1 Liver Transplantation

Thomas E. Starzl, M.D., Ph.D.

The concept of liver transplantation is a relatively recent one. The first descriptions of liver replacement in experimental animals were published less than 25 years ago (1,2), and the first attempt at clinical liver transplantation was not made until March 1, 1963 (3). In spite of continued efforts for the next 17 years, the great avalanche of human liver transplantations worldwide did not begin until 1980, only five years ago. A number of factors contributed to the growing interest in and success with orthotopic liver transplantation. Of these, the most important by far was the introduction of the new immunosuppressive agent, cyclosporine. In many of the contributions in this book, the influence of this drug will be described. Other topics to be considered will be an increased understanding of the anesthetic and intensive-care management of these patients, tissue matching, improvements in surgical techniques, and advances in organ procurement and preservation. My notations on some of these subjects will be superficial, but the topics will be fully developed by other authors.

IMMUNOSUPPRESSION

Truly long survival after liver transplantation between outbred mongrel dogs was achieved more than 20 years ago using azathioprine

Supported by Research Grants from the Veterans Administration and Project Grant No. AM-29961 from the National Institutes of Health, Bethesda, Maryland.

(4,5). One dog from that original study lived for more than 10 years.

The first extended survival of a human liver recipient was accomplished in the summer of 1967 (5), and the longest survival of any patient in the world today is now more than 15 years. This recipient, whose original disease was biliary atresia with an incidental hepatoma, was treated with azathioprine, prednisone, and antilymphocyte globulin (ALG).

Most of our liver recipients from 1963 through 1979 had this so-called triple-drug immunosuppression with azathioprine, prednisone, and ALG. In some patients, cyclophosphamide was substituted for azathioprine, and in a few others, lymphoid depletion was achieved with thoracic duct drainage instead of ALG. Details of these variations are summarized elsewhere (6). The failure of any of the variations to influence the survival after liver transplantation is evident from Figure 1.1. In the first trials from 1963 to 1976, only about one-third of the patients lived for as long as 1 year. In a smaller, second series of 30 patients treated from 1976 to 1978, the 1-year survival rose to 50%, but this improvement could not be sustained in the next 29 cases (Figure 1.1).

In 1976, Borel et al. (7) reported studies in rodents of a new immunosuppressive agent called cyclosporin A, and in late 1979, Calne and his associates (8) reported the first major clinical experience with this drug. On the basis of their experience they recommended that the drug be used alone for transplantation of the kidney, liver, or pancreas. However, it was immediately obvious in our first trials with cyclosporine in late 1979 that the full exploitation of the drug would not be possible without combining it with other agents, of which prednisone was the most important (9). By so doing in kidney recipients, it was possible to minimize the contribution of homograft rejection to poor renal function, and at the same time to ameliorate the drug's nephrotoxicity by reducing the requisite doses of cyclosporine. Since then, other drugs have been proposed and/or tried in modifications of the "pharmacologic cocktail" concept, but the cyclosporine-steroid combination remains the benchmark. The dose-limiting factor of cyclosporine has almost always been nephrotoxicity.

It is not hard to envision cyclosporine-steroid therapy as the modern analog of the original double-drug therapy with azathioprine and steroids. As a further analogy, the next logical step may

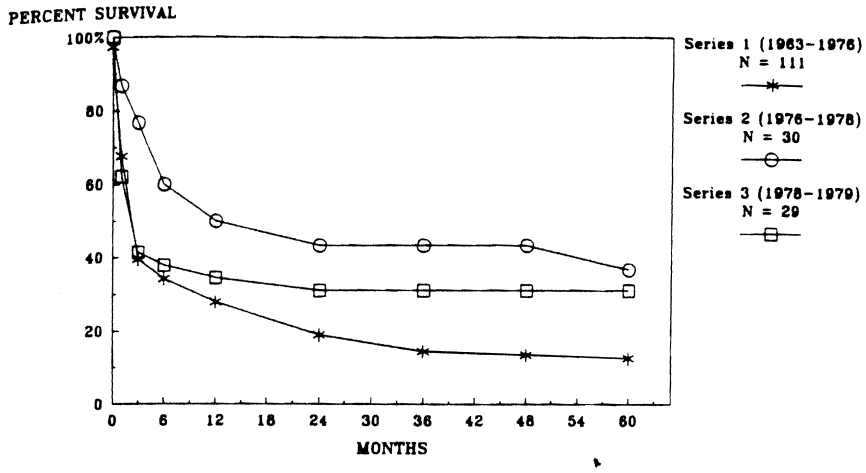


FIGURE 1.1. Results obtained over a 16-year period (1963–1979) using the conventional immunosuppression. Note the failure to improve the results despite the acquisition of considerable experience.

be the development of new "triple-drug" programs analogous to azathioprine, prednisone, and ALG but with cyclosporine-steroids being the baseline therapy to which one of the monoclonal ALG preparations that are undergoing preliminary clinical trials may be added.

Our present opinion is that monoclonal ALG such as that developed by Cosimi and his associates (*10*) should be used to "rescue" patients in whom rejection cannot be controlled with cyclosporine-steroid therapy or in whom there are severe limitations for one reason or another to the amounts of cyclosporine that can be safely given. Such limitations to cyclosporine dosage, which are almost imposed by the drug's nephrotoxicity, are particularly important in applying knowledge about immunosuppression to the transplantation of extrarenal organs such as the heart and liver, since secondary renal failure is common in patients with cardiac and hepatic disease. This complicates the use of the cyclosporine and completes a vicious cycle.

We have used OKT3 monoclonal antibody therapy in a number of our kidney and liver recipients. If rejection has developed despite cyclosporine-steroid therapy, reversal with OKT3 antibody usually has been striking. With the first dose of the monoclonal ALG, the circulating T-lymphocytes are practically eliminated. Recurrence

of rejection after the monoclonal antibody course has been completed has been far less common using baseline therapy with cyclosporine-steroids than previously reported with azathioprine-prednisone maintenance.

In 1980, cyclosporine and prednisone were used to treat 12 patients undergoing liver replacement. Two other liver recipients died on the operating table, for a total patient pool in that year of 14, of whom 11 (78%) lived out the first year. If one counted only those who actually survived the operation to be able to receive drug therapy, the success rate was 11 of 12 (91.7%).

These improved results became known in 1981 (*6*) and almost immediately a remarkable effect was seen on the case numbers. Increments occurred year-by-year, until in calendar year 1984 a total of 166 orthotopic liver transplantations were performed at the University of Pittsburgh. Augmented activity in other centers throughout the world has been documented elsewhere (*11*).

In our early trials of cyclosporine-steroid therapy, clinical judgment in managing the patients reflected a deliberate effort to balance the control of rejection against control of nephrotoxicity. Serum creatinine or BUN measures were used to guide the cyclosporine doses, using low-grade nephrotoxicity to set limits. When techniques became available for assessment of whole blood or plasma cyclosporine concentration using radioimmunoassay (RIA) or high-performance liquid chromatography (HPLC), it became popular to rely heavily on the results of these tests for management decisions. Recipients of liver transplantation have benefited from this practice since intestinal absorption of cyclosporine after liver transplantation has been unpredictable. To assure adequate cyclosporine blood concentrations, it frequently has been necessary to administer the drug both intravenously and by mouth for several days, weeks, or even months postoperatively. As absorption improves with the oral route, the intravenous doses are slowly reduced.

However, blind faith in the cyclosporine blood levels cannot be used to replace good clinical judgment since toxicity of the drug, including that affecting the liver as well as the kidney, does not have an absolute correlation with the blood level.

From 1963 through 1979, 170 patients were treated with conventional immunosuppression. The chances of living for a year after liver transplantation were only about 1 in 3 (Figure 1.2).

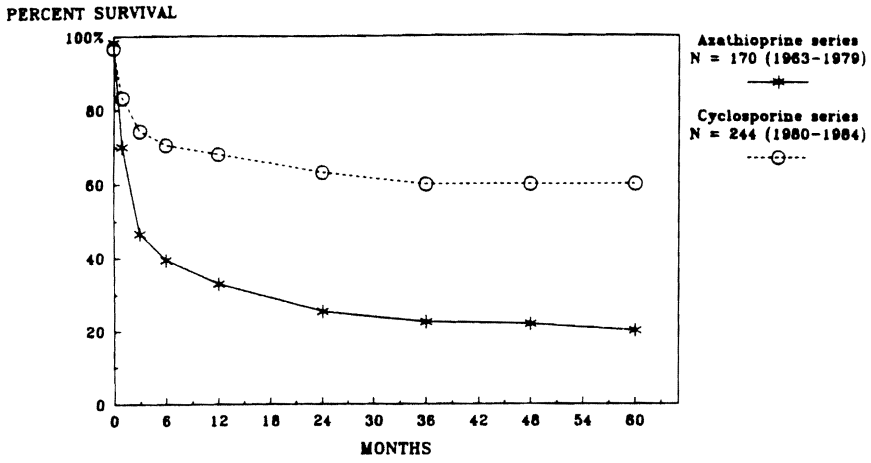


FIGURE 1.2. Marked improvement in results of liver transplantation after the introduction of cyclosporine-steriod therapy in early 1980.

Subsequently, 244 liver recipients were provided with cyclosporine-steroid therapy between March 1980 and July 1, 1984, allowing follow-ups (calculated in May 1985) of 10 months to more than 5 years. The chances of 1-year survival were more than doubled. Actuarial projections beyond 1 year indicate that these gains will be sustained for at least half a decade (Figure 1.2).

THE ROLE OF TISSUE TYPING

In patients treated with cyclosporine-steroids after renal transplantation, the antigen matching at the A, B, or D loci has had little influence on the results. Such matching has not even been attempted for liver recipients. It is unlikely that this kind of tissue matching will play a significant role in further developments in liver transplantation.

A surprising finding has been the remarkable resistance of the liver to hyperacute rejection (*6*). There has been no obvious penalty with transplantation of livers to recipients whose sera contain the cytotoxic antigraft antibodies that almost invariably lead to immediate loss of kidney grafts. Furthermore, many liver transplantations have been and are being carried out across the ABO blood-group barriers that frequently (although not invariably) cause hyperacute

rejection of kidneys as the consequence of antigraft isoagglutinins. These observations have simplified some of the logistical problems of liver transplantation by highlighting the nonrelevance of typing and matching with this organ.

IMPROVEMENTS IN TECHNIQUE

The technical principles of liver transplantation have been well worked out for almost two decades, but two highly significant developments have occurred in the last few years. These are perfection of pump-driven veno-venous bypasses and the standardization of biliary tract reconstruction.

The Veno-Venous Bypass

When liver transplantation was first carried out in dogs, an obligatory condition for success was decompression of the vena caval and portal venous systems that had to be occluded while the native liver was removed and the new organ was sewn in (1,2). In the first clinical trials it was found possible to omit this step (5), and for a number of years bypasses were not used. Without bypasses, the urgency with which the transplantation was performed was comparable to that in the early days of heart surgery when open cardiac operations were performed under inflow occlusion.

In the last three years, pump-driven veno-venous bypass techniques without heparin have been developed that have removed this urgency and allowed the avoidance of the venous hypertension that otherwise is inevitable during the anhepatic phase. The advantages include 1) improved intraoperative cardiovascular stability, 2) preservation of renal function by avoidance of the renal-venous hypertension, 3) diminished blood loss, 4) reduced trauma to the gastrointestinal tract by avoidance of the portal venous hypertension, and 5) creation of an operating-room ambience compatible with training a new generation of surgeons who in turn will set up numerous new centers in the United States and other countries.

The veno-venous bypass has changed the technical strategy of liver transplantation in important ways. In the past, when time

was such a critical factor during the anhepatic phase, it was impossible to obtain meticulous hemostasis in the bare areas opened up by removal of the diseased native liver. Even had there been time, it was often impossible to clean up and make dry the raw surfaces that were exuding blood at a voluminous rate because of venous hypertension. Control of bleeding by mechanical means was frequently impossible until the new liver was in place and until the obstructed venous beds were decompressed by opening the caval and portal venous anastomoses.

If veno-venous bypass is used, techniques can be applied whereby most or all of the bare areas are closed by running sutures. Although these maneuvers may require 1 h or longer before the anastomoses are started, the investment pays rich dividends later in ease of hemostasis.

Biliary Tract Reconstruction

Until about eight years ago, biliary tract reconstruction was called the Achilles heel of liver transplantation, with failure rates as high as 30–50%. At that time, the gallbladder usually was used for reconstruction, the pathway of bile excretion being from the common duct through the cystic duct and gallbladder and into the intestine. Duct-to-duct and duct-to-bowel reconstruction were not employed frequently.

Today, all biliary tract reconstructions are performed by one or the other of the techniques shown in Figure 1.3—namely, choledochocholedochostomy with a T-tube stent, or choledochojejunostomy to a Roux limb of jejunum. With these procedures, 90% or more of the biliary tract anastomoses are successful on the first occasion, and even when there are complications, they usually are easily rectified.

ORGAN REMOVAL AND PRESERVATION

Great advances have been made in multiple organ removal, and a relatively standard procedure is being used throughout most of the United States (*12*). The operation is done through a complete midline incision from the suprasternal notch to the pubis, including splitting of the sternum. The principle followed is to dissect the

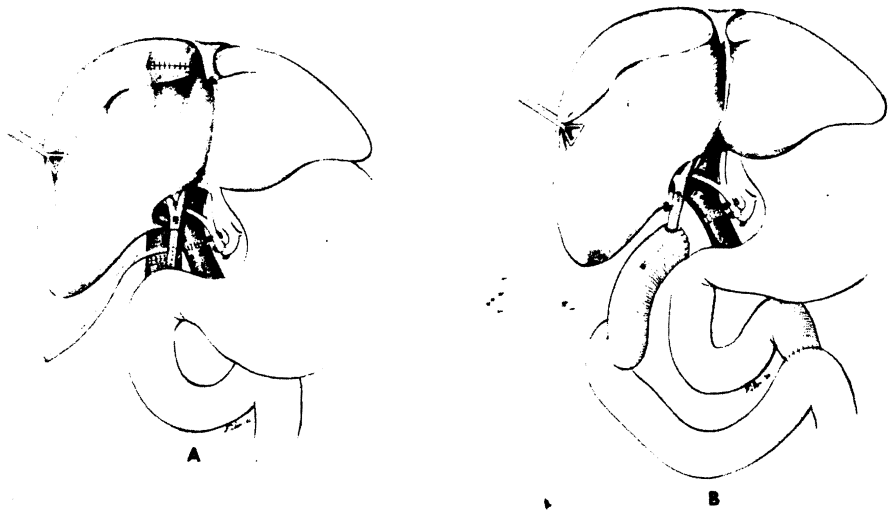
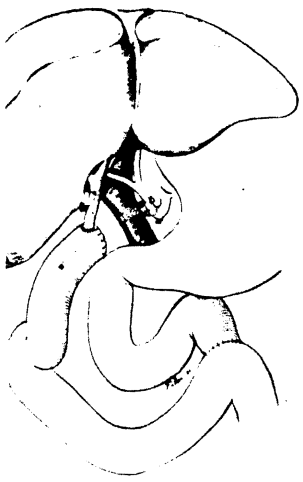


FIGURE 1.3. Completed orthotopic liver transplantation. (A) Biliary tract reconstruction with choledochocholedochostomy. (B) Biliary tract reconstruction with choledochojejunostomy, using a Roux limb. From *Hepatology* (*2:* 614–36) © 1982. By permission of the American Association for the Study of Liver Diseases.

aorta for cross-clamping at a level that will allow intraaortic infusion of cold fluids that will pass into the organs to be removed. If the liver is to be one of these organs, dissection of the liver hilum is carried out, after which the liver can be infused through both the aorta and portal vein (Figure 1.4). The kidneys also are cooled by the aortic perfusion. In the example shown in Figure 1.4, the liver and both kidneys are to be removed. With minor modifications, the heart can also be excised.

This procurement technique requires "brain death" conditions with stable cardiovascular function. An alternative with which we have had recent experience can be done swiftly, and in donors who have had cardiac arrest (11). With this so-called fast method, a cross-clamp is placed on the aorta near the diaphragm and cold solutions (usually the high potassium, high magnesium concentration Collin's solution) are infused rapidly. Blood enters the liver through the normal celiac axis route but also through the portal vein after passing through the splanchnic capillary bed (Figure 1.5). The portal venous blood quickly becomes almost red-cell free.



B

ansplantation. (A) Biliary
:hostomy. (B) Biliary tract
using a Roux limb. From
the American Association

llow intraaortic infusion
ıs to be removed. If the
ion of the liver hilum is
ıfused through both the
dneys also are cooled by
n in Figure 1.4, the liver
th minor modifications,

"brain death" conditions
ternative with which we
viftly, and in donors who
so-called fast method, a
the diaphragm and cold
ıigh magnesium concen-
lly. Blood enters the liver
t also through the portal
nic capillary bed (Figure
ɔmes almost red-cell free.

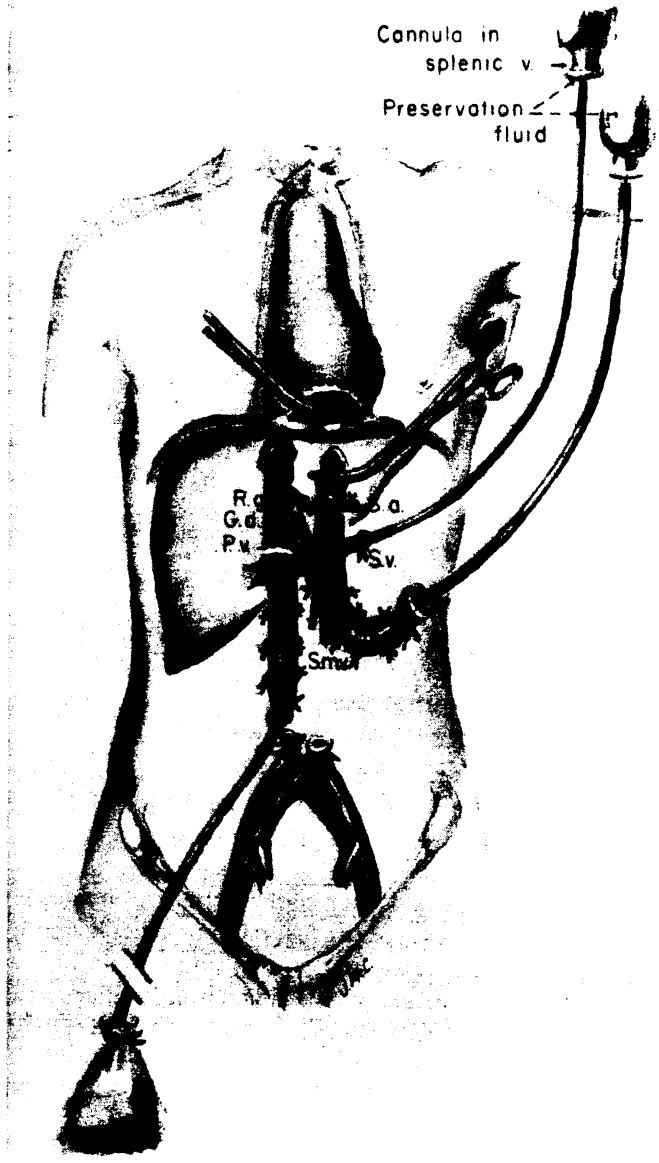


FIGURE 1.4 *In situ* infusion technique used when the kidneys and liver are removed from the same donor. R.g.a., right gastric artery; G.d.a., gastroduodenal artery; S.a., splenic artery; S.v., splenic vein; P.v., portal vein, and S.m.v., superior mesenteric vein. From *Surg Gynecol Obstet* 158:223–30 (1984). By permission of *Surgery, Gynecology, and Obstetrics.*

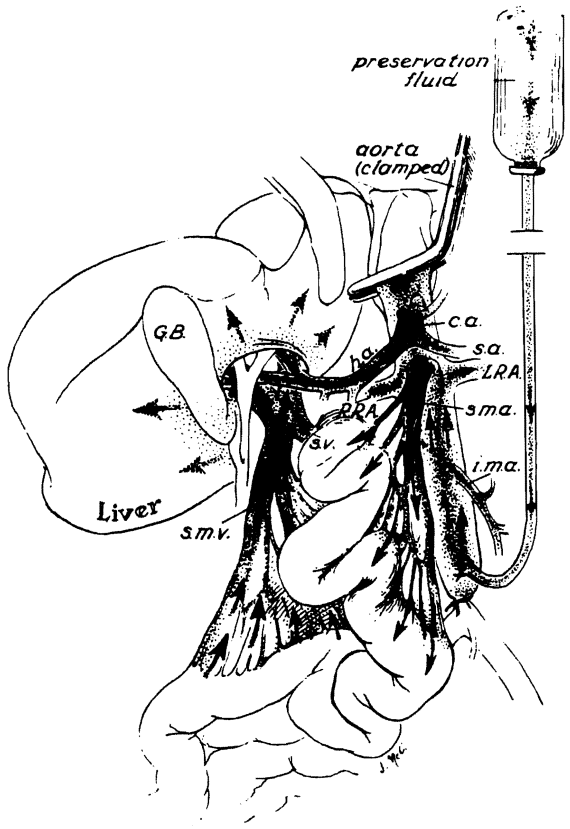
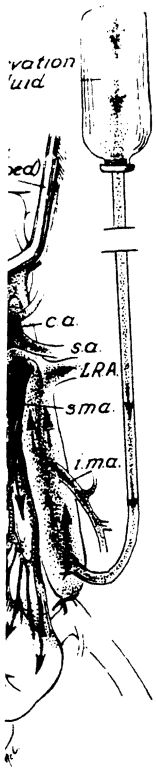


FIGURE 1.5. Method of rapid liver cooling that can be done without any preliminary dissection except for insertion of a distal aortic cannula and cross-clamping of the aorta at the diaphragm. The infusion fluid quickly get into the portal system via the splanchnic capillary bed, providing double inflow cooling. From *Transplant Proc* 17:250–58 (1985). By permission of *Transplantation Proceedings.*

The cold ischemia limit that is permissible for a human liver graft has been set arbitrarily at 10 h, but great efforts are made to work within a 5- or 6-h time frame. One of the most urgent needs in liver transplantation is the development of better methods of preservation. Any technique that would allow safe preservation of livers for the better part of a day would revolutionize the field overnight.



ing that can be done without
rtion of a distal aortic cannula
iaphragm. The infusion fluid
olanchnic capillary bed, provid-
Proc 17:250–58 (1985). By per-

rmissible for a human liver
ut great efforts are made to
ne of the most urgent needs
pment of better methods of
ld allow safe preservation of
ould revolutionize the field

TABLE 1.1. Indications for Liver Transplantation in 140 Adults

Indication	*Number*	*Percent*
Acute hepatic necrosis	3	2.1%
Budd-Chiari syndrome	5	3.6%
Cirrhosis	46	32.9%
Inborn errors of metabolism	11	7.9%
Alpha-1-antitrypsin deficiency	6	4.3%
Wilson's disease	3	2.1%
Tyrosinemia	1	0.7%
Primary biliary cirrhosis	36	25.7%
Primary hepatic tumors	13	9.3%
Secondary biliary cirrhosis	5	3.6%
Sclerosing cholangitis	19	13.6%
Other	2	1.4%

INDICATIONS FOR TRANSPLANTATION AND RESULTS

The indications for liver replacement in the developmental phase of this field have been documented elsewhere (*6*) and will not be mentioned here. Since the beginning of the cyclosporine era, 244 patients underwent this procedure between March 1980 and July 1, 1984. Tables 1.1 and 1.2 show the principal indications for these operations. In about 10% of cases, there were multiple pathologic diagnoses such as the incidental presence of primary hepatic malignancies in livers with a variety of underlying chronic diseases.

The profile of diseases in pediatric patients (less than 18 years) has been different from that in adults. In adults, postnecrotic cirrhosis has been the most important reason for proceeding (Table 1.1). Other common diseases in adults have been primary biliary cirrhosis and sclerosing cholangitis. In children, more than half of all the transplantations have been done for biliary atresia, the only other large group being a heterogeneous collection of inborn errors of metabolism (Table 1.2). The inborn errors, if they are hepatic-based, are cured permanently by liver replacement since the phenotype of the new liver remains that of the original donor (*5,6,11*).

TABLE 1.2. Indications for Liver Transplantation in 104 Children

Indication	*Number*	*Percent*
Biliary atresia	56	53.8%
Budd-Chiari syndrome	1	1.0%
Cirrhosis	10	9.6%
Familial cholestasis	7	6.7%
Inborn errors of metabolism	23	22.1%
Alpha-1-antitrypsin deficiency	15	14.4%
Wilson's disease	4	3.8%
Tyrosinemia	3	2.9%
Neonatal hepatitis	3	2.9%
Secondary biliary cirrhosis	1	1.0%
Sclerosing cholangitis	1	1.0%
Other	2	1.6%

Influence of Age on Survival

Aside from the fact that the disease profiles leading to transplantation are different in children versus adults, another justification for stratification into adult and pediatric categories is the influence of age on survival. It was noted in the days of conventional immunosuppression that the results were better in pediatric recipients (*6*). The disparity in results in pediatric versus adult cases has been even more striking during the cyclosporine era (*6,11*). The actuarial 5-year survival in adults is projected at about 50%, compared with more than 70% for the pediatric recipients. In view of the importance of the age factor, it will be important for groups reporting results to stipulate age distribution in their series. In our own experience using conventional immunosuppression from 1963 to 1979, half of the recipients were infants, children, and teenagers. In the subsequent years using cyclosporine, the pediatric component has never been this high (*11*).

With the appropriate age stratification, meaningful comparisons become possible between what was achievable in the precyclosporine era versus now. In adults, the projected 5-year survival after liver transplantation, while still unsatisfactory, is nearly three times better than it was previously. In children, the divergence

antation in 104 Children

Number	*Percent*
56	53.8%
1	1.0%
10	9.6%
7	6.7%
23	22.1%
15	14.4%
4	3.8%
3	2.9%
3	2.9%
1	1.0%
1	1.0%
2	1.6%

se profiles leading to trans-
rsus adults, another justifi-
d pediatric categories is the
d in the days of conventional
vere better in pediatric recip-
diatric versus adult cases has
cyclosporine era (*6,11*). The
projected at about 50%, com-
diatric recipients. In view of
will be important for groups
ibution in their series. In our
mmunosuppression from 1963
ants, children, and teenagers.
rine, the pediatric component

cation, meaningful compari-
was achievable in the precy-
the projected 5-year survival
till unsatisfactory, is nearly
sly. In children, the divergence

of results using conventional immunosuppression compared with the present time has been even more striking.

The Influence of Diseases upon Prognosis

There are no diseases for which transplantation has been carried out in the past that can be automatically precluded from future trials. Usually, the nature of the original disease has not profoundly influenced the outcome after transplantation. For example, the results in adults have been similar with such diverse diseases as primary biliary cirrhosis, sclerosing cholangitis, and inborn errors of metabolism. Nevertheless, there may be some high-risk diseases. So far, the results with postnecrotic cirrhosis and primary hepatic tumors have been inferior. With cirrhosis, the principal explanations have been the technical difficulties of the operation caused by the pathologic process, the generally poor condition of the cirrhotic patients, and almost universal recapitulation of their original chronic active hepatitis in B-virus carriers.

In patients whose reason for liver replacement was a primary hepatic malignancy that could not be removed by conventional subtotal hepatic resection, the early mortality has been quite low, with more than 80% of the recipients being alive at 6 months. The steady decline thereafter has been caused by recurrent tumors, which can be expected in 80% or more of patients who live long enough for metastases to be detected. The only acceptable results thus far have been in patients with the slow-growing and nonaggressive fibrolamellar hepatomas that recently have been recognized to be a favorable variant within the larger hepatoma category (*6,11*). It has been exceptionally disappointing to note that no patient in the world has ever been cured of a duct cell carcinoma by liver transplantation. This has been unexpected since the small duct cell carcinomas at the confluence of the right and left hepatic ducts (Klatskin tumors) were once thought to be an almost ideal indication for liver replacement.

In children, the results have been about the same in all of the main disease categories. It was thought once that the technical problems in frequently reoperated children with biliary atresia would result in an increased mortality. Almost all such infants and children have had portoenterostomies, and many have had multiple

later surgical interventions in and around the hepatic hilum. Although transplantation is technically much more difficult under such circumstances, there has been no demonstrable penalty in terms of either early or late survival.

The Role of Retransplantation

Before the cyclosporine era, retransplantation in the event of failure of the first liver was almost never successful (*6*). Twenty-one patients had retransplantations carried out between 1963 and 1979 under conventional immunosuppression, with only 4 patients living for as long as an additional 6 months. Even these 4 exceptional recipients died 6, 12, 13, and 16 months after retransplantation.

The effectiveness of retransplantation has improved greatly since the introduction of cyclosporine, with a subsequent 1-year survival of almost 50% (*6,13*). The success rate for patients whose grafts have been in place for some time and failed slowly because of rejection has been high. The worst results have been in patients with immediate and serious technical complications and those whose grafts have undergone a rapid and uncontrolled rejection in the first week or two.

The role of retransplantation in the future has been somewhat clouded by the enormous economic ramifications of early technical or other complications serious enough to warrant replacement of the graft. At the University of Pittsburgh hospitals, the costs of liver replacement averaged less than $100,000 if only one transplantation was performed. In contrast, the bills for patients receiving multiple grafts (usually two but as many as three) have been astronomical and have averaged almost three times as much as for patients treated successfully from the beginning.

Both in adults and in children, but particularly the latter, technical complications have played an important role in necessitating attempts at retransplantation (*13*). The lesson has been clear that if a perfect operation is not performed the first time for any reason, the cost will be prodigious and will have to be borne by the patient or, more commonly, the health insurance carrier. In future years it will become important to try to identify those patients for whom retransplantation offers little or no chance of survival, so that expensive and ineffective attempts can be avoided with some degree of accuracy.

SUMMARY

During the last five years, liver transplantation has become a service as opposed to an experimental operation. The most important factor in making this possible has been the introduction of cyclosporine-steroid therapy. At the same time, liver transplantation has been made more practical by improvements in anesthetic and surgical technique, including perfection of intraoperative veno-venous bypasses and the standardization of biliary tract reconstruction. Tissue typing and matching has played no role in improving the results of liver transplantation. With the demonstration that preformed antibody states are irrelevant, even avoidance of positive cross-matches caused by cytotoxic antibodies and observance of ABO blood-group barriers have become unnecessary if the recipient's needs are great.

With the exceptions of malignancy and cirrhosis, the nature of the underlying hepatic disease has not profoundly influenced the results. Retransplantation has played an important role in improving survival, although the costs of retransplantation have been extremely high. Many aspects of liver transplantation need to be improved, including the development of better methods of preservation that will allow the recipient operations to be done in a more leisurely manner and at more convenient times.

REFERENCES

1. Starzl, T. E.; Kaupp, H. A.; Brock, D. R.; Lazarus, R. E.; Johnson, R. V.: Reconstructive problems in canine liver homotransplantation with special reference to the postoperative role of hepatic venous flow. Surg Gynecol Obstet. *111*:733–743 (1960).
2. Moore, F. D.; Wheeler, H. B.; Demissianos, H. V.; Smith, L. L.; Balankura, O.; Abel, K.; Greenberg, J. B.; Dammin, G. J.: Experimental whole-organ transplantation of the liver and of the spleen. Ann Surg. *152*:374–387 (1960).
3. Starzl, T. E.; Marchioro, T. L.; von Kaulla, K.; Hermann, G.; Brittain, R. S.; Waddell, W. R.: Homotransplantation of the liver in humans. Surg Gynecol Obstet. *117*:659–676 (1963).
4. Starzl, T. E.; Marchioro, T. L.; Porter, K. A.; Taylor, P. D.; Faris, T. D.; Hermann, T. J.; Hlad, C. J.; Waddell, W. R.: Factors determining

short- and long-term survival after orthotopic liver homotransplantation in the dog. Surgery. *58*:131–155 (1965).

5. Starzl, T. E. (with the assistance of Putnam, C. W.): *Experience in hepatic transplantation*, W. B. Saunders, Philadelphia, 1969.
6. Starzl, T. E.; Iwatsuki, S.; Van Thiel, D. H.; Gartner, J. C.; Zitelli, B. J.; Malatack, J. J.; Schade, R. R.; Shaw, B. W. Jr.; Hakala, T. R.; Rosenthal, J. T.; Porter, K. A.: Evolution of liver transplantation. Hepatology. *2*:614–636 (1982).
7. Borel, J. F.; Feurer, C.; Gubler, H. U.; Stahelin, H.: Biological effects of cyclosporin A: A new antilymphocytic agent. Agents Action. *6*:468–475 (1976).
8. Calne, R. Y.; Rolles, K.; White, D. J. G.; Thiru, S.; Evans, D. B.; McMaster, P.; Dunn, D. C.; Craddock, G. N.; Henderson, R. G.; Aziz, S.; Lewis, P.: Cyclosporin A initially as the only immunosuppressant in 34 recipients of cadaveric organs: 32 kidneys, 2 pancreases, and 2 livers. Lancet. *2*:1033–1036 (1979).
9. Starzl, T. E.; Weil, R. III; Iwatsuki, S.; Klintmalm, G. B. G.; Schroter, G. P. J.; Koep, L. J.; Iwaki, Y.; Terasaki, P. I.; Porter, K. A.: The use of cyclosporin A and prednisone in cadaver kidney transplantation. Surg Gynecol Obstet. *15*:17–26 (1980).
10. Cosimi, A. B.; Burton, R. C.; Colvin, R. B.; Goldstein, G.; Delmonico, F. L.; LaQuaglia, M. P.; Tolkoff-Rubin, N.; Rubin, R. H.; Herrin, J. T.; Russell, P. S.: Treatment of acute renal allograft rejection with OKT3 monoclonal antibody. Transplantation. *36*:535–539 (1981).
11. Starzl, T. E.; Iwatsuki, S.; Shaw, B. W. Jr.; Gordon, R. D.: Orthotopic liver transplantation in 1984. Transplant Proc. *17*:250–258 (1985).
12. Starzl, T. E.; Hakala, T. R.; Shaw, B. W. Jr.; Hardesty, R. L.; Rosenthal, T. E.; Griffith, B. P.; Iwatsuki, S.; Bahnson, H. T.: A flexible procedure for multiple cadaveric organ procurement. Surg Gynecol Obstet. *158*:223–230 (1984).
13. Shaw, B. W. Jr.; Gordon, R. D.; Iwatsuki, S.; Starzl, T. E.: Hepatic retransplantation. Transplant Proc. *17*:264–271 (1985).