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Therapeutic ligation of the hepatic and splenic arteries

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THERAPEUTIC LIGATION OF THE HEPATIC AND SPLENIC ARTERIES

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THERAPEUTIC LIGATION OF THE HEPATIC AND SPLENIC ARTERIES

That medical management of cirrhosis of the liver is currently the treatment of choice is undisputed; however, in spite of the best efforts of the physician, such measures of treatment all too often do not suffice and the patient then succumbs to one or another of the many complications of cirrhosis to which he is especially susceptible; i. e., progressive liver failure, inanition with wasting ascites, or exsanguination after one or repeated bouts of hemorrhage from esophagogastric varices.

The relative incidence of the last two manifestations of cirrhosis of the liver, i. e., ascites and hemorrhage, has for many years commanded the attention of surgeons who have sought by operative measures to correct the existing complication.

In 1900, Preble, (1) analyzed the records of 60 fatal instances of gastro-intestinal hemorrhage occurring in patients suffering from hepatic cirrhosis. In 42 of the 60 cases, the esophagus had been examined at necropsy and varices were present in 35, (i. e. 85%). In 19 of these 42 cases the source of bleeding was noted. In 16 it was ruptured esophageal varices; in the remainder, ruptured gastric varices. In 6 of the 42 cases

examined at necropsy, no varices were found; the gastro-intestinal mucosa being said to be intact. In 1920, Blumenau, (2) reported that in a series of patients affected with obvious portal cirrhosis at the time of death, 19% died from ruptured esophageal or gastric varices and 19% from cirrhosis itself, i. e., hepatic insufficiency, which later in this paper will be shown to be vascular in origin and perhaps reversible by application of the technique in question.

In 1928, McIndoe (3) reviewed the problem and found that 50% of deaths in portal cirrhosis were due to vascular lesions. In view of this finding McIndoe began an extensive study into the cause of the clinical manifestations of cirrhosis. He concluded that along with gastro-intestinal hemorrhage, ascites, and edema, hepatic insufficiency was also of vascular origin and urged therefore that attention be directed to the portal system in further efforts at palliative treatment.

In 1945, Chaikin and Swhwimmer (4) reviewed 264 cases of portal cirrhosis and reported that in 63 hematemesis had occurred. In 12 of this group it was the first sign of cirrhosis and in 8 of those the first hemorrhage proved fatal. They also reported that in 93 of the 264 cases ascites was present.

Through the years a great number of interesting and

ingenious methods have been devised to surgically alleviate the always alarming and often fatal hematemesis of portal cirrhosis.

A classification (5) of these methods follows:

I. Efforts directed toward the varicosities themselves.

a. Insertion of suitable types of tubes with balloons - certainly the use of this type of tamponade may be a lifesaving procedure and it provides the means of successfully controlling hemorrhage while the condition of the patient is fortified by transfusions, vitamins, and general care preparatory for definitive treatment (6).

b. Injection of sclerosing agents - a procedure which is unsatisfactory because it is applicable only to the esophageal varices, whereas, the gastric varices are the commoner source of bleeding and also because of the multiplicity of the juxta-cardiac varices (7).

c. Excision of the lower one third of the esophagus and cardiac end of the stomach or excision of the entire stomach with anastomosis between the esophagus and jejunum - this method removes the areas containing vulnerable varices and the varices in the remaining part of the esophagus are thereby severed from their direct connections with the portal venous system via the

left gastric vein. Furthermore, such resections remove a large area of gastric mucosa, thereby reducing the amount of HCl and pepsin which appear to be important factors in the mechanism of erosion of the vulnerable varices.

II. Efforts directed toward correction of the underlying problem.

a. Omentopexy - one of the earliest surgical attempts to shunt blood away from the portal stream.

b. Splenic artery ligation - first reported by Blain (8) in 1918. This procedure has not been widely employed, however, recently the procedure has received some emphasis being found useful in some patients with intractable ascites whose condition is too poor to expect them to endure a very extensive procedure. This method seeks to reduce portal pressure by eliminating the percentage of portal flow received via the splenic vein.

c. Portacaval and Splenorenal shunts - a method of reducing portal pressure by introducing a by pass between the portal venous and systemic venous circulations. Shunt operations stem from the work of Eck (9) who in 1877, developed an operation whereby a fistula between the portal vein and inferior vena cava

was made in order that he might carry out experimental studies of diseases of the liver and the relation of the liver to metabolism. He suggested that an anastomosis between the two veins might be used to sidetrack the venous return in obstruction of the portal vein. The Eck fistula procedure was attempted in patients by several surgeons in 1910-12 in both France and Germany but with only a one to six month survival. The cause of the operative mortality was generally renal shut down from occluding the vena cava for too long a time during suture anastomosis of the portal vein to the vena cava. Recent interest in portacaval shunt resulted much from the non-suture method for blood vessel anastomosis devised by Blakemore and Lord (10). In 1947, Blakemore, (11) claimed that portacaval and splenorenal shunt were the two procedures most widely recommended for the alleviation of the complications of portal cirrhosis.

During the time since shunt procedures came into vogue, evaluation of the procedure has been made. Reinhoff, (12) and others (13) (7) (14) (6) report that the procedure is not satisfactory in the majority of cases. Their main criticism is that shunt procedures are formidable and technically difficult if not impossible. They further contend that such procedures subject an

already diseased liver to exhaustive anesthetic and surgical trauma and in some cases where severe liver malfunction is present lifesaving surgery may have to be denied the patient. Other criticism levels at the inadequacy of the procedure in preventing recurrence of complications of cirrhosis over a period of time. The contention is that shunt produces a temporary alleviation of varices, etc., but, with time, due to the progressive nature of the disease, portal pressure again increases and there is a recurrence of ascites, esophago-gastric varices, bleeding, etc.

Recently a different approach to the problem has been suggested, namely, that of alteration of the hepatic arterial circulation by ligation of the hepatic and splenic arteries. The proponents of this approach hold that it is a simple, nonexhaustive procedure which, therefore, is applicable to many patients which are non-operable otherwise. They also contend that it may by virtue of the rationale to be presented later in this paper bring about or be conducive to regeneration of liver parenchyma which of course is something very much to be desired in portal cirrhosis.

Ligation of the hepatic artery is not new. Reports are in the literature of ligation of the artery for a cure of aneurysm by Kehr (15), Kading (16), and Colmers (17). The problem of liver necrosis following ligation

will be covered elsewhere. Ligation of the splenic artery has been reported by Blain and Blain III (8).

Before turning to the rationale behind therapeutic ligation of the hepatic and splenic arteries in complicated portal cirrhosis consideration will be given to the anatomy, physiology, and experimental work upon which the soundness of such a procedure rests.

The coeliac artery as it arises from the abdominal aorta gives rise to three large branches. The left gastric, the splenic, and the hepatic arteries.

The left gastric (coronary) artery passes upward and to the left to the cardiac orifice of the stomach distributing branches to that part of the stomach and to the esophagus. The branches anastomose with the aortic esophageal arteries and with branches of the splenic artery. It then runs from left to right, along the lesser curvature of the stomach to the pylorus giving branches to both surfaces of the stomach and anastomoses with the right gastric artery - a branch of the hepatic artery.

The splenic artery has a tortuous course as it passes from right to left, where nearing the spleen, it divides into three sets of branches, the pancreatic

branches supplying the body and tail of the pancreas and anastomosing with the pancreatic branches of the pancreaticoduodenal and superior mesenteric arteries, the short gastric branches to the greater curvature of the stomach anastomosing with branches of the left gastric and left gastro-epiploic arteries, and the left gastro-epiploic artery, which runs from left to right on the greater curvature of the stomach anastomosing with the right gastro-epiploic and middle colic arteries as it supplies ascending branches to the stomach and descending branches to the greater omentum.

The hepatic artery ascends to the hepata portis where it divides into right and left branches which supply the corresponding lobes of the liver. Brunschwig (18) reports that there is an accessory or aberrant hepatic artery in 32 to 40% of humans. In its ascent it gives off the right gastric, the gastroduodenal, and the cystic arteries. The right gastric artery descends to the pyloric end of the stomach and in passing from right to left along the lesser curvature of the stomach anastomoses with the left gastric artery. The gastroduodenal artery is a short branch which descends between the superior part of the duodenum and the neck of the pancreas and divides at the lower border of the duodenum into two branches, the right gastro-epiploic,

which runs from right to left along the greater curvature of the stomach and anastomoses with the left gastro-epiploic artery - descending branches of this artery anastomose with the middle colic artery in the greater omentum, the superior pancreaticoduodenal artery, which descends between the contiguous margins of the duodenum and pancreas, supplying branches to both those organs and anastomosing with the inferior pancreaticoduodenal artery - a branch of the superior mesenteric artery. The cystic artery supplies the gallbladder (19).

Within the liver (3) the hepatic artery lies in close relationship to the portal vein within the portal spaces. Three distinct groups of branches arise from the artery. The vaginal branches, which form an intricate arteriolar plexus in the connective tissue of the portal space and undoubtedly are its main source of nourishment, apparently end in capillaries which communicate with both the portal vein and with the intercellular sinusoids. The vascular branches end directly in the sinusoids at the periphery of the portal space. Gad (20) described these arterial branches uniting with the portal venules at an acute angle, leaving a wedge-shaped valve between them. The capsular branches from the right and left hepatic arteries, which form an anastomosis via arteries and arterioles derived from

each over the capsule of the liver communicating with each other and there anastomosing with branches of the phrenic, internal mannary, lower intercostal, and other arteries. This was demonstrated by Segall (21), in 1923, by using an emulsion of barium sulfate which he injected into the vessels of the liver and followed up with radiographic technique. The anastomoses necessary were found present in the layers of the peritoneum which are reflected from the liver onto the diaphragm, in the areolar tissue between the diaphragm and the liver surface, around the walls of the inferior vena cava, and in the falciform ligament.

The other sources of arterial blood to the liver have been indicated above. A brief discussion, however, follows. The inferior phrenic artery as it passes from the aorta to the under surface of the diaphragm not only forms an anastomosis with the subcapsular branches of the hepatic arteries, but also its medial branch communicates with its fellow from the opposite side, the pericardiophrenic, and the superior epigastrics, while the lateral branches communicate with the same subcapsular plexus, the musculophrenics, the lower intercostals, and the left gastric, aortic, and inferior thyroid arteries by way of the branches it sends to the inferior vena cava and esophagus. There is on the right a branch of

the superior epigastric artery which extends into the falciform ligament to the liver and enters into anastomosis with the hepatic artery. The inferior epigastric artery by entering into anastomosis with the superior epigastric artery above the umbilicus is also, therefore, a potential source of arterial blood to the liver (19). In 1937, Huggins and Post, (22) reported finding fine arterioles present in the hepatic and portal veins and in the common bile duct readily apparent on injection of the aorta with barium sulfate followed by radiographic study.

It has long been known that ligation of the hepatic artery beyond its last tributary is fatal. This fact has been confirmed by many investigators (23) (24) (25) (27) (28). This is so in rabbits, cats, dogs, and man. In man a sufficient number of cases of sudden obstruction due to injury, embolus or accidental ligation of the artery, has occurred to establish that necrosis follows. In 1930, Cameron and Mayers, (23) almost simultaneously with Elis and Dragstedt, (24) noted the presence in such a necrosed liver of dogs of spore forming bacilli. These men stated the changes present in the liver following ligation of the hepatic artery beyond its last tributary in the following manner, "There is

massive necrosis of the liver which is soft, friable, malodorous and often containing many bubbles of gas. Histologically, there is total destruction of liver parenchyma which is crowded with millions of spore-forming bacilli." Cameron and Mayers, (23) at the same time, reported that if the ligation was not placed beyond the last tributary the animals lived and examination of their livers showed no change, thereby demonstrating the effectiveness of collateral circulation to the liver. In 1937, Huggins and Post, (22) showed that whereas subtotal removal of the arterial supply to the liver in one sitting was fatal, multiple stage ligation of the hepatic artery in dogs was attended by no change in the liver. Thus, demonstrating again, but more emphatically, the effectiveness of the collateral circulation to the liver. Their method was to first ligate the hepatic artery proximal to the gastroduodenal artery, then in four weeks ligation distal to the gastroduodenal artery, followed in a few weeks by removal of peritoneal attachments of the liver to the diaphragm, stomach, and posterior abdominal wall. Finally, even the phrenic arteries were ligated. They concluded that the liver becomes accommodated to deprivation of most of its arterial supply. These investigators theorized that the liver

necrosis observed following hepatic artery ligation was due to anaerobic infection, the bacilli either being present in the liver of dogs before ligation or having ascended from the gut in the presence of ischemia, which was facilitated by the decreased oxygen tension resulting from the ligation. In 1949, Markowitz, (25) proved that they were correct by preventing necrosis following the same procedure by the use of intramuscular penicillin. This latter work stimulated Chau (28) to repeat the work of Markowitz since the latter had made his discovery quite by accident and more work needed to be done for confirmation of such an hypophysis. Chau, (28) and his group, concluded that massive necrosis of the liver was due in dogs to the development of an overwhelming clostridial infection which was the result of sudden change in the intrahepatic environment toward anaerobic condition. Furthermore, since it was found necessary to protect the animals for only 48 hours with penicillin, some adaptive mechanism in that time came into play which increased oxygenation in the liver, thus, the liver was again demonstrated to have an amazing ability to develop collaterals. Finally, the significance of all this is that wide spread hepatic damage is not a necessary sequel to hepatic artery ligation.

There is a fundamental axiom in the ligation of any large vessel, this is that the closer to its source that the vessel is tied, the greater and more effective will be the collateral circulation. This holds true with respect to the hepatic artery. If the hepatic artery is ligated at its source collateral flow is ample and occurs mainly through the left gastric artery which anastomoses with the right gastric artery and hence into the hepatic artery, and to some extent through the inferior pancreaticoduodenal artery which anastomoses with the superior pancreaticoduodenal artery and hence into the hepatic artery through the gastroduodenal artery. If the splenic artery is not ligated collateral flow also occurs through the left gastro-epiploic artery which anastomoses with the right gastro-epiploic artery and hence through the gastroduodenal artery to the hepatic artery. The other channels are more apt to develop if ligation is carried out distal to the gastroduodenal artery and therefore are innumerated with that possibility. No doubt some of those channels develop before ligation in the cirrhotic liver. As was seen in the description of the arterial supply to the liver, anastomoses are so rich that one can tie off the coeliac axis or the hepatic, left gastric, and splenic arteries at the same time without in any way interfering with the circulation

to the liver provided the animal has been prepared with penicillin and streptomycin (29). In this latter case, flow would still occur via the superior mesenteric artery - inferior pancreaticoduodenal - superior pancreaticoduodenal gastroduodenal route and via middle colic - left gastro-epiploic - right gastro-epiploic - gastroduodenal route plus from other sources to be mentioned in connection with ligation of the hepatic artery distal to the departure of the gastroduodenal artery. Of course the factor of accessory or aberrant arteries is always present and, indeed, in certain cases may, because of their potential supply to the liver, defeat the purpose of this procedure as will be pointed out later in the body of this paper. If the hepatic artery is ligated distal to the gastroduodenal artery and if the splenic artery is ligated at its source, collateral flow to the liver develops mainly through the inferior phrenic arteries which anastomose with branches of the internal mammary artery, the lower intercostal arteries, and the aortic esophageal arteries and hence to the hepatic artery by way of the subcapsular plexus formed by artery and arteriolar branches of the left and right hepatic arteries. Accessory flow in this instance is also afforded by the aortic branches which travel with the

hepatic artery, portal vein, and common bile duct into the liver, and by the artery traveling to the liver in the falciform ligament. Lastly if one of the divisions of the hepatic artery is ligated collateral circulation will be ample since the right and left hepatic arteries form a rich anastomosis between themselves via the arteries and arterioles which form the subcapsular plexus already referred to. The splenic artery may be tied close to its source without producing necrosis of the spleen because of the rich blood supply through the short gastric and gastro-epiploic arteries.

The portal system includes all the veins which drain the blood from the abdominal part of the digestive tube (with the exception of the lower part of the rectum) and from the spleen, pancreas, and gallbladder. From these viscera the blood is conveyed to the liver by the portal vein.

The portal vein is formed by the junction of the superior mesenteric and splenic veins. It passes upward behind the superior part of the duodenum and then ascends in the right border of the lesser omentum to the right extremity of the porta hepatis where it divides into a right and left branch, which accompanied by the corresponding branches of the hepatic artery,

enter the substance of the liver. The right branch of the portal vein enters the right lobe of the liver, but before doing so generally receives the cystic vein. The left branch, crosses the left sagittal fossa, gives branches to the caudate lobe, and then enters the left lobe of the liver. As it crosses the left sagittal fossa it is joined by a fibrous cord, the ligamentum teres, and is united to the inferior vena cava by a second fibrous cord, the ligamentum venosum. Tributaries of the portal vein are:

The splenic vein follows the course of the splenic artery in a straight course from left to right to unite at a right angle with the superior mesenteric vein to form the portal vein. It receives blood from the short gastric, left gastro-epiploic, pancreatic, and inferior mesenteric veins which have the same distribution as the corresponding arteries. The inferior mesenteric vein, however, needs special attention as here is an important link between the portal and caval systems of veins. This vein begins in the rectum as the superior hemorrhoidal vein, which has its origin in the hemorrhoidal plexus, and through this plexuses communicates with the middle and inferior hemorrhoidal veins. The middle

hemorrhoidal being a tributary of the hypogastric vein, the inferior hemorrhoidal being a tributary of the internal pudendal vein which ends in the hypogastric vein - the hypogastric vein empties into the common iliac vein which in turn empties into the inferior vena cava. Tributaries of the inferior mesenteric vein are sigmoid veins from the sigmoid and iliac colon, left colic vein from the descending colon and left colic flexure.

The superior mesenteric vein returns the blood from the small intestine, from the cecum, and from the ascending and transverse portions of the colon. It begins in the right iliac fossa by the union of the veins which drain the terminal part of the ileum, the cecum, and vermiform process, and ascends between the two layers of the mesentary to unite behind the neck of the pancreas with the splenic vein to form the portal vein. Besides the tributaries which correspond with the branches of the superior mesenteric artery, viz., the intestinal, ileocolic, right colic, and middle colic veins, the superior mesenteric vein is joined by the right gastroepiploic and pancreaticoduodenal veins.

The coronary vein has the same distribution as the left gastric artery and as such receives esophageal veins-another link between the portal and caval venous systems.

The pyloric vein returns blood from the pyloric end of the stomach.

The cystic vein drains blood from the gallbladder, and accompanying the cystic duct, usually ends in the right branch of the portal vein.

The parumbilical veins which are small veins in the course of the ligamentum teres of the liver and of the middle umbilical ligament establish an anastomosis between the veins of the anterior abdominal wall and the portal, hypogastric, and iliac veins. The best marked of these small veins is one which commences at the umbilicus and runs with the ligamentum teres between the layers of the falciform ligament to end in the left portal vein (19).

Corrosion specimens of the portal vein (3) show that it consists of a massive system of branches ascending directly without cross anastomosis through five or six successive orders of division to the sinusoidal circulation. In general the branches are given off at right angles to the parent stem, while the sinusoids themselves arise from the tips of the venules. The hepatic artery lies in close relationship to the portal vein within the portal space and occasionally winds around it.

The hepatic veins have much in common with the portal veins. They, too, form a massive system of branches commencing at the central veins and passing through sublobular veins to the inferior vena cava by five or six successive orders of division. There are, however, certain distinguishing characteristics. The central veins receive their tributary sinusoids from the parenchyma throughout their whole length. The hepatic vein runs entirely alone and is surrounded by parenchyma throughout its course, with the intervention of a small amount of perivascular connective tissue which is an extension of the fibrous tissue of the portal spaces. There is no anastomosis either with the portal vein or with the hepatic artery except through the sinusoidal bed, and the two venous systems are always separated by parenchyma. Each portal vein lies midway between any two corresponding portal terminals at a distance representing half the diameter of the so-called hepatic lobule. Because of this, the cell mass assumes a certain foliated or lobulated appearance. The area of parenchyma drained by a central vein is by no means defined by connective tissue, nor is it in any sense a structural unit. The liver then is a continuous sheet of hepatic parenchyma regularly

and alternately pierced, supplied, and drained by the terminals of the portal and hepatic veins (3).

Coincident with the obliteration of the porta hepatic venous pathway as occurs in portal cirrhosis, collateral channels are gradually opened between the portal and caval systems. McIndoe (3) quotes Harris's classification of the sites of collateral circulation in portal venous obstruction. This is as follows:

(A) At the situations in the gastro-intestinal tract where absorbing epithelium comes in contact with protective epithelium, that is, the cardia and the anus. The former represents the site of anastomosis of the coronary vein of the stomach with the intercostal, azygos minor, and diaphragmatic veins of the caval circulation, here producing esophageal varices. Butler (7) divides these gastric and esophageal varices into internal and external. The internal occur in the lamina propria and in the submucosa and bulge into the gut lumen. The external are embedded in the outer fibrous coat of the esophagus and at the cardia become continuous with the dilated, tortuous, left gastric vein. The internal varices in the lamina propria are the important ones so far as bleeding is concerned. They extend from the cardia to the cricoid cartilage. Bleeding may occur anywhere in this area, but is most

frequent in the cardiac end of the stomach and in the lower most quarter of the esophagus. The cause of bleeding from the vulnerable internal varices is not always apparent, but the following possibilities should be considered. Trauma to the esophageal and gastric epithelium by food particles, autodigestion of the poorly nourished esophageal epithelium by regurgitated gastricjuice, congenital weakness of the vein walls, the degree of portal pressure increases the risk of erosion of the internal varices insofar as it causes them to bulge into the gut lumen. At the latter, i. e. anus, the superior hemorrhoidal vein of the portal circulation anastomoses with the middle and inferior hemorrhoidal veins of the caval circulation. Occasionally hemorrhoids develop, although they rarely become large and are usually not clinically important.

(B) At the site of obliterated embryologic circulation, that is, the falciform ligament containing the parumbilical veins.

(C) At all situations within the abdomen where the gastro-intestinal tract, its appendages or the glands develop from it, become retroperitoneal develop mentally or adherent to the abdominal walls pathologically. This includes the duodenum, small intestine,

colon, omentum, spleen and pancreas, containing the veins of Retzius, and the liver with its accessory veins of Sappey, both establishing an anastomosis between the portal and caval veins.

The blood flow through the normal as well as the cirrhotic liver is the result of the interdependence of the afferent circulation to the liver, the free communication between these two systems within the freely expansible tissue framework of the liver and the efferent circulation from the liver to the caval system (30).

The circulation entering the liver has two components, i. e., the hepatic artery with its small volume and high pressure and the portal vein with its large volume and low pressure. Burton-Opitz (31) estimate that under normal conditions the hepatic artery carries 25% of the total volume of blood reaching the liver under a pressure of approximately 125 mm. Hg. The portal vein, therefore, carrying the remaining 75% of the total volume of blood to the liver under a pressure of approximately 8-12 mm. Hg. Of the 75% via the portal vein, 30% is via the splenic, and 70% via the superior mesenteric veins (12).

That there is a free communication between the

hepatic artery and portal veins within the liver at the sinusoids and via direct arteriovenous communications between the branches of the artery and vein proximal to the sinusoids, as recognized by Herrick (30), had been noted before by Betz (32) and Gad (20), and has since been verified by others (3).

The freely expansible framework of the liver is perhaps the most important factor toward maintaining the proper balance between portal and arterial circulation to the liver since it houses the communications between the hepatic artery and portal vein where their relative pressures come to a common level (14).

The hepatic vein with its pressure roughly of 1-2 mm. Hg. facilitates the return of blood from the portal system to the vena cava which has a pressure of 0.5 mm. Hg. below the diaphragm which is still positive as compared with the intrathoracic pressure which varies from -2 to -5 mm. Hg. At the level of the right atrium the pressure in the vena cava is approximately 5 mm. of water (14).

McIndoe (3) in a classical study of the blood supply within the normal and cirrhotic liver found that in cirrhosis there is a marked diminution in the total hepatic vascular bed. The main portal trunks are attenuated and irregularly stenosed. Their larger

branches are given off at unusually abrupt angles and occasionally show irregular deviation to one side or the other as though having been pushed or pulled by an invisible force. The tiny portal veins are distorted and twisted, curled on themselves, and finally broken up into a network of stunted venules from which irregularly scattered terminals arise.

The same changes are present in the trees of the hepatic vein and artery, however, being more pronounced on the venous side. Markowitz, (25) in view of this relatively less change on the arterial side thought that one would be justified in assuming that in a cirrhotic liver the arterial supply is relatively increased. According to McIndoe (3) the most striking feature in the vascular change with cirrhosis is the total loss of normal regular porta hepatic venous relationships. The terminals of the two systems no longer alternate with one another but tend to be together and to assume a basket-like arrangement. The central veins are pushed to the periphery of the lobule and finally lie next to the portal vein, thus, there is a dissociation between the portal and hepatic venous systems which results in delimited free exit of blood from the portal sinusoids into the central veins with the production of increased portal pressure. As the

pressure rises a more direct communication is established between the branches of the hepatic artery and portal vein (14). This is a factor of great significance not only insofar that it contributes to increased portal pressure, but also in the basic rationale of the procedure in question.

Herrick, (30) in 1907, confirmed the existence of a freer communication between the arterial and portal venous elements experimentally. In his perfusion experiments using human normal and cirrhotic livers, he found that whereas in a normal liver there is a rise in portal pressure of 1 mm. Hg. for every 40 mm. Hg. rise in pressure on the arterial side, in a cirrhotic liver there was a rise in portal pressure of 1 mm. Hg. for every 6 mm. Hg. rise in pressure on the arterial side.

Nearly half a century after Herrick's observations were reported, Dock (33) carried out a similar study, which for the most part confirmed the results reported by Herrick. Using kerosene as a perfusion fluid to avoid edema, Dock carried out double perfusion experiments in the normal and in cirrhotic livers. Cannulas of suitable size were tied in the portal vein and the hepatic artery, and each was connected to a manometer. The pressure in each system could thus be varied at will and the flow under varying conditions of pressure measured.

The total portal and hepatic flow was found to average 2420 cc. per minute in normal livers, 2270 cc. in cirrhotic livers from alcoholics, 1880 cc. in nonalcoholic cirrhotics, and 900 cc. in one large fatty liver from an alcoholic. These figures were obtained with a portal pressure of 20 mm. Hg. and an arterial pressure of 100 mm. Hg. Measurements were made with portal pressure at 0 and arterial pressure at 100, with portal at 20 and arterial at 0; and with portal at 20 and arterial at 100. There was invariably a decrease in portal flow when the arterial inflow was increased. The decrease being as follows: in normal livers, 30%, in nonalcoholic cirrhotics, 21%, and in alcoholic cirrhosis 78%. Thus, a rise in pressure greatly above 20 mm. Hg. is necessary in cirrhosis to overcome arterial resistance and restore normal portal hepatic flow. From this experiment, Dock concluded that in portal cirrhosis the portal hypertension is higher than it would be if the arterial flow were reduced and therefore made the following suggestion, "in healed alcoholic cirrhosis, with ascites or danger of fatal hemorrhage, procedures to reduce hepatic arterial inflow may be worth consideration....."

Berman (27) in an excellent paper dealing with this subject summarizes the results of experimental work

on portal hypertension carried out over a period of several years as follows:

1. Ligation of the hepatic artery at the coeliac axis caused a fall in portal pressure of 10-20 mm. of water.

2. Ligation of the splenic artery after ligation of the hepatic artery caused an additional fall of 40-50 mm. of water.

3. Ligation of the splenic artery first caused a slight fall of 5-10 mm. of water; after the hepatic artery was ligated there was an additional fall of 40-60 mm. of water.

4. Ligation of the hepatic artery and then of the splenic artery one month later produced an additional fall in portal pressure.

5. If the splenic artery was tied first, then the hepatic artery 30 days later, there was a precipitous fall in portal pressure.

He concluded that experiments on dogs seemed to indicate that ligation of the hepatic and splenic arteries will produce a sustained fall in portal pressure and may be applicable in the treatment of portal hypertension.

As a consequence of the vascular changes considered above, portal hypertension gradually develops. With the rise in portal pressure collateral circulation develops

which in effect is a spontaneous Eck fistula between the portal vein and vena cava, allowing an ever increasing amount of portal blood to by pass the hepatic veins, thus divorcing the hepatic cells from their main blood supply. The point finally reached in this cycle leaves the hepatic cells with only the hepatic artery for blood supply. Hepatic insufficiency in cirrhosis is therefore as stated by McIndoe (3) in 1928, "an expression of vascular deficiency rather than a deficiency of liver cells."

McIndoe (3) substantiated his theory of 'divorce of liver cells from their main blood supply' by perfusion experiments. Showing that of 20 mm Hg. pressure in the portal vein in cirrhosis of the liver, 78-100% of the perfusion fluid passed directly into the collateral circulation and at most only 13% could be recovered from the hepatic vein.

Increased hydrostatic pressure within the portal vein is accompanied by a decrease in the osmatic pressure owing to the fact that the patient does not ingest sufficient protein and the liver fails to produce an adequate quantity of serum albumin. In addition the oxygen content of the portal blood is decreased because of stagnant anoxemia within the portal system. These factors are probably mainly responsible for

ascites which usually ensues. The decrease in osmotic pressure is perpetuated by the continued loss of albumin into the ascitic fluid (14).

The question of liver cell degeneration and regeneration as consequence of decreased portal flow and return of portal flow has partially been answered from an experimental point of view by various investigators, however, in man, regenerative evidence is still lacking following return of portal flow through the liver by the procedure in question (14).

In 1920, Rou and Larimore, (34) demonstrated that following ligation of a branch of the portal vein there was complete atrophy of the corresponding liver parenchyma with compensatory increase in size of the remainder of the organ.

In 1931, Mann, (35) found that liver regenerates very easily. They removed up to two-thirds of the organ and got complete regeneration provided portal flow was not disturbed. They demonstrated that if an Eck fistula had been made some time before removal of liver tissue hepatic regeneration did not occur.

Recently Wiles (36) has demonstrated that ligation of the hepatic artery has no effect upon regeneration of liver following partial hepatectomy.

The question posed above is of great significance in the procedure in question since in advanced portal cirrhosis the liver cells are 'divorced' from their main source of nourishment. Will it be possible to stimulate active liver cell regeneration by causing return to normal of portal direction of flow.

Moschowitz, (37) describes an effort on the part of the liver affected with portal cirrhosis to facilitate portal flow through the liver. He states that there is 'angiogenesis' in the cirrhotic liver attempting to establish a shunt between the portal and hepatic veins to compensate for the distortion and narrowing of the livers vascular content, in other words, an intrahepatic Eck fistula. A similar observation has been made by Berman (14).

Basically ligation of the hepatic and splenic arteries is done to accomplish two ends. The first of these is to decrease portal pressure thereby increasing the flow of portal blood to the liver which we have seen is of great importance in the alleviation of varices of the esophageal and for gastric veins, and in the production of conditions favorable to liver cell regeneration (35). Secondly to facilitate the formation of a new capillary bed in the liver, thereby providing nourishment for hepatic cells hence counteraction of the

vicious vascular cycle responsible for hepatic insufficiency. These ends are accomplished by ligation of the hepatic artery proximal to the gastroduodenal and right gastric arteries and by ligation of the splenic artery. Ligation of the hepatic artery cuts down pressure within the arterial tree of the liver, thus permitting the venous component to enter the sinusoid at a much lower pressure. Such a procedure also acts to eliminate one of the perpetuating forces responsible for the increase in portal venous pressure, i. e., the further the process of portal cirrhosis goes the more direct the communication between the arterial and venous components and hence the higher the portal pressure becomes. To carry this further, the higher the portal pressure the more blood portal and arterial is there which passes by way of venous collaterals to the caval system and therefore the more 'divorced' the hepatic cells become from their blood supply and so the more likely the advent of 'hepatic insufficiency'. Since ligation of the hepatic artery secondarily causes an increase in the lateral pressure proximal to the ligation arterial collaterals develop to the liver which facilitate the development of a new arterial capillary bed in the liver, thus providing for nourishment of the starved hepatic cells.

Hepatic artery ligation does not decrease the portal volume flow, therefore, lateral pressure within the liver remains unchanged. This is a factor which is of great importance since such a force could counteract the formation of new arterial capillaries by pressure occlusion of the arterial collaterals from which they would take origin. Provision is made, therefore, to decrease the portal blood flow until arterial collaterals can be formed, then 'revascularization' may take place. This is accomplished by ligation of the splenic artery, which in effect reduces the portal volume flow by 25-40 per cent per minute. Ligation of the splenic artery has the same effect otherwise as does ligation of the hepatic artery. Namely, there is an increase in lateral pressure proximal to the ligation and thence the formation of collaterals to the spleen via the short gastric and gastro-epiploic arteries which is sufficient to prevent necrosis. Ligation of the splenic artery is logical in patients with splenomegalia as accompanies portal hypertension of long standing since it permits collaterals to form in the pulp, thereby restoring the spleens ability to hold blood. This is true since in the late stages of portal hypertension the circulation of the spleen is converted from an open to an

almost closed one, seriously compromising the reservoir function of the organ. It is also useful in cirrhotics without splenomegalia because it increases the storage space of the organ. The immediate effect of splenic artery ligation is a decrease in the size of the organ. After collaterals form, the spleen increases in size. If this procedure acts in such a way as to induce hypersplenism, splenectomy may be done later. However, experiments seem to show that reducing the portal vascular bed by splenectomy increases to some extent the portal venous pressure. Clinically, splenomegalia is regarded as an unfavorable accompaniment of cirrhosis. This may be explained on the basis that the spleen has reached its storage capacity and is of no aid in diminishing the volume of blood reaching the liver (14).

Reinhoff (12) reported six cases and made mention of six others treated by Thoreck, Hunt, and Kunkel. All six patients reported were chronic alcoholics suffering from either severe ascites and/or bleeding from esophageal varices. The first of his series was operated on, June 7, 1947. All were prepared pre-operatively with 600,000 units of penicillin and one gram streptomycin per day for seven days. The operative procedure consisted of ligation of the hepatic artery distal to the departure of the gastroduodenal artery and splenic

artery ligation at its departure from the coeliac axis. Average hospital stay was one month. Follow-up of three and one-half years in the case of the first operated, indicate that the operation was entirely satisfactory. The other five are also without complications. These results are in spite of the fact that most have returned to their old habit, alcoholism.

Berman (29) and associates reported one case and mentioned five cases apparently all successfully treated. The patient in this instance was a 60 year old severe alcoholic with an 18 month history of gradually developing ascites, swelling feet, dyspnea and 60 pounds weight loss, who had had a recent episode of bleeding from the gastro-intestinal tract. He was treated by ligation of the hepatic artery proximal to the departure of the gastroduodenal artery and splenic ligation at the coeliac axis. A six month follow-up report indicates that the operation was successful. His bleeding had not recurred. He improved in strength, appetite, and general demeanor. He did develop a slight recurrence of ascites which receded as soon as the patient was placed on a restricted salt diet.

Altemeier (38) in a personal communication with Jahnke (13) reported 12 cases treated with encouraging

results.

Madden (39) reported seven cases treated since the time of Reinhoff's encouraging report. He reports highly unsuccessful results and, indeed, questions the efficacy of the procedure in the treatment of portal hypertension. He states that all his patients were alcoholics and were suffering cirrhosis complicated by hemorrhage and/or ascites. His procedure was to ligate the hepatic artery distal to the gastroduodenal artery departure in one and proximal to the departure of this artery in six. In six he ligated both the hepatic and splenic arteries. In one he ligated only the hepatic artery. He states that 50% died immediately post-operative. The first from cardiac arrest, second, on the third day post-operative from hemorrhage from multiple parts. The third from hematemesis 48 hours post-operatively. The fourth died from renal insufficiency on the fourth post-operatively day. The remaining three in his series found death a little later. The fifth patient operated on died at 8 months post-operatively from anopharyngeal bleeding and ascites. The sixth died at 7 months post-operatively of hematemesis, (he had an autopsy made in this instance and discovered that the hepatic artery had recanalized. The seventh died at three weeks post-operatively from hepatic failure

following severe hematemesis.

Jahnke (13) and coworkers reported one case. This patient was a 28 year old soldier with advanced post-hepatic cirrhosis of the liver complicated by esophageal varices and massive hematemesis. Treatment consisted of ligation and division of the hepatic and splenic arteries at the coeliac axis. Post-operative studies indicate that the surgical procedure was a failure on the basis of massive esophageal varices with measured pressure almost equal to that present at operation.

Chenoweth (6) reported two cases. The first was a 38 year old service station operator who had been diagnosed as cirrhosis 8 months prior to admission. He had been on a medical regimen since the time of diagnosis, however he developed hematemesis which resulted in admission, etc. During his stay in the hospital he had frequent episodes of hematemesis and in spite of treatment went down hill. Therefore surgery was decided upon. Ligation of the hepatic artery was done at its origin. When seen three months after the operation, this patient had had no further hematemesis, no ascites, or edema of the lower extremities. His appetite was good. To date this patient has remained

well. The second case was that of a 43 year old housewife admitted to the hospital because of massive hematemesis. She had previously been diagnosed as a cirrhotic. Ligation of the common hepatic and splenic artery as it entered the hilum of the spleen was done. Since operation, the patient has had no hematemesis. The spleen has decreased in size and she feels well to date. Both these patients were placed on penicillin and aureomycin for six days following the operative procedure.

In summarizing, consideration has been given to the problem of treatment of the complications of portal cirrhosis with special emphasis being given to the relatively near approach of ligation of the hepatic and splenic arteries. The relative advantages of this procedure from a technical as well as practical point of view have been pointed out as against other techniques employed for the control or prevention of the massive hematemesis and/or ascites of advanced portal cirrhosis.

A review of the vascular anatomy of the liver has been presented since upon factors herein does the logic of the procedure depend. It has been pointed out that the liver has an amazing ability to develop collateral circulation in event of hepatic artery ligation and an account of arterial anastomoses responsible for

this phenomenon has been given. The question of massive liver necrosis following hepatic artery ligation has been shown to be a solved problem since the advent of penicillin and streptomycin which protect against overwhelming clostridial infection while increased oxygen tension within the liver is being developed via collateral circulation. Venous supply and drainage of the liver have each been considered and an account of collateral circulation in the event of porta hepatic obstruction has been given.

It has been shown that the flow through the liver is interdependent upon three factors, namely, the flow entering the liver, the communications between these arterial and venous elements within the elastic tissue framework of the liver, and the flow from the liver.

Consideration of the vascular changes of portal cirrhosis has been given with special emphasis being directed toward the resultant changes in the interdependence of the factors mentioned above. Pertinent experimental work regarding nature andaffect of vascular change in portal cirrhosis has been cited. Briefly, the nature of vascular change in portal cirrhosis has been shown to be decreased intrahepatic vascular bed and more direct communication between the hepatic artery and portal vein, and the affect of these changes, portal

hypertension and hepatic insufficiency from 'divorce' of the liver cells from their main source of blood supply.

The question of liver cell regeneration has been considered from an experimental point of view.

Lastly the information presented in this paper has been pieced together in order to logically justify therapeutic ligation of the hepatic and splenic arteries, and a few cases summarized.

It is concluded that therapeutic ligation of the hepatic and splenic arteries is an entirely feasible procedure in the treatment of complicated portal cirrhosis because of the rich anastomoses which occur when the arteries are tied close to their origins, and because of the protection against massive liver necrosis due to clostridial infection afforded by penicillin and streptomycin. No conclusion has been reached as regards the origin of such infection in man.

It is also concluded that this procedure has much to offer in selected cases where shunt procedures are prohibitive due to their technically difficult nature.

One must also conclude that this procedure is aimed at accomplishing more than just palliative alleviation of symptoms, that is to say, that from a theoretical

point of view, ligation of the hepatic and splenic arteries may cause a tendency toward reversal of the pathological sequence of events responsible for the complications of portal cirrhosis.

Finally, it is realized that there are 'factors at large' as yet not adequately evaluated which in some instances have undoubtedly contributed to the unsuccessfulness in the application of the procedure. One such factor is the site selected for ligation, which must of necessity be individualized and, of course, the operator must always search for an aberrant or accessory hepatic artery because missing such a vessel could very easily nullify results. Another such factor is ligation of the splenic artery which, indeed, depends upon clinical judgement.

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