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One Stage Functional Hepatectomy in the Rat.*

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The recent demonstration by Blakemore and Lord[1] of a simple and efficient method for the nonsuture anastomosis of blood vessels has allowed the development in the rat of a technic for indirect anastomosis of the portal vein with the inferior vena cava by way of the left renal vein. This establishment of a portal-caval shunt, coupled with ligation of the hepatic artery, results in the preparation of a functionally hepatectomized animal.

Method. Adult male rats of the Long-Evans strain are anaesthetized with ether. A long midline incision is carried from the xiphoid process to the symphysis pubis. The major portion of the gastro-enteric tract is exteriorized to the left of the supine animal to allow adequate visualization of the portal vein and inferior vena cava. The exteriorized viscera are kept warm and moistened with saline gauze packs. The left renal vein is brought into the operative field and stripped of adjacent fat. The suprarenal and gonadal veins are ligated at a distance from the renal vein. The renal artery is ligated close to the aorta, and is then stripped away from the renal vein. The renal vein is ligated at its point of exit from the kidney and the latter organ is then excised. A control ligature is placed about the renal vein at the point of entrance into the inferior vena cava to prevent reflux of blood into the renal vein. A small thin-walled pyrex glass sleeve of appropriate size is then threaded over the renal vein. Under the binocular dissecting microscope, the ligature is removed from the free end of the renal vein and the vein is then cuffed or everted over the glass sleeve and tied securely in place with a fine silk ligature. The portal vein and hepatic artery are then isolated from the neighboring structures in the hepatic pedicle and are ligated at their points of entrance into the liver. A control ligature is employed as a temporary block to prevent blood flow through the open portal vein at the time of anastomosis with the free end of the renal vein. This temporary ligation is most easily carried out by using a rubber band as a ligature, tension being brought to bear on the vein by fastening the stretched rubber with a small mosquito hemostat. A small incision is then made in the wall of the portal vein between the 2 ligatures, and into this aperture is introduced the glass sleeve with the everted free end of the renal vein. The portal vein is then tied securely around the glass sleeve and the intervening renal vein. In effect, then, the intima of the portal vein is in direct contact with the intima of the renal vein, the glass sleeve remaining entirely extravascular in position. The temporary ligatures about the portal vein and renal vein are removed allowing free circulation of portal blood into the vena cava via the left renal vein. The viscera are replaced in the abdominal cavity and the incision is repaired. The animals recover rapidly from the anaesthetic and appear normal to outward appearances for a number of hours, save for moderately diminished activity.

The glass sleeve employed has an external diameter of 1.5 mm, and a length of 2.5 mm, but these dimensions are varied in accordance with the variation in size of the vessels in any particular animal. A small constriction in the glass sleeve facilitates tieing the veins in place. The portal vein will generally accommodate a cannula with external diameter of 2 mm. It is unnecessary to heparinize the animal. The operation, if car-

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1 Blakemore, A. H., and Lord, J. W., Jr., *J. A. M. A.*, 1945, **127**, 748.

ried out successfully, entails no blood loss. During the period of temporary portal vein obstruction, the intestines become markedly cyanotic, but normal color is regained immediately upon completion of the anastomosis and release of the temporary ligatures. The operation requires about 30 minutes. The major portion of this time is spent in preparing the renal vein and glass sleeve for insertion into the portal vein. The actual period of obstruction of the portal vein need not exceed 5 minutes.

If the hepatic artery be left patent, the rat will survive for an indefinite period with a complete portal-caval shunt (direct Eck fistula). These animals appear to be perfectly normal. Animals sacrificed 5 days after establishment of the portal-caval shunt show patent functioning anastomoses without evidence of portal obstruction. Secondary or delayed ligation of the hepatic artery may then be carried out at a later date.

Discussion. The survival time in a series of 12 unfasted adult rats averaged 11½ hours (range: 5-17 hours). The technic of nonsuture anastomosis of the portal vein to the inferior vena cava via the left renal vein obviates the use of a cannula directly in the bloodstream, and further does not require heparinization of the animal. The animals recover readily from the anaesthetic and seem normal for about two-thirds of the survival time, when they become progressively less active. Death usually occurred after a series of convulsive attacks. The animals were injected hourly after operation with glucose in saline solution by the subcutaneous route. At autopsy, the portal-renal anastomoses were patent. The liver was pale yellow in color and practically bloodless on incision. It is thought that the functionally hepatectomized rat or the rat with a portal-caval shunt is a useful preparation for experimental use.

Summary. A method is described whereby the portal vein is directly anastomosed to the left renal vein in the rat by a nonsuture method of blood vessel anastomosis. The complete direct Eck fistula produced in a one-stage operation coupled with ligation of the hepatic artery results in the preparation of a functionally hepatectomized animal. The survival time in a series of 12 rats thus prepared averaged 11½ hours.

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Viruses Inactivated by Mustard (*Bis*(β-chloroethyl) Sulfide) as Vaccines.

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For some years we have been using the rapidly advancing knowledge of protein chemistry in an attempt to find an agent other than formaldehyde that would inactivate viruses without destroying their antigenic nature. Formaldehyde reacts primarily with amino groups of protein but it also attacks other radicals. While some formalinized virus preparations are good immunizing agents many are not satisfactory, perhaps because the virus is not present in sufficient quantity. Reagents known to react with amino, tyrosine phenol, or SH groups of protein and several detergents have been used with disappointing results. Either the virus was not completely inactivated or else it failed to immunize animals to the active virus. It has been shown that mustard ($Cl—CH_2—CH_2)_2—S$ reacts with proteins[1] and it is our purpose here to report the tests we have made on the effect of this chemical on a number of viruses.

Eastern equine encephalomyelitis virus, fixed rabies virus, and hog cholera virus have been treated with chemically pure mustard.

[1] Berenblum, I., and Wormall, A., *Biochem. J.*, 1939, **33**, 75.