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TECHNIQUE OF ORTHOTOPIC LIVER ALLOTRANSPLANTATION IN DOGS

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The technique of orthotopic liver allotransplantation in dogs used by the authors at the Surgical Reseach and Transplantation Laboratory in Warsaw has been described. Some important technical modifications have been introduced in the experimental protocol to simulate the clinical situation when obtaining liver for transplantation. The donor remains hypotensive for about one hour before being sacrificed, removal of his liver begins approximately 5 minutes after death, warm ischemia time is prolonged to 20—30 minutes, and no heparin is used during the transplantaation procedure.

A large number of papers on experimental liver allotransplantation in dogs canbe found in the recent literature (Bonilla-Naar et al., 1963; Fonkalsrud et al., 1967; Mikaeloff et al., 1965; Moore et al., 1959, 1960; Starzl et al., 1960, 1965). Various techniques and numerous modifications have been described. In all experimental protocols the liver is removed from a healthy, normotensive, living animal. This does not correspond to the clinical situation where the prospective donor remains hypotensive for a certain period of time before death, and where the liver remains warm and unperfused for several minutes before cooling starts. These factors exert an unfavorable effect on graft integrity, affecting resumption of its function after transplantation and recipient survival.

In our experiments donor dogs remained hypotensive for about one hour before being sacrficed. Livers were taken only from cadavers, warm-ischemia time was prolonged to 20—30 min., recipients were not heparinized, transplanted livers were continuously cooled with balanced Ringer's solution during implantation.

METHOD OF OBTAINING LIVER FOR TRANSPLANTATION

The donor was being kept 3 days on a carbohydraterich diet and receives 300,000 u. of penicillin daily. Anesthesia was given with a small dose of ether. Barbiturates are absolutely contraindicated. The femoral artery

was dissected, and 500 ml of blood was collected into a plastic bag with ACD preservative. The dog remained hypotensive for 30—40 minutes. Collected blood was transfused later to the recipient. The next step was the intravenous administration of 3 mg/kg of heparin. Three minutes later, the donor was sacrificed with an intravenous bolus of 20 ml of 10% potassium chloride.

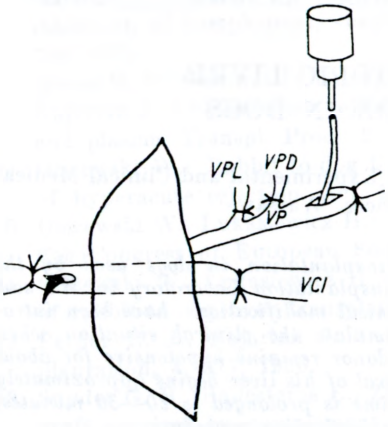

Fig. 1. Colling of the liver. *VP*-portal vein, *VPD* — pancreato-duodenal vein, *VCI* — inferior vena cava, *VPI* — pyloric vein.

About 2—3 minutes later a long midline incision from the neck down to the pubis was made, and the abdomen and thorax were opened. The infrahepatic segment of the inferior vena cava et the level of the right adrenal vein was ligated. The distal part of the superior mesenteric vein, the pyloric vein, and the pancreato-duodenal vein were also ligated. A cannula was introduced into the portal vein, and the liver was washed out with 1 500 ml Ringer's solution of 4°C with 20 ml of 5% sodium bicarbonate and 300,000 u. of penicillin (Fig. 1). The surface temperature of the liver decreased to 6—8° in about 15 minutes time.

At the time of cooling, the left hepato-phrenic ligament was ligated, then cut. Also, the peritoneal folds between the liver and phrenic crura were divided. The next step consisted in ligation and division of the smaller omentum, and then of the hepatoduodenal ligament with the right gastric artery, common bile duct, and small veins (Fig. 2). Small tributaries of the portal vein were ligated and divided, the main trunk of the vein being cut distally to the cannula. The liver was slightly displaced upwards, so that the hepatic artery could be better exposed. All the tributaries of the hepatic artery with the splenic artery were ligated. The main trunk of the celiac artery was cut close to its origin from the aorta. The inferior vena cava divided at the level of the right suprarenal vein. The peritoneal

fold between the liver and the diaphragm crura were also cut. Next, the suprahepatic infradiaphragmatic vena cava was cut transversely very close to the liver (Fig. 3). If it is cut high above the liver the phrenic veins can be inadvertently divided and remains open when the clamp is removed from the IVC.

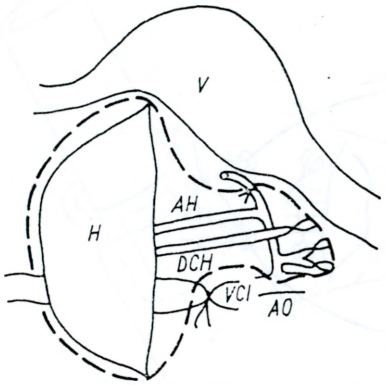

Fig. 2.

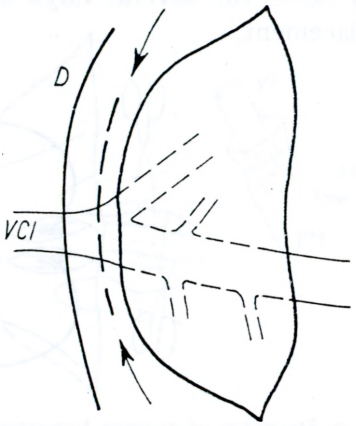

Fig. 3.

Fig. 2. Dissection and division of hepatic vessels and neighbouring structures. *DCH* — common bile duct, *AH* — hepatic artery, *AO* — aorta, *VCI* — inferior vena cava, *V* — stomach, *H* — liver. Dotted line indicates the site of division of ligaments fixing the liver.

Fig. 3. Level of dividion of the suprahepatic inferior vena cava. *D* — diaphragm, *VCI* — inferior vena cava.

The hepatic artery was flushed with 50 ml of cold Ringer's solution. The cannula was left in the portal vein and a cool drip was continued until the anastomoses of the IVC with the recipient veins were completed.

RECIPIENT

The body weight of the recipient should be about the same as that of the donor so that the size of the transplanted liver remains similar to that of the removed liver. This is very important for three reasons: 1) technical problems due to disparity between the lumen of donor and recipient vessels are avoided, 2) a small transplanted liver produces a high resistance for recipient splanchnic blood flow, 3) a large liver may displace other organs and cause kinking of portal vein and IVC anastomoses. The recipient was pretreated for 3—5 days with 300,000 u. of penicillin and 3 g oral Neomycin daily.

Dogs were premedicated with 0·3—0·5 mg of atropine sulfate intravenously, then anesthetized with halothane in the concentration of 5 vol%. After induction they were intubated, and anesthesia was continued with 1·5—2·5 vol% of halothane.

A venous cut-down was made on the forelimb, and a plastic cannula for the continuous intravenous drip was introduced into the vein. It remained there for several days after transplantation, being used for fluid replacement.

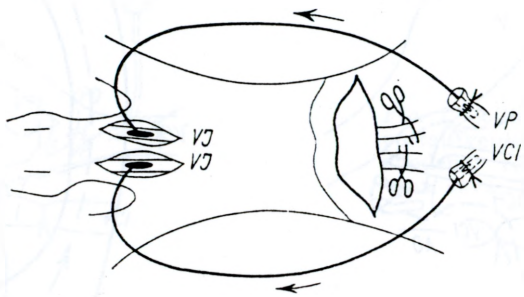

Fig. 4. Diagram of venous bypasses decompressing the portal and inferior vena cava circulation. *VP* — portal vein, *VCI* — inferior vena cava, *VJ* — jugular vein.

The first step of the transplantation procedure in the recipient was the creation of a venous bypass decompressing the inferior vena cava and the portal circulation (Fig. 4). The right jugular vein and inferior vena cava were cannulated on one side, and the left jugular vein and portal vein on the opposite side. A logitudinal 5 cm long incision was made on the neck, and the jugular vein was exposed. Only its anterior aspect was freed, the other parts being left intact. This technique helps to avoid constriction of the vein. The peripheral part of the vein was ligated, and the proximal part was intubated with a 8—10 mm wide cannula filled with heparinized saline and connected to tubing to be introduced later into the inferior vena cava or the portal vein.

HEPATECTOMY IN THE RECIPIENT

A midline incision between the xiphoid process and symphysis pubis was made. The right suprarenal vein was ligated and divided between the ligatures. The infrahepatic portion of the inferior vena cava was freed from the adjacent structures. The next step of the operation was right nephrectomy. The stump of the renal artery served for anastomosis with the grafted hepatic artery. The kidney capsule was divided, and the renal artery was exposed down to its origin from the aorta. The longest possible

segment of the artery was left to make the anastomosis with hepatic artery easier. The left triangular ligament was ligated and cut, and the peritoneal fold between the liver diaphragmatic crura was carefully divided. The gastrohepatic ligament and the common bile duct were divided. At that

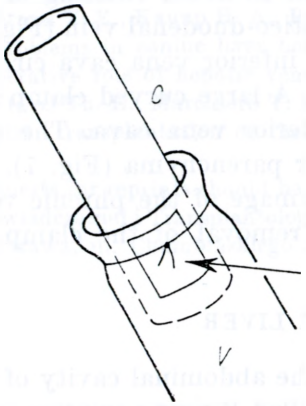

Fig. 5.

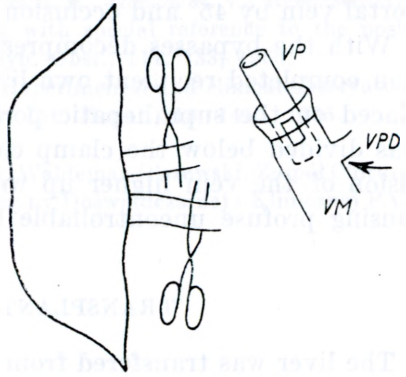

Fig. 6.

Fig. 5. Fixation of the cannula in the portal vein and inferior vena cava. *V* — vein, *C* — cannula.

Fig. 6. Occlusion of the pancreatoduodenal vein by inadvertent placement of the ligature close to the vein's origin (arrow). *VP* — portal vein, *VPD* — pancreatoduodenal vein, *VM* — mesenteric vein.

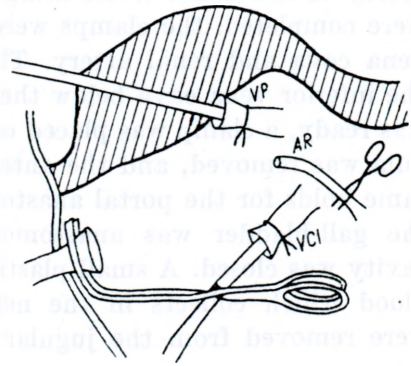

Fig. 7. Abdominal cavity after hepatectomy. Clamps placed on the infradiaphragmatic vena cava, infrahepatic vena cava (*VCI*), renal artery, (*AR*) and portal vein (*VP*).

time, also, other structures such as the hepatic artery and portal vein were exposed. The artery was divided close to the liver hilum, and the portal vein was meticulously dissected down to the liver.

The peritoneal fold between the liver and right diaphragmatic crus was cut, its small arteries having been previously ligated. The inferior vena cava and portal vein were now ready for cannulation. A clamp was placed

on the inferior vena cava above the renal veins, and another on the same vein close to the liver. The vein was divided. Its lumen was intubated with the tubing with one end already in the jugular vein. A ligature was placed on the vein wih cannula and tied on a plastic pad (Fig. 5). The, clamp was taken off of the tubing to allow free blood flow from the lower part of the body to the jugular vein. Using the same technique, the portal vein was cannulated. Attention should be paid to avoid twisting of the portal vein by 45° and occlusion of the pancreatico-duodenal vein (Fig. 6).

With the bypasses decompresing portal and inferior vena cava circulation completed recipient own liver is removed. A large curved clamp was placed on the suprahepatic portion of the inferior vena cava. The vein was divided below the clamp close to the liver parenchyma (Fig. 7). Division of the vein higher up would lead to damage of the phrenic veins causing profuse uncontrollable bleeding after removal of the clamp.

TRANSPLANTATION OF THE LIVER

The liver was transfered from the donor to the abdominal cavity of the recipient. It was continuously perfused with chilled Ringer's solution until the venous anastomoses were completed. The suprahepatic portion of the inferior vena cava of the donor and recipient were anastomosed with a continuous 3—0 silk suture. The anastomosis should be water-tight to avoid postoperative bleeding from the suture line. The next step was an end-to-end anastomosis of the renal artery of the recipient with the hepatic artery of the donor liver, using 5—0 silk. When those two anastomoses were completed. the clamps were removed from the suprahepatic inferior vena cava and renal artery. The third anastomosis was made between the inferior vena cava below the liver. When the posterior row of sutures was ready, a clamp was placed on the vein above the renal veins, the cannula was removed, and the anterior row of sutures was put on fast. The same holds for the portal anastomosis. Careful hemostasis was made, and the gall-bladder was anastomosed to the duodenum. The abdominal cavity was closed. A small plastic drain was left in the abdomen to drain blood which collects in the neighborhood of the transplant. Cannulas were removed from the jugular veins.

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