DNA and Protein Metabolism After Liver Autotransplantation

S.K.		Tamvakopoulos
H.T.		Randall
J.		VanLancker

Division of Surgical Research, Rhode Island Hospital and the Sections of Surgery and Pathology, Division of Biological and Medical Sciences, Brown University, Providence, USA.

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Authors' address: S. K. Tamvakopoulos, M. D.; H. T. Randall, M. D. and J. Van-Lancker, M. D., Division of Surgical Research, Rhode Island Hospital, Providence, RI 02902 (USA).

Technique Materials Methods

Heterotopic liver autotransplantation is carried out to the diaphragmatic surface of the spleen [13, 14, 15] in Albino-Sprague-Dawley rats of 150–200 g each, in two stages.

In the first stage, adhesions were created between the diaphragmatic surface of the spleen and the inferior surface of the left lobe of the liver, in order to create collateral circulation from the spleen to the liver. The liver, usually the edge of the left lobe, is attached with two 2–0 chromic catgut stitches to the spleen, and then a capsulectomy is performed over the opposing surfaces of both organs.

In order to provide bile drainage in the piece of liver to be transplanted and prevent pressure atrophy due to proliferation of bile canaliculi, catheterization of the main bile duct of the autotransplant is accomplished with a fine polyethylene tube directed through the common duct. In a second stage, three weeks later, the portion of liver to be auto-transplanted, usually a part of the left lobe of about 3–5 g, is separated with scissors and left attached to the splenic bed. A partial hepatectomy may be performed at the same time in order to stimulate liver regeneration and ascertain the effect of a humoral factor [10, 11].

Histological examinations are carried out monthly. Glucose-6-phosphatase [8] levels of protein [6] and DNA content [6] are determined in tissue homogenates.

Attempts of liver autotransplantation date back to 1895. CAMERON [1] credits Allessandri as the first, who tried to evaluate whether liver autografts survive and function.

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Free grafting in one stage or grafting in two stages, dividing the original blood supply, following establishment of collateral circulation, have been employed since then, but results have generally been disappointing. The ultimate fate of liver grafts, placed in the anterior chamber of the eye, mesotestis, peritoneum, subcutaneous tissue, etc. has been atrophy and degeneration, secondary to lack of blood supply and to pressure necrosis, due to proliferation of bile ducts following transplantation [2, 3, 4, 5, 7, 9, 12].

In view of the remarkable regenerating ability of liver, success in establishing an intact and functioning portion in an heterotopic location could open new vistas for clinical application and does provide a method for study of liver regeneration in experimental animals.

It is, therefore, very worthwhile to study whether hepatic cells placed heterotopically would respond to a humoral stimulus, after partial hepa-tectomy of the non-transplanted liver and proceed to hypertrophy, proliferate, and organize into a functioning organ resembling liver. It is the purpose of this communication to report on results achieved by a method of heterotopic liver autotransplantation previously described [10,11].

Fig. 1. Maintenance of liver architecture six months after liver autotransplantation. Liver tissue separated from splenic tissue by capsule.

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Results

Maintenance of histological architecture and survival of the autotrans-plant was established by histological criteria for as long as six months following separation from the main organ (fig. 1).

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NORMAL 24 HOUR TRANSPLANTED
REGENERATING

Fig. 2. Glucose-6-Phosphatase activity in normal, 24 hour regenerating and autotransplanted liver. (24 hours after partial hepatectomy.)

NORMAL 24 HOUR TRANSPLANTED
REGENERATING

Fig. 3. DNA content (colorimetric test) in normal, regenerating and autotransplanted liver. (24 hours after partial hepatectomy.)

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NORMAL 24 HOUR TRANSPLANTED
REGENERATING

Fig. 4. Tissue protein content in normal, regenerating and autotransplanted. (24 hours after partial hepatectomy.)

Glucose-6-phosphatase determinations have shown enzyme levels identical to normal liver four months following separation of the auto-transplant from the main organ (fig. 2).

DNA and protein content were the same in the transplant as in the main liver segment. When the rats were partially hepatectomized by the method of Higgins and Anderson, regeneration in the autotransplant paralleled regeneration in the main organ, as measured by the incorporation of H_3 thymidine into DNA (fig. 3).

Discussion

Failure in autotransplantation of the liver is attributed to lack of blood supply and to pressure necrosis due to proliferation of bile canaliculi following transplantation. Anoxic necrosis occurs if adequate blood supply is not provided in the autotransplanted portion. Proliferation of bile ducts occurs because of their greater potential for growth compared to hepato-cytes. Atrophy of hepatocytes follows due to pressure.

Satisfactory results and a functioning autotransplant can therefore be obtained only if these two factors are eliminated.

The reported technique provides a logical experimental model for the study of survival, growth and regeneration of the autotransplanted liver

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as well as additional insight into the events of hepatic function in an heterotopic location.

Results reaffirm the existence of a humoral factor stimulating liver regeneration following hepatectomy. These results seem also to indicate that an intact portal circulation is not necessary for liver regeneration following partial hepatectomy.

Summary

A new technique for functional liver autotransplantation in the diaphragmatic surface of the spleen is described as carried out in the rat.

Maintenance of liver architecture and finding of normal protein and DNA levels has been accomplished for as long as six months following separation from the main organ.

The autotransplant responds to partial hepatectomy in a fashion similar to regeneration of the non-transplanted liver as indicated by determination of tissue protein levels and rate of incorporation of H_3 thymidine into DNA.

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