

# INTRODUCTION

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Liver transplantation is now a recognized therapeutic option for patients with progressive, irreversible liver disease, acute or chronic, or life-threatening hepatic metabolic disturbances, in whom conventional forms of medical therapy offer no prospect for prolonged survival (*Pimstone et al., 1990*).

Canine liver grafts were shown to function after transplantation to the pelvis by Welch in 1955. Orthotopic liver transplantation in dogs was attempted by Cannon in 1956 and performed successfully by Moore in 1959.

The first attempt at liver allotransplantation in man was made by Starzl at the University of Colorado on March 1, 1963. Ensuing attempts in Denver, Boston, and Paris were unsuccessful until 1967, when the first extended survival of a human liver allograft recipient was achieved by Starzl. The addition of cyclosporine immunosuppression by Calne in 1978 and then combination therapy with cyclosporine and prednisone by Starzl in 1980, as well as better liver preservation and surgical techniques, improved the prospects for clinical liver transplantation (*Bollinger and Stickel, 1991*).

Liver transplantation gained impetus following a National Institutes of Health (NIH) Consensus Development Conference on Liver Transplantation in June 1983, which concluded that liver transplantation "is a therapeutic modality for end-stage liver disease that deserves broad application" (*Pimstone et al., 1990*).

There are two general approaches to transplantation of the liver. With the first method, the host liver is removed and replaced with a homograft (orthotopic transplantation). The alternative technique is the insertion of an

extra liver (auxiliary homotransplantation) at an ectopic site. The most encouraging results have been with ortotopic transplantation (*Starzl et al., 1991*).

The epidemiology of pediatric liver disease is such that it concentrates the need for orthotopic liver transplantation (OLT) in a population younger than 2 years, yet more infants die of liver failure than become organ donors. Strategies have been developed to attempt to increase the numbers of available transplantable tissues. Reducing the size of a large donor liver so that it can be transplanted orthotopically into a small recipient. The split-liver transplant is based on the fact that the one potentially usable lobe, discarded during a reduced-size liver transplant procedure, is further dissected so that it is also used as a free functioning graft. The concept of living related liver transplants has now evolved into reality but has only been made possible in the clinical setting by the recent advances in hepatic surgery (*Broelsch and Lpoyd, 1993*).

One of the most important advantages of the liver, is resistance to antibody-mediated (humoral) rejection. Whereas kidneys and hearts usually are destroyed by hyperacute rejection in patients whose serum contains cytotoxic antibodies of the IgG class which are directed against HLA and other antigens in the donor, livers are spared this fate in most cases (*Starzl et al., 1991*).

At present one year survival rates of 70-80% and higher are widely attained, with data suggesting that five years survival rates of 60-70% are likely (*Bismuth et al., 1988*). These improved results can be related to more careful patient selection with great emphasis on nutritional status, to better surgical techniques and postoperative care, to greater willingness to

retransplant after rejection, and to better immunosuppression, particularly with cyclosporine (*Sherlock, 1989*).

Transplant surgery is a major endeavor for both the transplant center and the team that calls for a commitment from all parties involved. The basic requirements include:

- qualified surgeons capable of and willing to perform the procedure;
- hepatologists who have a good working relationship with the operating surgeons;
- an active renal dialysis program;
- adequate intensive care and operating room facilities with staff capable of accommodating transplant surgery;
- an active infectious disease program capable of recognizing unusual viral, fungal, and protozoal infections;
- a blood bank that can provide the necessary blood products on demand, often with little advance warning;
- a pathologist with special interest in liver and transplant histopathology;
- a psychiatric and social service to support patients and their families, a broad-based community support program that include housing for patients and their families;
- an adequate staff, including transplant coordinators, transplant fellows, laboratory support, and enough persons in each group to prevent "burn out".

The last is particularly important, as success in transplantation requires obsessive and demandingly meticulous attention to detail 24 hours per day, 365 days a year. This in effect requires at least two experts in each area committed to all levels of patient care (*Pimstone et al., 1990*).