

Refinements in the Surgical Technique of Liver Transplantation

THOMAS E. STARZL, M.D., Ph.D., SHUNZABURO IWATSUKI, M.D.,
CARLOS O. ESQUIVEL, M.D., Ph.D., SATORU TODO, M.D.,
IGAL KAM, M.D., STEPHEN LYNCH, M.D., ROBERT D. GORDON, M.D.,
and BYERS W. SHAW Jr., M.D.

At one time, the operation of orthotopic liver transplantation was viewed as too difficult and dangerous to be practical on a large scale. The image of the procedure as one requiring a virtuoso surgical team has changed during the last few years as the result of technical improvements. These have put the operation within the capability of many competent general and vascular surgeons. In this account, we will discuss various aspects of this still complex undertaking, with emphasis on those recently clarified details that stand above others in importance and significance.

DONOR OPERATION

Orthotopic hepatic transplantation is an exercise in futility without a well-preserved and promptly functioning liver. At the present time, liver grafts usually are removed as part of a multiple organ procurement, which can be performed easily in brain-dead donors without jeopardizing any of the organs.¹ When the liver is used, the most common organ combinations in order of frequency are liver and kidneys; liver, kidneys, and heart; and liver, kidneys, and heart-lung. We do not remove the liver and pancreas from the same donor because the arterial blood supply of both organs is based on the donor celiac axis.²

From the Department of Surgery, University of Pittsburgh Health Center, University of Pittsburgh, Pittsburgh, Pennsylvania.

Reprint requests: Dr. Starzl, Dept. of Surgery, 3601 Fifth Ave., Room 103, Falk Clinic, Pittsburgh, PA 15213.

The technique of multiple organ removal can be learned in a systematic way in heart-beating cadavers, using techniques of hemostasis and tissue handling that are the same as for patients who are expected to survive. However, once the techniques of organ cooling and extirpation are learned in this way, a "fast" method may be used that has major advantages under some circumstances. We will mention here the "standard" and "fast" techniques in that order.

Standard Donor Operation

The principle is to carry out a preliminary dissection that will allow eventual termination of the procedure by rapid core cooling in situ by selective infusion of chilled fluids into the organs that are to be removed.¹ This is done through a complete midline incision from the suprasternal notch to the pubis. If the liver is one of the organs to be taken, the hilar structures of the liver are dissected free. The aorta is encircled just below or just above the diaphragm for later cross-clamping, and cannulas are inserted into the distal abdominal aorta and splenic vein for the infusions (Fig. 1).

When all is in readiness, a moderately rapid infusion of lactated Ringer's solution into the portal system is started (Fig. 1). If this infusion is done with caution, it does not jeopardize the donor's cardiodynamic status, although the body temperature may slowly decrease into the 30 to 32°C range. The liver can be felt to cool, and when this is evident, or if the patient becomes unstable, the aorta is cross-clamped at the diaphragm, and cold preservation fluid is introduced rapidly through the aortic

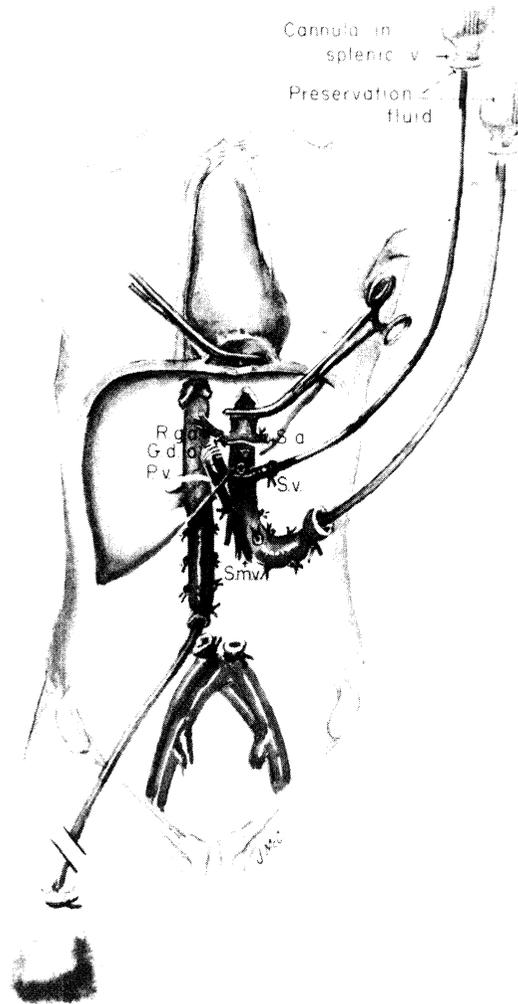


FIG. 1. In situ infusion technique used when the kidneys and liver are removed from the same donor. R.g.a.: right gastric artery; G.d.a.: gastrooduodenal artery; S.a.: splenic artery; S.v.: splenic vein; P.v.: portal vein; S.m.v.: superior mesenteric vein. (Reproduced with permission from Starzl et al.¹)

cannula at the same time as the portal infusion continues. The vena caval blood is allowed to drain out into the wound or into a floor bag (Fig. 1).

If the aortic cross-clamping at the diaphragm and the cold infusions are carefully timed, warm ischemia is eliminated for the kidneys as well as for the liver, which is already partially cooled by the preliminary portal infusion. The protection of the kidneys has been reflected in a very high rate of prompt function of the renal homografts obtained at multiple organ procurements.³ The exact constituency of the preservation fluid infused into the aorta is probably not so critical as the timing just described. Most centers prefer the potassium-rich Collins solution for cold infusion of the aorta and for a final infusion through the portal vein.

After the organs are cold, the origin of the celiac axis is detached from the aorta. The portal vein is freed and the infrahepatic vena cava is transected. The liver is removed with a piece of diaphragm and with part of the right adrenal gland so that the right adrenal vein easily may be identified later and ligated at its entry into the retrohepatic inferior vena cava. The liver is placed immediately in a fluid-filled bag. The bag is packed in ice until the liver is taken out in the recipient's operating room for final dissection and removal of extraneous tissue in an ice basin on a back table.

In at least a third of donors, the hilar dissection will be complicated by arterial anomalies, whereby some or all of the liver is supplied by branches of the left gastric artery, superior mesenteric artery, or direct branches from the aorta instead of by ramifications of the common or proper hepatic artery. Special techniques have been devel-

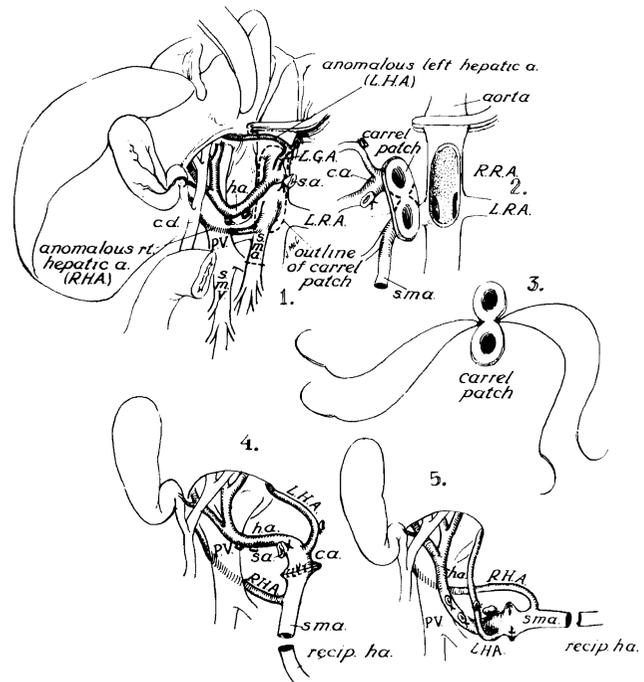


FIG. 2. Methods used to reconstruct a complex donor anomaly (1) split arterial supply to the liver originating from the left gastric artery (LGA), celiac axis (c.a.), and superior mesenteric artery (s.m.a.); (2) a patch of anterior aorta, including the origins of the celiac axis and superior mesenteric artery, is removed. The renal artery orifices are protected, (3) folding of the aortic patch permits safe anastomosis of the celiac axis to the superior mesenteric artery, (4) the superior mesenteric artery distal to the right hepatic artery is used for anastomosis to the recipient artery (recip.h.a.), (5) the reconstructed arterial supply of the graft may be rotated to match the orientation of the host vessel. s.a.: splenic artery; L.R.A.: left renal artery; R.R.A.: right renal artery; P.V.: portal vein; s.m.v.: superior mesenteric vein. (Reproduced with permission from Gordon et al.⁵)

oped that allow all such livers to be used.⁴⁻⁶ These have in common the conversion of multiple vessels into a single trunk by back table dissection and anastomoses, or other reconstructive maneuvers (Fig. 2).

Fast Donor Operation

Preparation of the liver and the preliminary steps for kidney removal in a heart-beating cadaver donor require 1½ to 2 hours of an experienced surgeon's time, or longer than this for beginners. Once the basic operation has been mastered, a modification of technique may be desirable in some circumstances.⁷ With the modification, no preliminary dissection is necessary except for encirclement of the proximal aorta, and cannulation of the terminal aorta or one of the iliac arteries (Fig. 3). If the heart is to be removed, the cardiac surgeon is asked to proceed as if no other organs were involved, but

with the proviso that a warning be given when effective circulation ceases. At that moment, the aorta is cross-clamped at the diaphragm, and an infusion of cold Collins solution is started in the distal aorta.

The liver becomes blanched and free of blood with surprising rapidity providing the distal inferior vena cava is incised or bled off into a bag. Within 2 or 3 minutes, the liver is palpably cold. At the same time, the intestines become blanched, and blood in the portal vein becomes clear and hemoglobin-free. Thus, perfusion of the liver is assured via both the hepatic artery and the portal vein (Fig. 3).

In adults, 2 to 3 liters of cold Collins solution rapidly infused into the distal aorta are required to bring the liver into a cryoprotective range of less than 28°C. After this has been achieved, the aortic infusion can be slowed. The main nonhepatic branches of the celiac axis can be ligated swiftly and the hilar dissection can be completed in a matter of a few minutes in the bloodless field. The portal vein is cleaned inferiorly to the junction of the splenic and superior mesenteric veins and these individual tributaries are divided. By lifting the portal vein anteriorly, the possibility of a missed right hepatic artery coming from the superior mesenteric artery (see earlier) can be promptly excluded. The liver is then excised the same as with the standard technique, leaving fragments of diaphragm and adrenal gland with the specimen. Infusion of the kidneys via the aorta can be continued slowly as nephrectomies are performed.

With the ability to carry out all dissections in a bloodless field using the rapid method, it is possible to carry out multiple organ removal, including the heart, liver, and both kidneys in about a half hour. With this technique, satisfactory livers can be removed from donors with absent or ineffective heartbeat. This may be a necessary condition of liver harvest in countries that do not have "brain death" laws. More commonly, the method can be used to terminate procurement quickly in patients who become unstable during the standard dissection.

The quality of the liver grafts with the rapid method is as good as with the more tedious standard operation. However, the disadvantage is that a much higher level of skill is required to do the rapid operation safely. The skill is automatically learned by prior experience with the standard procedure. With either approach, the integrity of the donor surgeon must be beyond question, since failure to reveal information about technical surgical accidents or other problems in the donor operation may result in the recipient surgeon making an irrevocable commitment to go forward, with tragic results.

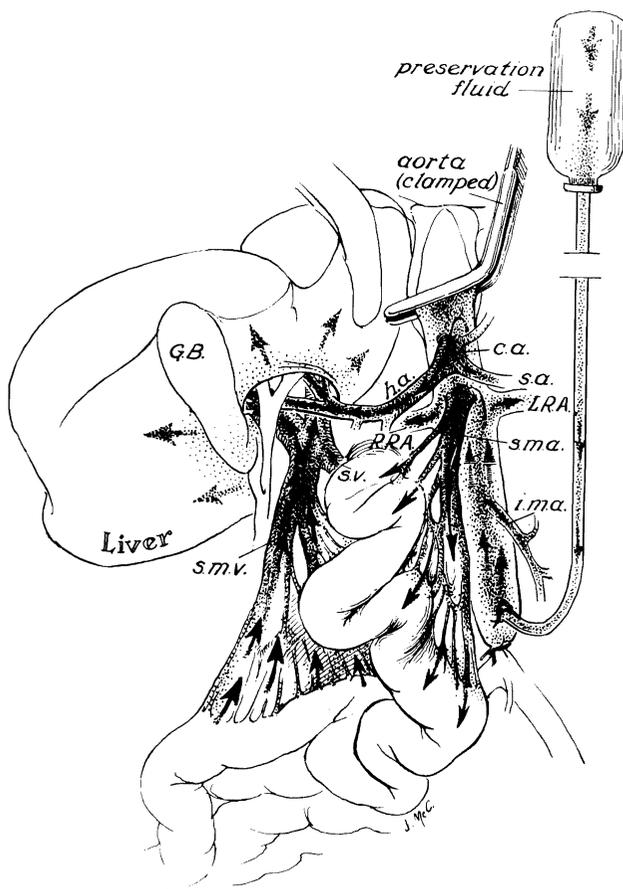


FIG. 3. Method of rapid liver cooling that can be done without any preliminary dissection except for insertion of a distal aortic cannula and cross-clamping of the aorta at the diaphragm. The infusion fluid quickly gets into the portal system via the splanchnic capillary bed, providing double inflow cooling. G.B.: gallbladder; i.a.a.: inferior mesenteric artery; see Figure 2 for other abbreviations. (Reproduced with permission from Starzl et al.⁷)

RECIPIENT OPERATION

The recipient procedure may be long, physically demanding, and stressful. Its component parts are so dissimilar that a single surgeon operating from skin-to-skin may find it difficult to adjust to the changing pace. At the outset, removal of the diseased liver may be one of the most bloody experiences in a surgeon's life. Yet the subsequent performance of the vascular anastomoses can be among the most delicate and sophisticated, especially in very small children. Obtaining perfect hemostasis after the new liver has been revascularized is often a tedious third phase that, if not accomplished, will ruin all that has gone before. At the end, the biliary tract reconstruction becomes the final thread on which the enterprise is suspended. In some centers, various parts of the procedure are being done by independent and fresh teams. However, the total responsibility still rests with a single surgeon who must understand each part of the operation.

Operative Exposure

A right subcostal incision is almost always used for the recipient operation, but its exact location is dictated by previous right upper quadrant incisions, and by the size and configuration of the liver. Extensions are also variable, but an upper midline component has been particularly valuable if the xiphoid process is excised. The xiphoid excision permits access to the hepatic veins and suprahepatic vena cava. In the majority of cases, the patients end up with a bilateral subcostal incision, with a superior midline T extension. Thoracic extensions are almost never needed.

Making the incision and obtaining exposure of the proposed operative field can be a major task, particularly if there have been previous right upper abdominal operations, as is often the case. It may be necessary to abandon delicate conventional techniques of hemostasis with small hemostat bites and tying, and to resort to continuous hemostatic sutures at the cut edge of the fascia and peritoneum, using polypropylene (Prolene suture that will slip easily through the tissues.

Once the abdomen is entered, an effort is made to find a plane of dissection just outside of the liver capsule if there are major subhepatic adhesions. Movement away from this plane invites disruption of major varices that may be large enough to cause disastrous or even lethal hemorrhage during the preliminary dissection.

Recipient Hepatectomy

There is no single best way to remove a diseased native liver. Once exposure has been obtained, it is important to assess the condition of the liver and to decide on whatever technical approach the abnormal anatomy will permit. In some patients, efforts to mobilize the liver from the hepatic fossa can cause lethal hemorrhage unless the hepatic arterial and portal venous blood supply are ligated first. In other recipients, it may be absolutely impossible because of scarring from previous operations or because of massive formation of varices to dissect individually the structures of the portal triad. Finally, the method of hepatectomy, as well as the conduct of the rest of the operation, are largely determined by whether or not veno-venous bypasses are going to be used.

Venous Bypass Question

When liver transplantation was first attempted in dogs,^{8,9} survival was not possible without using veno-venous bypasses that transmitted blood without a pump from the inferior vena cava and the portal vein into the superior vena cava while the lower venous systems were obstructed during the anhepatic phase. With the first human trials, it was learned that the use of such bypasses was not an obligatory condition for survival,⁴ and they were abandoned for almost 20 years.

With no provision to decompress the obstructed splanchnic and systemic venous beds, every liver replacement in patients was carried out in a crisis atmosphere comparable to that of open cardiac surgery under inflow occlusion. Even when the occlusion time was limited to that required for performance of the two vena caval and the portal anastomoses, damage to the splanchnic and systemic capillary beds often was evident grossly with petechial hemorrhages and edema. With occlusion of both the vena cava and the portal vein, hemorrhage from the thin-walled varices and from all other raw surfaces of the operative wound was predictably amplified. The bleeding often could not be controlled by any mechanical means until decompression was accomplished by opening of the vena caval and portal venous anastomoses of the new liver.

In 1982 and 1983, a pump-driven veno-venous bypass system without recipient heparinization was developed, tested in dogs,¹⁰ and eventually brought to the clinic.^{11,12} The technique made it possible to carry out venous bypass from the lower to the upper half of the body (Fig. 4) for as long as 4 or 5

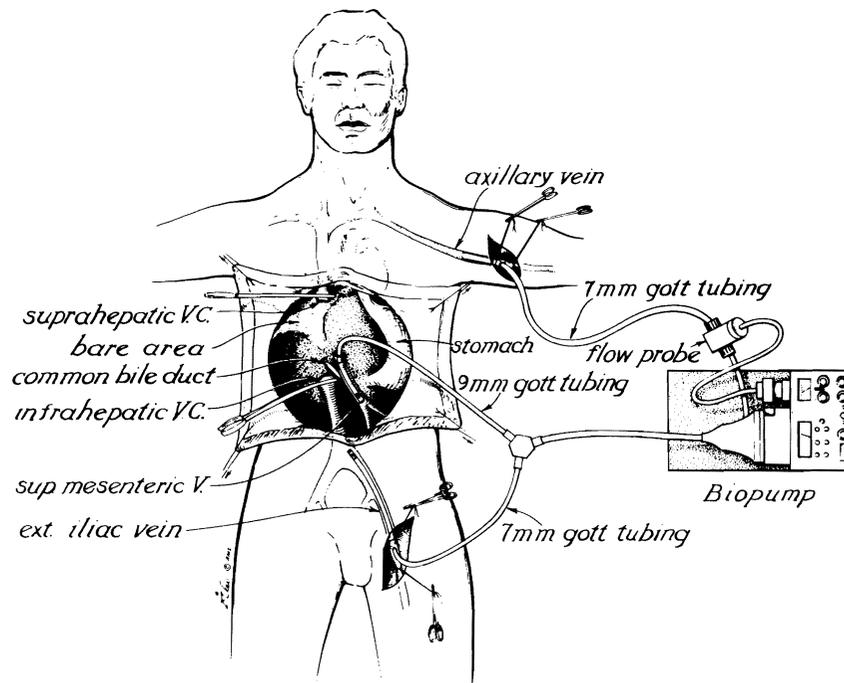


FIG. 4. Pump-driven bypass. (Reproduced with permission from Griffith et al.¹¹)

hours without obvious harm to the recipient, as will be described by Shaw et al in the next article in this issue of *Seminars*. With this development, it became possible to modify many aspects of the recipient operation in adults, including the technique of hepatectomy, as will be described next. More complete earlier accounts of other details of hepatectomy can be found elsewhere.^{4,13}

Hepatectomy on Bypass

The extent of preliminary dissection can be greatly decreased if a veno-venous bypass is to be used. The individual structures of the hilum usually are skeletonized, but no other areas need be invaded. When the bypass is ready for implementation, the hepatic artery and the common duct are ligated. The portal vein cannula for the veno-venous bypass is inserted as well as a femoral cannula, allowing both the splanchnic and systemic systems to be brought into the veno-venous circuit. Entry into the superior vena caval system usually is via the axillary vein (Fig. 4). In adults, 1 to 6 liters of blood per minute are bypassed. Simultaneous obstruction of the portal vein and inferior vena cava should cause little change in blood pressure or other measures of cardiovascular function.

With the hemodynamic stability afforded by the veno-venous bypass, it is possible to systemati-

cally divide all other structures that are holding the liver, including the infrahepatic vena cava. The triangular ligaments and the leaves of peritoneal reflection that make up the coronary ligament are cut if these have not been incised already (Fig. 5). The bare areas are entered on both the right and left sides. After these maneuvers have been carried out, the right hepatic lobe can be retracted into the wound. If it has not been possible to encircle the inferior vena cava, this can be done now just below or above the liver, and eventually at both locations. The liver can then be shelled out on the stalk defined by the vena caval connection (Fig. 5), and the vena caval cuff for eventual anastomosis can be developed.¹³

Once the liver has been removed, it is possible using veno-venous bypass time to close all the raw surfaces that were created during the hepatectomy.¹⁴ This is usually done with a continuous polypropylene suture, beginning at the tip of the right triangular ligament and continuing this centrally in rows that eventually are connected (Fig. 6). The superior leaf of the coronary ligament can be the starting point, with continuation into the bare area itself and eventually to the inferior portion of the coronary ligament (Fig. 6). When these continuous suture lines are eventually incorporated into a single suture line, all of the right bare area may be eliminated if desired (Fig. 6). The same principle is

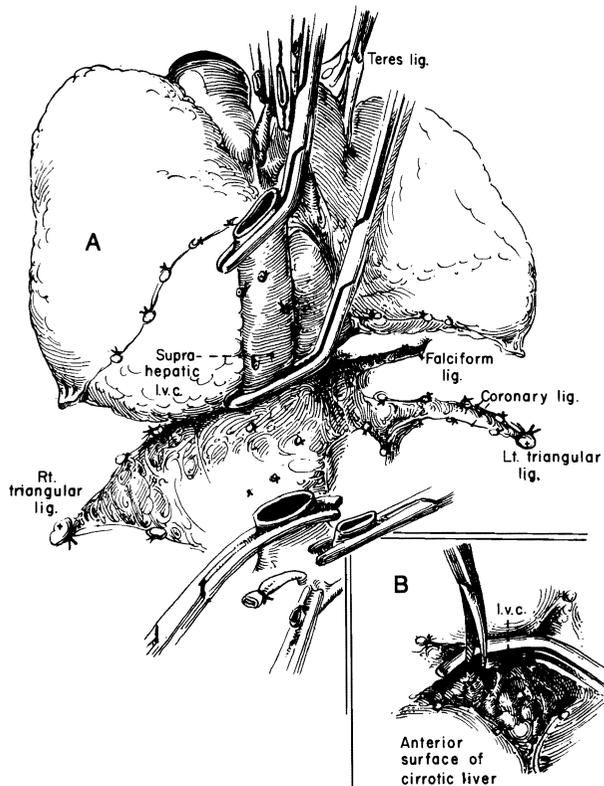


FIG. 5. Operative field after retrograde liver mobilization. The last-remaining structure, the suprahepatic inferior vena cava (I.v.c.), has been clamped above the liver. Inset: Technique for mobilization of a suitable length of suprahepatic vena cava after placement of clamp. In adults, this usually involves cutting away cirrhotic liver tissue over the frequently distorted and foreshortened right and left hepatic veins. (Reproduced with permission from Starzl et al.¹³)

followed in dealing with the left triangular and falciform ligaments.

Another line of continuous suture that is of vital importance is that behind the excised recipient inferior vena cava, where the right adrenal gland and its tied-off vein have been left behind. This closure has a superior-inferior orientation and usually requires at least a double layer (Fig. 6). By the time this final suture line has been completed, virtually all of the bare areas will have been eliminated. The time necessary for these hemostatic maneuvers is 30 to 90 minutes, an investment that was not feasible before veno-venous bypasses were used. If major hemorrhage occurs from the hepatic fossa after the new liver is revascularized, it is usually from the graft itself or from one of the anastomoses rather than from raw recipient tissues.

Veno-venous bypasses have been routinely used only for patients of adult size. Infants and small children tolerate venous occlusion reasonably well and the systematic use of an extracorporeal bypass

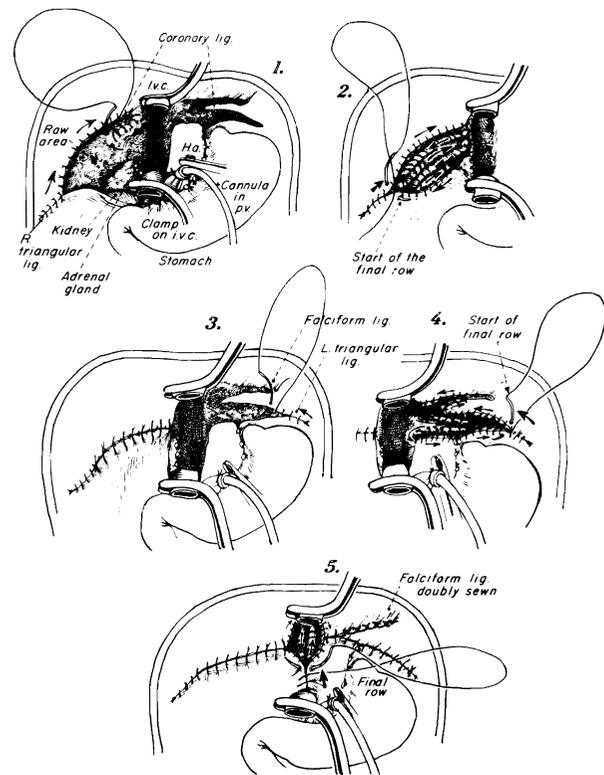


FIG. 6. 1, 2: Elimination of raw surfaces in the right bare area with continuous sutures. 3, 4: Similar treatment of the left triangular and falciform ligaments, eliminating all raw surfaces. 5: Closure of bare area in the bed of the excised retrohepatic inferior vena cava. Failure to obtain good initial hemostasis from this region can lead to the loss of liters of blood during and after the actual transplantation. (Reproduced with permission from Starzl et al.¹⁴)

system for them has been avoided. Nevertheless, low flow veno-venous bypasses are feasible and useful in some pediatric cases, and their use will undoubtedly be more common in years to come.¹⁵

Vascular Anastomoses

If adequate cuffs have been developed, the anastomoses of the vena cavae above and below the liver are readily performed. During construction of the lower vena caval anastomosis, the liver is flushed with lactated Ringer's solution to remove entrapped air from its major veins and to rid the graft of the highly concentrated potassium that is contained in the preservation fluid. Failure to observe these precautions can result in air embolus or cardiac arrest from hyperkalemia.¹⁶

When reconstructing the portal venous and hepatic arterial circulations, performance of a flawed anastomosis with subsequent thrombosis usually either will cause death or will precipitate the

need for retransplantation. To obviate these possibilities, particularly in children who have small vascular structures, special techniques have been described that, in essence, are designed to prevent anastomotic strictures.¹⁷ The anastomoses of the hepatic artery and portal vein are done in the usual way with a continuous polypropylene suture, but a so-called growth factor is left by tying the sutures at a considerable distance from the vessel wall (Fig. 7). After flow is restored through the hepatic artery or portal vein, the excess of the suture recedes back into the vessels and redistributes itself throughout the circumference of the suture line (Fig. 7). If an additional single suture is placed at the point where the two ends of the continuous suture line meet, thus preventing distraction of the lips, the amount of hemorrhage at the time of flow restoration is surprisingly small. Suture materials other than polypropylene are not satisfactory for this technique. The polypropylene is so slippery that it is not caught by adventitia and can easily work itself back through the entire circumference of the suture line.

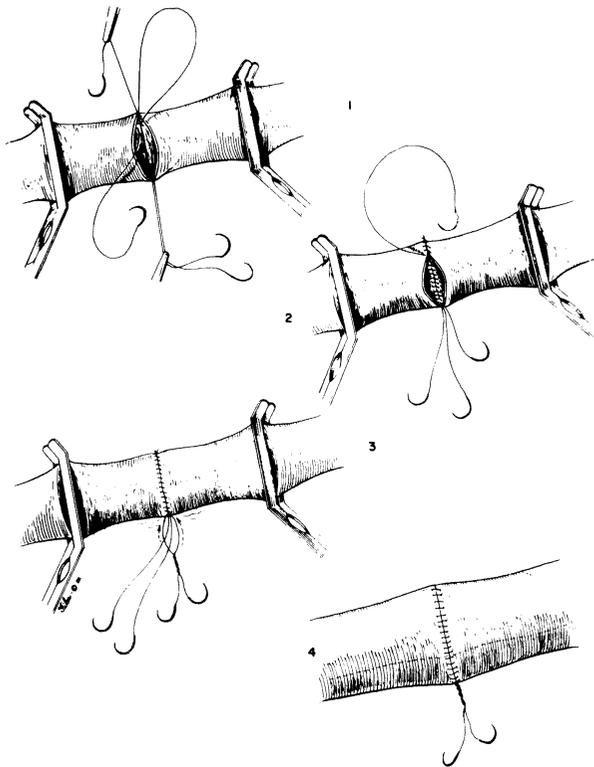


FIG. 7. Method of avoiding strictures of small vascular anastomoses. See text for explanation. (Reproduced with permission from Starzl et al.¹⁷)

Biliary Reconstruction

The many techniques used for restoration of the biliary tract after transplantation are summarized in Figure 8. At the present time, we recommend only duct-to-duct reconstruction with a stent (Fig. 8a), or if this is not possible, a choledochojejunostomy to a jejunal Roux limb (Fig. 8b). All of the other methods of reconstruction have had too high a rate of morbidity or mortality to warrant their continued use.

Calne¹⁸ prefers the procedures shown in Figure 8c and d, whereby the homograft common duct is anastomosed to the gallbladder and the fundus of the gallbladder in turn is attached to the recipient common duct or intestine. Although Calne has been

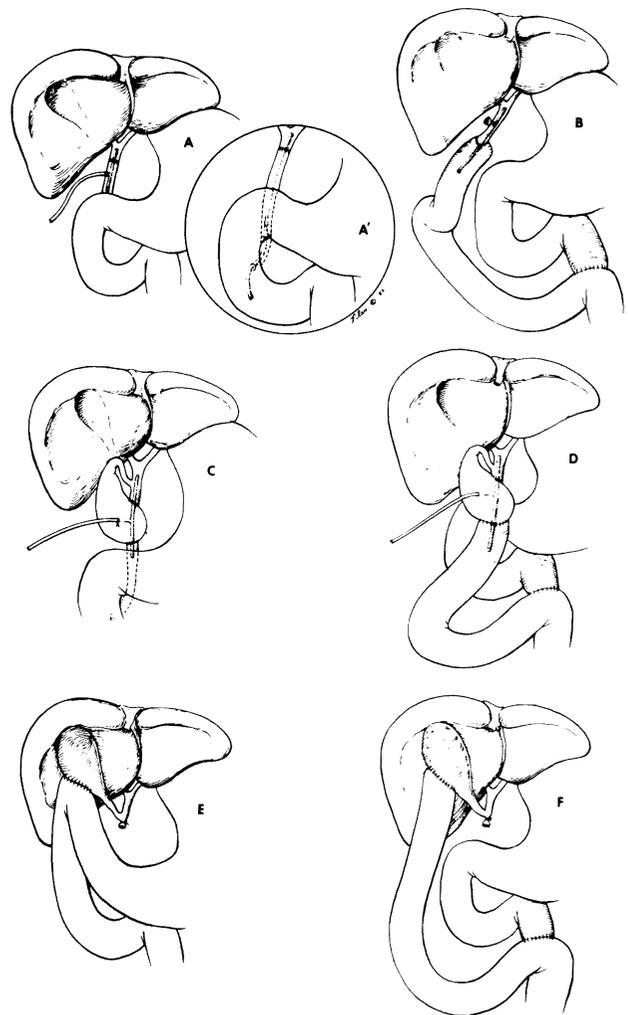


FIG. 8. Methods of biliary tract reconstruction that have been used with liver transplantation. The techniques shown in E and F are so defective that they have been abandoned. Depending on the anatomic and clinical circumstances, each of the other methods may be useful in individual cases. (Reproduced with permission from Starzl et al.¹⁹)

satisfied with the results of this procedure, its use has been on the decline in most European as well as American centers.

Need for Hemostasis

One of the most difficult lessons about liver transplantation that has had to be learned, and relearned from time to time, has been the necessity for total hemostasis before closing. The assumption that nature will take care of the problem if effective liver function is provided by a homograft has proved to be a vain hope on many occasions. Even if the patient has received a virtually nonfunctioning graft, perfect hemostasis usually can be achieved if the surgeon is persistent. Under these circumstances, the anesthesiologists have been able to promote clotting with fresh blood products, including platelets, and in the event of severe fibrinolysis by using epsilon-aminocaproic acid. Our policy has been not to close wet wounds under any circumstances. Many hours of tedious and exhausting effort may be required, but are eventually rewarded by complete hemostasis. After hemostasis has been accomplished, closed sump drains are placed in two or three locations above and below the liver and the wound is closed with nonabsorbable sutures.

When the patient is moved to the intensive care unit, a new full range of potential complications must be avoided or managed, as will be described elsewhere in this issue of *Seminars*.

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

REFERENCES

1. Starzl TE, Hakala TR, Shaw BW Jr, et al: A flexible procedure for multiple cadaveric organ procurement. *Surg Gynecol Obstet* 158:223-230, 1984.
2. Starzl TE, Iwatsuki S, Shaw BW Jr, et al: Pancreaticoduodenal transplantation in humans. *Surg Gynecol Obstet* 159:265-272, 1984.
3. Shaw BW Jr, Hakala TR, Rosenthal TR, et al: Combination donor hepatectomy and nephrectomy and early functional results of allografts. *Surg Gynecol Obstet* 155:321-325, 1982.
4. Starzl TE (with the assistance of Putnam CW): Experience in Hepatic Transplantation. Philadelphia, W.B. Saunders Company, 1969.
5. Gordon RD, Shaw BW Jr, Iwatsuki S, et al: A simplified technique for revascularization of liver homografts with a variant right hepatic artery from the superior mesenteric artery. *Surg Gynecol Obstet* 160:474-476, 1985.
6. Shaw BW Jr, Iwatsuki S, Starzl TE: Alternative methods of arterialization of the hepatic graft. *Surg Gynecol Obstet* 159:490-493, 1984.
7. Starzl TE, Iwatsuki S, Shaw BW Jr, Gordon RD: Orthotopic liver transplantation in 1984. *Transplant Proc* 17:250-258, 1985.
8. Moore FD, Wheeler HB, Demissianos HV, et al: Experimental whole organ transplantation of the liver and of the spleen. *Ann Surg* 152:374-387, 1960.
9. Starzl TE, Kaupp HA, Brock DR, et al: Reconstructive problems in canine liver transplantation with special reference to the postoperative role of hepatic venous flow. *Surg Gynecol Obstet* 111:733-743, 1960.
10. Denmark SW, Shaw BW Jr, Griffith BP, Starzl TE: Venovenous bypass without systemic anticoagulation in canine and human liver transplantation. *Surg Forum* 34:380-382, 1983.
11. Griffith BP, Shaw BW Jr, Hardesty RL, et al: Venovenous bypass without systemic anticoagulation for human liver transplantation. *Surg Gynecol Obstet* 160:270-272, 1985.
12. Shaw BW, Martin DJ, Marquez JM, et al: Venous bypass in clinical liver transplantation. *Ann Surg* 200:524-534, 1984.
13. Starzl TE, Porter KA, Putnam CW, et al: Orthotopic liver transplantation in 93 patients. *Surg Gynecol Obstet* 142:487-505, 1976.
14. Starzl TE, Iwatsuki S, Shaw BW Jr, et al: Factors in the development of liver transplantation. *Transplant Proc* 17: October, 1985.
15. Kam I, Lynch S, Todo S, et al: Low flow venovenous bypasses in small animals and pediatric patients undergoing liver replacement. *Surg Gynecol Obstet*, 1986.
16. Starzl TE, Schneck SA, Mazzoni G, et al: Acute neurological complications after liver transplantation with particular reference to intraoperative cerebral air embolus. *Ann Surg* 187:236-240, 1978.
17. Starzl TE, Iwatsuki S, Shaw BW Jr: A "growth factor" in fine vascular anastomoses. *Surg Gynecol Obstet* 159:164-165, 1984.
18. Calne RY, Ed: Liver Transplantation: The Cambridge-King's College Hospital Experience. London, Grune & Stratton, 1983.
19. Starzl TE, Iwatsuki S, Shaw BW Jr: Transplantation of the human liver. In: Schwartz SI, Ed: *Abdominal Operations*, 8th ed. (Maingot) East Norwalk, CT: Appleton-Century-Crofts, 1985, pp 1687-1722.