The first successful renal graft in man

Harold Ellis

Today, organ transplantation – of kidney, liver, heart, lung or pancreas, alone or in combination – is accepted as a more or less routine operative procedure, yet the first successful organ graft in man took place a mere 50 years ago, on December 23 1954.

At the end of the 18th century, John Hunter, of St George's Hospital, London, grafted healthy teeth, obtained at a price from indigent donors, to the gums of wealthier recipients. This was successful, as teeth are relatively inert antigenically. In 1804, Guiseppi Baronio demonstrated that free skin autografts in sheep would survive, but not grafts taken from one animal to another – the experimental basis of much of modern plastic surgery. However, the studies of Alexis Carrel (1873–1944) provided the basis of both the surgical technique and the biological problems of organ transplantation in the early 20th century.

After qualifying in Lyons, Carrel moved first to Chicago and then to the Rockefeller Institute of Medical Research in New York. Having developed the methodology of small blood vessel anastomosis still used today, by 1914, he showed that a dog's kidney could be transplanted and attached to the vessels in its neck and would maintain the animal in health after removal of the other kidney. However, transplantation of a kidney from one animal to another invariably failed in a short time. He had overcome the technical problems of organ transplantation, although the biological problems of rejection remained. These were not to be overcome until the 1960s. Carrel received a Nobel Prize in 1912.

The first human kidney graft was performed by Yu Voronoy in Kiev in 1933. The graft was taken from a young man who had died 6 hours before, and given to a woman aged 26 years dying of renal failure following ingestion of mercury in a suicide attempt. The graft failed to function and she died 2 days later. By 1949, Voronoy had performed six such grafts, but with no substantial, even temporary, function in any of them. So we come to the 1954 operation, performed by Joseph Murray and Hartwell Harrison at the Peter Bent Brigham Hospital, Boston (Merrill et al, 1956).

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The patient was a 24-year-old man admitted in October in advanced renal failure, who had a twin brother. He was drowsy, hypertensive, oedematous, disorientated and became frankly psychotic. He responded well to 4 hours of dialysis on the rather primitive Kolff artificial kidney, in the days before the vascular shunt and other advances made repeated and frequent dialyses technically possible.

A full-thickness skin graft was exchanged between the twins and took perfectly. The patient's condition worsened. By 12 December he was in congestive heart failure, oedematous up to the knees, had a pleural effusion, hepatomegaly, papilloedema and gross hypertension. A biopsy of the skin graft at 31 days showed perfect survival. The twins' blood matched in all eight of the blood group systems then known. Hospital records showed that the twins had shared a common placenta, and each had the relatively rare Darwin's tubercle of the ears, which their two siblings did not. The twins had identical eye colours, as well as iris structure and pigment patterns, again unlike their siblings.

On 23 December the twins were operated upon in adjacent theatres. A normal left kidney was removed from the healthy twin and grafted to the other twin's iliac vessels extraperitoneally in the right iliac fossa (*Figure 1*). The ureter was implanted in the bladder – a technique which has become the standard pattern today. The total operating time was 3.5 hours. On release of the vascular clamps, the graft kidney became turgid and pink, with immediate copious flow of urine.

The subsequent course of both patients was smooth. Later, the patient had both diseased kidneys removed; they were shrunken, fibrosed and showed typical changes of advanced chronic glomerulonephritis. A year later, the patient was well, normotensive and carrying out unlimited physical activity. Intravenous urography showed prompt excretion of contrast, which was well concentrated.

By 1961, at least 25 more renal transplants between identical twins had taken place, 17 by the Boston team, with 14 long-term survivors, the longest 7 years after surgery. Joseph Murray received the Nobel Prize for Medicine in 1990.

There still remained the biological problem of rejection of non-identical renal grafts. The solution to this began with the demonstration by Roy Calne in 1961 that dogs could accept unrelated renal grafts using the purine analogue 6-mercaptopurine, work that was rapidly applied to successful kidney grafts between unrelated human donors. HM

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Merrill P, Murray E, Harrison H et al (1956) Successful homotransplantation of the human kidney between identical twins. *JAMA* **160:** 277

Figure 1. The first successful human renal transplantation. The renal artery is anastomosed end-to-end with the internal iliac, the renal vein end-to-side with the common iliac, and the donor ureter mucosa-to-mucosa with the bladder. This technique served as the prototype for subsequent renal grafts to this day.