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Effect of Complete Hepatic Vein Ligation on Portal Pressures and Ascites Formation in Dogs with Porta-Caval Shunts.* (20160)

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Bollman(1) stated, "Because of the anatomic relation of the liver to the inferior vena cava, no suitable technic has been devised for direct constriction of the hepatic veins." Simonds and Brandes(2) and Brandes(3) studied the effects of obstructing the hepatic veins by use of a mass ligature technic employing a soft rubber tube as a tourniquet to occlude the veins. Child and associates(4) occluded the hepatic veins in the *Macaca mulatta* monkey by placing a polythene tube in the inferior vena cava held in place by a ligature above and below the entrance of the hepatic veins. Most investigators have relied on supra-diaphragmatic constriction of the inferior vena cava to produce increased intrahepatic and portal pressures in the study of ascites production. The purpose of this study was to develop a technic for complete individual occlusion of the hepatic veins, and to determine the effects of such occlusions on portal pressures, liver function, pathologic changes in the liver, and ascites formation.

Methods. Healthy mongrel dogs were used. Preliminary efforts showed that total ligation of the hepatic veins resulted in 100% mortality. Immediately after occlusion of the last hepatic vein the inferior vena cava collapsed almost completely and the animals died in acute shock from pooling of blood in the portal system in a period of 5 to 30 minutes. If the compression of the portal outflow was released just before the heart stopped, the dogs recovered completely. In each case the last vein to be occluded was the large proximal vein just below the diaphragm which drains all of the liver except the right lateral lobes (Fig. 1). If this vein was left untied, dividing all of the others, the dogs survived indefinitely with no ill effects. To attain survival in dogs with total ligation of the hepatic veins a porta-caval shunt had to be done in conjunction with the ligation. This allows portal blood to flow directly into the inferior vena cava, and the hepatic artery inflow to the liver then escapes into the inferior vena cava in a retrograde manner through the proximal segment of the portal vein and the porta-caval anastomosis. Fifteen dogs weighing 11 to 22 kg were prepared and studied in this manner. A thoracoabdominal approach through the right tenth interspace, dividing the diaphragm from its costal attachment to the hiatus of the inferior vena cava, was employed to divide the hepatic veins. The vena cava in this area not only is intimately adherent to the diaphragm, but also is surrounded by liver, and must be dissected from these attachments before the division of the individual hepatic veins is begun (Fig. 2).

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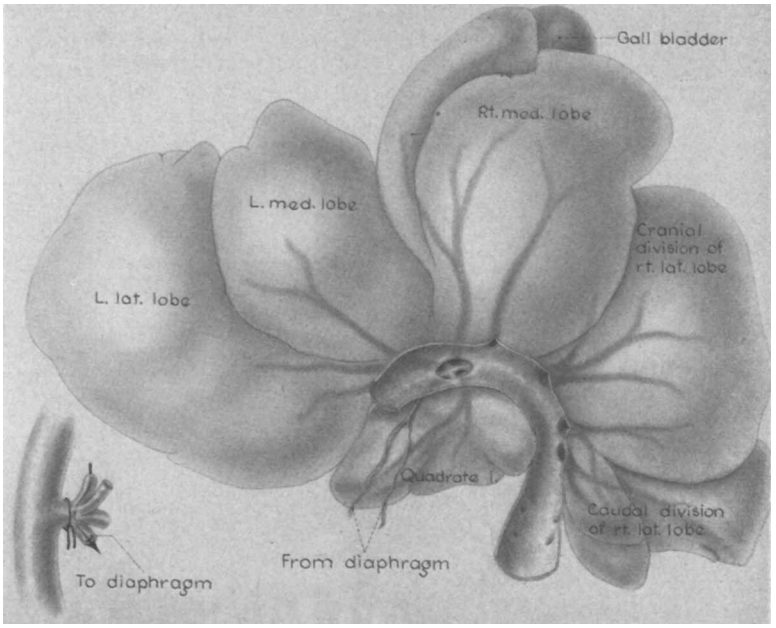

FIG. 1. Drawing illustrating major hepatic veins emptying into the inferior vena cava and areas of liver drained by them. Note diaphragmatic vein emptying into large proximal hepatic vein. Inset shows the possibility of collateral circulation behind a ligature placed on this vessel.

The dissection is started distally separating the inferior vena cava from its investing sheath and is then carried proximally by gently dissecting the vena cava from its liver bed dividing the hepatic veins between ligatures of 2-0 silk as the veins are encountered. The 2-0 ligatures are reinforced with stick ties of 3-0 silk. There are innumerable small vessels present in addition to the 5 large veins shown in Fig. 1. This part of the dissection is made difficult by the fact that the hepatic veins are large and bifurcate very close to their junction with the inferior vena cava. To give added length to the veins the liver substance is dissected back for a short distance along the veins. If the hepatic veins are divided too close to the inferior vena cava, part of the wall of the latter vessel is included in the ligature, which not only partially occludes the lumen of the inferior vena cava, but also increases the hazard of slipping of the ligatures. The large proximal vein is merely ligated instead of ligated and divided because of its size and difficulty of exposure. Before this last vein is occluded, a side to side porta-caval anastomosis is done utilizing a single Pott's clamp. The full available width of the clamp is used resulting in an anastomosis measuring 1 x 2 cm. When the procedure outlined above is completed there is a possibility for collateral venous drainage from the liver to the diaphragm present behind the ligature on the large proximal vein as shown in the insert in Fig. 1. If this small diaphragmatic vein is obstructed at the time the hepatic veins are ligated, the operative mortality approaches 100% even with an adequate porta-caval shunt. However, its value as a collateral diminishes as readjustments in the circulation take place because this vein was filled with clot in 14 of the 15 dogs in this study at the time of autopsy. Post-operatively the dogs were maintained on a standard kennel diet with whole milk supplement. Liver function and blood studies were done periodically, the onset and amount of ascites recorded, and the animals reexplored transabdominally to obtain portal pressures and liver biopsies after 2 to 5 weeks. Portal pressures were done in a branch of the right gastro-epiploic vein. The animals were followed for periods of 2 to 28 weeks. At autopsy the porta-caval shunts ranged from .7 x .9 cm to 1 x 3 cm. The majority were 1 x 2 cm.

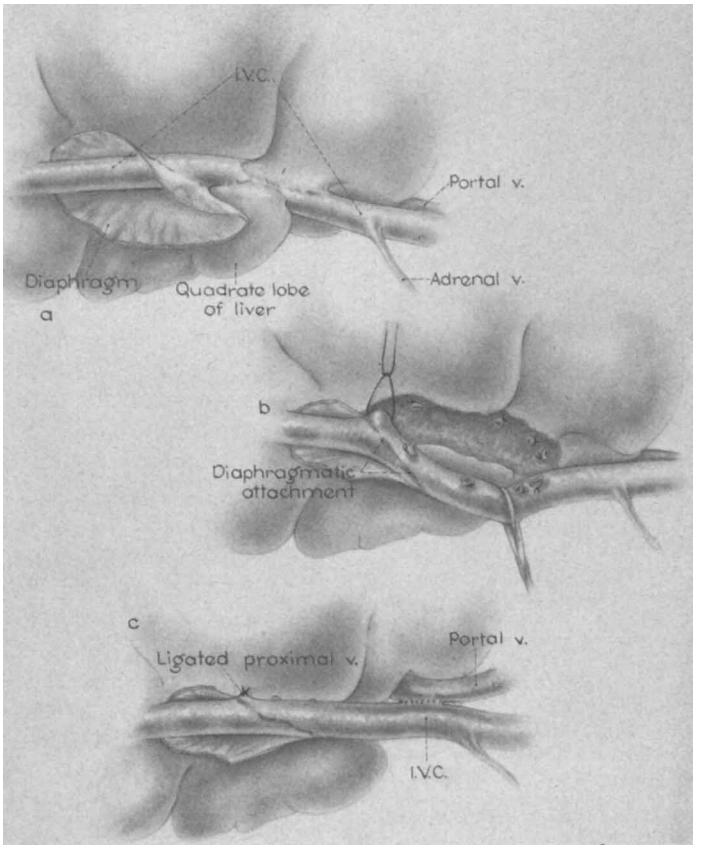

FIG. 2. Outline of main steps in individual occlusion of hepatic veins in conjunction with a porta-caval anastomosis. A. Inferior vena cava exposed showing its intimate relationship to the diaphragm and dorsal surface of the liver. B. Inferior vena cava has been dissected from its liver bed by ligating and dividing all hepatic veins except the most proximal vein. The porta-caval anastomosis is done at this stage. C. Porta-caval anastomosis completed, and ligature tied down around the large proximal vein. Major hepatic veins are much larger than represented here, and there are also numerous small veins which have to be ligated and divided.

Results. Effects on portal pressures and ascites formation. There was no uniformity in the development of increased portal pressures or ascites (Table I). Portal pressures were measured in the 15 dogs and ranged from 11 to 68 cm of water. Pressures in control dogs ranged from 11 to 15 cm. Ten dogs or 66% had portal pressures that were elevated above 19 cm of water. Four dogs or 27% had pressures from 15 cm to 19 cm, and one dog had a pressure of 11 cm of water. Eight or 53% of the 15 dogs in which portal pressures were measured developed ascites high in protein content which became apparent within 2

TABLE I. Effects of Total Hepatic Vein Ligation in Dogs with Porta-Caval Shunts.

Dog No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Portal pressure, cm H_2O	11	15	15	16	17	19	20	22	26	28	32	42	43	58	68
Ascites	+	—	+	—	—	+	—	+	+	—	+	—	—	+	+
Central necrosis & congestion	2+	+	2+	2+	+	3+	+	2+	3+	3+	3+	3+	2+		4+
Serum albumin, g/100 cc	1.6	2.2	1.7	1.6	1.7	2.8	2.3	1.8	1.8	1.6	1.5	2.1	1.7	3.8	2.0
Total serum protein, g/100 cc	5.0	5.3	4.7	6.5	7.1	5.2	6.2	5.5	4.7	6.3	4.7	6.4	6.4	4.3	4.9
% BSP* retention	17	7	6	6	7	6	5	12	7	7	9	19	6	5	8

* Control dogs show less than 6% retention in 45 min.

FIG. 3. Dog 11 showing marked ascites and collateral circulation in abdominal wall. This dog formed 22 liters of ascitic fluid over a period of 3 months and required repeated paracentesis.

weeks. The ascites varied from 200 cc in one dog to 22 liters in another, the latter amount of fluid being removed over a period of 3 months. The total proteins in the ascitic fluid averaged 3.6 g/100 cc with an albumin content of 1.0 g %. Those animals with marked ascites showed collateral vessels in the abdominal wall (Fig. 3). No esophageal varices or large collaterals in the region of the diaphragm were observed.

Laboratory studies. The blood sugar, blood urea nitrogen, and serum bilirubin were normal in all dogs. The hemoglobin values ranged from 7.8 to 16.0 g. Serum protein levels were low in general, especially the albumin fraction. These values are shown in Table I, along with the bromsulfalein clearance values.

Pathology. Grossly the livers were large and congested with rounded edges. Exudate and adhesions were present over the surface. There were dilated lymphatics and large lymph nodes in the hilar region. None of the dogs used in this study showed residual hepatic veins emptying into the inferior vena cava at the time of autopsy, and there was no instance of incomplete ligature or recanalization of the large proximal vein. Clots in various stages of organization were present in the hepatic veins at the site of their occlusion. Microscopically the sinusoids were dilated and filled with blood or amorphous pink staining material. Varying degrees of central necrosis and degeneration of the liver cell cords were found ranging from minimal changes to a marked degree of destruction. No signs of fibrosis or regeneration were present. In some sections thickened capsule and dilated subcapsular lymphatics were seen.

Discussion. This is the first time that survival following occlusion of the hepatic veins has been reported. Child, McClure, and Hays(4) observed survival in monkeys up to 3 hours following supportive treatment. Complete occlusion of the hepatic veins results in marked congestion of the liver with subsequent death from shock due to pooling of blood in the portal system. The porta-caval shunt acts as an avenue of escape permitting the blood in the liver to leave the portal bed. This retrograde blood flow through the porta-caval anastomosis can readily be seen at the conclusion of the anastomosis and may be demonstrated more clearly by temporarily occluding the portal vein on the intestinal side of the porta-caval shunt. The presence of free communications between the arterial and portal venous systems in the liver is thus established by these experiments.

There was no correlation between the size of the porta-caval shunt and the subsequent elevation of portal pressure; in fact, the dog with the smallest shunt in the series did not develop either an elevated portal pressure or ascites. It is difficult to explain such findings, but the work of Madden(5) and his associates gives some insight to this problem. These investigators have shown by injection studies in human cadavers that pre-existing natural porta-caval shunts were present in 4 out of 8 cadavers studied. Such pre-existing shunts may also explain the wide variations in portal pressures in the dogs studied in this experiment.

Volwiler and associates(6,7) stress the importance of hepatovenous congestion and increased liver lymph flow, and McKee *et al.*(8) have shown the effect of serum protein and salt on ascites production. In the present study an attempt was made to correlate the development of ascites with an increase in the portal vein pressure, a decrease in serum albumin, or with the degree of liver damage as shown in the microscopic sections or the bromsulfalein test. Examination of Table I reveals that there was no consistent correlation found between any one of these factors and the degree of ascites formation in the dogs in this experiment. This finding would suggest that the formation of ascites more likely was due to a combination of factors rather than to any single one.

Summary. 1. A successful technic for individual ligation and division of the hepatic veins in the dog is described. 2. Complete occlusion of the hepatic veins is uniformly fatal in dogs. However, if a porta-caval shunt is also done, the dogs will survive. 3. Fifteen dogs prepared in this manner were studied, and 66% of them developed a significant elevation of the portal pressure. 4. Ascites developed in 53% of the dogs, but the ascites could not be correlated with the increased portal pressures, decreased serum proteins, or pathological changes in the liver.

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Some Relationships Between Intracranial Pressure and EEG Frequency in Cats.* (20161)

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This report describes some relationships existing between intracranial pressure and the EEG pattern in the curarized, unanesthetized cat.

Methods. Each cat was anesthetized with vinyl ether (Vinethene), and a wide midline skull exposure made. Four small holes were drilled through the skull, one over each parietal region and one over each side of the cerebellum. These holes were so placed as to center approximately over the motor cortices and cerebellar lobes. Screw-in type EEG electrodes were placed in these holes. Each animal was then tracheotomized and injected with dihydro-beta-erythroidin hydrobromide§ to eliminate muscle activity and then placed on artificial respiration. A number 18-gauge spinal needle was then inserted into the cisterna magna through the foramen magnum and the needle connected by means of a short rubber tube to a Statham strain gauge pressure transducer. The output of the transducer activated a high-gain amplifier coupled to a

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