

TOTAL SURGICAL REMOVAL OF THE LIVER IN RABBITS.

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Total surgical removal of the liver in the rabbit without impairment of the portal and caval circulation has not hitherto been reported. A method has been devised for the purpose of work in this laboratory. It would seem to be desirable to report its technique not only because of the wide use of the rabbit as an experimental animal but because of the frequency with which it has been employed in studies upon the relation of the liver to carbohydrate metabolism (1).

Excision of the liver necessitates occlusion of the portal vein. Moreover the intimate attachment of the organ to the vena cava requires the removal of a segment of this vessel as well, if a complete and satisfactory liver ablation is to be obtained. In the normal rabbit the obstruction of either, or both, of these veins is followed by death so rapidly that in a method for hepatectomy channels must be provided for the immediate return of caval and portal blood to the heart. Markowitz and Soskin (2) have reported a technique for inducing a collateral circulation in dogs without an Eck fistula. At a preliminary operation the portal vein and vena cava are partially occluded with ligatures which constrict the lumina of these vessels to about one-fifth the original size. After some weeks collaterals to the veins are so well developed that the liver may be removed without impairment of the portal circulation. The present method is a modification of this technique.

Our first attempts with the rabbit were unsuccessful. The vena cava and portal vein had been approached directly, and exposed on the right side of the abdomen. The consequent injury to the ventral surface of the liver and the peritoneum of this region resulted in massive adhesions among the injured parts, preventing removal of the liver without great blood loss. It therefore became imperative to devise a method whereby these veins could be approached, and

partially ligated, from the left side of the abdomen, without exposing the liver, leaving the right side free of adhesions that would hinder the later hepatectomy.

Anatomical Peculiarities of the Rabbit's Liver.

The liver of the rabbit consists of two relatively separate masses connected by a thin isthmus of parenchyma. The larger mass, comprising the three cephalad lobes, has been termed the "main liver" and the smaller portion, the "posterior lobe mass" (3). Each possesses its own arteries, ducts and branches of the portal vein. The main portal trunk on approaching the liver divides to send its first branch to the "lobe mass." At about this level it also receives a tributary—the superior pancreatico-duodenal vein—and in this region too the hepatic artery comes to lie close to the vessel and accompany it to the liver. Still another tributary, the left gastro-epiploic, enters the portal vein about 1 cm. cephalad to the juncture of the portal and superior pancreatico-duodenal veins. The relationship of these structures is by no means constant. Thus, for example, the superior pancreatico-duodenal vein may enter the portal stream either below or above the great branch of the portal to the "posterior lobe mass" of the liver. As the aim of the preliminary operation is the establishment of a portal obstruction so great that it will induce the development of a collateral circulation, it is necessary to produce this obstruction caudad to the first branch of the portal vein, that to the "lobe mass." Unfortunately the tributaries mentioned above, the superior pancreatico-duodenal and the left gastro-epiploic, usually enter the portal vein above this site of election and, as our experience has shown, will serve as by-passes, whereby portal blood reaches the "main liver." To cut off this source of supply it is necessary to ligate the two small vessels individually.

The Preliminary Operation.

The shaved skin of the rabbit is swabbed with 60 per cent alcohol and under ether anesthesia the abdominal cavity is exposed from the level of the ensiform to the umbilicus by an incision 1 cm. to the left of the mid-line. The relatively bloodless mid-region is thus left intact for the incision of the secondary operation. The stomach is pressed upward, covering the liver, and the portal vein is approached from the left side and sufficiently freed of the surrounding tissue for a

silk ligature, soaked in petrolatum, to be passed about it. The ligature is placed just caudad to the branch to the "posterior lobe mass" and to the junction of the superior pancreatico-duodenal and portal veins. Great care should be exercised to place the ligature around the vein only, leaving intact between it and the liver the peritoneum adherent to its right side, thus preventing all contact between silk and the liver. Only if this is successfully accomplished will adhesions fail to develop.

The ligature is tied down so as to include not only the vein but the end of a glass rod. This end is bent at a right angle to the main shaft and is laid parallel to the vessel for ease in tying. It should taper slightly so that it can be readily withdrawn after the tie has been accomplished leaving the vein partially ligated, with a lumen equal to the size of the rod. The diameter of the latter should be 2 mm. for a 2 kilo animal.

The superior pancreatico-duodenal vein is tied near its junction with the portal, and likewise the small vein which arises on the caudad surface of the pylorus and leads into the portal about 1 cm. above the entrance of the superior pancreatico-duodenal vein. At times this vessel may enter the portal vein just dorsal to the pylorus. Both these procedures, carried out without injury to the peritoneum of the right side of the abdomen, are essential; for as already mentioned these veins, unless occluded, enlarge with extreme rapidity and soon provide an adequate supply of blood to the liver. The ligation of the small left gastro-epiploic vein can be carried out only by a dissection along the posterior wall of the pylorus. The vein receives, as a rule, one or more tributaries. It should be inspected along its entire course and the ligature placed below the last tributary, a delicate procedure which exposes the bile duct and portal vein in this region as well.

Finally partial occlusion of the vena cava is effected from the left side of the abdomen. As a first step the superior mesenteric artery is identified and the peritoneum perforated on the left side of the mesentery just cephalad to this artery and just ventral to the aorta. A small glass spatula covered with vaseline is introduced into the aperture and worked between the vessel and the peritoneum anterior to it. A threaded ligature passer introduced along the track thus made is turned posteriorly about the vena cava, thus carrying a ligature around the vessel, just caudad to the right adrenal body. The lumen of the vena cava is then reduced to 2 mm. by tying the ligature about the removable glass rod as in the case of the portal vein.

Recovery from the operation is usually rapid and a collateral circulation soon develops about the liver. In a few days, if the procedure has been successful, evidences of this fact appear, in a notable enlargement of the veins of the abdominal wall. The development of this collateral circulation is so rapid that one can totally occlude the portal vein and the vena cava 5 days after the primary operation without the appearance of any untoward symptoms. This has been done in 4 instances as a control experiment to demonstrate the existence of an adequate by-pass for the blood about the liver. In our later work, however, we have gener-

ally allowed an interval of 3 weeks to elapse between the primary and secondary operations. This not only affords ample time for the development of the new vascular bed about the liver but suffices for the animal's complete return to general health. Liver extirpations have been done successfully as late as 6 months after the preliminary operation.

Hepatectomy in the Rabbit.

The incision for hepatectomy in the rabbit should run in the mid-line from ensiform to umbilicus. A ligature is placed around the entire gastrohepatic omentum, including in the one tie the portal vein, bile duct and hepatic artery. The vena cava is ligated just cephalad to the right adrenal gland, and again just cephalad to its union with the hepatic veins from the "main liver," and severed between. The structures in the gastrohepatic omentum are cut cephalad to the tie placed about them. The liver can now be removed *in toto*, after cutting its ligaments to the diaphragm and dividing the peritoneum on either side of the vena cava in the regions where this is intimately attached to the liver. No stump of hepatic tissue need be left.

A diaphragmatic vein enters the right side of the vena cava slightly caudad to the entrance of the hepatic veins from the "main liver." This small vessel must be tied and cut between ligatures.

In certain instances it may be of advantage to remove the "main liver" early in the operation, immediately after tying the gastrohepatic omentum, thereby gaining working space for the more difficult steps. This is done by snipping the ligamentous attachments between the "main liver" and diaphragm and throwing a stout ligature around the former, tying it down closely upon the vena cava. The "main liver" is then cut away above this ligature. In the final stage of the operation, its stump is removed.

DISCUSSION.

The clinical picture in the rabbit, deprived of the entire liver, needs only brief mention for in all important particulars it is like that in the liverless dog, described by Mann (4). As is now well known, hepatectomy in the dog is followed by pronounced hypoglycemia with an accompanying train of typical symptoms. Further, this condition fails to appear when the diminution of blood sugar is prevented by administrations of glucose. The postoperative state in the liverless dog may be divided into two clearly defined stages, the first characterized by the hypoglycemic symptoms, the second, even if glucose be given, by coma terminating in death.

All these phenomena have their counterpart in the rabbit, as our observations upon these animals deprived of 90 per cent of the liver

(5) have already shown. Completely hepatectomized animals treated by the administration of dextrose in 25 per cent solution *per os* or in 5.4 per cent solution intravenously in sufficient amounts to keep the blood sugar concentration at or about 125 mg. per cent behave normally for from 12 to 32 hours. In this first stage no untoward symptoms appear. As a rule only slight variations of the pulse and respiratory rate are noticed, together with an increase in body temperature of 1 to 1.5°. Finally, in spite of the glucose administrations, certain phenomena usher in what may be called the second stage. Now the animal when placed on the floor no longer investigates its surroundings in the ordinary way but hops blindly in a straight line, striking any object in its path, even a brilliantly lighted wall. Later on evidences of muscular weakness and ataxia appear; the animal sits with sprawling legs and drooping head. Left in the cage it will be found with nose pressed in a corner. In the next few hours, although care is taken that the blood sugar level does not fall below normal, the weakness progresses and the movements become more ataxic. The animal falls to one side in attempting to move and cannot rise again, or it lies with sprawling legs unable to raise its head or draw the limbs under the body. The temperature becomes subnormal; the respiratory movements are labored and less frequent, and the pulse is slower too. The corneal reflex and knee jerk previously present are lost and complete flaccid paralysis, save of the respiratory muscles, sets in. For a period Cheyne-Stokes respiration may occur, after which the respiratory rate falls to 8 per minute or even lower, and while the pulse rate remains at about 30 per minute the heart sounds progressively weaken. After varying periods up to 40 hours death comes on, with respiratory failure, the heart continuing to beat for 10 minutes or more after respiration has ceased.

At the present time we can venture no explanation of the later symptoms. It is of importance now merely to call attention to the close similarity of the postoperative events in the liverless rabbit and dog, a similarity which permits us to infer perhaps that the major functions of the organ are much the same though the one creature is herbivorous and the other omnivorous.

SUMMARY.

A technique is described for total removal of the liver of the rabbit without circulatory difficulties as a result. The method requires a preliminary operation to induce a development of portal and caval collaterals.

Rabbits deprived of the liver in this manner if given glucose live for varying periods up to 40 hours. Before death they show the same disturbances as do hepatectomized dogs. They die early, of hypoglycemia, unless provided with sugar.

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