

## Case histories

### Liver transplant

Life, as an old *Punch* cartoon has it, is largely a question of the liver, and this meatiest of organs has taken a leading role in most visions of human anatomy, ancient and modern. Two 19th-century developments—the emergence of the new discipline of experimental physiology, and the appearance of the laboratory as a site for making reliable clinical knowledge—shaped our understanding of the liver. In pursuit of the mechanisms by which the body maintained a stable *milieu intérieur*, the French physiologist Claude Bernard discovered the role of the liver in synthesising carbohydrates. His work highlighted the complexities of the liver's functions, responsible for “internal secretion” of glucose into the blood and the “external secretion” of bile into the lumen of the gut.

By the end of the 19th century, as historian Thomas Schlich has shown, surgeons and physicians were deploying a new modular conception of the body, in which parts could—at least in principle—be repaired or replaced. Schlich observes that two assumptions underlie modern transplant surgery: that the replacement of an isolated organ can provide a definitive cure for particular diseases, and that an organ from one body can safely and sustainably perform the same function in another. In 1902 the French surgeon Alexis Carrel, borrowing techniques from lace-makers, devised an intricate procedure for reconnecting blood vessels, and also showed that well perfused organs could be kept alive outside the body for days. Carrel's work won him the 1912 Nobel Prize in Physiology or Medicine, but experiments showed again and again that even technically successful grafts between different individuals almost always failed within a few days.

Before World War 1 some researchers had suggested that graft rejection might be the result of an immune reaction. At the Rockefeller Institute in the 1920s and 1930s the American pathologist James Bumgardner Murphy began to tease out the role of lymphocytes in immunity, and in Melbourne in the late 1940s the Australian immunologist Frank Macfarlane Burnet proposed that the immune system distinguished “self” from “non-self” antigens through a process of selection before birth. During World War 2, the zoologist Peter Medawar worked with the Scottish plastic surgeon Thomas Gibson, trying to use cadaveric skin grafts to treat the extensive burns sustained in firebomb raids. Their efforts were constantly frustrated, but Medawar noted that successive grafts from one donor to the same recipient were rejected more and more quickly, suggesting a process of rapid “adaptive immunity”.

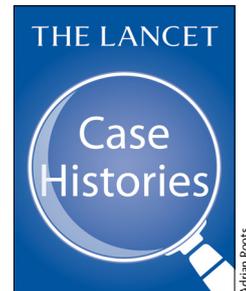
Burnet and Medawar shared the 1960 Nobel Prize in Physiology or Medicine for their work on immune tolerance. From the early 1950s Medawar had been experimenting with the new steroid cortisone, known to have an immunosuppressant side-effect, and in 1959

Roy Calne, working at Addenbrooke's Hospital, began to use azathioprine, a highly toxic drug which offered the first practical prospect of managing graft rejection. In 1963 the American surgeon Thomas Starzl of the University of Colorado attempted the first human liver transplant, on a 3-year-old child with congenital biliary atresia. A patient on whom Starzl operated in July, 1967, became the first liver transplant recipient to survive longer than a year, and the following year Calne performed the first successful liver transplant in Europe, on a 46-year-old woman.

Starzl, Calne, and their colleagues continuously refined their procedures, incorporating HLA tissue typing to reduce the need for immunosuppression, but through the 1970s long-term survival rates remained low. In 1980, Calne introduced cyclosporine, which prompted an increase in long-term success and helped to make liver transplant a standard part of the contemporary surgical repertoire. Around the globe, though, rapid and life-saving improvements in surgical technique and postoperative care have run alongside protracted arguments over the ethics, economics, and regulation of transplantation and the availability of donor organs. Public debates have often focused on high-profile cases in which transplants to treat alcohol-induced liver failure failed after their recipients returned to drinking. The technical triumphs of transplant medicine have generated a set of legal and philosophical complexities fit to rival the functional intricacies of the liver itself.

Richard Barnett

richard@richardbarnettwriter.com



For more on **Case histories** see [Comment Lancet 2016; 387: 211](#), [Perspectives Lancet 2016; 387: 217, 737, 1265, 1711, 2082, 2495](#), and [Lancet 2016; 388: 228, 649, 1148](#)

**Further reading**

Lederer S. *Flesh and blood: organ transplantation and blood transfusion in twentieth-century America*. New York, NY: Oxford University Press, 2008

Schlich T. *The origins of organ transplantation: surgery and laboratory science, 1880-1930*. Rochester, NY: University of Rochester Press, 2010

Starzl TE. *Organ transplantation: a practical triumph and epistemologic collapse*. *Proc Am Philos Soc* 2003; **147**: 226-45

