently examined 11 of the hand transplant recipients, under the society's auspices. "Despite claims by some surgeons, most of the patients have regained only protective sensation and not the ability to discriminate between two points, which is the finer sensibility that we take for granted," Dr. Lee said. Protective sensation is the most basic level of nerve feeling - the warning signal that keeps people, for example, from burning themselves on a stove. Yet finer sensory discrimination is needed for writing and distinguishing among objects.

"The hand transplant patients, obviously, are grateful they have some sensation, rather than just a stump," Dr. Lee said. "But the transplant is still not anywhere close in terms of restoring the everyday function they had before they lost their hand, largely because of incomplete nerve regeneration." Transplant patients can move their new hands and fingers by retraining muscles in their natural arm to pull on the newly connected tendons. In interviewing patients and their families, Dr. Lee said he was deeply impressed with the psychological benefits hand transplants offered, particularly among those who have lost both hands.

### **Always a Need for Donors**

Organ transplantation has become so successful that today the biggest problem is a drastic shortage of organ donors. "Organ transplantation is an advance that we can't take full advantage of because of a lack of donor organs," said Dr. Charles B. Carpenter, a pioneer in transplant medicine at the Brigham and Women's Hospital.

While the general rule is that organs from younger donors fare best, doctors are now using organs from older donors with a success that once did not seem possible. In one case, a 92-year-old woman's liver extended the life of a 62-year-old patient, also a woman, for 4½ years, said Dr. William J. Wall, who performed the transplant at the London Health Sciences Center in London, Ontario, in 1993. It is believed to be the oldest organ ever used. Because of the shortage, doctors and desperate patients have increasingly turned to live donors, many of them unrelated to the recipients. Since 2001, the number of kidneys from living donors has continued to surpass those from cadavers.

Although thousands of Americans receive transplants each year, thousands more die waiting for an organ. As of Monday, 10,603 people had donated an organ this year, but 87,292 awaited one. The organ shortage is aggravated by the fact that many recipients require multiple transplants. Nearly half of donor organs from cadavers wear out after a decade or more because of a poorly understood phenomenon known as chronic rejection, said Dr. Tilney, of Brigham and Women's. That fact shows how far scientists need to go to make long-term survivors like Mr. Phillips the norm instead of the exception. Few experts see a solution to the shortage of donor organs unless they find a way to reduce the number of people who need new organs. Vaccines and other prevention measures against illnesses like hepatitis C and alcoholism would help achieve this. But even if such measures were available, a shortage would still be likely. So imaginative researchers are seeking ways to grow a patient's cells in the laboratory to fashion a new organ, and even to give human patients animal organs. At Massachusetts General Hospital in Boston, for example, Dr. David Sachs's team is experimenting with organs from a breed of pig. In the studies, organs are safely transplanted from one animal to another without immunosuppressive drugs. Dr. Sachs cautiously predicted that a pig-to-human xenotransplant would be attempted in less than a decade, and possibly "in a couple of years."

Meanwhile, the half century of success with organ transplants has given thousands of people new chances. Chris Klug, a snowboarder and a liver transplant recipient, used his to win an Olympic bronze medal in 2002. "How much more complete might the world have been if Mozart had been treated with renal transplantation instead of dying of kidney disease at the age of 34?" Dr. Starzl mused.