

# The effect of liver disease on the need for venous decompression during the anhepatic phase of canine orthotopic liver transplantation

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In at least one important way, an erroneous conclusion was reached from animal experimentation about the technical requirements for successful orthotopic transplantation of the human liver. During the anhepatic phase, it is necessary to cross-clamp the great veins which drain the intestine and the lower half of the body. It was soon learned that normal dogs rapidly developed shock and almost inevitably failed to survive operation if the stagnant venous pools were not decompressed. Eventually, methods were developed in which external plastic catheters were used to temporarily permit runoff from the occluded inferior vena caval and splanchnic systems into the cervical veins, bypassing the obstruction.<sup>1, 3</sup> The same precaution was taken in the first clinical attempts at liver replacement.<sup>5</sup>

Subsequent experience has proved that simultaneous occlusion of the portal vein and inferior vena cava can be tolerated in human subjects for a long enough time to permit recipient hepatectomy and the insertion of a new liver.<sup>2, 4</sup> It has been suggested that the relative safety with which this could be done was due to the presence of venous collaterals secondary to the underlying hepatic disease.<sup>2</sup>

In the present study, this hypothesis has

been tested in dogs. Liver injury was produced by ligation of the common duct. Several months later, orthotopic homotransplantation was performed without any provision for venous decompression.

## METHODS

Twelve mongrel dogs weighing 10 to 25 kilograms were subjected to cholecystectomy and ligation and division of the common duct. In addition, all periportal tissue was also divided sparing only the skeletonized hepatic artery and portal vein. Portal pressure was measured.

Two to 3 months later, the animals were re-explored and the portal pressure was determined again. Orthotopic hepatic transplantation was then carried out with non-related mongrel donors of approximately matching size. The vascular structures entering and leaving the liver were all reconnected with end-to-end anastomoses. During the anhepatic phase external bypasses were not used. Postoperatively, the animals were treated with azathioprine, prednisolone, and horse anticanine-lymphocyte globulin.

## RESULTS

At the time of the first operation, the portal pressures ranged from 7 to 13 cm. of water. Postoperatively, the stools became acholic. The serum bilirubins rose to 4 to 13 mg. percent along with marked rises in the alkaline

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phosphatase, serum glutamic oxalacetic transaminase, and serum glutamic pyruvic transaminase. Eventually, the animals became wasted and had prolonged prothrombin times. The serum protein concentrations fell from about 6 Gm. percent to an average of 3.5 Gm. percent. Half the dogs developed ascites, and in two of these there was over 5 L. of intraperitoneal fluid at the time of re-exploration; the latter two animals had become azotemic by this time. Death terminated two of the 12 experiments before transplantation could be attempted.

The 10 remaining dogs were subjected to orthotopic liver transplantation despite the fact that they were all seriously ill by this time. Upon reopening the abdomen, portal pressures were measured at 27 to 35 cm. of water. Extensive venous collaterals were found in the abdominal wall, the retroperitoneal space, and in all the viscera. The presence of large and thin-walled veins in the gastrohepatic ligament made dissection of the portal triad unusually difficult. During the anhepatic phase when the portal vein and inferior vena cava were cross-clamped for 45 to 60 minutes, the intestines remained pink and motile.

One of the dogs was lost intraoperatively because of a technical accident. Two more died 1 day later without having regained consciousness. The other seven recovered promptly from anesthesia and were able to walk around on the following day; several began to eat. There was invariably a prompt alleviation of the hyperbilirubinemia and usually the depressed prothrombin times were restored toward normal. However, all seven animals which survived operation died after 3 to 10 days. Their extremely debilitated state seemed to be the most important factor. Pneumonitis was regularly found. None of the dogs had secondary rises in serum bilirubin before death, although some of the livers had pathologic findings suggestive of early rejection.

#### DISCUSSION

When the portal vein and suprarenal inferior vena cava are abruptly cross-clamped

in normal dogs, a dramatic and rapidly evolving lethal syndrome is produced. Within a few minutes the intestines become first deeply cyanotic and then black. The kidneys and the other contents of the retroperitoneal space undergo similar changes. The blood pressure falls precipitously, and death usually follows within 20 to 30 minutes.

None of these events in the present study were observed in the animals which had been conditioned by long-term extrahepatic biliary obstruction. These dogs had developed extensive venous collaterals and moderate portal hypertension. Obstruction of the great veins draining the splanchnic bed and the lower portion of the body for as long as 1 hour did not cause grave cardiodynamic consequences. The intestines did not change color at all. These observations support the hypothesis that the presence of hepatic disease eliminates or reduces the need for decompressing bypasses during the anhepatic phase of orthotopic liver transplantation.

#### SUMMARY

After common duct ligation in dogs, it is possible within 2 to 3 months to safely cross-clamp the portal vein and suprarenal inferior vena cava for at least 1 hour during the course of orthotopic liver replacement. The lack of serious hemodynamic consequences under these circumstances as opposed to those in normal animals is apparently explained by the increased venous collaterals that develop in the course of liver disease.

#### REFERENCES

1. Moore, F. D., Wheeler, H. B., Demissianos, H. V., Smith, L. L., Balankura, O., Abel, K., Greenberg, J. B., and Dammin, G. J.: Experimental whole organ transplantation of the liver and of the spleen, *Ann. Surg.* 152: 374, 1960.
2. Starzl, T. E., Groth, C. G., Brettschneider, L., Moon, J. B., Fulginiti, V. A., Cotton, E. K., and Porter, K. A.: Extended survival in 3 cases of orthotopic homotransplantation of the human liver, *SURGERY* 63: 549, 1968.
3. Starzl, T. E., Kaupp, H. A., Brock, D. R., Lazarus, R. E., and Johnson, R. U.: Reconstructive problems in canine liver homotransplantation with special reference to the post-

- operative role of hepatic venous flow, *Surg. Gynec. & Obst.* **111**: 733, 1960.
4. Starzl, T. E., Marchioro, T. L., Huntley, R. T., Rifkind, D., Rowlands, D. T., Jr., Dickinson, T. C., and Waddell, W. R.: Experimental and clinical homotransplantation of the liver, *Ann. New York Acad. Sc.* **120**: 739, 1964.
  5. Starzl, T. E., Marchioro, T. L., von Kaulla, K., Hermann, G., Brittain, R. S., and Waddell, W. R.: Homotransplantation of the liver in humans, *Surg. Gynec. & Obst.* **117**: 659, 1963.