S P L E N I C A N D P O R T A L V E N O G R A P H Y

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"For the truth is there is no one method method of science ....The task of the man of science is first to observe the appearances which Nature presents, then to ascertain what lies behind those appearances, and, lastly to link together his conclusions and observations in general laws. How he does this is not a matter of much concern, so long as he does it. Nor need he, as a man of science, concern himself with the question of what are the ultimate truths behind all the appearances that Nature presents to us. He has but to express general laws accord-:ing to the knowledge of his day, knowing full well that a day will almost certainly come when his general laws and the ideas on which they are based will have to be modified or replaced....
He will deal only with the knowledge that he has, knowing full well that further work may throw new light on his investiga-tions."

Charles Singer (1922).

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INTRODUCTION

INTRODUCTION

In 1945 Blakemore and Lord published their work on the treatment of Banti's Syndrome by anastomosing the splenic to the left renal vein, or the portal vein to the inferior vena cava. In the same year Whipple (1945) classified portal hypertension into cases with an obstruction in the portal system outside the liver, and those with a block inside the liver, the result of hepatic fibrosis. The cases with extrahepatic blockage of the portal circulation present clinically as cases of Banti's Syndrome. In this latter group repeated haematemeses are a common, and often fatal symptom. The operation of porta-caval anastomosis has as its main object the lowering of the pressure in the portal system, with a reduction in the frequency, and severity of the haematemeses. The operations are difficult and dangerous, and the patients suitable for operation must be selected carefully. The exact site of obstruction causing portal hypertension must be determined either at, or preferably before operation, as it will determine the type of operation. Thus an anastomosis between the portal vein and the inferior vena cava will be useless if haematemeses are the result of obstruction of the splenic vein.

The obstruction is likely to be intrahepatic if the liver function tests are disturbed. To localize extrahepatic obstructions, surgeons have done pressure studies of the portal vein and its branches at

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operation (Blakemore and Lord, 1945; Blalock, 1947). Whipple (1945), also at operation, has injected diodone into a branch of the portal vein to determine the site of obstruction radiologically. During the last few years several indirect methods of estimating the portal circulation time were reported, e.g. the rate of absorption of acetylene (Henning et al, 1950) or dyes (Souidan, 1950) from the intestinal tract. However, they were of no value in locating the site of obstruction.

As the cases of Banti's Syndrome all have big palpable spleens, the possibility suggested itself of injecting a radio-opaque dye into the spleen, hoping that its rapid passage into the splenic vein might show the splenic and portal veins on an X-ray film. This seemed to be the only method of localizing an obstruction in the portal system pre-operatively.

To determine the rate of blood flow in the portal vein, a series of experiments on guinea pigs were performed. The results, however, were inconclusive. Dogs were next investigated. To have a readily available spleen for injection, the spleens were exteriorized in eleven dogs by Barcroft's method (Barcroft, 1926; Barcroft and Stephens, 1928) by placing the spleen between the skin and the muscles of the abdominal wall. On injecting a radio-opaque dye (diodone 70%) into the substance of these subcutaneous spleens, it was possible to visualize radiologically the portal and splenic veins as well as some of their tributaries. The dye flowed

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into the splenic vein the moment the injection was started, and 20 cc. dye took about ten seconds to leave the spleen completely.

The intrasplenic injections of dye did no damage to the spleen. The procedure was, therefore, carried out in humans with enlarged spleens. In addition a few normal spleens were injected at operation. An X-ray exposure was made at the end of a rapid injection of 20 cc. 70% diodone. The results were the same as in the dog, both the splenic and portal veins being demonstrable. Thus, not only can the site of portal obstruction be localized pre-operatively, but the presence of portal hypertension is shown on the X-ray film by a marked collateral circulation of veins.

This new method of demonstrating the portal circulation in the intact animal and human being is also useful in investigating the blood flow in the portal system. The procedure is easy to do and because it is made into the splenic pulp the dynamics of the portal circulation cannot be disturbed. No increase in portal pressure during rapid injection of the dye into the spleen at laparotomy, was found in dogs. There is a constant filling defect where the superior mesenteric vein joins the portal. This is confirmatory evidence that the blood flow and pressure in the portal vein are not disturbed by the injection. The intra-abdominal pressure is not altered, as a laparotomy is not done. It is, therefore, most likely that the true physiological state of the circulation in the portal vein

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is demonstrated.

This method indicates the velocity and direction of blood flow in the splenic and portal veins. The size of these vessels and the density of the dye in them give an approximate idea of the volume of blood flow in the portal system. "Streamlining" of the blood in the portal vein may be shown but the dye usually fills the right and left lobes of the liver equally well. Transient spasm of the splenic vein may occur. This shows that the veins of the portal system can contract and dilate.

The behaviour of the dye in the spleen is interesting. It leaves the spleen very rapidly, indicating that the venous sinuses probably drain the pulp directly. The dye does not diffuse through the splenic pulp on injection, and is usually drained by only one branch of the splenic vein. The spleen appears to function as if it were divided into compartments. This fits the histological appearance of the spleen, which is divided into segments by fibromuscular septa.

The intrahepatic branches of the portal vein may be radiologically visible. This is a useful method of studying the intrahepatic cir-lation, and can be investigated further. This thesis is concerned mainly with the blood flow in the portal vein and its branches. Before report-:ing and discussing the experiments and results, the

../literature

literature on the blood flow and pressure in the portal system will be reviewed, and the anatomy of the portal circulation will be outlined.

HISTORICAL REVIEW

CHAPTER 1 : The Blood Flow in the Portal Vein

CHAPTER 11: The Blood Pressure in the Portal Vein

CHAPTER 1

A REVIEW OF THE LITERATURE ON THE BLOOD FLOW IN THE PORTAL VEIN

The liver and spleen are organs that have interested physiologists and anatomists from the earliest days. Galen (130 - 200 A.D.) believed that the body was governed by the liver, heart and brain, and that ingested food was carried from the intestine via the portal vessel to the liver. In the latter this "chyle" was transformed into "Natural Spirits" which was distributed to the rest of the body. The liver was the centre of the venous system of the body, a view which was also held by Andreas Vesalius (1514 - 1564; quoted by Singer, 1922).

Although William Harvey (1578 - 1657) discovered the circus movement of the blood in the 17th century, the experimental investigation of the portal circulation was only started towards the end of the 19th century. As late as 1932 McNee (1932) stated in his Croonian lectures on the liver and spleen, "We know a good deal about the dynamics of the systemic and pulmonary circulations but far less about the portal". The investigation of the portal circulation has been difficult because of its double set of capillaries with their resistances.

This review on the blood flow in the portal circulation will be followed by a separate historical

../survey

survey of the blood pressure in the portal system. Streamlining of the portal blood will be discussed in a later section of the thesis.

THE VOLUME OF BLOOD FLOW IN THE PORTAL SYSTEM

The results of the various workers and the methods they employed are summarized in Tables 1, 11 and 111 (Pages 8 to 10). Table 1 shows the volume of blood flow in the portal and splenic veins, Table 11 the total flow of blood through the liver, and Table 111 the blood flow in the hepatic artery and portal vein in relation to the total liver flow.

It should be noted that when Ludwig's stromuhr is being used the portal vein has to be occluded for 15 minutes during the insertion and, therefore, the physiological flow through the vessel is disturbed. However, the results correspond to those obtained by the thermostromuhr. Although the direct current thermostromuhr is more sensitive than that of Rein (Grodins et al, 1941), both appear equally reliable.

	Author	Values obtained in cc./minute Minimum	Maximum	Average.	Method	Subject	Remarks
1)	Schmid (1908)	20 per 100 Gms Splanchnic Organs	30	25	Ludwig's Stromuhr	Cats and Dogs	Tributaries enter the portal vein at the hilum of the liver in the dog. These must be ligated before insertion of the stromuhr.
2)	Burton-Opitz (1911 c)	123 (30 cc./minute per 100 Gms. splanchnic organs)	565	268	Ludwig's Stromuhr	Dogs	-
3)	Barcroft and Shore (1912)	9.6	28.6	-	Direct collection of blood	Cats	The portal flow was not influenced by feeding the animals
4)	Grab, Janssen and Rein(1929)	125	340	200	Rein's Thermostromuhr	Dogs	The portal flow = 80% of total liver flow = 45% of flow in the inferior vena cava
5)	Blalock and Mason (1936)	265	535	373	Direct collection of blood	Dogs	Portal flow is not directly related to the liver weight
6)	Soskin, Essex, Herrick & Mann (1938)	227	307	256	Thermo-Stromuhr	Dogs	-
7)	Grindlay, Herrick &Mann (1941)	145	505	345	Thermo-Stromuhr	Dogs	-
8)	Grodins, Osborne, Ivy & Goldman (1941)	-	-	270	Direct Current Thermostromuhr	Dogs	Average flow in a dog weighing 15 Kg.
		The Volume Flow in the Splenic Vein					
	Burton-Opitz (1909)	17	137	57	Ludwig's Stromuhr	Dogs	Results showed wide variations

TABLE 1 : THE VOLUME FLOW IN THE PORTAL VEIN

Author	Blood Flow in cc./minute				Method	Subject	Remarks
	Minimum	Maximum	Average	Per 100 Gms. Liver weight			
1) Burton-Opitz(1911 c)	-	-	-	84	Ludwigs Stromuhr	Dogs	-
2) MacLeod & Pearce (1914)	-	-	390	95.4	Direct collection of blood from the hepatic veins	Dogs	The hepatic artery was occluded to estimate the portal flow and vice versa
3) Blalock and Mason (1936)	313	612	387	82	Direct collection of blood from the hepatic veins	Dogs	-
4) Barcroft and Shore (1912)	-	-	-	33 - 48	Collection of blood from the hepatic veins	Cats	-
5) Grindlay, Herrick and Mann (1941)	252	620	-	-	Rein's Thermostromuhr	Dogs	-
6) Grodins,Osborne,Ivy and Goldman (1941)	-	-	-	86	Direct Current Thermostromuhr	Dogs	-
7) Bearn, Billing and Sherlock (1951)	-	-	800 cc per square metre body surface	-	Catheterization of the hepatic veins	Humans	Bromsulphthalein clearance by liver and Fick principle used for estimating the hepatic flow

TABLE 11 : THE TOTAL HEPATIC BLOOD FLOW

Author	The Hepatic arterial flow as percentage of the liver flow			The portal flow as percentage of the liver flow	Flow in Hepatic Artery in cc./minute	Method	Subject	Remarks
	Minimum	Maximum	Average.					
1)Burton-Opitz (1911 c)	25	33	30	70	26 per 100 Gm.Liver	Stromuhr	Dogs	-
2)Barcroft and Shore (1912)	12	60	39	61	-	Collection of Blood	Cats	-
3)MacLeod and Pearce (1914)	26	32	-	68 - 74	-	Collection of Blood	Dogs	-
4)Grab, Janssen and Rein (1929)	12	22	-	78 - 88	-	Rein's Thermostromuhr	Dogs	-
5)Schwiegk (1932 a)	20	25	-	75 - 80	-	Rein's Thermostromuhr	Dogs	-
6)Blalock and Mason (1936)	-	-	20	80	48 - 119	Collection of Blood	Dogs	-
7)Soskin,Essex,Herrick and Mann (1938)	-	-	38	62	154	Rein's Thermostromuhr	Dogs	Grindlay et al found that the hepatic arterial flow was 33-65 cc/min.in unanaesthetized, as compared with 102 cc/min. in anaesthetized dogs. The portal flow was the same in both
8)Grindlay, Herrick and Mann (1941)	15	40	-	60 - 85	102	Rein's Thermostromuhr	Dogs	
9)Grodins,Osborne,Ivy and Goldman (1941)	-	-	37	63	11 -50 per 100 Gms Liver	Direct Current Thermostromuhr	Dogs	

TABLE 111 : THE RELATIVE BLOOD FLOWS IN THE HEPATIC ARTERY AND PORTAL VEIN

To measure the blood flow in the portal vein by collection of its blood, a horizontal glass tube is connected to it, the vein is occluded distally and the amount of blood that flows into the glass tube during a known period (usually five to ten seconds) measured. This method is not accurate and it is strange that results obtained by it correspond so closely to those derived from the other methods.

Although the observations of Barcroft and Shore were made on cats, their results appear inaccurate when compared with those of the other workers. The average flow in the portal vein of dogs varies from 200 to 375 cc. per minute. This figure appears to be reliable. The liver receives from 82 to 95 cc. blood per 100 g. per minute, of which the portal vein supplies 60 to 85%.

Burton-Opitz was the only worker to investigate the blood flow in the splenic vein, but these results show such wide variations that they are unreliable.

NORMAL VARIATIONS IN THE PORTAL FLOW

Normal variations in the portal flow occur. Burton-Opitz did not detect them with Ludwig's stromuhr, but by using the more sensitive thermostromuhr, Schwiegk (1932 a) noticed rhythmic changes occurring at 20 to 30 second intervals. These changes were confirmed by Barcroft and his co-workers (1932) who also noticed rhythmic contractions of the intestine and spleen in dogs. These contractions may be responsible for the variations in the portal flow.

../A pulse

A pulse is present in the portal vein (Feil and Forward, 1922). When the blood flows through the splanchnic vessels the cardiac pulse is retained but the delay in passage leads to a fall of the portal pulse with systole and a rise with diastole. Cellina (1934), as well as de Castro et al (1935), mentioned that the portal veins have a "contractile arterial-like function".

The portal flow varies with respiration. Notwithstanding the "suction effect" of inspiration on the hepatic veins, the flow decreases, to rise with expiration (Schmid, 1909). Schmid also showed that the portal flow falls when the intrabronchial pressure is raised, e.g. during straining. This fall can be accounted for by a diminished venous return to the heart leading to a smaller cardiac output and a drop in aortic blood pressure.

THE CONTROL OF THE PORTAL BLOOD FLOW

The physiological factors that control the blood flow in the portal system can be classified as follows:-

(a) Factors regulating the Portal Inflow of Blood

(1) The main factor appears to be the arterio-venous pressure difference in the splanchnic vessels. Although this pressure difference is great (75 - 80 mm Hg - Jaure, 1932), most of it is spent in overcoming the vascular resistance. The smaller part left acts as a driving force to the

../blood

blood in the portal system. Accordingly, a drop in aortic blood pressure will result in a decreased portal flow. The portal flow, therefore, depends partly on the cardiac output.

(2) Burton-Opitz (1909) has shown that contraction of the spleen leads to a temporary rise in portal flow. The contractions of the spleen and intestine that occur at regular intervals may be a factor in forcing the blood along the portal system. Contraction of the spleen in dogs occurs in response to stimuli, such as exercise, starvation, and fear, and under these conditions the portal flow may be raised.

(3) Both Schmid (1909) and Jauré (1932) mentioned that the intra-abdominal pressure may force the blood along the portal vein. However, the blood flow in the portal system does not decrease at laparotomy when the intra-abdominal pressure is equal to the atmospheric pressure. Also, a rise in intra-abdominal pressure will raise the pressure in the peripheral and central end of the portal system to the same extent. The intra-abdominal pressure cannot influence the portal flow.

(b) <u>The Intrahepatic Resistance</u>

(1) Jaure (1932) thinks that the liver with its "tight capsule" must constitute a severe resistance to the portal blood. That it does not do so is shown by the relatively low pressure in the portal vein i.e. 8 - 20 cm. water. The pressure

../difference

difference between the portal and the hepatic veins is 8 - 15 mm. mercury. In spite of this small pressure difference a large volume of blood flows along the portal vein. This difference in pressure must play a role in the control of the portal flow e.g. a rise of pressure in the hepatic veins will diminish the portal flow. Daniel, Prichard and Neyell (1952 b) have shown that there is no obvious change in the portal flow with marked swelling of the liver cells.

(2) The tone of the portal branches in the liver regulates the portal flow to a large extent. It has been shown by Tait and Cashin (1925) that vessels of the portal system contract, even to the extent of obliterating the lumen, on direct mechanical stimulation. The work of Daniel and Prichard (1951 a) needs special mention. These authors studied the portal circulation in rats by serial X-ray photography after the intra-portal injection of thorotrast. In the majority of animals the dye outlined the portal branches throughout the liver. In a third of the rats the peripheral branches did not fill. This latter "restricted intrahepatic circulation" of portal blood was present in all rats after partial hepatectomy. The blood was shunted through the main branches of the portal vein and it reached the hepatic veins one second earlier than in the group in which the peripheral portal branches were visible. This "restricted intrahepatic circulation" may also occur after injecting adrenaline or stimulating the splanchnic nerves, and it shows that

../the portal

the portal vein branches are under vasomotor control.

(3) It has been suggested by Jaure (1932) that the liver acts as a pump that forces the portal blood into the inferior vena cava: the pulsations of the intrahepatic branches of the hepatic artery are transmitted to the walls of the portal branches (giving the latter a pumping action). That this is incorrect is shown by the actual increase in portal flow after occlusion of the hepatic artery.

(c) <u>The Pressure and Flow in the Hepatic Artery</u>

It has been suggested by Jaure (1932) and Schneider (1933) that the faster flow in the hepatic arterial branches may have a "water-suction" effect on the more slowly flowing portal blood, where the two streams meet in the liver. This suggestion has been disproved by the increase in portal flow that occurs on experimental occlusion of the hepatic artery (MacLeod and Pearce, 1914; Baer and Roessler, 1927; Bauer et al, 1932; Schwiegk, 1932 a; McMichael, 1932). A rise in the hepatic arterial pressure and flow leads to a smaller portal flow. There is a partial reciprocal relationship between the flows in the hepatic artery and portal vein. This is probably regulated by the pressure in the intrahepatic sinusoids e.g. a rise in hepatic arterial flow will increase the sinusoidal pressure, thus raising the resistance to the portal flow which, accordingly, diminishes.

It has been mentioned by MacLeod and Pearce (1914) that the calibre of the portal venules is

../readily

readily influenced by changes in the closely adjacent branches of the hepatic artery. This is extremely unlikely as marked changes in the size of the hepatic cells do not affect the portal flow (Daniel et al, 1932 b).

The work of Burton-Opitz (1911) must be mentioned here. He found that there was a 25 - 33% fall in the hepatic arterial flow when the portal vein was occluded. However, when the associated drop in aortic blood pressure was prevented by a shunt between the spleen and left renal veins, the blood flow in the hepatic artery rose by 40 to 50%.

THE RELATIONSHIP BETWEEN THE BLOOD FLOW AND PRESSURE IN THE PORTAL VEIN.

There is no direct relationship between the blood flow and the pressure in the portal system (Bauer et al, 1932; Schwiegk, 1932 a; Carnot et al, 1932 b; Wiggers et al, 1946.) When the portal pressure rises in the presence of portal obstruction, the flow is diminished. On the other hand, a marked increase in the inflow of blood, as occurs with splanchnic vaso-dilatation, raises the portal flow as well as the portal pressure. The following graphs have been drawn from the results of Burton-Opitz (1914). They show the great variations in portal pressure that can occur with minimal changes in flow.

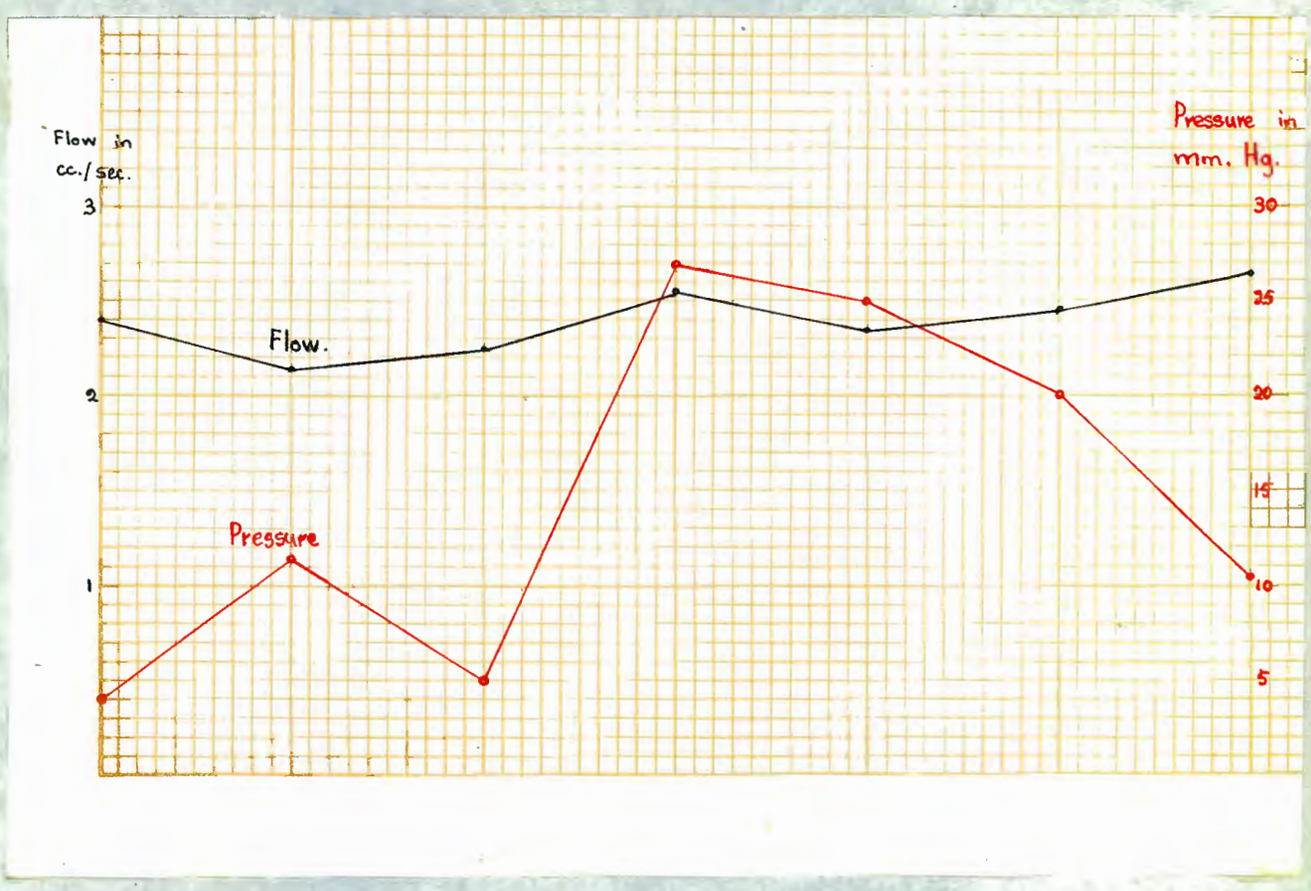

Flow in cc./sec.
3
2
1
Flow.
Pressure
Pressure in mm. Hg.
30
25
20
15
10
5

Fig. 1

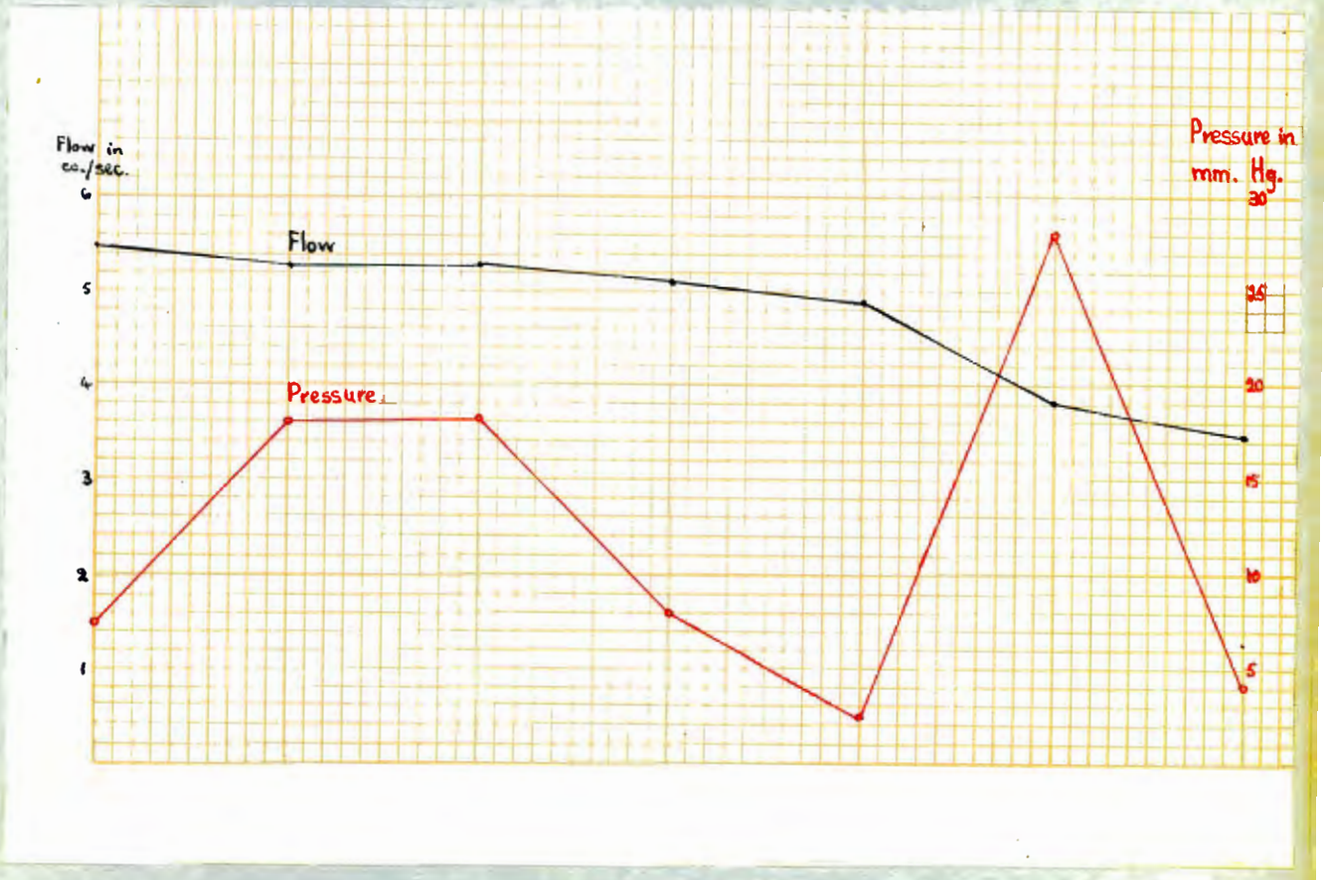

Flow in cc./sec.
6
5
4
3
2
1
Flow
Pressure
Pressure in mm. Hg.
30
25
20
15
10
5

Fig. 2

The variations in tone of the portal vessels influence the portal pressure more than the portal flow. It must be pointed out that Wiggers, Opdyke and Johnson (1946) stressed the low resistance offered by the vasomotor tone of the portal vessels. They estimated the portal resistance as 0.0174 (resistance = $\frac{\text{pressure gradient}}{\text{flow}}$ = $\frac{6\text{mm Hg}}{345\text{ cc/min.}}$ in portal system). Compared with this figure the hepatic arterial resistance is 1.14.

That the portal system may adapt itself to a great increase in blood flow with a minimal rise in pressure, has been shown by various workers. Carnot and his co-workers (1932 b) raised the portal flow in dogs by 230 cc per minute by anastomosing the right renal artery to the portal vein. The portal pressure did not rise more than 2 cm water. This adaptability of the portal circulation to an increase in its blood volume has been stressed by other workers who showed that, in dogs, rapidly infused fluids tend to collect in the portal system (Roberts and Crandall, 1933; Chiarolanza, 1951).

THE EFFECTS OF NERVE STIMULATION ON THE PORTAL CIRCULATION.

The effect of stimulation of the splanchnic nerves on the portal circulation is shown in Table IV (Page 20). Burton-Opitz (1912 b) described four phases on stimulating the splanchnic nerves in dogs:

(1) There is an immediate drop in the systemic and portal pressures and in the portal flow. This is

../followed

followed by:

(ii) A marked elevation of portal and systemic pressures and an increased portal flow.

(iii) The portal pressure and flow next fall while the systemic blood pressure remains elevated. Complete cessation of blood flow may occur.

(iv) In the fourth phase there may be a slight rise in portal pressure and flow before normal values are established.

The splanchnic nerves carry vaso-constrictor impulses to the portal vein and its intrahepatic branches. Stimulation of these nerves raises the portal pressure by means of this vaso-constrictor effect. At the same time the portal flow is usually, but not always, diminished. This effect is probably the result of splanchnic vaso-constriction, which diminishes the flow into the portal system.

The spinal outflow of the vasoconstrictor fibres to the portal vein and its branches was traced to the lower seven dorsal and upper two lumbar nerve trunks by Francois-Frank and Hallion (1896). However Bayliss and Starling (1894 b) found that these vaso-constrictor nerves leave the cord in the third to eleventh dorsal nerve roots. The main fibres are carried in the fifth to the ninth roots. The findings of the latter authors appear to be more reliable.

../Table 1V

Author	Effect on the Portal Flow	Method	Subject	Remarks
Burton-Opitz (1909)	See remarks	Stromuhr	Dogs	The flow in the splenic vein rose temporarily and then dropped to 30 - 50% normal. The same effect was obtained by stimulating the splenic pedicle.
Griffith and Emery (1930)	-	Liver volume measured with a plethysmograph	Cats	There was a decrease in liver volume. This suggests that vaso-constriction of the portal branches occurred.
Eckardt (1935)	Diminished	Rein's thermostromuhr	Dogs & Cats	The hepatic venous outflow increased
Daniel and Prichard (1951 a)	-	Serial angiograms of the portal system	Rats	There was constriction of the intrahepatic portal branches, whereas the portal vein was dilated.

TABLE IV : STIMULATION OF THE SPLANCHNIC NERVES

The effects of stimulating the vagus and the postganglionic nerves in the hepatic pedicle and sectioning the spinal cord are shown in Table V (Page 22) Because of portal vasodilatation on stimulation of the central end of the cut vagus nerve, Griffith and Emery concluded that the splanchnic nerves also carry vasodilator fibres. However, it is more likely that this effect was obtained by the inhibition of the sympathetic vasoconstrictor impulses.

From the results of Griffith and Emery it appears that the postganglionic fibres in the hepatic pedicle carry vasoconstrictor impulses to the branches of the portal vein and hepatic artery.

Author	Nerve Stimulated	Effect on the portal flow	Method	Subject	Remarks
Burton-Opitz (1911 b)	Hepatic Pedicle	None	Stromuhr	Dogs	The author concluded that the portal vein was not under vasomotor control
MacLeod and Pearce (1914)	Hepatic Pedicle	None	Collection of blood from hepatic veins	Dogs	The hepatic artery was ligated to measure the portal flow
Griffith and Emery (1930)	Hepatic Pedicle	-	Liver volume measured with plethysmograph	Cats	The liver volume was diminished. The authors concluded that the terminations of the hepatic artery and portal vein were constricted.
Griffith and Emery (1930)	Central end of cut vagus	-	Liver volume measured with plethysmograph	Cats	Increased liver volume: the author concludes that vasodilator fibres are carried in splanchnic nerves.
Griffith and Emery (1930)	Peripheral end of cut vagus	-	Liver volume measured with plethysmograph	Cats	No effect on liver volume: the vagus contains no fibres that supply portal branches
Bayliss and Starling (1894 a)	Transection of the spinal cord	Diminished	Direct collection of blood	Dogs	The simultaneous fall in aortic pressure led to a reduced splanchnic blood flow.

TABLE V : THE EFFECTS OF STIMULATION OF NERVES OTHER THAN THE SPLANCHNICS, ON THE PORTAL SYSTEM

THE EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON THE PORTAL BLOOD FLOW.

The changes in the portal flow after the administration of adrenaline are shown in Table Vl (page 25). It will be noticed that when adrenaline is administered into a systemic vein, the portal flow is increased. This is probably the result of an increased cardiac output and splanchnic vasodilatation. However, when it is administered in small doses into the portal vein, the portal flow is diminished because of an increased hepatic resistance. The latter is confirmed by a corresponding rise in portal pressure. This raised intrahepatic resistance cannot be due to swelling of the liver cells, as suggested by Schwiegk (Daniel and his colleagues, 1952 b, have shown that swollen liver cells do not obstruct the portal flow.) Adrenaline relaxes the hepatic sphincter of dogs (Bauer et al, 1932). Therefore, it must constrict the portal branches in the liver and so increase the hepatic resistance to the portal flow.

The results of Schmid do not correspond with those of the other workers and are not acceptable. It must be pointed out that when a large amount of adrenaline is injected into the portal vein, it overflows into the general circulation, with a resultant increase in cardiac output, fall in splanchnic resistance and raised portal flow.

Burton-Opitz (1914) found that the hepatic arterial flow and pressure were not affected when adrenaline was injected into the portal vein; nor did it affect the portal pressure and flow when given into the hepatic artery. These results indicate that the branches

../of the

of the portal vein and those of the hepatic artery have separate vasoconstrictor mechanisms.

The different effects of adrenaline and noradrenaline on the portal circulation of humans are shown by the results of Bearn and his colleagues Table Vl.

Author	Effect on Flow	Route of Administration	Dosage	Method	Subject	Remarks
Burton-Opitz (1912 d)	Increased	Intravenously	6-8 minims of 1-1000	Stromuhr	Dogs	-
Burton-Opitz (1912 d)	Slightly raised	Into portal vein	6-8 minims of 1-1000	Stromuhr	Dogs	The portal pressure was also raised
MacLeod and Pearce (1914)	Diminished	Into portal vein	-	Direct collection of blood	Dogs	From their results these authors concluded that adrenaline causes constriction of the intra-hepatic portal vessels.
Baer and Roessler (1927)	Diminished	Into portal vein	-	Perfusion of isolated liver	Dogs, Cats and goats	
Schwiegk (1932 a)	Increased	Intravenously	-	Thermostromuhr	Dogs	The author thought that the increased flow was the result of contraction of the spleen
McMichael (1932)	Diminished at first then increased	Intravenously	0.5 cc of 1-1000	Liver plethysmograph	Cats	Adrenaline had no effect on the wall of the main portal vein
Schmid (1909)	Diminished	Intravenously	"Small"	Stromuhr	Dogs	The portal flow dropped from 0.77cc second to nil. The hepatic vascular resistance was increased.
Bearn, Billing and Sherlock (1951)	-	Intravenous adrenaline	0.10 µg per Kg. body wt. per min.	Catheterization of the hepatic veins, Bromsulphthalein clearance by liver and the Fick principle	Humans	Splanchnic vascular resistance diminished. There was a 200% increase in the liver flow
Bearn, Billing and Sherlock (1951)	-	Intravenous Nor-Adrenaline.	0.15-0.20 µg.per Kg body wt. per min.		Humans	Splanchnic vascular resistance increased. There was a 25% decrease in the liver flow.

TABLE : V1 : THE EFFECT OF ADRENALINE ON THE PORTAL FLOW

Table VII (Page 27) shows the effects of drugs (other than adrenaline), food, temperature changes and haemorrhage on the portal flow. It must be pointed out that these are isolated observations, none of which has been confirmed by other workers.

Author	Agent	Route of Administration	Effect on Flow	Method	Subject	Remarks
Schmid (1909)	Digitalis	-	Increased	Stromuhr	Dogs	The portal flow increased from 1.89 to 3.39 cc per second. The splanchnic vessels were dilated and the portal pressure was raised
Baer and Roessler (1927)	Histamine	Into the portal vein	-	Perfusion of isolated liver	Dogs	Contraction of the hepatic veins occurred
Schwiegk (1932a)	Posterior Pituitary Extract	Intravenously	Diminished	Rein's Thermo-stromuhr	Dogs	The flow through the spleen was diminished as well.
Schwiegk (1932 b)	Atophan	Intravenously	Diminished	Rein's Thermo-Stromuhr	Dogs	-
Schwiegk (1932 b)	Glucose	By mouth	Increased by 200%	Rein's Thermo-Stromuhr	Dogs	When glucose was given intravenously the the portal flow rose by only 10%
Schwiegk (1932 a)	Cold (External)	Applied to surface of body	Increased by 60%	Rein's Thermo-Stromuhr	Dogs	-
Schwiegk (1932 a)	Heat (external)	Applied to surface of body	Diminished	Rein's Thermo-stromuhr	Dogs	-
Schwiegk (1932 a)	Artificial pyrexia	-	Increased	Rein's Thermo-stromuhr	Dogs	Produced by 20 mg. tetra-beta-naphthylamine administered intravenously
Blalock and Levy (1937)	Haemorrhage	-	Diminished by 50%	Direct Collection of blood	Dogs	Haemorrhage was produced till the aortic pressure fell to 80-100 mm Hg.
Grodins, Osborne, Ivy and Goldman (1941)	Sodium dehydrocholate	Intravenously	Diminished	Direct current Thermostromuhr	Dogs	The hepatic arterial flow as well as the excretion of bile were increased
Blalock and Levy (1937)	Histamine	Intravenously	Diminished	Direct collection of blood	Dogs	The normal portal flow averaged 417 cc per minute

TABLE V11 : THE EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON THE PORTAL FLOW

THE RATE OF BLOOD FLOW IN THE PORTAL SYSTEM

Observations on the rate of the portal flow have been few. It is 43 mm per second in the splenic vein of dogs according to Burton-Opitz (1909), Daniel and Prichard in their angiographic studies in rats, mentioned that the transhepatic portal circulation time was 1.5 to 3 seconds. They did not study the rate of flow in the extrahepatic portal vessels. Hahn, Donald and Grier (1945) showed that radio-active phosphorus, injected into a branch of the splenic vein, reached the liver lobules within three seconds.

An attempt was made by Souidan (1950) to measure the portal circulation time in humans. The "vein-urine" time is the time taken by a dye, given intravenously, to appear in the urine. When the dye is given by mouth the "stomach-urine time" is determined. The difference between these two is the "portal circulation time", which was 19 to 25 minutes in 70% of tested normal humans. However, this "portal circulation time" gives no idea of the rate of blood flow in the portal system. It mainly measures the time taken for the dye to be absorbed from the stomach. The same applies to the method of Henning and his co-workers (1950), who administered acetylene-gas intraduodenally and noticed the time taken for it to be excreted in the breath.

THE PORTAL FLOW AND LIVER MAINTENANCE

McMichael (1937) has mentioned that the liver of rabbits gets very little of its oxygen supply from the portal blood. However, when the hepatic artery is ligated,

../the portal

the portal vein may be able to supply the liver parenchyma with sufficient oxygen to prevent necrosis (Cameron and Mayes, 1930). Blalock and Mason (1936) have shown that the liver of dogs needs 0.045 cc oxygen per gram per minute. Table VIII (Page 30) shows the percentage oxygen saturation in the portal system, as well as the relative amounts supplied by the portal vein and hepatic artery to the liver. The reciprocal relation between the portal and arterial flows ensures an adequate oxygen supply to the liver.

Ligation of the portal vein or its main branches will lead to atrophy of the part of liver deprived of portal blood (Bainbridge and Leathes, 1907); Cohnheim and Litten, 1876; Gray, 1951). Hypertrophy of that part of the liver with its portal flow intact, will take place. This hypertrophy results from vascular congestion, caused by an increased portal flow. In the same way will hepatic venous congestion, produced by obstructing the hepatic vein, stimulate regeneration of the liver when its portal flow has been interfered with (Gray, 1951). Although atrophy of the liver occurs in dogs in the presence of an Eck fistula, Blakemore (1952) has found that its establishment in humans enables the liver to regenerate with improvement in its functions.

In conclusion, it should be pointed out that, although the portal flow plays a part in the maintenance of the liver, its role is far less important than that of the hepatic arterial supply.

Author	% O_2 Saturation in the portal vein	Volumes % O_2 tension in the portal blood	% O_2 Saturation in the hepatic artery	% O_2 saturation in the hepatic veins	Subject	Remarks
Barcroft and Shore (1912)	23-30	5-6	-	-	Cats	-
Schwiegk (1932 a)	51-61	10-12	84-88	33-39	Dogs	The liver receives 55-60% of its O_2 from the portal blood. On obstructing the portal flow, the flow in the hepatic artery increases 50 - 100%
McMichael (1937)	-	-	-	-	Cats and rabbits	The liver receives 62.5% of its O_2 from portal blood. This drops to 35% in shock when the aortic blood pressure falls.
Snyder (1942)	50	10	85	-	-	-
Le Veen, Mulder and Prokop (1952)	75	15	95	-	Humans	The O_2 saturation in the portal blood is reduced to 20% in shock. This is associated with a marked increase in the hepatic arterial flow

TABLE V111 - THE PERCENTAGE OXYGEN SATURATION IN THE PORTAL SYSTEM

CHAPTER 11

A REVIEW OF THE LITERATURE ON THE BLOOD PRESSURE IN THE PORTAL VEIN.

Compared with the difficulties in determining the blood flow in the portal vein, the estimation of the portal pressure has been a simple procedure. Many workers have measured the normal portal pressure and a number have investigated its variations under physiological and under experimental conditions.

In recent years surgeons have used the portal blood pressure as a measure of the success of a shunt-operation for portal hypertension. Some have also determined the normal portal pressures in human beings during operations for other conditions.

The pressure in the portal system has been most easily measured by connecting a glass manometer filled with saline or 3.8% sodium citrate solution, to a tributary of the portal vein. Variations in the height of the zero-level of the manometer may have accounted for differences in the normal portal pressure. Few workers have mentioned this level in their experiments. The majority have probably measured the pressure from the level of the hepatic pedicle or portal vein (Leger, Albot and Array, 1951). The portal pressure in dogs is the same with the abdomen open or closed (Feldberg, Schilf and Zernik, 1928), but is probably lower in standing, than in supine dogs (Hoffbauer, Bollman and Grindlay, 1947).

Table IX (Page 33) summarizes the normal portal pressures, as measured by the various workers (results recorded in mm. mercury have been changed to

../ cm.water

cm. water - the specific gravity of mercury is 13.6. Those recorded in cm. saline, water, plasma, sodium citrate and magnesium sulphate are comparable). It will be noticed that most pressures fall between 7 and 20 cm. water in dogs, cats, rats and humans. There is a consistency in the results, whether the pressure was measured in the portal, splenic, or superior mesenteric veins. The differences recorded by Burton-Opitz (Table IX) between the pressures in these veins are not significant.

Author	Pressure in cm.water Minimum	Maximm	Average	Solution in Manometer as used by author	Vein used for Measuring Pressure	Subject	Remarks
1)Von Basch (1876)	-	-	9.1	Mercury	Portal	Dogs	-
2)Bayliss and Starling (1894 a)	-	-	9.3	25% Magnesium sulphate	Splenic	Dogs	The magnesium sulphate was coloured with methylene blue. Veins draining the spleen were ligated.
3)Schmid (1908)	9	20	-	Mercury	Portal	Cats and Dogs	The pressure rose on inspiration and fell on expiration
4)Burton-Opitz (1909)	13.6	15.6	13.7	Mercury	Splenic	Dogs	-
5)Burton-Opitz (1909)	-	-	12.1	Mercury	Portal	Dogs	-
6)Burton-Opitz (1909)	-	-	20	Mercury	Superior Mesenteric	Dogs	-
7)Bainbridge and Trevan (1917)	-	-	9.5	2.5%Sodium Citrate	Splenic	Dogs	-
8)Manwaring, Brill and Boyd (1923)	9.5	17.7	12.2	Mercury	Portal	Dogs	-
9)Feldberg (1929)	7	17	-	Water	Splenic	Cats	The pressure rose 0.5 to 2 cm. with each inspiration
10) Feldberg, Schilf and Zernik (1928)	5	18	-	Ringer's Solution	Splenic	Dogs	The pressure rose with each inspiration. The splenic artery was ligated and the abdomen closed round the manometer
11)Clark (1928)	-	-	6	Sodium Citrate	Splenic	Cats	-
12)Carnot, Gayet and Merklen (1930 a)	-	-	17	Water	Superior Mesenteric and splenic	Dogs	-
13)McMichael (1932)	8	10	-	5% Sodium Citrate	splenic	Cats	The pressure rose on inspiration and fell on expiration.A splenectomy was done and the abdomen closed round the manometer

TABLE 1X:THE BLOOD PRESSURES IN THE PORTAL SYSTEM

(Continued on Page 34)

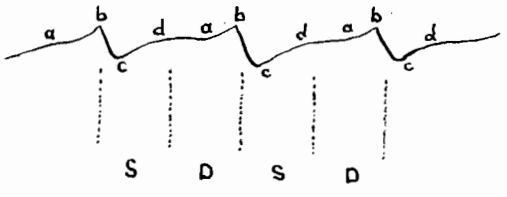
Author	Pressure in Cm.water Minimum	Maximum	Average	Solution in manometer as used by author	Vein used for measuring pressure.	Subject	Remarks
14)Wiggers,Opdyke and Johnson (1946)	12.8	28.6	16.3	Mercury	Portal	Dogs	The pressure in the inferior vena cava was 8.2 cm.
15)Hoffbauer,Bollman and Grindlay (1947)	4	10	-	Sodium Citrate	Portal	Dogs	Pressure measured with dogs standing The catheter was inserted into the portal vein via the splenic vein.
16)Daniel,Prichard and Neyell (1952 b)	-	-	10.6	Saline	Portal	Rats	The pressure was not raised by swelling of the liver cells
17)Grindlay and Bollman (1952)	7	11	-	Water	Portal	Dogs	There was a 12-21 cm. rise in pressure after a 70% partial hepatectomy.
18)Rousselot (1939)	7	36	19.1	Water	Tributaries of Portal	Humans	Pressure measured in 15 normal humans at laparotomy
19)Thompson,Caughey, Whipple and Rousselot (1937)	10.5	12.0	11.6	Water	Portal	Humans	Pressure measured in 3 normal humans at laparotomy
20)Auvert (1950)	10	12	-	Water	Portal	Humans	Measured at laparotomy
21)Leger,Albot and Auvert (1951)	10	20	-	Plasma	Portal	Humans	Zero point taken as level of hepatic pedicle i.e. midway between anterior and posterior body walls.
22)Gray (1951)	13.6	23.5	-	Water	Portal	Humans	Zero point taken as anterior border of vertebral column. 62% of humans fell between 16-21 cm

TABLE 1X : THE BLOOD PRESSURE IN THE PORTAL SYSTEM (concluded)

NORMAL VARIATIONS IN THE PORTAL PRESSURE

1) Variations with the Pulse

Feil and Forward (1922) established the presence of a pulse in the portal vein of dogs. They connected a cannula, introduced into the portal vein, with a Wigger's optical manometer, and obtained a tracing of the pulse as shown in Figure 3



S : Systole
D : Diastole

FIGURE 3

It will be noticed that the tracing rises during diastole and falls during systole. This is explained by by the delay of blood flowing through the splanchnic vessels. This delay varies from 0.02 to 0.07 (average 0.04) seconds. The authors think that the waves a-b and b-c are the result of mechanical factors e.g. the impulse of the heart transmitted through the diaphragm; c-d-a

../denotes

denotes the flow of blood into the portal system. The cardiac pulse, therefore, is not abolished by the splanchnic vessels, but is present in the portal vein and varies with the cardiac output and splanchnic vascular resistance.

McQueen (1927), who noticed a pulse in the hepatic sinusoids during transillumination, (studies on the livers of toads) suggested that the portal pulse is due to contractions of the right auricle, transmitted through the liver. Although this suggestion does not seem a likely one, it is known that the liver may show pulsations corresponding to the venous pulse (Groedel, 1946; Hamilton, 1946).

Schwiegk (1932 b) noticed waves of the same nature as Hering-Traube waves in portal pressure tracings. These were more prominent in the splenic than in the superior mesenteric veins.

2) Variations with Respiration

There is a small rise in portal pressure during inspiration and a fall during expiration. (See Table IX: Schmid, Feldberg, Feldberg et al and McMichael). Wiggers, Opdyke and Johnson (1946) suggested that the descent of the diaphragm on inspiration raised the intra-abdominal pressure with a corresponding rise in portal pressure. However, the same variations with respiration are noticeable when the abdomen is open and the intra-abdominal pressure is zero. If the "suction effect" of inspiration on the flow in the inferior vena cava and hepatic veins were a factor (as suggested by Schmid, 1908) the portal pressure would have fallen during inspiration. The

../descent

descent of the diaphragm on inspiration causes a certain degree of rotation of the liver. The latter may raise the portal pressure by obstructing the hepatic venous outflow.

3) Variations with Intra-abdominal Pressure

Hoffbauer, Bollman and Grindlay (1947) showed that a rise of intra-abdominal pressure during straining e.g. with vomiting or defaecation, raised the portal pressure in dogs. The latter remained elevated longer than the intra-abdominal pressure, which was measured by a manometer connected to a balloon inside the peritoneal cavity. They also found that ingestion of food raised the portal pressure. Their results on the effect of intra-abdominal pressure have been confirmed by Bellis and Wangensteen (1939).

4) Variations with Posture

Hoffbauer and his co-workers found that the portal pressure was slightly lower in standing than in supine dogs (See Table IX, Hoffbauer et al, 1947). The difference in pressure is small and of doubtful significance; nor have their findings been confirmed.

THE CONTROL OF THE PORTAL PRESSURE

Feldberg, Schilf and Zernik (1928) have stated that the portal pressure depends on the aortic blood pressure, the splanchnic vasomotor tone and the hepatic resistance. Factors that may control the pressure in the portal system will be discussed separately.

1) The Cardiac Output

This influences the portal pressure by

../maintaining

the aortic blood pressure. When the latter falls during haemorrhage (Table XlV, Page 52) or during obstruction of the thoracic aorta (Table X, Page 39), the portal pressure falls.

2) Respiration

The effect of respiration on the portal pressure has already been noticed. It will be seen from Table X that asphyxia or an increased intrabronchial pressure raises the portal pressure in dogs. However, Schmid's figures show only small changes, which are of doubtful significance.

3) The Splanchnic Vascular Resistance and Portal Blood Flow.

Although there is no direct relationship between the portal flow and blood pressure, the results of various workers (Table X) indicate that the portal pressure rises when the portal blood volume is markedly increased. This increase in portal flow must be great to raise the portal pressure; Grindlay and Bollman (1952) showed that there was no rise in portal pressure with a reversed Eck fistula (i.e. all the blood in the inferior vena cava below the liver is shunted through the portal vein) in dogs. Splenectomy does not lower the normal portal pressure in dogs (Carnot et al, 1932 b), but in humans with portal hypertension it decreases the portal blood flow by 40% and lowers the pressure (Linton et al, 1947; Rienhoff, 1951).

The splanchnic vascular resistance may influence the portal pressure by controlling the portal inflow of blood (Feldberg; Schilf and Zernik, 1928). Bauer and his colleagues (1932) point out that a diminished splanchnic resistance will raise the portal flow as well as pressure. It must be mentioned that Carnot, Gayet and Merklen (1932 b) found no change in the portal pressure after denervation of the superior mesenteric and coeliac arteries in dogs.

Author	Experimental Procedure	Effect (Increase:↑ Fall :↓)	Pressures in cm. Water Before	After	Method: Solution in Manometer	Vein used for measurement	Subject	Remarks
1)Bayliss and Starling (1894 a)	Obstruction of the thoracic aorta	↓	-	-	25% Magnesium Sulphate	Splenic	Dog	-
2)Erlanger and Gasser (1949)	Obstruction of the thoracic aorta	↓	8	2.7	Mercury	Splenic	Dog	The fall in portal pressure was the result of a diminished portal inflow
3)Mall (1902)	Contraction of the spleen	↑		250	Mercury	Splenic	-	The splenic contraction acts as a pump and the portal pressure only rises momentarily
4)Carnot,Gayet and Merklen (1932 b)	Anastomosis between right renal artery and the portal vein	Slight ↑	17	19	Water	Splenic	-	The portal blood flow was increased by 230 cc/min. Rise in portal pressure was not significant
5)Bayliss and Starling (1894 a)	500 cc Saline was rapidly infused intravenously	↑	9.7	32.0	25% Magnesium Sulphate	Splenic	Dog	Gradual return to normal - 15 minutes later pressure still 19 cm
6)Bayliss and Starling (1894 a)	Asphyxia	↑	9.7	14.4	25% Magnesium Sulphate	Splenic	Dog	Portal pressure fell with the aortic pressure
7)Schmid (1908)	Raised intrabronchial pressure	↑	11.4	14.1	Mercury	Portal	Dog	It is doubtful whether the rise is significant
8)Cohn and Parsons (1950)	Anastomosis between the aorta and the portal vein with venous graft	↑	8.4	36.8	Water	portal	Dog	After 2 weeks the portal pressure was still elevated, averaging 36.8 cm.
9)Chiarolanza (1951)	Intravenous infusions of saline, 5% glucose and blood	↑	-	-	-	Portal and tributaries	Dog	The author concludes that intravenous fluids tend to collect in the portal system

TABLE X : THE EFFECTS OF VOLUME CHANGES IN THE PORTAL CIRCULATION ON THE PORTAL PRESSURE.

4) The Vascular Tone of the Portal Vein and Its Branches

The portal vascular resistance in the liver is a most important factor in controlling the portal blood pressure (Bauer et al, 1932). Drugs that cause portal vasoconstriction (Table XII) readily raise the pressure.

5) The Blood Flow and Pressure in the Hepatic Artery

Compression of the hepatic artery lowers the portal pressure (Jaure, 1932; Rienhoff, 1951). A rise in hepatic arterial pressure elevates the pressure in the portal vein (McMichael, 1932). These results are consistent and reliable. An increased flow or pressure in the hepatic artery may raise the pressure in the portal vein by obstructing its flow at the hepato-portal junctions in the liver.

The work of Herrick (1907) may be cited here. By perfusion of livers removed at autopsy, he found that the portal pressure rose 1 mm Hg for every 40 mm Hg. increase in hepatic arterial pressure. However, in cirrhotic livers the corresponding rise in portal pressure was 8 mm Hg. These results suggest that only gross changes in hepatic arterial pressure will affect the portal pressure. McIndoe (1928) however, has been unable to confirm these results of Herrick.

6) The Intestinal Volume and Intra-Abdominal Pressure

Jarish and Ludwig (1927) found that an increased intestinal volume raises the portal pressure. However, Bellis and Wangensteen (1939) noticed the reverse. From these contradictory results it appears that the intestinal volume does not control the portal pressure. The effects

../of intra-abdominal

of intra-abdominal pressure have already been mentioned.

7) <u>The Position of the Animal</u>

This has been discussed

8) <u>The Pressure in the Systemic Veins</u>

There is no relation between the pressures in the portal vein and in the inferior vena cava (Bainbridge, and Trevan 1917; Bellis and Wangensteen, 1939). The graph shown in fig. 4, drawn from the findings of Rousselot (1939), shows that the portal pressure is not related to the venous pressure in the upper limb. This was confirmed by Thompson and his co-workers (1937).

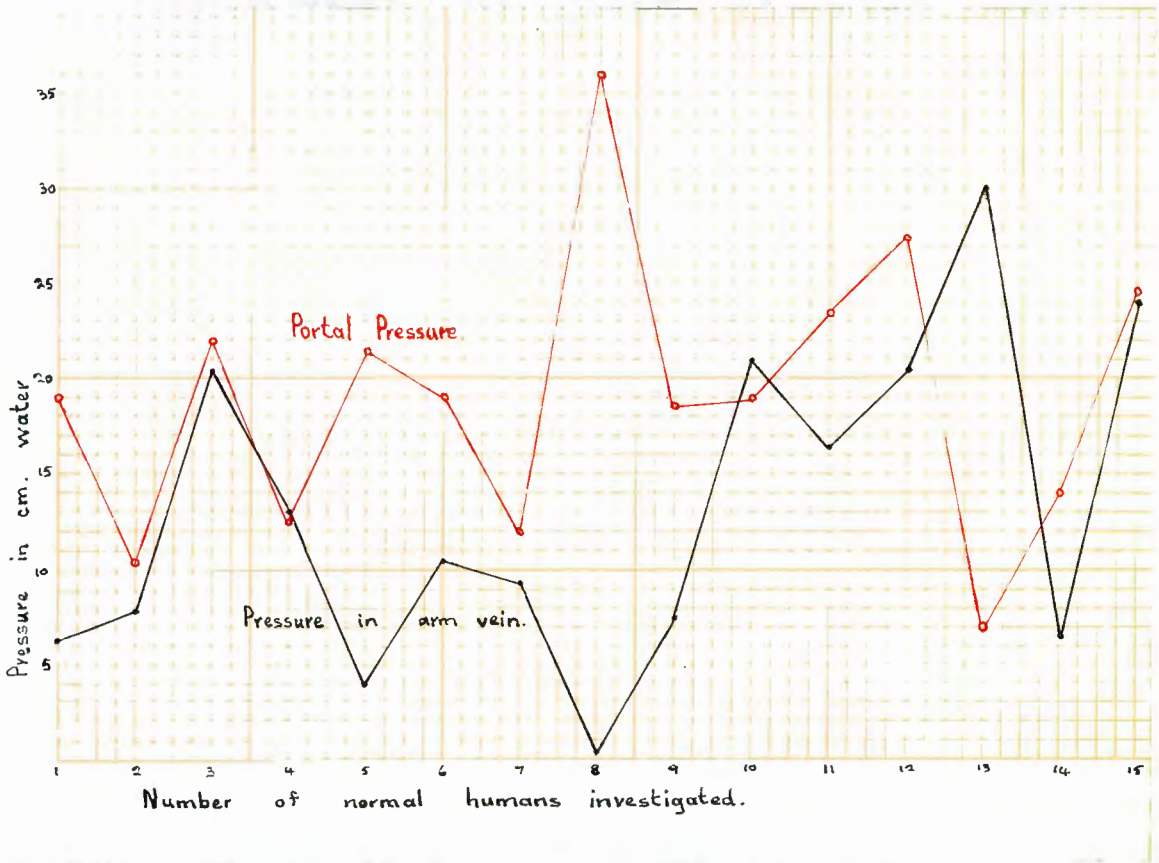


Fig.4

Bellis (1942) found that the portal pressure in humans varies with the venous pressure in the ankle veins and is about 10 cm higher. The relation between the two pressures is indicated in the following graph (fig. 5). This relationship has not yet been confirmed by other workers.

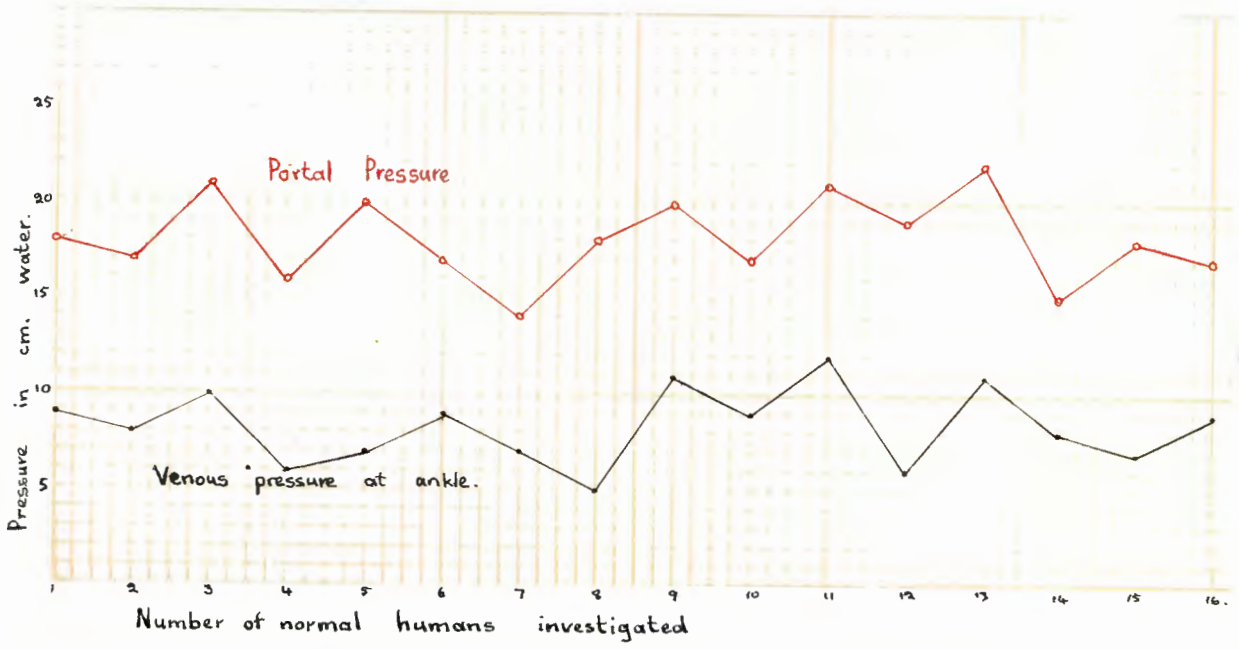


Fig.5

It can be concluded that the portal pressure is controlled mainly by the splanchnic vascular resistance which regulates the inflow of blood, and the intrahepatic portal vascular resistance. The latter depends on the tone of the portal branches, and probably also to a small extent on the flow and pressure in the hepatic artery. Apart from inspiration, which causes a slight rise, the other factors do not appear important in the control of the portal pressure.

THE EFFECTS OF STIMULATION OF NERVES ON THE PORTAL PRESSURE.

The effects of stimulating the splanchnic and vagus nerves are shown in Table XI (Page 45). The rise in portal pressure on splanchnic nerve stimulation appears

../to be

to be the result of vasoconstriction of the intrahepatic portal branches. This vasoconstriction also occurs when the post-ganglionic nerves in the hepatic pedicle are stimulated (Daniel and Prichard, 1951 a; Burton-Opitz, 1914). It must be pointed out that Burton-Opitz (1912 b) observed four phases in the dog on splanchnic nerve stimulation:

(i) There was a brief drop in portal pressure (associated with a diminished flow and a low aortic pressure), followed by

(ii) A marked rise in portal pressure (with a raised portal flow and aortic pressure).

(iii) Another drop in pressure occurred (associated with a diminished portal flow and high aortic pressure).

(iv) In the last phase there was a return to normal values. However, the variations in portal pressure in these four phases were never greater than 5 - 6 mm Hg, and these results of Burton-Opitz must be confirmed before they can be accepted.

Stimulation of the vagus nerve appears to raise the portal pressure. As it does not do so in the dog after the spinal cord has been transected (Bayliss and Starling, 1894 a), the mechanism by which it elevates the portal pressure is probably a central one: inhibition of vasoconstrictor impulses in the splanchnic nerves will lower the splanchnic vascular resistance and the resultant increased portal flow will raise the pressure in the portal system. Another possible mechanism is the following: blood accumulates on the right side of the heart because of the cardiac standstill on vagus stimulation. This

../accumulation

accumulation leads to congestion of the hepatic veins with a corresponding backpressure on the portal outflow of blood, and a rise in pressure. However, this latter mechanism is unlikely in view of Bayliss and Starling's findings, mentioned above.

Author	Nerve stimulated	Effect (Increase: ↑ Fall: ↓)	Pressures in Cm Water Before	After	Method - Solution in Manometer	Vein used for pressure measurement	Subject	Remarks
1)Bayliss and Starling (1894 a)	Splanchnic	↑	9.7	19.0	25% Magnesium Sulphate	Splenic	Dog	The pressure took two minutes to reach a normal level after cessation of stimulation
2)Francois-Frank and Hallion (1896)	Splanchnic	↑	-	-	-	-	-	At the same time the liver decreased in size
3)Schmid (1908)	Splanchnic	↑	14.8	15.2	Mercury	Portal	Dog	The rise in pressure was preceded by a slight fall. The pressure differences are too small to be significant and the results are unreliable
4)Burton-Opitz (1909)	Splanchnic	↑	13.6	55	Mercury	Splenic	Dog	On cessation of stimulation the pressure fell to 8 cm. It then gradually returned to normal
5)Carnot,Gayet and Merklen (1930 a)	Splanchnic	↑	-	-	Water	Splenic & Superior Mesenteric	Dog	There was an initial rise, then a small drop,followed by another rise
6)Bayliss and Starling (1894 a)	3rd to 11th Thoracic Nerve Roots	↑	9.7	14	25% Magnesium Sulphate	Splenic	Dog	The spinal outflow to the portal vein is from the 3rd to 11th thoracic nerve roots (Bayliss and Starling(1894 b)
7)Bayliss and Starling (1894 a)	Vagus	↑	10.6	20.4	25% Magnesium Sulphate	Splenic	Dog	The rise in pressure only occurred when the heart started beating after an initial cardiac standstill.
8)Carnot,Gayet and Merklen (1930 a)	Vagus	↑	17	Splen:19 Sup. Mesnt:22	Water	Splenic & Superior Mesenteric	Dog	The cardiac output and aortic pressure dropped. The rise in pressure might have resulted from hepatic venous congestion
9)Wiggers,Opdyke and Johnson (1946)	Vagus	↑	-	-	Mercury	Portal	Dog	-
10)Burton-Opitz (1909)	Splenic Plexus	↑	13.6	41.4	Mercury	Splenic	Dog	Splenic contraction raised the pressure by increasing the volume flow in the splenic vein. The rise in pressure was proportionate to the intensity of the stimulation
11)Bayliss and Starling (1894 a)	Transection of the spinal cord	↓	9.7	7.3	25% Magnesium Sulphate	Splenic	Dog	Stimulation of the vagus after spinal cord section had no effect on the pressure,suggesting that the vagus has a central effect,acting via the splanchnics

TABLE XI : THE EFFECT OF NERVE STIMULATION ON THE PORTAL PRESSURE

THE EFFECTS OF ADRENALINE AND OTHER DRUGS ON THE PORTAL PRESSURE.

The effect of adrenaline on the pressure in the portal system is shown in Table XII (Page 48). It will be seen that the rise in pressure is related to the amount of adrenaline given (Burton-Opitz) and the duration of its administration (Bainbridge and Trevan). The pressure rises whether adrenaline is given intravenously or into the portal vein. Therefore, adrenaline appears to act on the liver. Bainbridge and Trevan (1917) found that the increase in portal pressure was related to an increase in liver size and they suggested three possible modes of action for adrenaline.

(i) It may obstruct the venous outflow from the liver, thus also accounting for the observed increase in liver size.

(ii) It may constrict the intrahepatic branches of the portal vein.

(iii) It may cause swelling of the liver cells with compression of the sinusoids and obstruction to the portal flow. That this explanation is not a valid one has been shown by Daniel and Prichard (1952 b): marked swelling of the liver cells did not raise the portal pressure in rats. Most workers have noticed, contrary to the observations of Bainbridge and Trevan, a reduction in liver size on adrenaline administration; adrenaline appears to act by constricting the intrahepatic portal branches. It is not possible to explain the findings of Carnot, Gayet and Merklen (1932 b) who found that

../adrenaline

adrenaline raised the portal pressure when the liver had been bypassed by means of an anastomosis between the portal vein and right renal vein. However, the findings of these latter workers have yet not been confirmed.

The effects of other drugs on the portal pressure are shown in Table XIII (Page 49). Posterior pituitary extract raises the splanchnic vascular resistance with a lowering of the portal flow and pressure. It is possible that it also lowers the hepatic resistance, as suggested by Clark (1928).

Author	Route of Administration	Dosage	Effect (Increase: ↑ Fall : ↓)	Pressures in Cm Water Before Administration	Pressures in Cm Water After Administration	Method: Solution in Manometer	Vein used for Measurement	Subject	Remarks
1) Schmid (1908)	Intravenously		↑	8.6	23.3	Mercury	Portal	Dogs	-
2) Burton-Opitz (1912 f)	Into portal vein	-	↑	13.6	51.7	Mercury	Portal	Dogs	The rise occurred 2-3 seconds after injection. The rise in portal pressure directly varied with the amount of adrenaline given and the duration of the injection. The author concludes that adrenaline obstructs the portal flow.
3) Burton-Opitz (1912 f)	Intravenously		↑	-	-	Mercury	Portal	Dogs	-
4) Bainbridge and Trevan (1917)	Into portal vein	1 cc of 0.1% sol.	↑	9.5	40	25% Sodium Citrate	Splenic	Dogs	The rise in portal pressure was preceded by a small drop for 15-30 seconds. The rise lasted 2-3 minutes - it was related to the duration of adrenaline Administration. Occlusion of the hepatic artery had no effect on the results. The pressure in the inferior vena cava remained the same
5) Bainbridge and Trevan (1917)	Into portal vein	1 cc of 0.1% sol.	↑	-	20	2.5% Sodium Citrate	Splenic	Cats	
6) Carnot, Gayet and Merklen (1930 a)	Intravenously	-	↑	17	26 (splenic) 24 (sup.mesent.)	Water	Splenic & Superior Mesenteric	Dogs	-
7) McMichael (1932)	Intravenously or into portal vein	-	↑	-	-	5% Sodium Citrate	Splenic	Cats	A splenectomy was first done
8) Wiggers, Opdyke & Johnson (1946)	Intravenously	-	↑	-	-	Mercury	Portal	Dogs	-

TABLE XII : THE EFFECT OF ADRENALINE ON THE PORTAL PRESSURE

Author	Chemical Agent	Route of Administration	Effect (Increase: ↑ Fall: ↓)	Pressures in cm. water Before Administration	Pressures in cm. water After Administration	Method: Solution in Manometer	Vein used for measurement	Subject	Remarks
1) Bainbridge and Trevan (1917)	Posterior Pituitary Extract	Into portal vein	↓	19	2	2.5% Sodium Citrate	Splenic	Dogs	-
2) Clark (1928)	Posterior Pituitary Extract	Intravenously	↓	-	-	Sodium Citrate	Splenic	Cats	The hepatic resistance was diminished and the splanchnic resistance increased
3) Carnot, Gayet and Merklen (1930 a)	Posterior Pituitary Extract	- do -	↓	-	-	Water	Splenic & Superior Mesenteric	Dogs	-
4) McMichael (1932)	Posterior Pituitary Extract	- do -	↓	-	-	5% Sodium Citrate	Splenic	Cats	Same result on administration of pituitrin after occlusion of the splenic and superior mesenteric veins
5) Schmid (1908)	Digitalis	-	↑	13.3	17.7	Mercury	Portal	Dogs	Rise in pressure associated with and increased portal flow
6) Bainbridge and Trevan (1917)	Barium Chloride	Into portal vein	↑	9.5	13.5	2.5% Sodium Citrate	Splenic	Dogs	-
7) Carnot, Gayet and Merklen (1930 b)	Acetyl choline	Intravenously	Variable	-	-	Water	Splenic & Superior Mesenteric	Dogs	-
8) Carnot, Gayet and Merklen (1930 b)	Amyl Nitrate	Inhalation	No Effect	-	-	Water	Splenic & Superior Mesenteric	Dogs	-

TABLE XIII: THE EFFECTS OF CHEMICAL AGENTS - OTHER THAN ADRENALINE - ON THE PORTAL PRESSURE

THE EFFECTS OF SHOCK AND HAEMORRHAGE ON THE PORTAL PRESSURE

Table XlV (Page 52) shows the effects of haemorrhage and histamine - or peptone - shock on the portal pressure. Histamine and peptone, injected intravenously or into the portal vein, raise the pressure in the portal system of dogs. These drugs do not elevate the portal pressure in cats (Feldberg, Table XlV). These results can be explained by the presence of a sphincter in the hepatic veins of dogs. (Bauer et al, 1932; Mautner and Pick, 1922; Elias and Feller, 1926). Mautner and Pick showed that histamine stimulates the hepatic sphincter to contract. This will reduce the portal outflow and raise the portal pressure.

Feldberg (1929) has noticed two types of reactions when histamine or peptone is injected into the portal system of cats:

(a) There may be a fall in portal pressure with a gradual return to normal, as shown in fig. 6

Fig. 6

(b) The fall in pressure may be followed by a secondary rise above normal (fig. 7)

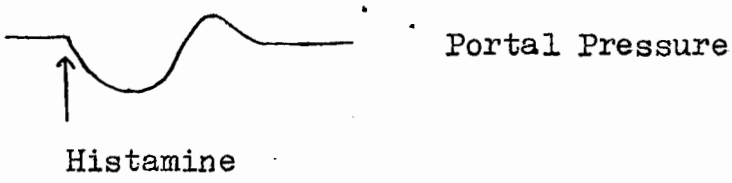


Fig. 7

The fall in portal pressure depends on a corresponding fall in aortic pressure and the author thinks that the secondary rise in the second type of reaction is the result of a temporary increase in hepatic resistance.

Author	Method of Shock Production	Effect (Increase: ↑ Fall: ↓)	Pressures in Cm. Water Before	After	Method: Solution in Manometer	Vein used for measurement	Subject	Remarks
1) Bayliss & Starling (1894 a)	Haemorrhage (200 cc loss)	↓	9.7	4.2	25% Magnesium Sulphate	Splenic	Dogs	-
2) Wiggers, Opdyke & Johnson (1946)	Haemorrhage	↓	-	-	Mercury	Portal	Dogs	Returned to normal values with re-infusion of the blood
3) Wiggers, Opdyke & Johnson (1946)	Intravenous Histamine	↑	-	-	Mercury	Portal	Dogs	The histamine produced "histamine-Shock"
4) Feldberg (1929)	Intravenous Histamine	Small ↓	-	-	Water	Splenic	Cats	-
5) Essex and Thomas (1950)	Histamine Intravenously or ascaris extract	↑	7	30	Water	Portal	Dogs	Rise in pressure probably due to hepatic venous constriction. "Ascaris extract" a shock factor
6) Feldberg, Schilf & Zernik (1928)	Histamine or Peptone Intravenously	↑	-	-	Ringer's Solution	Splenic	Dogs	Large doses of these drugs were used to produce shock
7) Feldberg, Schilf & Zernik (1928)	Histamine or Peptone Intravenously	Marked ↑	-	-	Ringer's Solution	Splenic	Dogs	Small doses were used
8) Manwaring, Brill & Boyd (1923)	Intravenous Peptone	↑	12	30	Mercury	Portal	Dogs	Pressure returned to normal gradually over 8 - 12 minutes
9) Carnot, Gayet and Merklen (1930 b)	Intravenous Peptone	↑	17	30 in splenic | 34 in sup. mesenteric	Water	Splenic & Supeior Mesenteric	Dogs	Shock was produced by the peptone

TABLE XIV : THE EFFECT OF SHOCK AND HAEMORRHAGE ON THE PORTAL PRESSURE

THE EFFECTS OF OBSTRUCTING THE BLOOD FLOW IN THE PORTAL SYSTEM ON ITS PRESSURE.

Table XV (Page 55) summarizes the results of different workers on obstructing the portal flow. During the rise in portal pressure on complete occlusion of the portal vein at the hilum of the liver, the aortic blood pressure falls, and the animal dies from shock in 30 to 60 minutes. Grindlay and Bollman (1952) have shown that incomplete occlusion of the portal vein does not necessarily raise the portal pressure.

It will be noticed that the rise in pressure on occluding the hepatic veins is much smaller than that on portal vein occlusion. This difference can be explained by the presence of anastomotic veins between the liver and the systemic venous system (e.g. veins run in the round ligament to the umbilicus and from the bare surfaces of the liver to the diaphragm).

The portal pressure is raised in humans with portal obstruction e.g. in cirrhosis of the liver (Rousselot, 1939; Linton et al, 1947).

McMichael appears to be the only worker who has measured the pressure on peripheral occlusion of the portal vein (Table XV). That the pressure does not drop to zero may have been explained by an inflow of blood from the branches of the hepatic artery in the liver. However, on occlusion of the hepatic artery the pressure remains at 5 cm. water. An increased tone in the portal branches and hepatic veins may keep the portal pressure at this level.

../From this

From this review of the literature, it appears that the normal portal pressure in animals and humans is fairly constant. It ranges from 7 to 20 cm. water usually, and its height mainly depends on the tone of the portal branches in the liver. This vascular tone is under nervous and hormonal control.

Author	Site of Obstruction	Effect (increase: ↑ fall : ↓)	Pressures in Cm. Water Before Obstruction	After Obstruction	Method: Solution in Manometer	Vein used for pressure measurement	Subject	Remarks
1) Bayliss and Starling (1894a)	Portal vein at hilum of liver	↑	8.9	60-80	25% Magnesium Sulphate	Splenic	Dog	-
2) Manwaring, Brill and Boyd (1923)	Portal vein at hilum of liver	↑	-	-	Mercury	Portal	Dog	Pressure rose to the level of the Aortic blood pressure
3) Feldberg, Schilf & Zernik (1928)	Portal vein at hilum of liver	↑	-	-	Ringers Solution	Splenic	Dog	Pressure rose to two-thirds of the height of the aortic blood pressure
4) Auvert (1950)	Portal vein at hilum of liver	↑	-	60-90	Water	Portal	Dog	Pressure rose 0.5 cm with each heartbeat
5) McMichael (1932)	Peripheral occlusion of portal vein	↓	10	5	5% Sodium Citrate	Splenic	Cat	
6) Bayliss and Starling (1894a)	Occlusion of hepatic veins by occluding Inferior Vena Cava above liver	↑	8.9	22.6	25% Magnesium Sulphate	Splenic	Dog	-
7) Manwaring, Brill & Boyd (1923)	- ditto - Inferior Vena Cava tied above & below liver	↑	12	25	Mercury	Portal	Dog	-
8) Simonds and Brandes (1925)	Occlusion of hepatic veins by ligature round base of liver	↑	-	2 X normal	-	-	Dog	-

TABLE XV : THE EFFECTS OF OBSTRUCTION TO THE PORTAL OUTFLOW ON THE PORTAL PRESSURE

A N A T O M Y O F T H E P O R T A L S Y S T E M

CHAPTER 1 1 1

CHAPTER 111

THE ANATOMY OF THE PORTAL SYSTEM

The portal system of veins conveys the blood from the abdominal part of the digestive tube, spleen, pancreas and gall bladder to the liver. In most text-books on anatomy, the portal system is described as having a constant anatomical pattern, but variations are common. In this section the most common pattern will be described and the important major variations will be mentioned.

The Portal System in Man

The portal vein and its tributaries are shown semi-diagrammatically in fig. 8. The portal vein is formed at the level of the second lumbar vertebra, behind the neck of the pancreas and in front of the inferior vena cava, by the union of the superior mesenteric and splenic veins. These two veins meet at an angle of 90°. The average length of the portal vein is 6 to 8 cm. and its average diameter is 1 to 2 cm. (Douglass et al, 1950; Segall, 1923). From its origin it ascends in the right free border of the lesser omentum, in front of the foramen of Winslow, to the right side of the porta hepatis. Here it divides into right and left branches. The right branch receives the cystic vein before it enters the liver. The smaller but longer left branch gives off vessels to the quadrate and caudate lobes and then enters the left lobe. It also receives the para-umbilical veins and it is connected with the umbilicus by the ligamentum teres, and with the inferior vena cava by the ligamentum venosum. During its passage in the free edge of the lesser omentum, the portal vein

receives the superior pancreatico-duodenal vein on its right side, immediately above the first part of the duodenum. The right gastric vein joins it somewhat higher and anteriorly. On the left side the portal vein may receive an accessory pancreatic vein (fig. 8). Lymphatics and the hepatic plexus of nerves surround the portal vein.

The splenic vein is a non-tortuous vessel (Gray, 1942) which averages 15 cm. in length and 0.5 cm. in diameter (Douglass et al, 1950). It commences at the hilum of the spleen by the union of five to six branches. These branches, which drain the spleen, are 3 to 4 cm. long. They may be larger than the splenic vein itself (Douglass et al, 1950). The latter passes with a downward inclination to the right side across the posterior abdominal wall, behind the pancreas.

Four to five short gastric veins and the left gastroepiploic vein from the stomach, join the splenic vein at is origin. Behind the pancreas it receives many short pancreatic veins and 2 cm. from its termination the inferior mesenteric vein, which ascends from the rectum, opens into it.

The superior mesenteric vein drains the small bowel, caecum, appendix, ascending colon and the greater part of the transverse colon. While it ascends in the mesentery of the small intestine it receives the jejunal, ileal, ileocolic, right and middle colic veins. The right gastroepiploic and the inferior pancreatico duodenal veins open into it below the third part of the duodenum. The average diameter of the superior mesenteric vein is 8 to 9 mm. (Douglass et al, 1950) and its average length is 6.0.cm. (Purcell et al, 1951).

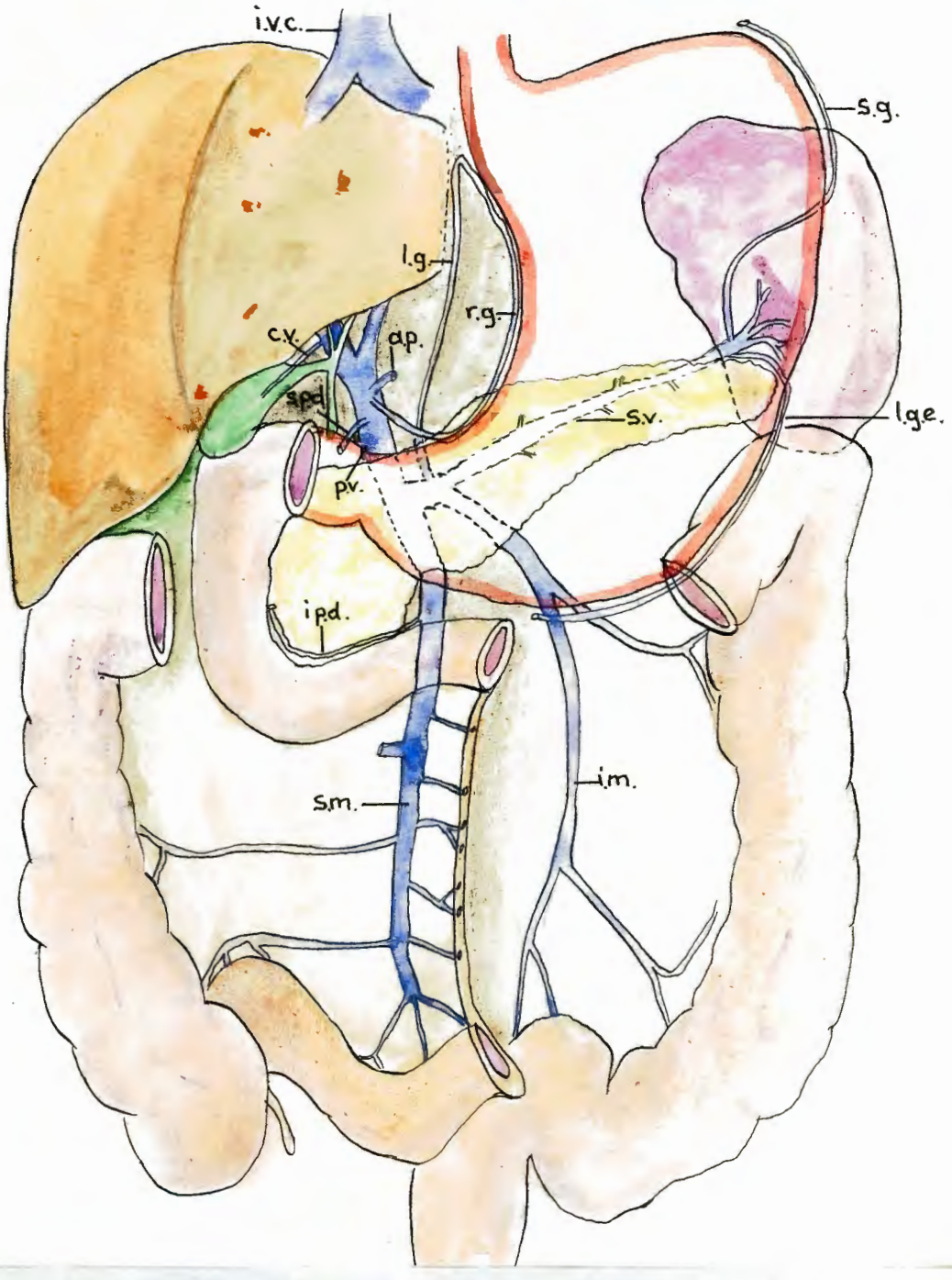


Fig. 8 THE PORTAL SYSTEM IN THE HUMAN

a.p.	accessory pancreatic vein
c.v:	cystic vein
i.m:	inferior mesenteric vein
i.p.d:	inferior pancreatico-duodenal vein
i.v.c:	inferior vena cava
l.g:	left gastric vein
l.g.e:	left gastro-epiploic vein
p.v:	portal vein
r.g:	right gastric vein
s.g:	short gastric veins
s.m:	superior mesenteric vein
s.p.d:	superior pancreatico-duodenal vein
s.v:	splenic vein

The left gastric vein drains the anterior and posterior surfaces of the stomach along the lesser curvature. It runs upwards in the lesser omentum towards the cardia, where it receives a few oesophageal veins. Turning downwards and backwards behind the lesser sac, it terminates at the junction of the splenic and portal veins, above the first part of the duodenum.

The most common pattern of the portal system has been described. Important variations of this pattern are concerned with the terminations of the left gastric and inferior mesenteric veins. The former opens at the junction of the splenic and portal veins in 60 per cent of humans, into the left border of the portal vein in 25 per cent and into the splenic vein in 15 per cent (Douglass et al, 1950). However, it practically always joins these veins within two cm. of the angle formed by them (Purcell et al, 1951). Occasionally it runs upwards and opens into the portal vein inside the liver (Holmes and Lovitt, 1951).

The inferior mesenteric vein terminates into the splenic vein in 38 per cent of humans, into the superior mesenteric vein in 30 per cent and at the junction of these two veins in 32 per cent (Douglass et al, 1950). Occasionally it divides into two branches, one of which joins the superior mesenteric and the other the splenic vein (Purcell et al, 1951).

The Portal System in the Dog

It will be seen from fig. 9 that the anatomy of the portal system in the dog closely resembles that of man. Only features that are dissimilar to the human will

../be mentioned

be mentioned. The portal vein of the dog is 4 to 6 cm. long and has a diameter of 6 to 8 mm. (Feil and Forward, 1922). At the hilum of the liver it divides into a right and a larger and longer left branch. The right branch divides into two, supplying the two right hepatic lobes. The left runs on for 5 cm., giving three branches to the three intermediate lobes of the liver on the way, and terminates in five branches; two supply each of the two left lobes and the fifth goes to the quadrate lobe (Copher and Dick, 1928).

The splenic vein, which has a diameter of 3 to 8 mm. (Burton-Opitz, 1909), joins the superior mesenteric vein at an angle of 45°. The left gastric vein enters the upper border of the splenic 2 cm. from its termination. However, it may open into the portal or at the junction of the portal and splenic veins.

The superior mesenteric vein is larger than the splenic and it lies in a direct line with the portal. It is joined by the inferior mesenteric vein, 1 to 2 cm. from its termination. The latter vein drains the whole colon in the dog, and its two tributaries may enter the superior mesenteric vein separately.

The upper pancreatico-duodenal vein terminates into the portal vein 2 cm. below the hilum of the liver. The lower one joins the superior mesenteric vein 5 cm. from its termination.

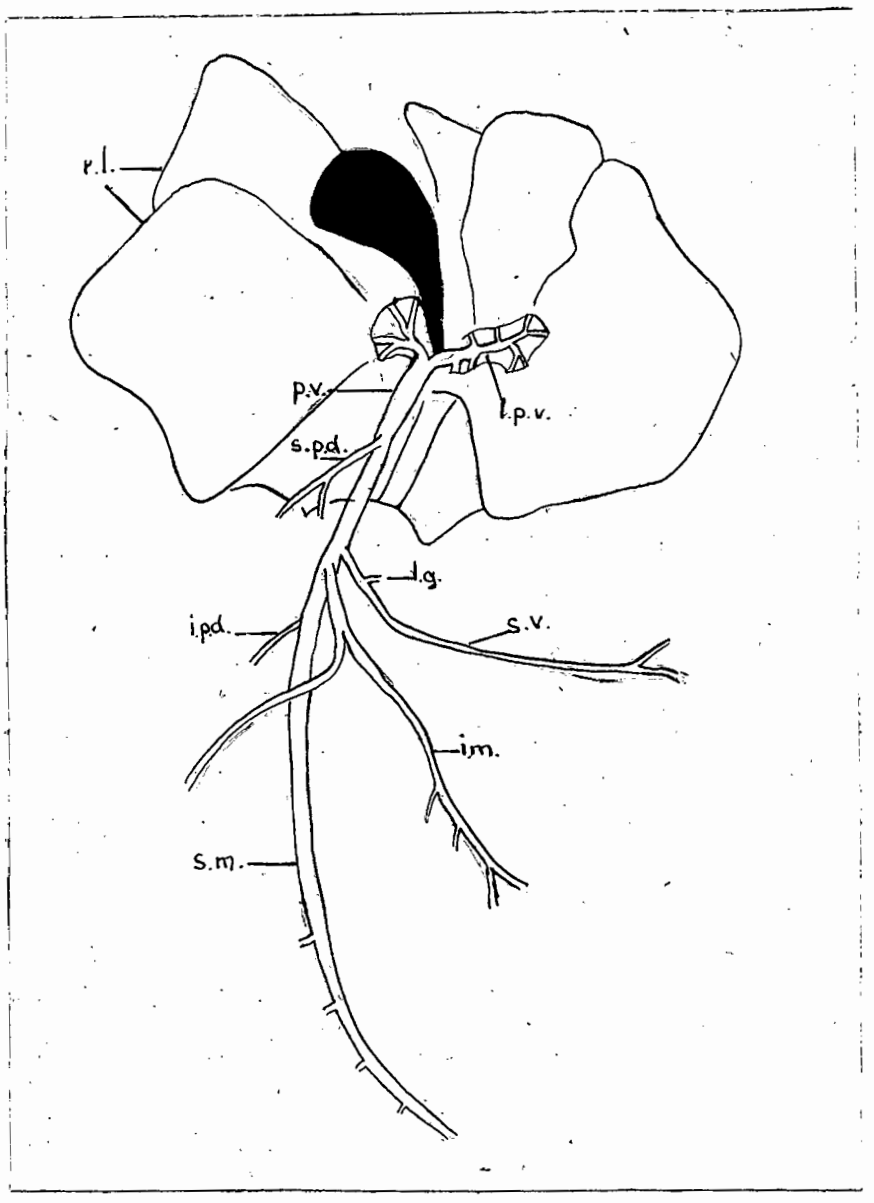


Fig. 9 Diagram of the Portal Vein and its Tributaries in the Dog

i.m. : inferior mesenteric vein
i.p.d.: inferior pancreatico-duodenal vein
l.g. : left gastric vein
l.p.v.: left branch of portal vein
p.v. : portal vein
r.l. : two right hepatic lobes
s.m. : superior mesenteric vein
s.p.v.: superior pancreatico-duodenal vein
s.v. : splenic vein.

The Portal Branches in the Liver

By injecting the portal vein with barium sulphate and taking stereoscopic X-ray photographs, Segall (1923) traced its intrahepatic branches as far as their seventh divisions in human livers removed at autopsy. The larger divisions left the large branches at angles of 60° to 90°. There was a sudden decrease in size at the fifth to the seventh divisions and the angles formed by them were 80° to 100°. They terminated round Glisson's capsule without anastomosing with one another. Mall (1906) estimated that the portal system of the dog consisted of 80,000 branches of the fifth and 956,000 branches of the sixth order.

It should be pointed out that the liver, in both man and dog, is divided physiologically into two lobes by a vertical plane which passes through the gall bladder fossa and the hepatic veins (Barlett et al, 1914; McIndoe and Counseller, 1927; Copher and Dick, 1928). The only communication between these two lobes is the intercellular sinusoids.

Pei-Lin Li (1940) studied the histology of the veins of the human portal system. He found that circular muscle fibres were prominent in the tunica media (the tunica media of the inferior vena cava contains mainly longitudinal muscle fibres) and that it was rich in elastic fibres. In cases of persistent portal hypertension the intima was thickened and the circular muscle of the media was hypertrophied. The same author also described a "splenic sphincter" in the splenic vein at its junction with the superior mesenteric. At this "sphincter" the intima was thickened and the circular muscle of the media was

../three to four

three to four times as thick as elsewhere.

Valves are present in the veins of the portal system in the foetus and newborn infant (Gray, 1942). They atrophy and disappear but may persist in a degenerative form in the adult.

Communications between the Portal and Systemic Venous Systems

The portal system communicates with systemic veins at the following sites.

1) At the lower end of the oesaphagus the gastric and oesophageal veins anastomose with the inferior hemiazygos vein.

2) In the retroperitoneal tissues the anastomosis of Retzius is formed between veins of the ascending and deseending colon, duodenum and pancreas and those of the diaphragm and kidneys.

3) At the umbilicus the veins in the falciform ligament meet the superior and inferior epigastric veins, to form the accessory portal system of Sappey. The veins in the falciform ligament also communicate through the diaphragm with the azygos vein.

4) At the lower end of the rectum the superior rectal communicates with the middle and inferior rectal veins.

5) On the convex surface of the liver veins anastomose freely with those of the peritoneal ligaments and diaphragm.

6) Occasionally the ductus venosus remains patent, forming a direct communication between the left branch of the portal vein and the inferior vena cava.

OBSERVATIONS

C H A P T E R 1 V

O B S E R V A T I O N S.

GROUP A - OBSERVATIONS ON GUINEA PIGS

Material and Methods

Twelve adult guinea pigs were used, each weighing between 500 and 600 Gms.

In six guinea pigs it was attempted to measure the rate of blood flow from the splenic pulp to the portal vein. Intraperitoneal nembutal and open ether were used as anaesthetic and the abdomen opened by a transverse or left subcostal incision. The portal vein, in the lesser omentum, and the spleen were exposed. A lateral hole was cut in the portal vein and dyes or other substances were injected into the splenic pulp. The blood flowing from the portal vein was examined for the injected material and the time noted from its administration until its appearance in the portal vein. Table XVI (page 66) summarizes these experiments. It shows the material used for injecting, the methods of recognizing it in the portal blood, and the results.

It was noticed that the spleen appeared contracted and relatively bloodless when exposed in the anaesthetized guinea pig, and the blood flow through the spleen was observed in and additional six guinea pigs. In four animals a substance was injected intracardially and the splenic pulp examined

for its presence. In the other two animals the effect of an adrenolytic drug (dibenamine) on the spleen was observed. This second series of experiments with the results are summarized in Table XVll (Page 67).

Results and Conclusions:

It will be noticed from the results in Tables XVl and XVll that the guinea pig was an unsatisfactory animal to use in investigating the rate of blood flow from the splenic pulp to the portal vein. Probably as a result of the anaesthetic and of operative trauma, the spleen was contracted and so avascular that practically no blood flowed in the splenic vein (Experiment 6, Table XVll). Dibenamine was not effective in preventing the spleen contracting.

It is likely that the much diminished blood flow in the contracted spleen accounted for the inability to demonstrate the presence in the portal blood of material injected into the splenic pulp. (Table XVl).

The results of these experiments on guinea pigs were inconclusive and it was decided to investigate dogs in the subsequent series of experiments.

No.of Experiment.	Material used for injecting spleen	Amount Used	Method of recognising the presence of the injected material in the Portal Vein.	Results
1	Methylene Blue Solution	0.5 cc	Inspection of portal blood for colour change	(1) No dye was visible in the portal blood (2) The spleen was contracted and the splenic vein narrow; it was 1½ to 2 inches in length
2	Mixture of methylene blue and methyl red solutions	0.5 cc	Inspection of portal blood for colour change	(1) No dye visible in portal blood (2) Spleen contracted
3	Liquid paraffin	0.5 cc	Smears taken at two second intervals from portal blood and examined microscopically for fatty droplets.	No fatty droplets observed in the portal blood
4	Indian Ink	0.5 cc	Smears taken at two second intervals from portal blood, and examined under phase contrast microscope	No Indian ink particles seen in portal blood
5	Potassium Ferricyanate	1.0 cc	Swabs taken at two second intervals from portal blood were dipped in a solution of ferriperchloride and examined for a prussian blue reaction	Potassium ferricyanate which leaked from the surface of the spleen during injection contaminated all the swabs.
6	Potassium Ferricyanate	1.0 cc	- ditto -	The superior mesenteric vein was clamped to diminish the portal flow, but no potassium ferricyanate was demonstrated in the portal blood

TABLE XVI : EXPERIMENTS ON INJECTING THE SPLEENS OF GUINEA PIGS

No.of Experiment	Material injected intracardially	Amount	Method of observing the splenic blood flow	Remarks and Results
1	Solution of methylene blue and methyl red	1.0 cc	Pulp of spleen inspected and smears made were examined microscopically	No dye seen macro- or microscopically
2	Liquid Paraffin	0.5 cc	- ditto -	Fatty droplets were present in the smears made from the splenic pulp
3	Solution of Brilliant Cresyl-red	1.0 cc	- ditto -	No dye seen macro- or microscopically
4	Potassium ferri-cyanate solution	1.0 cc	Liver, lungs, spleen, kidneys and muscle tested with ferri perchlor-ide solution for prussian blue reaction	Reaction strongly positive in liver and lungs; faintly positive in kidneys and spleen and negative in muscle. The faintly positive reaction indicates that very little blood flows through the spleen
5	Dibenamine (injected after exposure of spleen)	0.5 cc of 1% solut-ion	Spleen exposed and observed. Splenic vein cut, distal end clamped and flow of blood from proximal end observed	The dibenamine, which is an adrenolytic drug, did not cause any dilatation of the spleen and almost no bleed-ing occurred from the proximal end of the cut splenic vein
6	Dibenamine(injected intraperitoneally before operation started)	0.5 cc of 1% solu-tion	- ditto -	The spleen was about 50% larger than in previous ex-periments. However, on cutting the splenic vein it contracted and there was almost no bleeding from the proximal end of the cut splenic vein

TABLE XV11 : OBSERVATIONS ON THE SPLENIC BLOOD FLOW IN GUINEA PIGS

GROUP B - OBSERVATIONS ON DOGS AND HUMANS

Material and Methods:

To investigate the blood flow in the portal system two methods suggested themselves:-

1) The rate of blood flow could be measured by injecting a radio-active substance into the splenic pulp and determining its appearance in the liver with a Geiger counter.

2) It appeared possible that a radio-opaque material injected into the spleen might flow into the splenic and portal veins, which could then be demonstrated radiologically. It was decided to investigate the latter method.

(a) Experiments on Dogs and Rabbits

The spleen was exteriorized in eleven adult dogs so that it could be readily available for the injection of radio-opaque materials. In five dogs Barcroft's method (Barcroft and Stephens, 1927; Barcroft, 1926) (fig 10) was used and in six the spleen was placed outside the abdominal muscles but covered by skin (fig.11). (See appendix 1 for detail).

Five dogs died in the post-operative period. In the six that survived eighteen experiments were done, in some as long as two years after the exteriorization of the spleen. In these experiments the dog was anaesthetized with intravenous pentothal. It was placed supine on an X-ray table and a radio-opaque dye was injected rapidly into the splenic pulp, using a 20 cc. syringe and a needle having a diameter of one millimetre. The injection was made over a period of two to ten seconds. In some

../experiments

Fig. 10 (Dog V). Photograph of dog with a completely exteriorized spleen.

Fig.11 (Dog 1V). Photograph of dog with a subcutaneous spleen (the arrow points to the spleen).

experiments rapid serial X-ray exposures were made with an automatic casette changer. In others the animal was fluroscoped and an X-ray photograph taken when necessary. The details of these experiments are summarized in Table XVlll (Page 72). It will be noticed that diodone was the radio-opaque dye used in all the experiments except the first three.

As 70% diodone is alleged to be a highly irritating substance, its effect on intraperitoneal injection in two rabbits was observed. One received 2 cc., and the other 1 cc 70% diodone intraperitoneally. The former was killed on the 10th day and the latter after three months. In neither was there any evidence of peritoneal irritation or adhesions and histological sections from the liver, lungs, spleen and kidneys were normal.

In experiment D5 (Table XVlll) a non-exteriorized spleen which was exposed at laparotomy, was injected. In Experiment D16 an attempt was made to pass a polythene catheter, two millimetres thick, through the splenic pulp into the splenic vein, but it failed. It should also be noted that, although the portal veins of the dogs used in experiments 7 and 9 had been ligated, both animals remained in excellent health.

Subsequently this method was applied to humans.

(b) Experiments on Humans

Eighteen experiments were done on twelve humans. The spleen was enlarged and palpable in eleven and of normal size in one. The clinical diagnosis in 10 of the 11 cases with enlarged spleens, was portal hypertension due to

../hepatic fibrosis

hepatic fibrosis. The other one was a case of congenital haemolytic anaemia, which presumably, had a normal portal circulation.

The experimental procedure in these cases was as follows: The patient was premedicated with omnopon or pethidine and tested for sensitivity to diodone by injecting a few minims of 70% diodone intravenously. He was then placed supine on an X-ray table and the site of the splenic injection infiltrated with 2% novocaine. In the first three experiments the injection was made over the spleen below the left costal margin. In the others the needle was inserted through the left 9th or 10th intercostal spaces between the anterior and posterior axillary lines. A lumbar puncture needle 10 to 12 cm. long and with a diameter of 1 mm, was attached to a 20 cc syringe which contained 50% or 70% diodone, heated to body temperature. The patient was told to hold his breath and the needle inserted downwards, medially and backwards, penetrating the left pleural cavity and the diaphragm. The spleen could be felt being engaged at 3 to 4 cm and the needle was inserted a further 2 cm. The diodone was injected over a period of 6 to 10 seconds (once in less than 5 seconds) and towards the end of the injection an X-ray exposure was made. Plates were also taken 10 seconds and 10 minutes later.

The details of these experiments are summarized in Table XIX (Page 74). It will be noticed that most patients had spleens palpable four finger's breadth below the costal margin. A general anaesthetic was used

../in experiment

No.of Experiment	No.of Dog.	Position of Spleen	Dye used	Amount	Method of X-ray Examination	Remarks
D 1	11	Outside Skin	Thorotrast	5 cc	Serial X-ray photographs at one second intervals	The dog collapsed during the experiment, showing marked contraction of its spleen
D 2	11	-ditto-	-ditto-	5 cc	Serial X-ray photographs at 0.5 second intervals	Dog in good condition
D 3	11	-ditto-	-ditto-	2 cc	Fluoroscoped only	-
D 4	11	-ditto-	70% diodone	5 cc	Fluroscoped and X-ray photographs taken	Dog died at end of experiment
D 5	V	Normal	-ditto-	5 cc	- ditto -	The spleen was exposed and injected at laparotomy and thereafter exteriorized
D 6	IV	Under Skin	50% diodone	3 cc 5 cc 5 cc	- ditto -	Dye injected into different parts of the spleen
D 7	1V	-ditto-	-ditto-	10 cc	- ditto -	Experiment done two weeks after the portal vein had been ligated. The dog was in excellent health
D 8	V	Outside Skin	-ditto-	10 cc	- ditto -	-
D 9	V	-ditto-	70% diodone	10 cc	- ditto -	Experiment done four weeks after the portal vein had been ligated. The dog was in excellent health

TABLE XV111 (i) THE INJECTION OF RADIO-OPAQUE DYE INTO THE SPLEENS OF DOGS

No.of Experiment	No of Dog	Position of Spleen	Dye Used	Amount	Method of X-ray Examination	Remarks
D 10	1V	Under Skin	50% diodone	10 cc	Fluroscoped and X-ray photographs taken	-
D 11	V	Outside Skin	-ditto-	10 cc	- ditto -	Experiment done after a portacaval anastomosis had been done on the dog
D 12	V111	Under Skin	70% diodone	20 cc	- ditto -	-
D 13	V11	-ditto-	-ditto-	20 cc	- ditto -	-
D 14	V111	-ditto-	-ditto-	20 cc	- ditto -	An anastomosis between the hepatic artery and portal vein had been done three weeks before
D 15	V11	-ditto-	-ditto-	20 cc	- ditto -	A portacaval anastomosis had been done three days before
D 16	1V	-ditto-	-ditto-	20 cc	- ditto -	An attempt was made to pass a No. 2 polythene catheter into the splenic vein through the splenic pulp. This failed - the catheter coiled in the spleen. The dye was injected through the catheter
D 17	V111	-ditto-	-ditto-	20 cc	Serial X-ray photographs at one second intervals	An aortogram was done on the dog at the same time
D 18	X1	-ditto-	-ditto-	20 cc	Serial X-ray photographs at end of injection, five seconds and 15 seconds later	-

TABLE XV111 (ii) (Continued) : THE INJECTION OF RADIO-OPAQUE DYE INTO THE SPLEENS OF DOGS

No.of Experiment	No.and initials of patient	Clinical Diagnosis	Dye used	Amount	Method of introducing Needle into Spleen	Remarks
H 1	1 F.v.Z	Portal Cirrhosis	70% diodone	5 cc 10 cc	Needle inserted below left costal margin	The spleen was palpable well below the costal margin.The patient was fluoroscoped and X-ray photographs were taken. There were no ill effects.
H 2	11 P.B.	None	-ditto-	10 cc	-ditto-	The spleen was palpable 3 fingers below the costal margin Patient fluoroscoped and X-ray photographs taken
H 3	11 P.B.	None	-ditto-	10 cc	-ditto-	1)X-ray taken at end of injection which took 5 seconds 2)Patient ran a temperature afterwards and complained of pain over the spleen. However he recovered fully.
H 4	111 McL.	Portal Cirrhosis	-ditto-	15 cc	Needle inserted through 9th intercostal space in mid-axillary line	1)Patient obese with a 3 finger splenomegaly. Oesophageal varices present on Ba-swallow 2)X-ray exposure made at end of injection. 3)Patient vomited and had a small haemoptysis after injection, but recovered fully 4)Pressure in the superior mesenteric vein was 29 cm water at operation two days later
H 5	1V M.S.	Chole-cystitis	-ditto-	18 cc	Needle through 10th inter-costal space in posterior axillary line and directed into spleen at laparotomy for cholecystectomy	1)Exposure made at end of injection 2)The spleen was of normal size 3)There was no bleeding from the splenic surface at the end of the injection
H 6	V E.F.	Portal Cirrhosis	-ditto-	20 cc	Needle through 10th inter-costal space in mid-axillary line	1)Spleen enlarged down to the umbilicus. Firm. 2)X-ray exposure made at end of injection 3)The patient complained of pain in the left shoulder and at the site of injection for a short time afterwards

TABLE XlX (i) SPLENIC INJECTION OF RADIO-OPAQUE DYE IN HUMANS

No.of experiment	No.and initials of patient	Clinical Diagnosis	Dye Used	Amount	Method of introducing needle into spleen	Remarks
H 7 *	V1 H.K.	Splenic Vein thrombosis	70% diodone	20 cc	Through 9th intercostal space in posterior axillary line	1) The spleen was palpable 4 fingers below the costal margin 2) The X-ray exposure was made at the end of injection with patient tilted 30° on to his right side.
H 8	V1 H.K	-ditto-	-ditto-	20 cc	- ditto -	Patient in supine position. X-ray photograph taken at end of injection
H 9	V E.F.	Portal Cirrhosis	-ditto- -ditto-	20 cc 20 cc	Through 10th intercostal space in anterior axillary line	Spleen palpable well below costal margin. X-ray photographs taken at end of injection, 5 seconds and ten minutes later.
H 10	V11 L.D.	-ditto-	-ditto-	20 cc	Through 9th intercostal space in anterior axillary line	1) Spleen palpable 4 fingers below costal margin. Oesophageal varices on Ba-swallow. 2) X-ray photographs taken at end of injection, 5 seconds and 10 minutes later
H 11	V111 N.K.	Nodular hyperplasia of liver	-ditto-	10 cc	- ditto -	1) Spleen enlarged 4 fingers down. 2) X-ray exposure made at end of the injection. The patient was unable to hold his breath.
H 12	V111 N.K.	-ditto-	-ditto-	20 cc	- ditto -	The injection was made while the patient was breathing quietly. Films were taken at the end of injection, five seconds and ten minutes later. There were no ill effects
H 13	1X K.S.	Portal Cirrhosis	-ditto-	20 cc	- ditto -	1) The spleen was palpable 5 fingers down. 2) X-ray films were taken at end of injection, 5 seconds and 10 minutes later

*Case reported in Lancet, March 15th, 1952, p.530 (appendix 2)

TABLE XIX (ii) (Continued) SPLENIC INJECTION OF RADIO-OPAQUE DYE IN HUMANS

No.of Experiment	No. and Initials of Patient	Clinical Diagnosis	Dye Used	Amount Used	Method of introducing needle into spleen	Remarks
H 14	X R.N.	Portal Cirrhosis	70% Diodone	8 cc	Through 10th intercostal space in anterior axillary line	1) The spleen was enlarged to 4 fingers below the costal margin. 2) Serial x-rays were taken at 0.5 - 1 second intervals. The syringe broke after 8 cc.dye had been given. The films were over exposed
H 15	X1 J.N	Bilharzial Liver (made histologically)	-ditto-	20 cc	Through 9th intercostal space in anterior axillary line	1) Serial X-rays taken at 1 second intervals. 2) Some difficulty in injecting the dye rapidly enough - it took 6-10 seconds
H 16	X11 V.P.	Congenital Haemolytic Anaemia	50% Diodone	20 cc	Through 9th intercostal space in midaxillary line	1) The spleen was palpable 2-3fingers below the costal margin. Areas of calcification were present in it 2) The injection was done under general anaesthesia before the abdomen was opened for a splenectomy.The anaesthetist stopped the patient's breathing and an X-ray was taken at the end of the injection. The needle was 6.5 cm in length and the injection was made more rapidly-within 5 seconds. 3) At laparotomy there was no bleeding from the splenic surface. There was a subcapsular haematoma(1 cm^2) at the site of the injection

TABLE XIX (iii) (continued) SPLENIC INJECTION OF RADIO-OPAQUE DYE IN HUMANS

in Experiment H5, in which a normal spleen was injected at laparotomy, and in experiment H16, in which the spleen was injected before the abdomen was opened for a splenectomy. The anaesthetist prevented these two patients from breathing during the injection. In Experiments H 11 and H 12 the patient was breathing quietly while the splenic injection was being made, but no harm was done.

Experiments H1 and 2 were done under fluoroscopy. Serial X-ray photographs at one second intervals, were taken in Experiments H 14 and H 15. In the fourteenth only 8 cc. dye was injected; the force on injecting was so great that the syringe broke. In the last experiment a needle of 6.5 cm length was used and the injection was made with less force and greater speed.

No apparent harm was done by these injections. Some patients suffered from nausea and vomiting a few seconds after the injection had been made. This was due to the diodone. There were no hypersensitivity reactions. Case 111 had a small haemoptysis immediately after the injection. This was presumably caused by trauma to the base of the left lung. For a few days there was a slight pyrexia with tenderness over the spleen in Case 11, but he recovered fully. Experiments were repeated on patients V, V1 and V111 - on the same day in the latter and on consecutive days in Case V1. There were no ill effects.

The spleen was removed as part of the medical treatment in patients 111, V1, X1 and X11. No puncture wound was visible on the surface of the spleens but all

../showed

showed on section a haemorrhagic area. Except in the spleen of Case 111 (fig. 12) this area was never larger than one square cm.

In addition to these experiments attempts were made to inject three normal spleens, not exposed at operation; these attempts failed.

Fig. 12 (Experiment H 4 - Patient 111)

The photograph shows a transverse section of an enlarged human spleen which was removed at a shunt-operation, three days after an intrasplenic injection of diodone had been done. The intrasplenic haematoma (indicated by the arrow) is larger than usual.

R E S U L T S

The results on injecting radio-opaque dye into the splenic pulp were similar in dogs and man, and the features in both groups were as follows:

Within a second of the intrasplenic injection of diodone, the latter was seen fluroscopically to be flowing into the splenic and portal veins and in the portal branches in the liver (figs.13 - 16, Page 86). The apex of the dye could be followed under X-ray screen or by rapid serial X-ray photographs (figs.17-19). Figs. 17-19 were taken at ½ second intervals. In fig. 17 the apex of the dye is just inside the portal vein, in fig. 18 the larger branches in the liver are filled and the finer hepatic branches are shown in fig. 19.

The photographs so obtained with thorotrast and 70% diodone were good, but although 50% diodone was used satisfactorily in the dog, it was not radio-opaque enough when used in man (fig. 20).

In Experiment H 1 the dye appeared to remain in the spleen. In Experiment H 2 the dye left the spleen quickly but was not visible in the portal system. The dye was probably injected into the peritoneal cavity in Experiment H 3, but there were no serious ill effects. The dye did not flow from the splenic to the portal vein in patient V1, in whom thrombosis of the splenic vein was proved at laparotomy (figure 34).

../In two

In two dogs with exteriorized spleens, the portal vein had been ligated before the experiments were done (Experiments D 7 and D 9). A lateral anastomosis between the hepatic artery and portal vein was done on dog VIII (Experiment D 14); in dogs VII and VIII aortograms were done in an attempt to show the hepatic arterial branches in the liver (fig.s 42 and 43).

The radio-opaque dye could also be injected through a polythene catheter introduced into the spleen (Experiment D 16). It will be noticed that the exteriorized spleen retained its normal blood supply (fig.13).

An X-ray photograph taken 10 minutes after the splenic injection invariably showed the dye being excreted by the kidneys (figs. 21 and 40).

The portal venogram, obtained by the intrasplenic injection of diodone (50 or 70%) showed the following features.

1) Rate of Flow

The dye flowed from the spleen to the liver with great rapidity. Within 0.5 seconds after injection the dye could be seen in the portal vein and a second later it filled the small portal branches in the liver (figs. 17-19). The rate of flow was also observed under the fluroscope in dogs and in Experiment H 15 serial X-ray photographs showed the same rapid flow in man, in spite of the presence of an intrahepatic portal obstruction (figs. 22 and 23). In Experiment H 14 the dye was in the splenic vein one second after injection and it filled the portal vein and the finer branches in the liver respectively one and two seconds later.

.../The relative

2) The Relative Volume-Flow in the Portal System

The apex of the column of dye was clearly visible (fig. 17) and it left the spleen with such force that it caused a "bolus-effect". It was observed even with small amounts of dye. However, the density with which the splenic and portal veins were demonstrated, was related to the amount of dye injected. These veins remained visible as long as the injection was being made into the spleen and for 10 to 20 seconds afterwards (fig.15).

The sizes of the splenic and portal veins were clearly shown (fig.16). When the latter was large the dye appeared diluted (figs. 28 and 29). In some experiments the splenic vein was wide and tortuous (fig. 24).

3) Spasm of Splenic Vein

This was observed fluoroscopically a few times. It occurred immediately after the dye had been injected. In Experiment D 4 the splenic vein went into severe spasm when the dog died (fig. 25). Slight spasm was demonstrable by serial X-ray photographs in Experiments D 12 (figures 26 and 27).

4) The Filling Defect at the Entrance of the Superior Mesenteric Vein.

This was a finding in the great majority of Experiments (figs. 13, 16-19 and 28). When the injection was made rapidly in subjects with an intrahepatic portal obstruction, there was a reflux of dye into the superior mesenteric vein (fig. 32). A reflux into branches joining the splenic vein at the hilum of the spleen was also seen in the majority of experiments, (figs.16 and 31).

../Dilution

Dilution of the diodone occurred after the splenic vein was joined by the superior mesenteric (figs. 16 and 28). Some dilution was occasionally seen at the splenic hilum, where the veins draining the spleen formed the splenic vein (fig. 20).

5) "Streamlining" in the Portal Vein

In the majority of experiments the dye filled the portal vein homogeneously. However, in some of the venograms it flowed mainly along the left half of the portal vein (figs. 14 and 28). In one instance the dye flowed along the right side (fig. 27) and in another along the centre of the portal vein (fig. 30).

Filling of the liver lobes with diodone was variable. In some experiments mainly the left lobe was filled (fig.14), whereas in others the right contained most dye (figs. 16 and 20). Both lobes were filled equally in most of the venograms.

6) Direction of Flow

The direction in which the dye flowed in the portal system could be observed under the fluroscope. It passed to the liver directly, filling only the splenic and portal veins and the intrahepatic portal branches. However, in the presence of portal vein obstruction in both man and dog, the dye also flowed into other veins, sometimes to the exclusion of the portal (fig. 33). Fig. 34 shows that the direction of flow had been changed completely; the dye flowed from the splenic to the short gastric veins and then to the portal via the left gastric vein. The latter vein is also shown in figs. 29 and 31. In fig. 31 the inferior mesenteric vein is visible.

../Two kinds

Two kinds of collateral circulations were demonstrated after experimental obstruction of the portal vein.

(a) A peripheral collateral circulation occurring round the spleen (figs.35 36 and 41), and

(b) a central type round the block in the portal vein (fig. 37

Experiments D 11 and D 15 were done after a portacaval anastomosis, and figure 38 shows the dye flowing into the inferior vena cava at the site of the anastomosis. It will be noted that "streamlining" is shown by the dye in the upper part of the inferior vena cava.

7) <u>The Behaviour of the Dye in the Spleen.</u>

It has been pointed out already that the diodone left the splenic pulp quickly (fig. 17 was taken 0.5 seconds after the injection was started). It was occasionally delayed for about one second in the spleen in subjects with portal vein obstruction. The dye did not diffuse throughout the spleen but remained localised to a segment, whence it was drained by a single vessel that joined the splenic vein at the hilum (fig. 28). In some experiments more than one segment was injected, and the dye flowed through two or more branches into the main splenic vein (figs. 23, 29 and 32). The reflux of diodone into branches draining non-injected segments of the spleen, has already been noted.

In Experiment H 16, injection of the dye was

.../made just

made just underneath the capsule of the spleen, but it flowed into the splenic vein without difficulty (fig.20).

Most of the diodone left the spleen within 10 to 20 seconds after cessation of its administration. Some, however, remained in the spleen for 10 minutes or longer, disappearing slowly over a period of 24 hours. It presented a typical honeycombed appearance (figs.21, 39 and 40).

8) The Behaviour of the Dye in the Liver

The branches of the portal vein in the liver were visible on the X-ray photographs in both man (figs. 16, 20, 24, 29 and 32) and dog (figs. 13-15 and 19). Although these branches were not shown clearly enough to demonstrate a definite pattern, they appeared to be fewer, coarser and further apart in patients with hepatic cirrhosis (figs. 24 and 30) than in the normal human (fig. 16).

It was not possible to trace the circulation of dye through the liver except in Experiment D 18. Here the finer intrahepatic portal branches were filled five seconds after injection (fig. 14). Ten seconds later the liver showed a dense shadow and the dye was visible in the inferior vena cava (fig. 15).

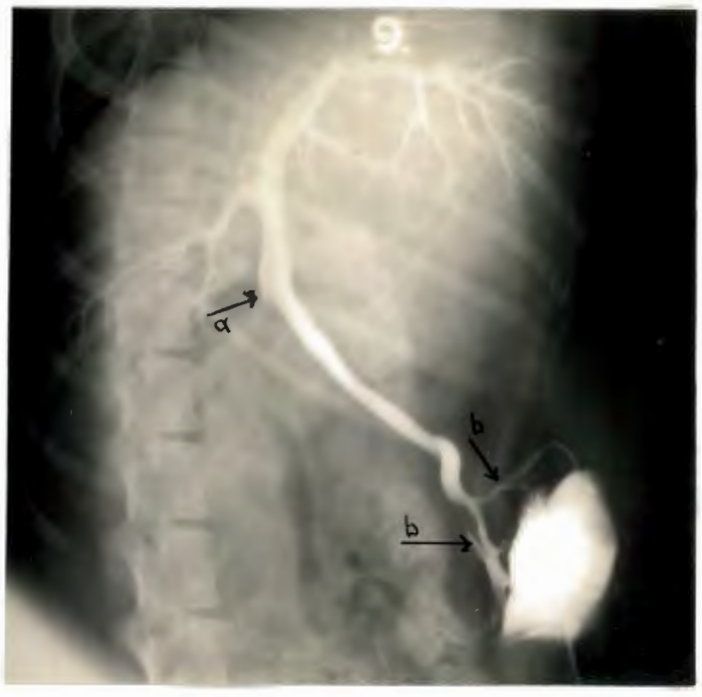


Fig.13 (a) (Experiment D 18 - Dog X1)
Radiograph taken after injecting
20 cc 70% diodone into spleen

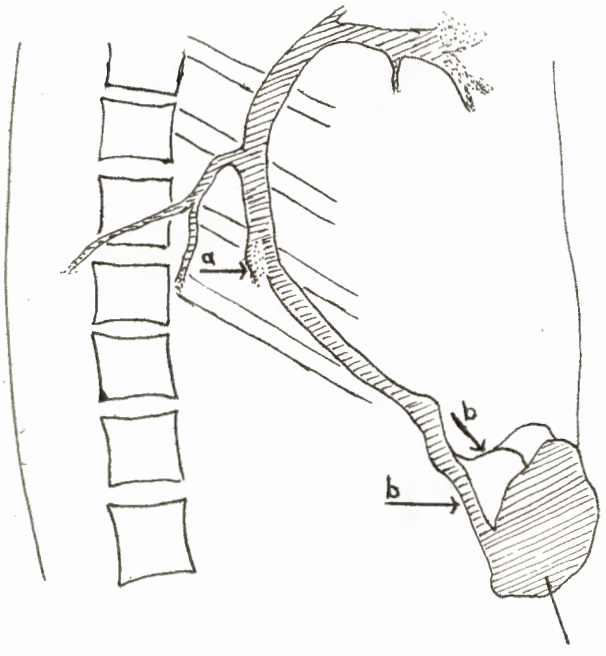


Fig. 13 (b) Diagram of original venogram shown
in fig. 13 (a)

Note in both figures:

(1) The defect at the entrance of the superior mesenteric vein (arrow a)

(2) The three veins draining the dye from the splenic pulp (arrows b)

(3) The intrahepatic portal branches are visible.

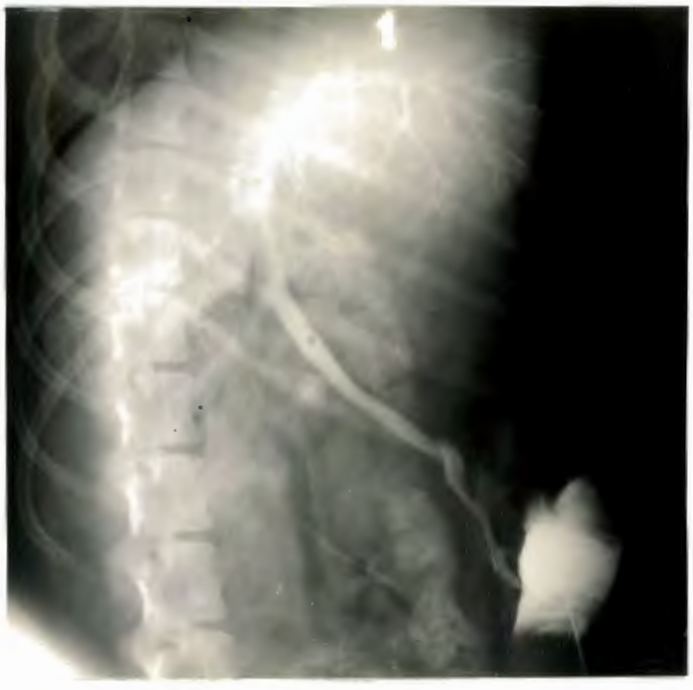


Fig 14 (Experiment D 18 - Dog X1)

Radiograph taken five seconds after fig.13(a) The diodone fills the smaller branches of the portal vein.

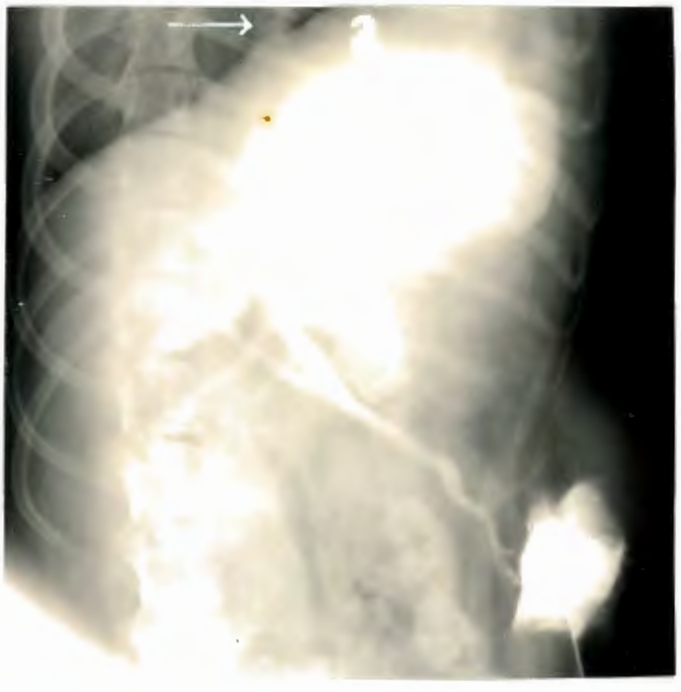


Fig. 15 (Experiment D 18 - Dog X1)

Radiograph taken ten seconds after fig. 14. The diodone demonstrates the inferior vena cava (arrow) and the liver casts a dense shadow.

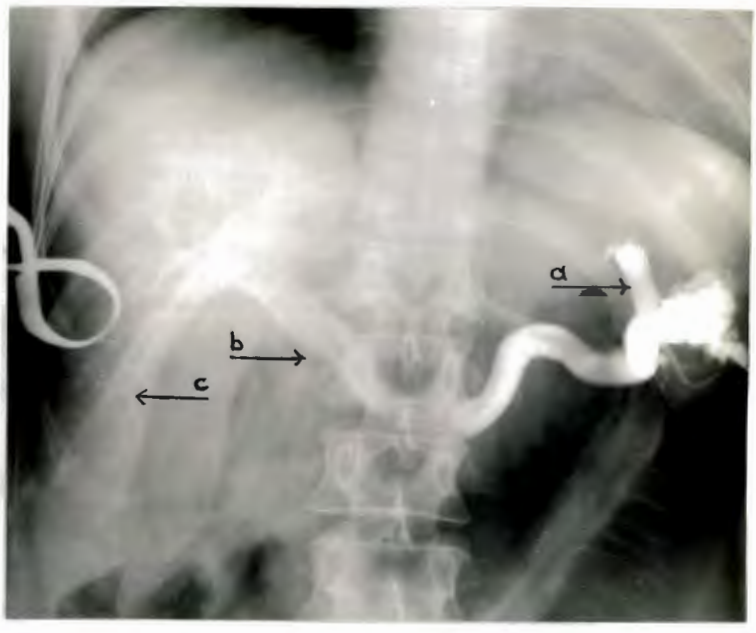


Fig. 16 (a) (Experiment H 5 - Patient 1V)
Radiograph showing a normal human portal venogram.

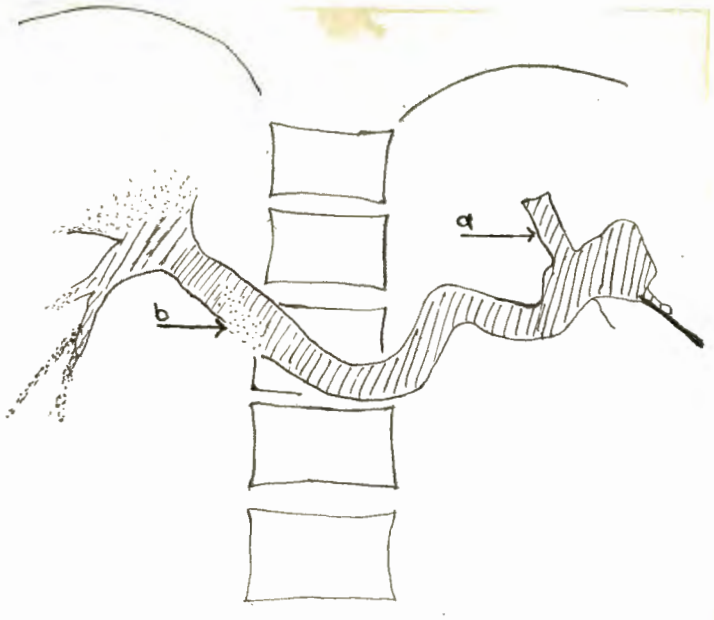


Fig. 16 (b) Diagram of original venogram shown in fig.16(a)
Note in both figures:

(1) The reflux of diodone into a large branch of the splenic vein (arrow a).

(2) The defect at the entrance of the superior mesenteric vein (arrow b).

(3) The dilution of the dye in the portal vein, after the superior mesenteric vein has entered it.

(4) The dye in the right lobe of the liver (arrow c).

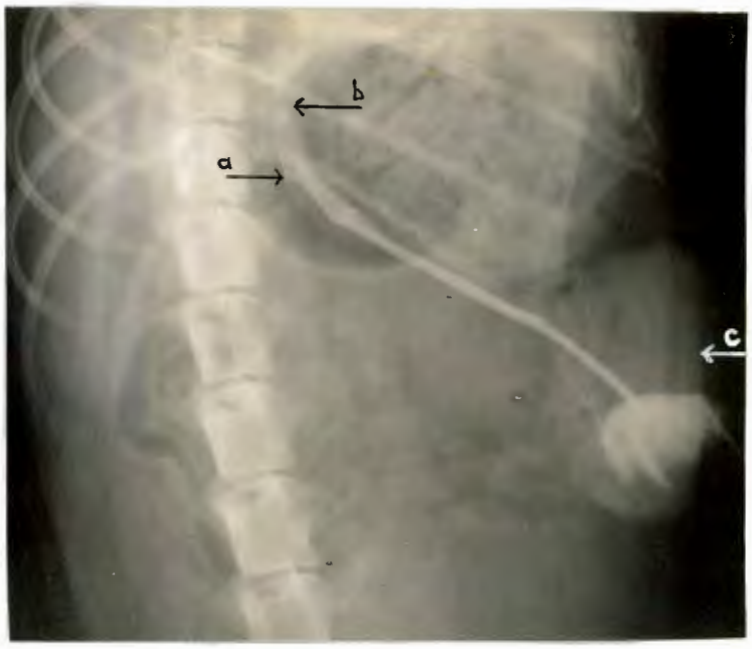


Fig.17 (a) (Experiment D 1 - Dog 11)
Radiograph taken 0.5 second after the injection of diodone into the spleen was started

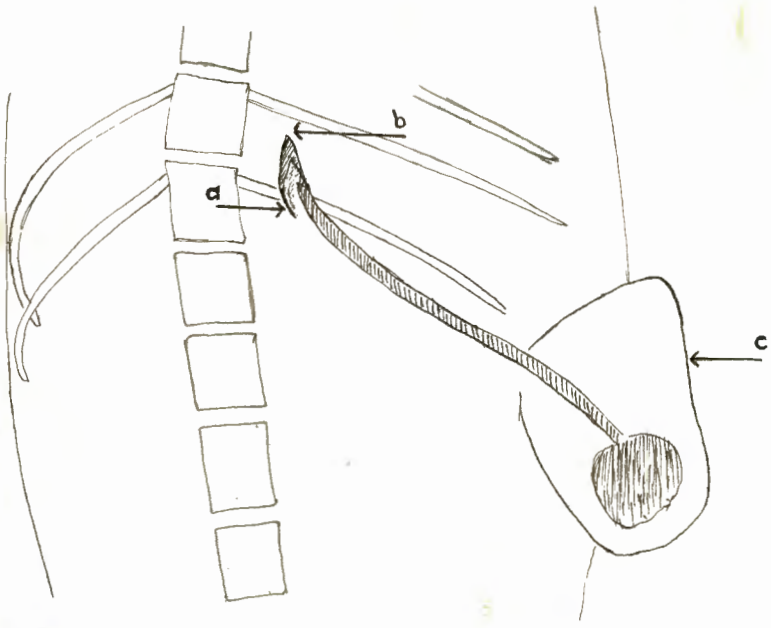


Fig.17 (b) Diagram of original venogram shown in fig.17(a)

These figures demonstrate:

(1) The rapid flow of diodone in the splenic vein

(2) The filling defect at the entrance of the superior mesenteric vein (arrow a) (arrow b points to the apex of the dye in the portal vein and arrow c to the exteriorized spleen).

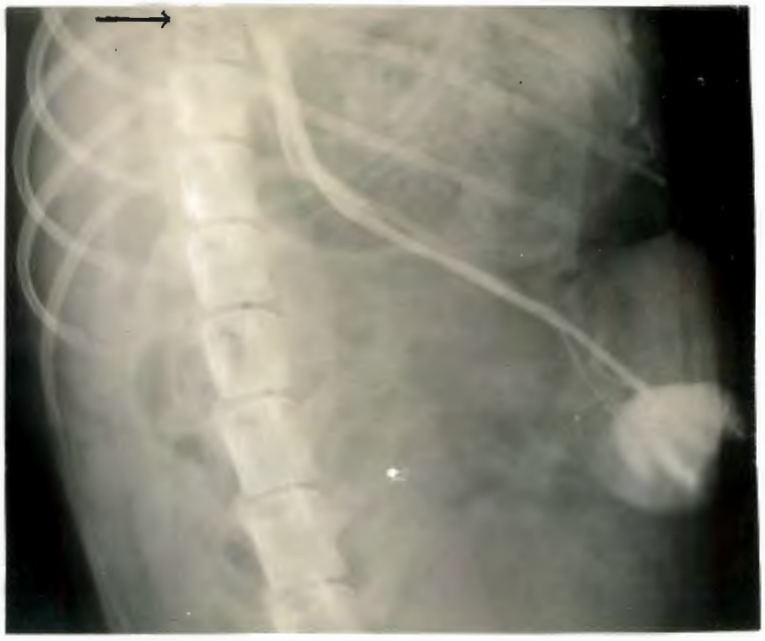


Fig. 18 (Experiment D 1 - Dog 11)

Radiograph taken 0.5 second after fig.17(a) The dye fills the larger portal branches in the liver (arrow)

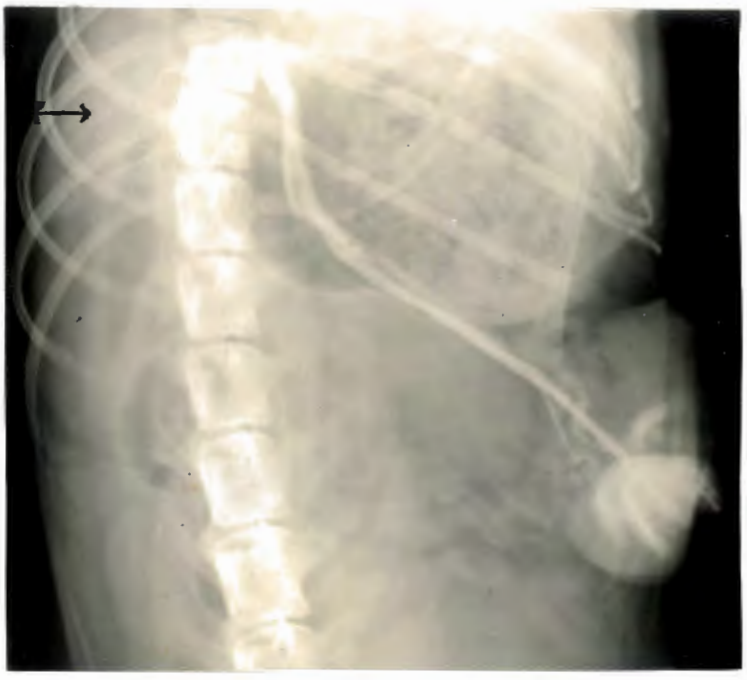


Fig.19 (Experiment D 1 - Dog 11)

Radiograph taken one second after fig. 18, The dye now fills the small intrahepatic portal branches (arrow)

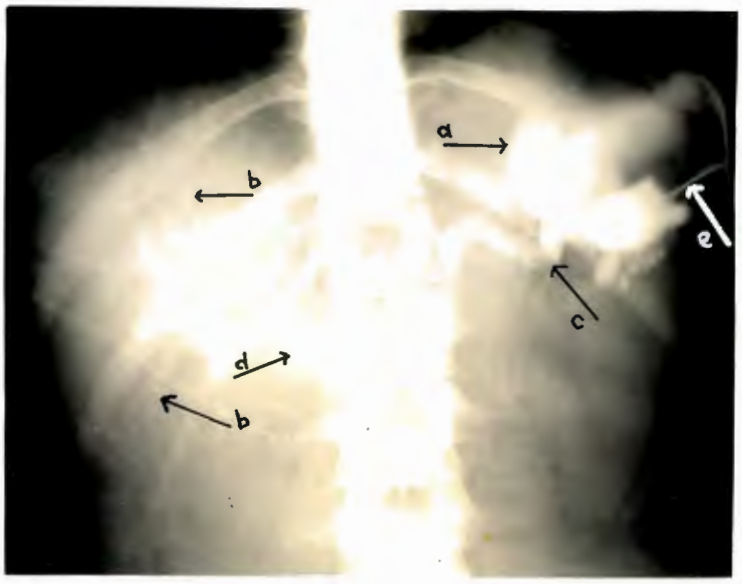


Fig. 20 (Experiment 20 - Patient Xll)

Radiograph taken after injecting 20 cc. 50% diodone into the spleen. The opacity above the spleen (arrow a) is an area of calcification. The portal branches in the liver are shown (arrows b) and the dye is diluted at the hilum of the spleen (arrow c). (Arrows d and e point to the portal vein and the needle in the spleen respectively)

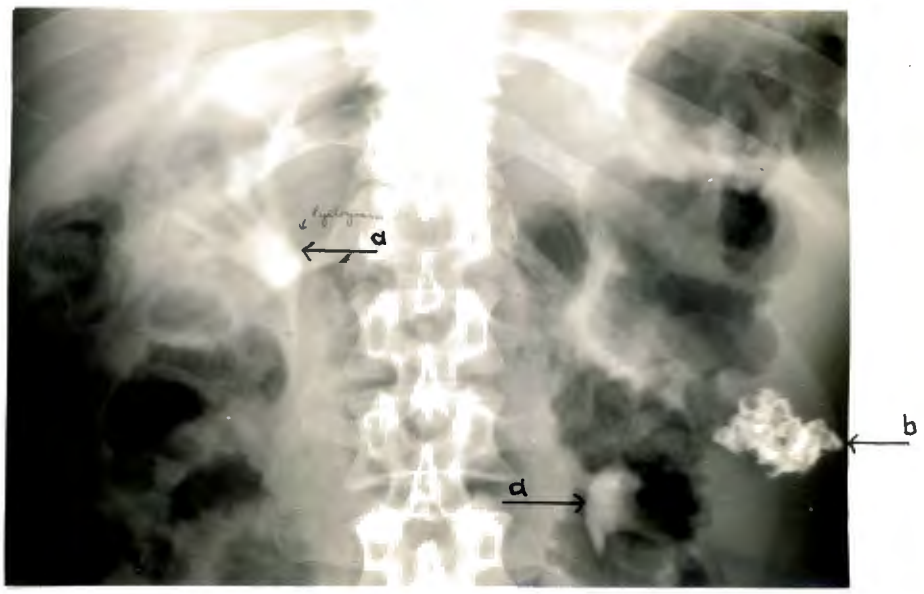


Fig. 21 (Experiment H 10 - Patient V11)

Radiograph taken ten minutes after a portal venogram had been done.
Note: (1) The pyelograms obtained (arrows a)
(2) The honeycombed appearance of the dye that has remained in the spleen (arrow b)

Fig. 22 (Experiment H 15 - Patient X1)

Radiograph taken one second after the injection of diodone in the spleen was started. The arrow points to the apex of the dye in the splenic vein.

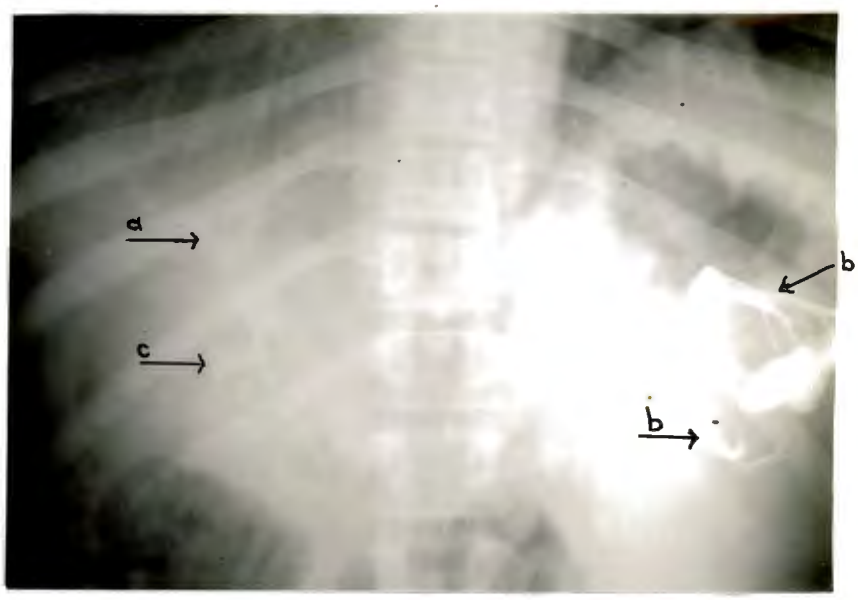


Fig. 23(a) (Experiment H 15 - Patient X1)
Radiograph taken one second after fig.22

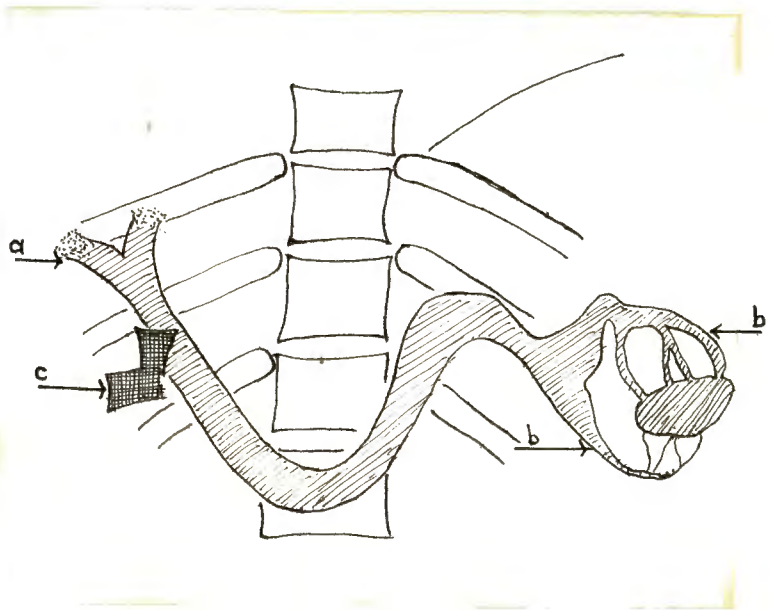


Fig. 23 (b) Diagram of original venogram shown in fig.23(a)
Note in both figures:
(1) The apex of the dye in the portal vein (arrow a). When compared with fig.22 the rapid rate of blood flow in the portal system is demonstrated.
(2) The diodone leaves the spleen by four "compartmental" veins (arrows b)
(3) A pyelogram is obtained on the right side (arrow c). This is the result of a venogram done 15 minutes earlier.

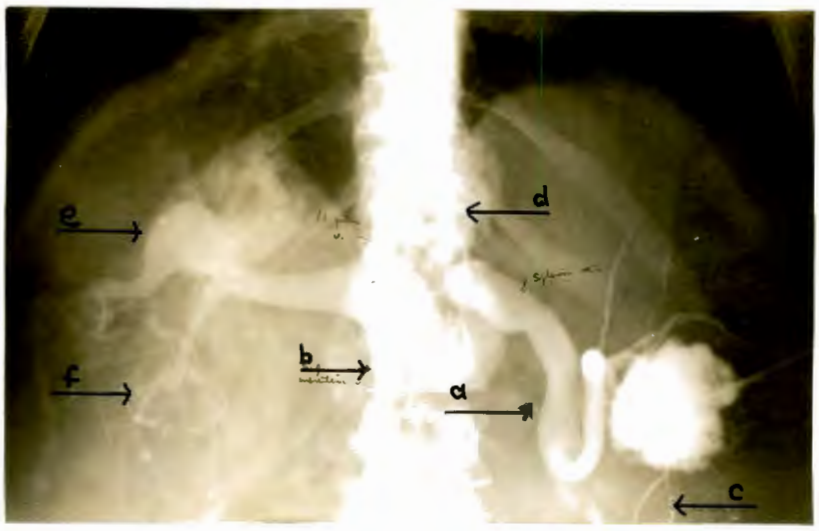


Fig. 24 (a) (Experiment H 13 - Patient IX)
Radiograph taken after injecting 20 cc diodone into the spleen.

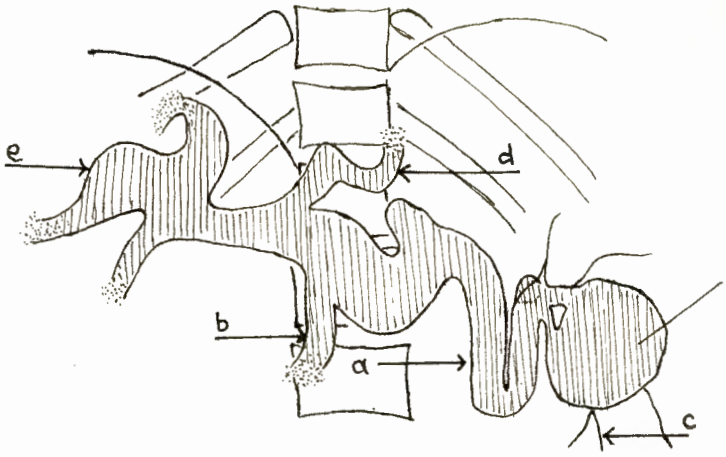


Fig. 24 (b) Diagram of original venogram shown in fig.24(a)

Note in these figures:
(1) The large tortuous splenic vein (arrow a)
(2) The reflux of dye into the superior mesenteric vein (arrow b)
(3) The collateral veins round the spleen (arrow c)
(4) The dye in the left gastric vein (arrow d)
(5) The dilated portal vein (arrow e)
(6) The coarse pattern of the portal branches in the liver (arrow f).

These features suggest the presence of portal hypertension, secondary to cirrhosis.

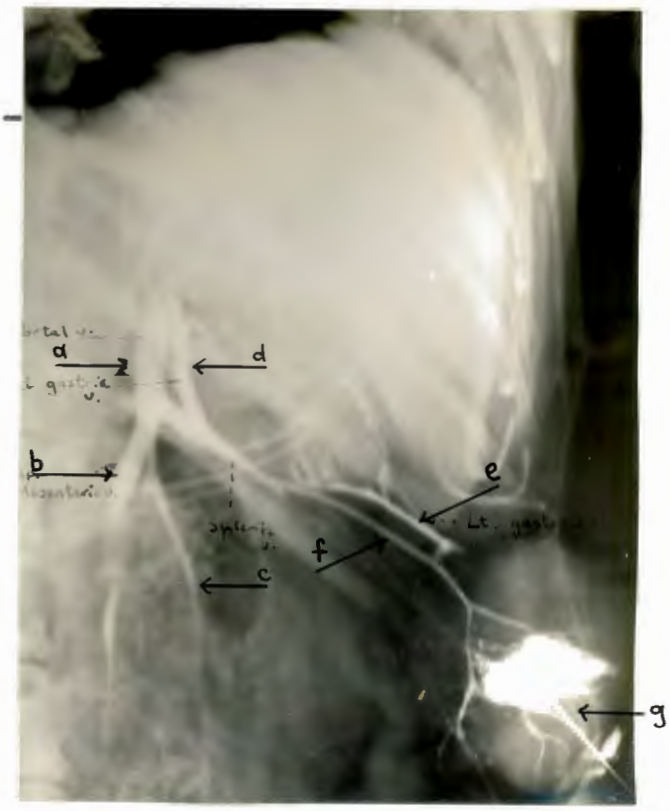


Fig. 25(a) (Experiment D 4 Dog 11)

Radiograph of Portal Venogram done at death.

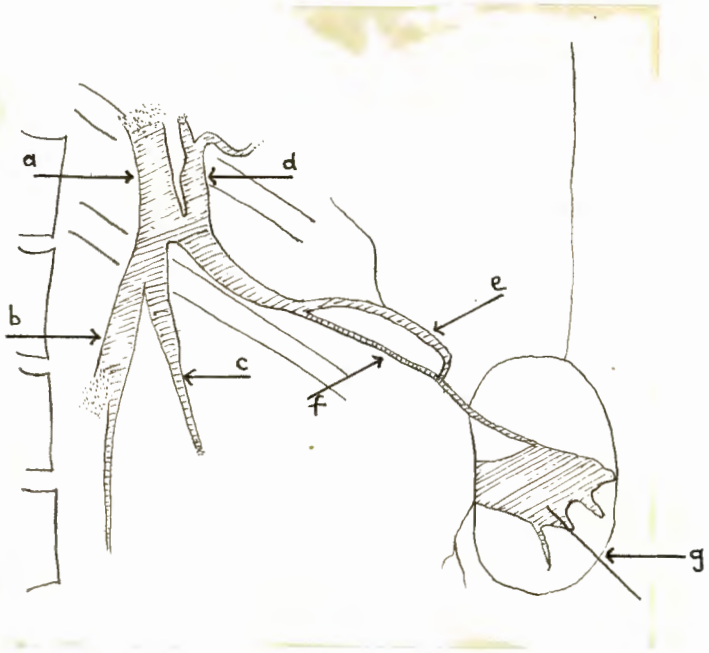


Fig. 25(b)

Diagram of original venogram shown in fig.25 (a)

These figures demonstrate the tributaries of the portal vein, filled with dye (a: portal vein; b:superior mesenteric vein; c: inferior mesenteric vein; d: left gastric vein; e: left gastro-epiploic vein).
Note also the marked spasm of the splenic vein that has occurred at death (arrow f). (Arrow g points to the exteriorized spleen with the needle in situ)

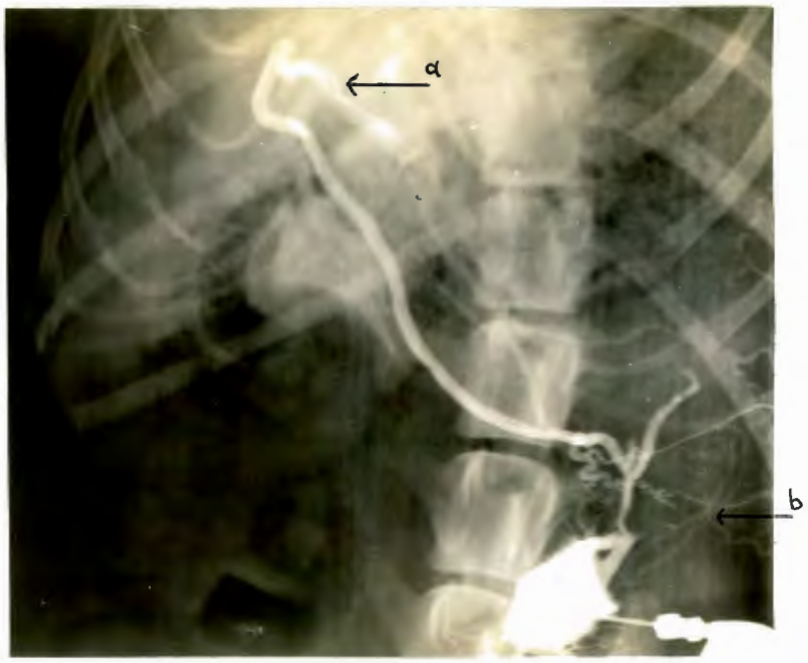


Fig. 26 (Experiment D 12 - Dog VIII)

Radiograph taken while injecting diodone into the spleen. Arrow a points to the dye in the portal vein and arrow b to the collateral circulation that has developed round the subcutaneous spleen.

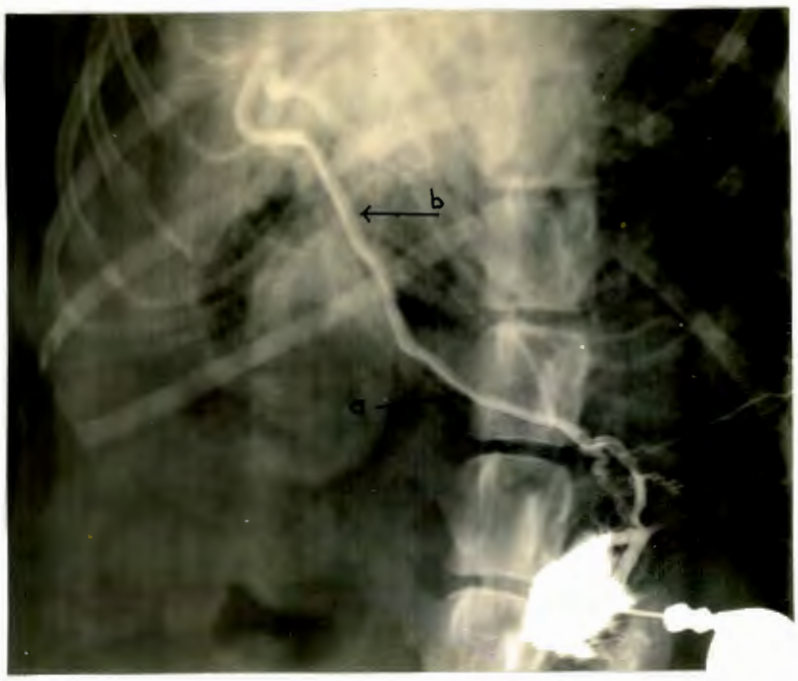


Fig. 27 (Experiment D 12 - Dog VIII)

Radiograph taken a few seconds after fig. 26
It shows (1) A mild degree of spasm of the splenic vein (arrow a - compare with fig. 26)

(2) More dye flows along the right border of the portal vein (arrow b); it is probably displaced by the flow from the left gastric vein.

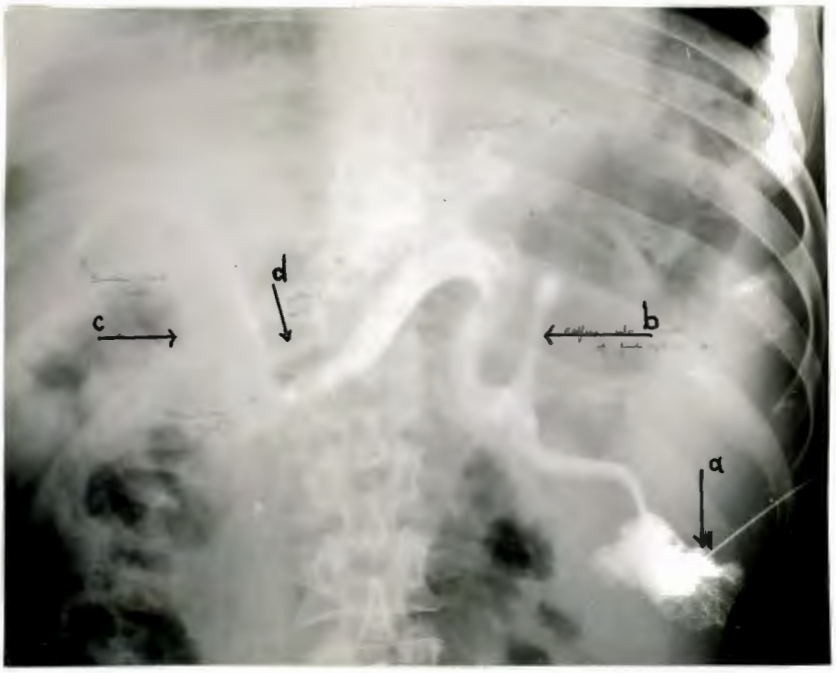


Fig. 28 (a) (Experiment H 10 - Patient V11)

Radiograph obtained after injecting 20 cc 70% diodone into the spleen

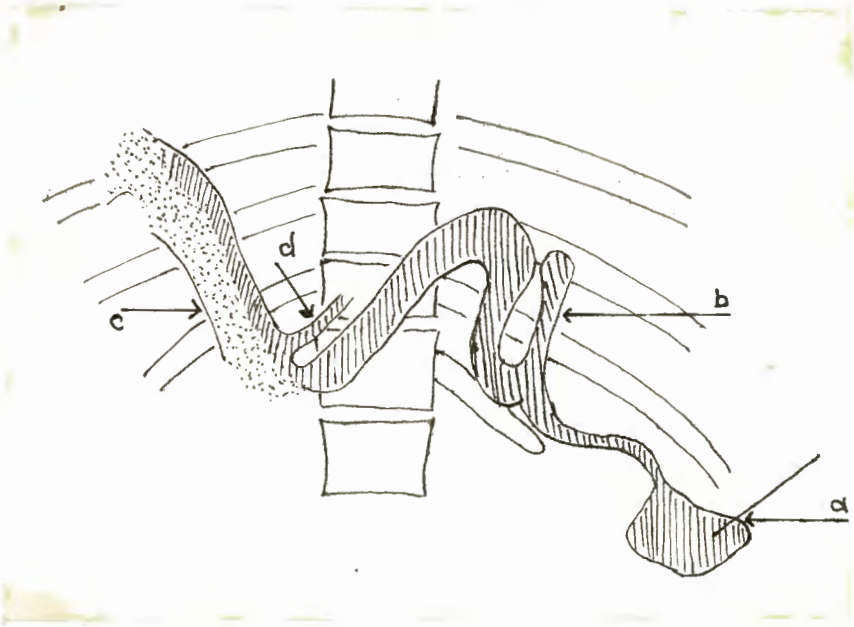


Fig. 28 (b) Diagram of original venogram shown in fig 28(a)

Note in both figures:

(1) The dye and needle in the spleen (arrow a)
(2) The reflux of dye into a large tributary of the splenic vein (arrow b)
(3) The "streamlining" of the dye in the dilated portal vein (arrow c).
(4) The dye in the left gastric vein (arrow d) indicative of the presence of portal obstruction.

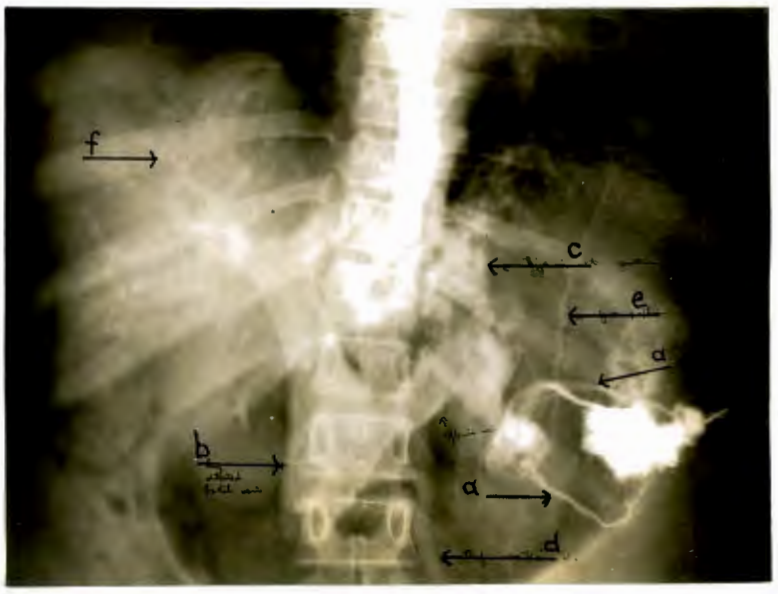


Fig. 29 (Experiment H 12 - Patient VIII)

Radiograph obtained on injecting 70% diodone into the spleen of a patient with cirrhosis of the liver.

It shows:

(1) The diodone leaving the spleen by three segmental veins (arrows a)

(2) A dilated portal vein (arrow b)

(3) The presence of dye in the veins round the cardiac end of the stomach (arrow c), in the inferior mesenteric (arrow d) and in the left gastro-epiploic vein (arrow e)

(4) The coarse pattern of the intrahepatic portal branches (arrow f)

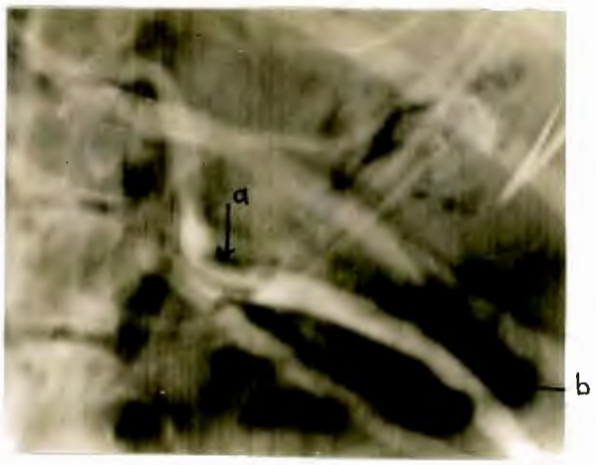


Fig. 30 (a) (Experiment D 6 - Dog 1V)
Radiograph taken on injecting 5 cc 50% diodone into spleen.

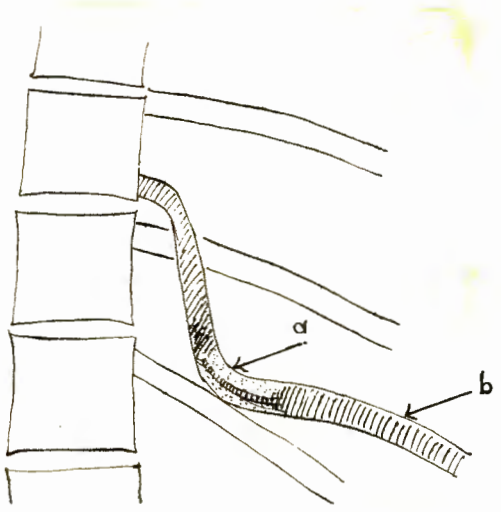


Fig. 30 (b) Diagram of original venogram shown in fig.30(a)

These figures show that the diodone has been forced to occupy a central stream in the portal vein (arrow a) by the incoming blood from the left gastric vein above and the superior mesenteric vein below. These three streams, however, soon become mixed.
(Arrow b points to the splenic vein)

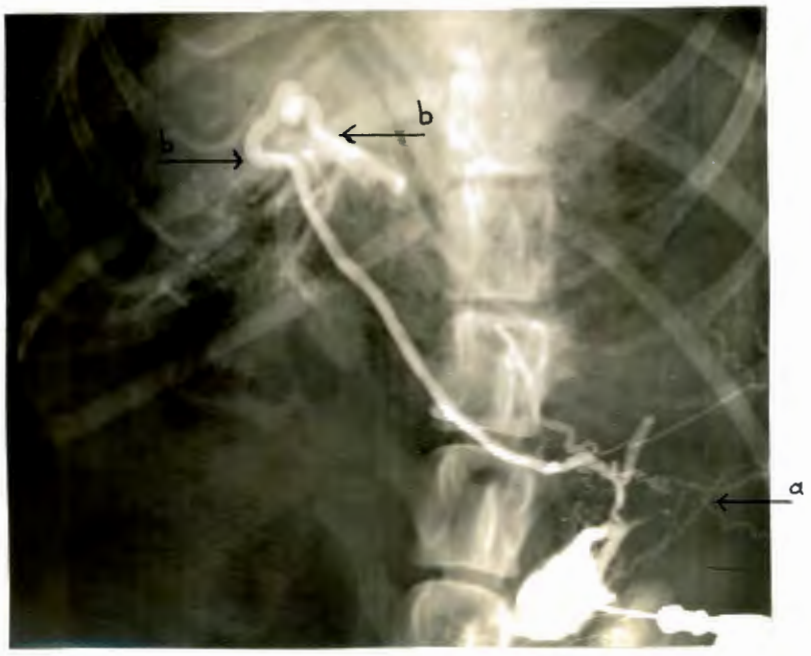


Fig. 31 (Experiment D 12 - Dog VIII)
(See also figs. 26 and 27)

Radiograph obtained on injecting 70% diodone into a subcutaneous spleen of a dog. It demonstrates that the subcutaneous spleen retains its normal venous drainage by the splenic vein; however, a collateral circulation also forms round the spleen (arrow a). (Arrows b point to the portal vein)

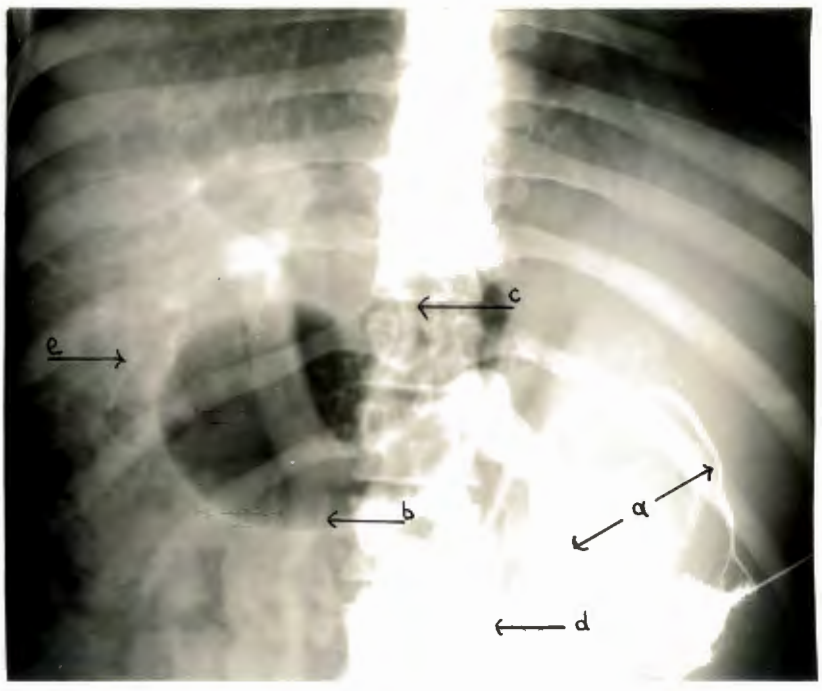


Fig. 32 (a) (Experiment H 9 - Patient V)
Radiograph taken after injecting 70% diodone into the spleen

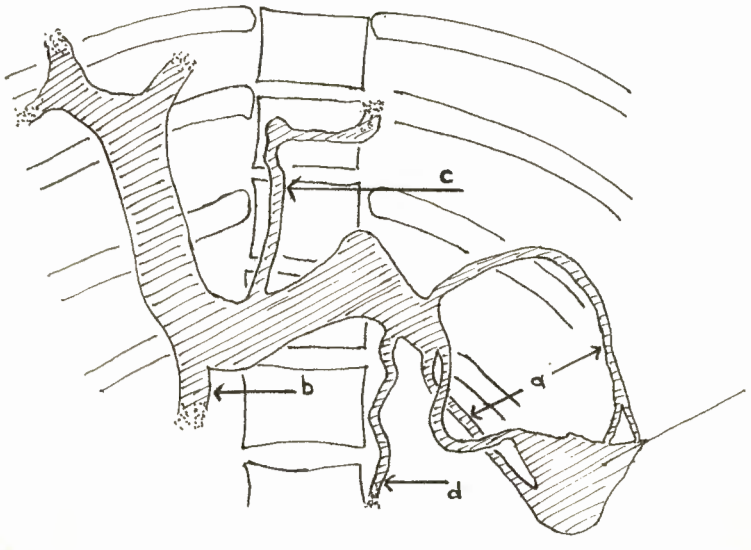


Fig. 32 (b) Diagram of original venogram shown in fig.32(a)

Note in both figures:

(1) The dye leaves the spleen by more than one vein (arrows a)
(2) The reflux of dye into the superior mesenteric vein (arrow b) suggests the presence of portal obstruction
(3) Collateral veins are shown: arrow c points to the left gastric and arrow d to the inferior mesenteric vein
(4) The intrahepatic portal branches are coarse (arrow e).

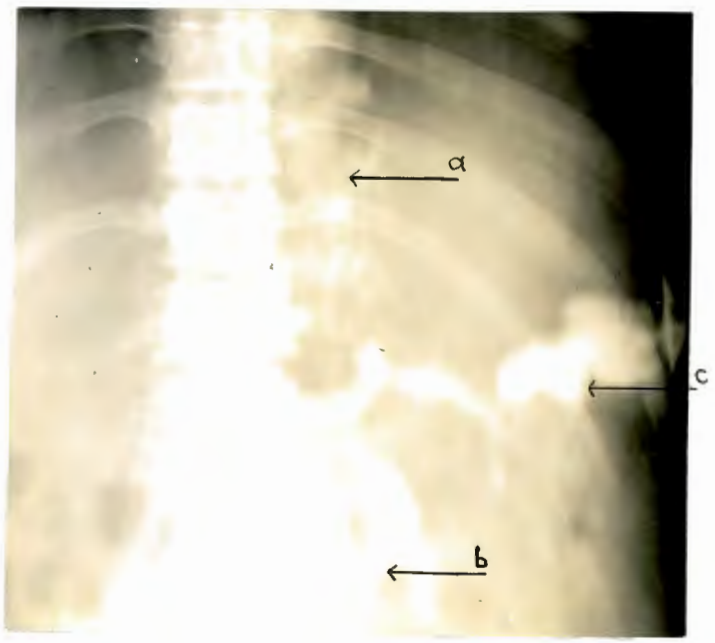


Fig. 33 (a) (Experiment H 4 - Patient 111)

Radiograph taken after injecting 15 cc 70% diodone into the spleen

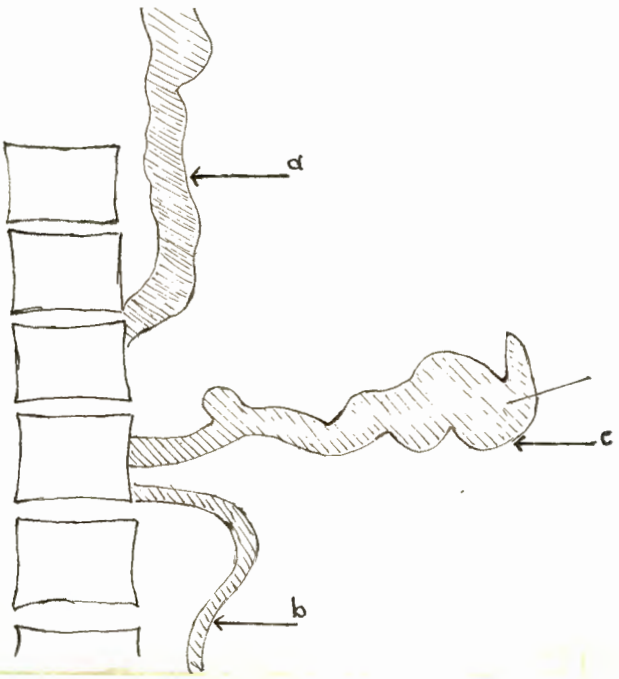


Fig. 33 (b) Diagram of original venogram shown in fig.33(b)

These figures show:

(1) A big dilated left gastric vein (arrow a)
(2) The inferior mesenteric vein (arrow b)
(3) The absence of dye in the portal vein.

These features suggest that severe portal obstruction is present.

(Arrow c points to the dye in the spleen)

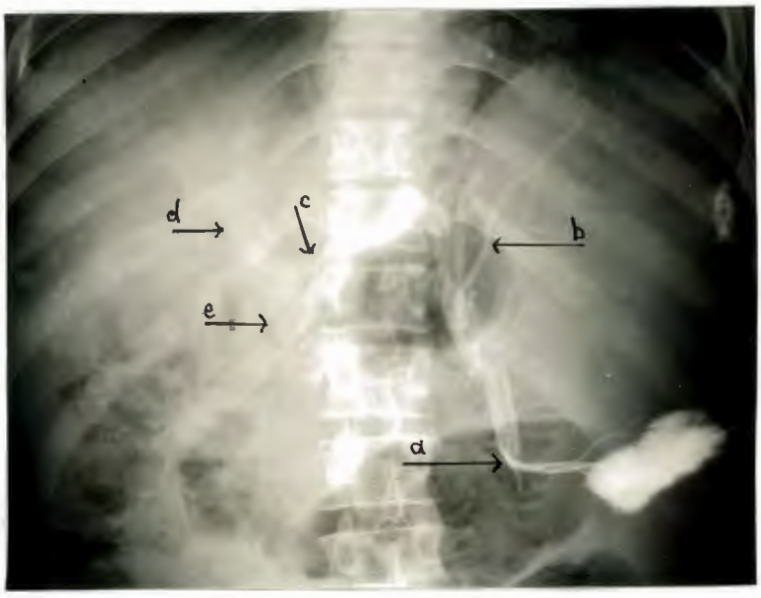


Fig. 34 (a) (Experiment H 8 - Patient V1)

Radiograph showing the presence of obstruction to the flow of diodone in the splenic vein.

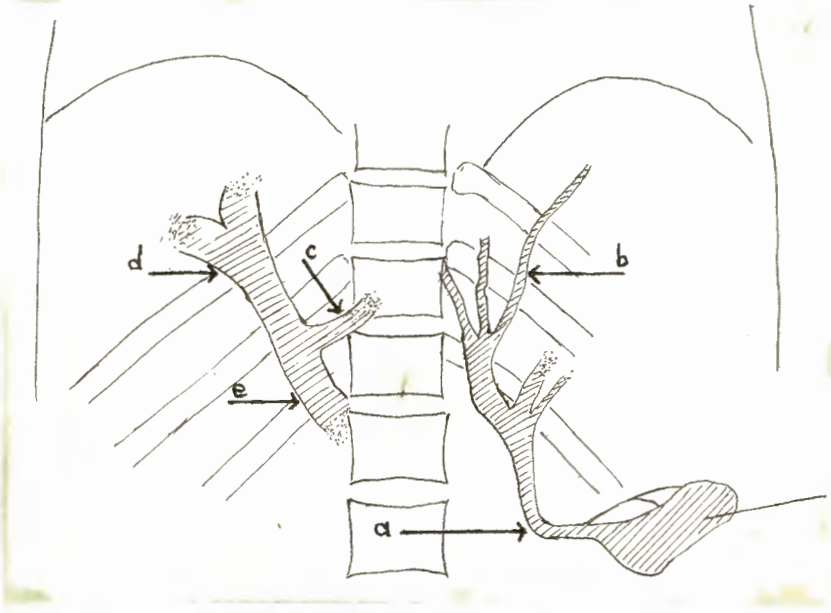


Fig. 34 (b) Diagram of original venogram shown in fig.34(a)

These figures show the presence of a block in the splenic vein (arrow a); the dye flows along the left gastro-epiploic and short gastric veins (arrow b), to the left gastric (arrow c) and thus to the portal vein (arrow d). (Arrow e points to a reflux of dye into the peripheral part of the portal vein).

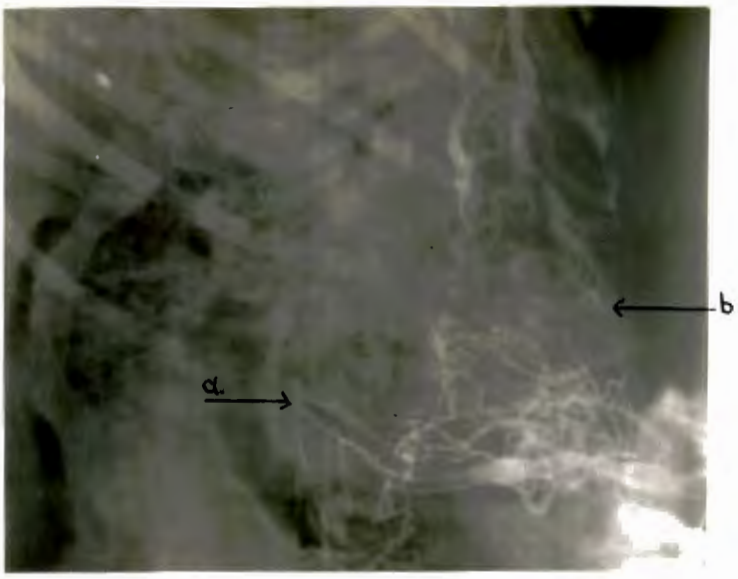


Fig. 35 (Experiment D 11 - Dog V)

Radiograph obtained on injecting diodone into the spleen after a portacaval anastomosis had been done. The anastomosis has become thrombosed (arrow a) and a marked collateral circulation has developed round the spleen (arrow b).

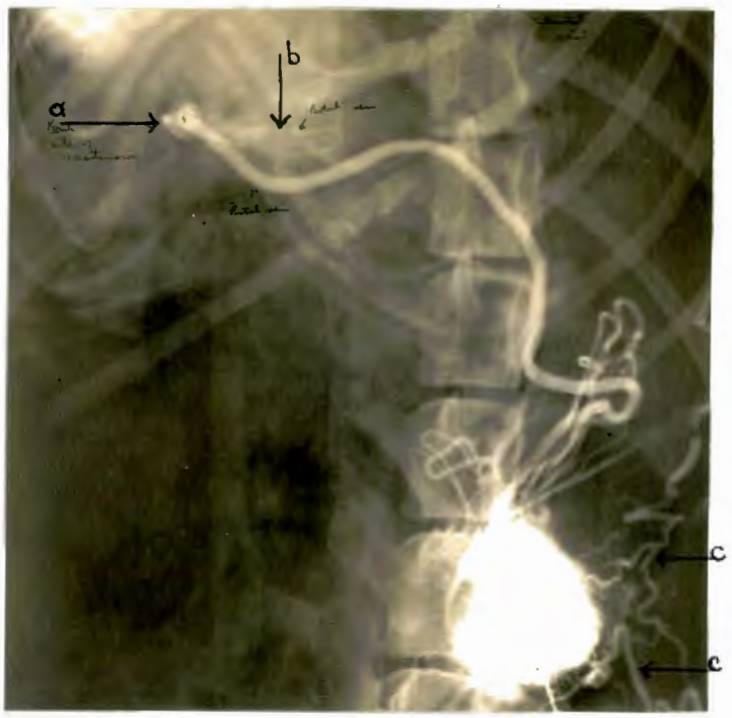


Fig. 36 (Experiment D14 - Dog VIII)

Radiograph obtained on injecting diodone into the spleen after a hepato-portal anastomosis had been done.
Note:(1) The kink in the portal vein at the site of the anastomosis (arrow a)
(2) The dilution of the dye in the portal vein (arrow b)
(3) The collateral circulation that has formed round the spleen (arrows c)

Fig. 37 (Experiment D 9 - Dog V)

Radiograph obtained after injecting 70% diodone into a subcutaneous spleen, four weeks after the portal vein had been ligated. It demonstrates:

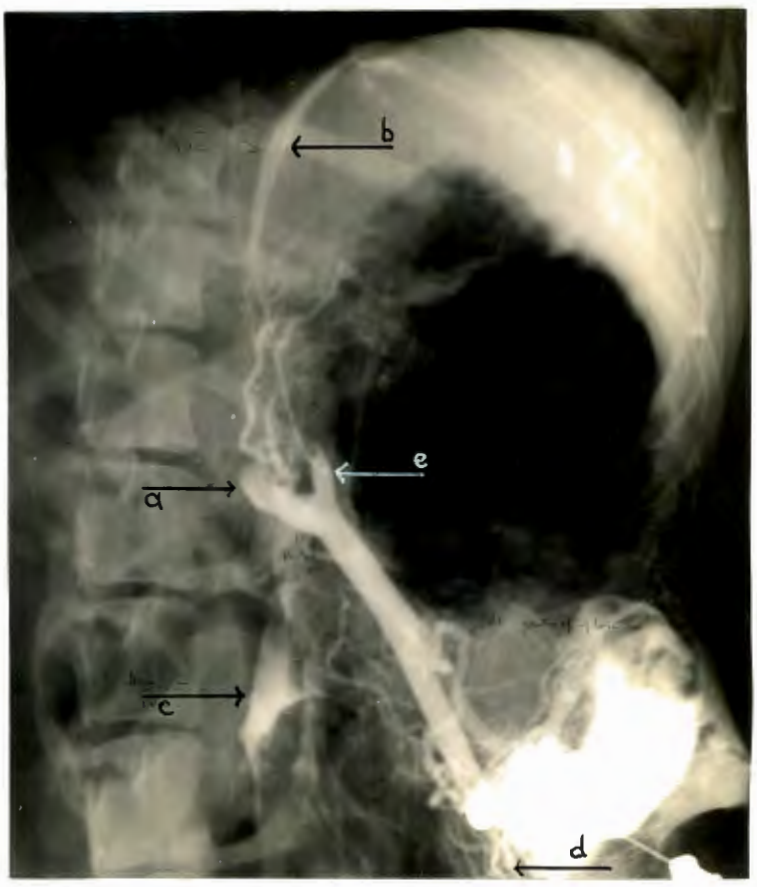
(1) The block in the portal vein (arrow a)

(2) The collateral circulation round the block (arrows b)

(3) The extensive collateral circulation round the spleen (arrow c)

(Arrows d and e point to the left gastric and splenic veins, respectively).

Fig.38
(Experiment D 15 - Dog V11)



Portal venogram obtained after a portacaval anastomosis. Arrow a points to the site of the anastomosis and arrows b and c point to the dye in the inferior vena cava. The dye flows along the left anterior border of the upper part of the vena cava (arrow b). The collateral circulation round the spleen (arrow d) has resulted from its subcutaneous position. Note the dye in the left gastric vein (arrow e)

Fig.39
(Experiment H 8 - Patient V1)

Radiograph taken ten minutes after a portal venogram had been done. The arrow points to the dye that remains in the spleen. It has a honeycombed appearance.

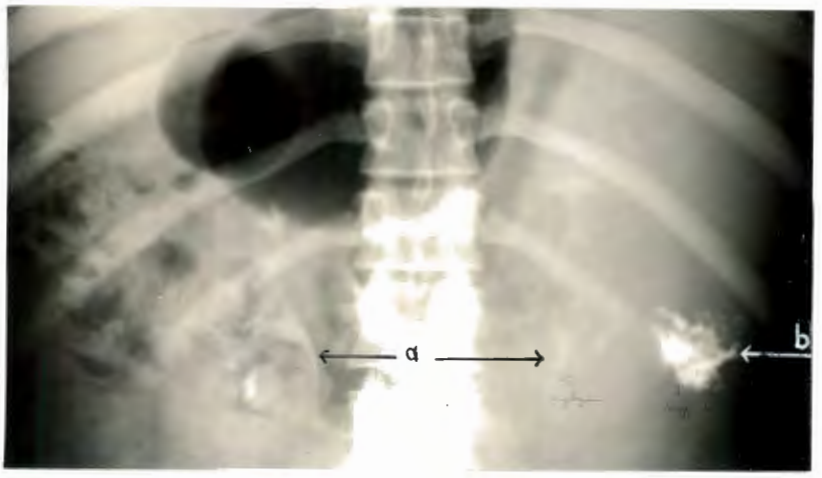
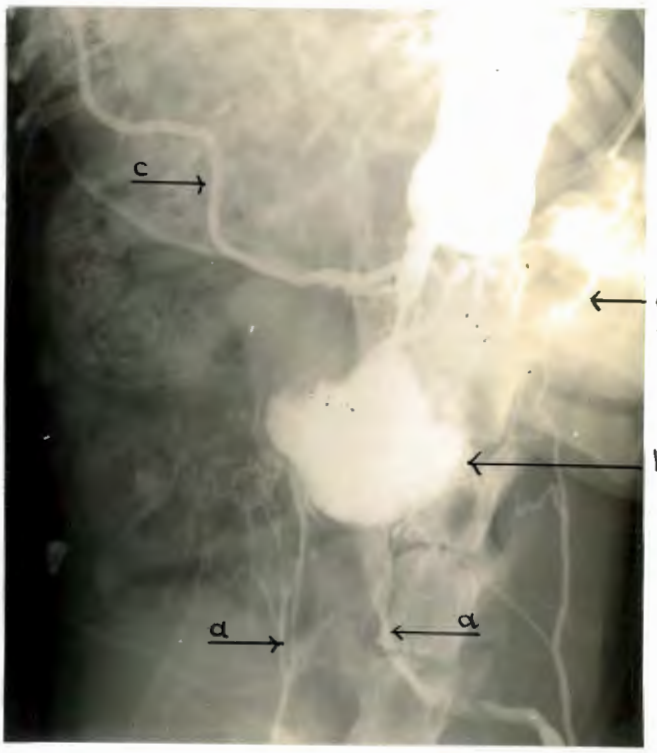


Fig. 40 (Experiment H 9 - Patient V)

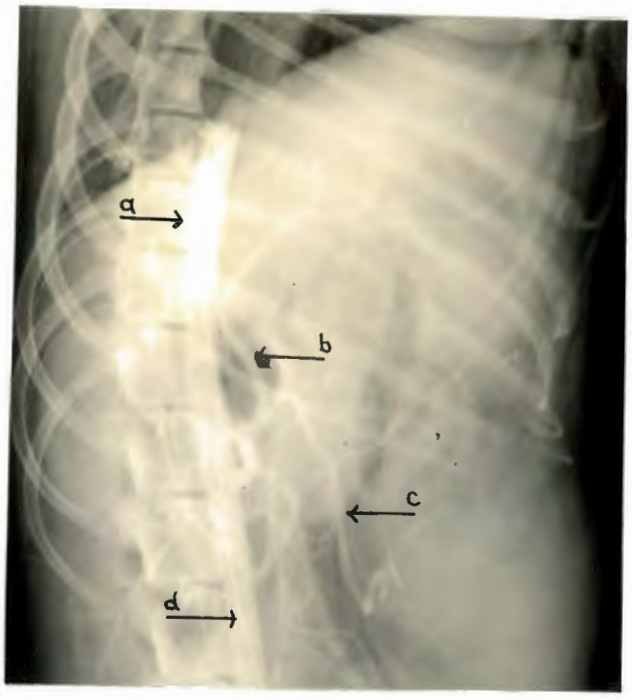
Radiograph taken ten minutes after a portal venogram had been done. It shows a bilateral pyelogram (arrows a) and the dye remaining in the connective tissue of the splenic pulp (arrow b)

Fig. 41 (Experiment D 17 - Dog VIII)



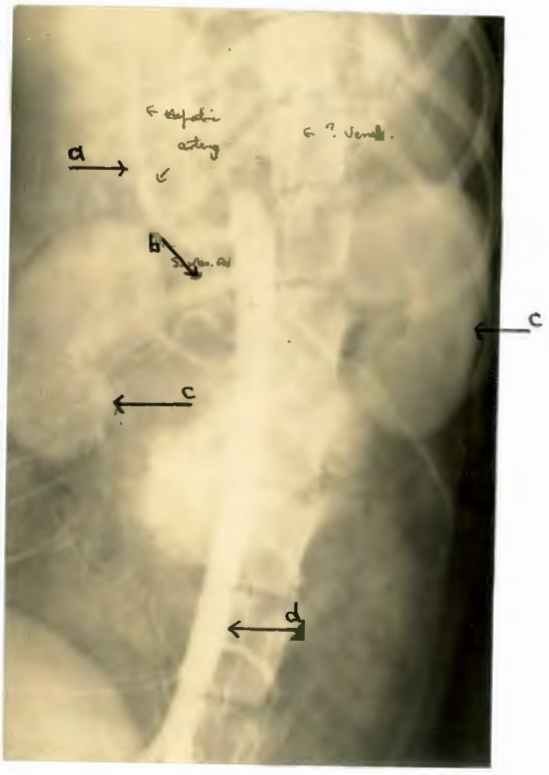
Portal venogram eight months after hepato-portal anastomosis had been done in a dog with a subcutaneous spleen. It shows a marked collateral circulation round the spleen (arrows a) (Arrow b points to the dye in the spleen and arrow c to the splenic vein).

Fig.42
(Dog V11)



Radiograph taken on injecting 20 cc 70% diodone into the aorta through a polythene catheter. It shows the aorta (arrow a), and the hepatic and splenic arteries (arrows b and c respectively). The hepatic branches in the liver were not visible. (Arrow d points to the catheter in the aorta).

Fig 43
(Dog V111)



Radiograph obtained on injecting 20 cc 70% diodone into the aorta. The branches of the aorta are shown but not the intrahepatic arterial branches (Arrow a; hepatic artery; b: superior mesenteric artery; c: kidneys; d: aorta).

GROUP C - OBSERVATIONS ON THE PORTAL PRESSURE IN DOGS

In addition to the observations on the intra-splenic injection of a radio-opaque dye, the blood pressure in the portal vein of the dog was investigated.

Material and Methods

Experiments were done on six adult dogs. They were anaesthetized with intravenous pentothal, intratracheal ether and oxygen. In the supine position a laparotomy was done through a midline or left subcostal incision. In three dogs the portal vein was exposed and a needle, connected with a glass manometer containing a solution of 3.8% sodium citrate, was inserted into it. In the other three the manometer was attached to a number 2 polythene catheter, which was inserted and tied into a branch of the splenic vein. The tip of the catheter lay just inside the portal vein.

The pressures in the portal vein under various experimental conditions were taken (Table XX, Page 111). All pressures were read with the level of the hepatic pedicle as the zero-point. The portal pressure and the effects of occluding various vessels were noted. The hepatic artery and portal vein were occluded in the right free border of the lesser omentum. The portal vein was clamped on the peripheral side of the needle (or catheter) as well as at the hilum of the liver. The inferior vena cava was compressed immediately above the liver by inserting a hand under the diaphragm. The portal pressure under these conditions was registered. Twenty cc saline was

../rapidly injected

rapidly injected into the splenic pulp while observing the pressure. Thereafter the needle was removed from the portal vein and haemorrhage stopped by local pressure. When a polythene catheter was used, the branch of the splenic vein was tied after its removal. The abdomen was then closed.

Severe haemorrhage occurred during the dissection of the portal vein in dogs 9 and 10. It was much easier to measure the pressure by means of the polythene catheter inserted through the splenic vein.

Results

These are summarized in Table XX (Page 111). All the pressures were measured in centimetres of 3.8% sodium citrate solution. It will be noticed that when the pressure dropped from a high level, it did so during expiration, remaining stationary during inspiration. The drop with each expiration was 0.5 to 1.0 cm. sodium citrate.

The pressure rose slowly on central occlusion of the portal vein and on occluding the inferior vena cava, taking one to two minutes to reach its maximum.

No. of Dog	Normal Pressure	On peripheral occlusion of portal vein.	On central occlusion of portal vein	On occlusion of the hepatic artery	On occlusion of the Inferior Vena Cava above the liver	On injecting 20 cc saline into spleen	Remarks
9	11.0	Not measured	60* +	11.0	29.0	11.0	Manometer connected to needle in portal vein. The same method used in measuring the pressure in dogs 10 and 12
10	10.0	3.0	61* +	10.5	27.0	10.0	On release of central portal occlusion the pressure dropped 1 cm. with each expiration (remaining stationary with inspiration) to normal level.
12	11.0 (11.0)**	5.0	66.0	9.0	35.0	11.0	1) Pressure in portal vein on occluding I.V.C. + hepatic artery: 37 2) Normal pressure in I.V.C. : 7.0 3) Pressure in I.V.C. on occluding it above the liver : 29
13	11.0 (12.0)***	5.0	70.0	13.0	31.0	12.0	1) Manometer attached to polythene catheter. Same method in dogs 14 and 15 2) Pressure on occluding I.V.C. + hepatic artery artery : 31
14	12.5 (13.0)***	11.5	64.0	10.0	22.0	12.5	1) Pressure on peripheral occlusion of portal vein+ hepatic artery occlusion : 11.5 2) On release of central portal occlusion the pressure dropped 0.5 cm with each expiration (remaining stationary with inspiration) to normal level.
15	12.0 (13.0)***	10.5	90* +	11.5	25.5	13.0	1) On release of central portal occlusion the pressure dropped 0.5 cm. with each expiration (remaining stationary with inspiration) to normal level 2) Normal pressure in I.V.C : 5.0 3) Pressure in I.V.C. on occluding it above the liver : 19.0

* The manometer could not register a higher pressure.

** The pressure was again measured at the end of the experiment, but in the splenic vein.

*** The pressure was again measured at the end of the experiment, in the portal vein.

TABLE XX : BLOOD PRESSURES IN THE PORTAL VEIN IN CM. 3.8% SODIUM CITRATE SOLUTION

D I S C U S S I O N

CHAPTER V : The Portal Venogram

CHAPTER Vl: The Portal Pressure

CHAPTER Vll: The Blood Flow through the Spleen

CHAPTER Vlll: The Hepatic Circulation and Future Work.

C H A P T E R V

D I S C U S S I O N

THE PORTAL VENOGRAM AS A METHOD OF INVESTIGATING THE PORTAL CIRCULATION.

The first portal venogram in man was done by Whipple (1945). He injected diodone into a tributary of the portal vein in patients suffering from portal hypertension, to determine the site of obstruction at operation. During the last few years his method has been used on humans with normal portal circulations, and on others with portal hypertension (Child et al, 1951; Durand et al, 1950; Leger et al, 1951a; Santy and Marion, 1951; Moore and Bridenbaugh, 1950).

Franklin and Janker (1937) employed the portal venogram to study the effect of respiration on the hepatic outflow of blood. They injected thorotrast into the splenic and superior mesenteric veins of dogs and cats, and took serial X-ray photographs with a cine-camera. The vessels of the portal system became tortuous on inspiration and there was a backflow of blood from the inferior vena cava into the hepatic veins on expiration. Recently, Daniel and his co-workers (1951 a and b; 1952 a and b) have reported a series of observations on rats and other animals. They injected thorotrast into a tributary of the portal vein and studied the portal and hepatic venous circulations radiologically by serial X-ray photographs. Although the portal pressure remained unchanged, the authors mentioned that their method might disturb the mechanics in the portal system. The portal venograms mentioned

../above have

above have all been obtained by injecting the dye into a branch of the portal system, either directly or through a polythene catheter. A laparotomy under general anaesthesia has been necessary.

In 1948 Glynn and his colleagues injected India ink into the spleen of dogs and noticed that the ink was carried to the liver where it stained the sinusoids. In 1951 Malventi injected a radio-opaque dye into the spleen of rabbits, guinea pigs and dogs. By means of radiographs he studied the appearance of the dye in the spleen. In the same year Abeatici and Campi (1951) reported the radiological visualization of the portal system on injecting 6 to 9 cc 70% diodone into the spleen of dogs. The diodone flowed into the splenic and portal veins, demonstrating them radiologically. This method was applied to humans by Leger and his co-workers (1951 b), who injected the spleen at laparotomy as well as through an intact abdominal wall.

By studying the portal venograms reported in this thesis, observations of physiological importance have been made. These will now be discussed.

1. THE VELOCITY OF BLOOD FLOW IN THE PORTAL VEIN

It can be assumed that the rate at which the dye flows in the splenic and portal veins indicate the velocity of blood flow in them. This rate, which appears to be the same in both veins, is fast in dogs and man. (fig.17-19). The distance from the spleen to the hilum of the liver varies from 15 to 25 cm. in man, and averages 15 cm. in dogs. As the dye reaches the liver hilum about one second

../after its

after its administration into the spleen, the rate of blood flow in the splenic and portal veins must be 15 to 25 cm. per second, in both man and dog. This figure does not correspond to the results of Burton-Opitz (1909) and Abeatici and Campi (1951). The former author, by using Ludwig's stromuhr, estimated that the rate of flow in the splenic vein of dogs was 4.3 cm. per second. The latter authors only noticed the dye in the portal vein 3 to 4 seconds after it had been injected into the spleen. However, the stromuhr is not an accurate instrument to measure the rate of blood flow in a vessel, and the observations of Abeatici and Campi were made on only two animals. The fast rate recorded in this thesis has been a constant finding.

How rapid the velocity of the blood in the portal vein is (15 - 25 cm. per second), is shown when it is compared with the velocity in the femoral vein (6 cm. per second, Fulton, 1946) or in the carotid artery (30 to 50 cm. per second, Fulton, 1946; Evans 1941). Contraction of the spleen may increase the rate of blood flow in the splenic and portal veins; but the enlarged and palpable human spleen does not contract when the dye is injected; nor does the exteriorized spleen of the dog, although capable of contracting, show any recognisable decrease in size when injected.

The pressure in the portal vein of the dog averages 12 cm. water and that in the hepatic veins 6 cm., giving a pressure gradient of 6 cm. water in the liver. This, although small, appears to be the only factor which controls the rapid rate of flow in the portal vein.

../The inflow

The inflow of blood into the portal system can influence the velocity of flow only by raising the portal pressure. It has been noted that when the volume flow in the portal vein is increased enormously, the portal pressure is only slightly raised. It can, therefore, be concluded that the rate of blood flow in the portal system has, for practical purposes, no relation to the volume flow. The fast rate can only be explained by a very low resistance offered by the hepatic sinusoids. The portal venules open directly into the sinusoids and they are much wider than capillaries (Gray, 1942).

In the presence of cirrhosis the hepatic resistance to the the portal flow is raised. The rate of blood flow remains approximately the same (figs.22 and 23), as the associated increase in portal pressure raises the pressure gradient in the liver. The latter may reach 45 cm. water. In the presence of portal hypertension, blood is shunted into collateral channels and the flow to the liver is diminished. Notwithstanding the reduced flow in the portal vein, the velocity of blood remains the same.

2. THE VOLUME OF BLOOD FLOW IN THE PORTAL SYSTEM

A survey of the literature showed that the volume flow in the portal vein varies from 200 to 375 cc. per minute in dogs. The total hepatic flow in man is 800 cc. per minute per square metre body surface, or 1440 cc. per minute in the average adult (Bearn et al, 1951). As the portal vein supplies 60 to 85% of this amount, the volume flow in the portal vein of adult man is 860 to 1220 cc per minute or about 1 litre per minute.

../The degree

The degree of dilution of the dye in the portal venogram indicates the relative amounts of blood flowing in the tributaries of the portal system. Very little dilution takes place in the splenic vein (figs. 13 and 16), as the volume of blood entering it through the left gastro-epiploic, short gastric and pancreatic veins, is small compared with the flow from the spleen. When the dye reaches the superior mesenteric vein it is immediately diluted (figs. 13 and 16). Therefore, a greater amount of blood flows in the superior mesenteric than in the other branches which enter the splenic vein. This is borne out by the anatomical sizes of these veins. The left gastric vein may open into the portal instead of into the splenic vein. The dilution of diodone in the portal vein will then be due to the combined flows in the superior mesenteric and left gastric veins. The density of the dye depends on its concentration and on the "softness" of the X-ray photograph. The former depends on the speed of injection and on the amount of diodone given. However, it is the relative density in the vessels that is important.

It has been observed that the diodone shows a "bolus effect" and that its apex is visible fluoroscopically. It must, therefore, leave the spleen in large quantities. This is not due to contraction of the spleen. The "bolus effect" indicates that the quantity of blood that enters the portal vein through the splenic, is proportionately large. It may be as much as 40% of the total portal flow in humans with

../enlarged spleens

enlarged spleens (Linton et al, 1947).

The sizes of the splenic and portal veins are shown by the portal venogram. The volume of blood flowing through a vessel is not directly proportionate to its size. However, as the blood pressure is the same in the larger veins of the portal system, their sizes will indicate the relative amounts of the blood flowing through them. When the portal flow is obstructed inside the liver the portal vein is dilated and the splenic vein is tortuous. The size of the former probably indicates the severity of the portal hypertension, and thus the degree of obstruction present. However, in the presence of a raised portal blood pressure, the size of the portal vein is no indication of the amount of blood flowing through it.

3. SPASM OF THE SPLENIC VEIN

The historical surveys on the flow and pressure in the portal system indicated that the intrahepatic branches of the portal vein can vary in tone and are constricted by adrenaline and by splanchnic nerve stimulation. The portal and splenic veins are distensible (Daniel and Prichard 1951 b; Franklin and Janker, 1937), but not all workers agree that they can contract. McMichael (1932) found that adrenaline had no effect on the wall of the splenic vein and Snyder (1942) stated that the portal vessels are devoid of smooth muscle and cannot respond to drugs. However, Pei-Lin Li (1940) has shown that the walls of these veins contain many circular smooth muscle fibres. Segments of the portal vein contract under the influence of adrenaline (Edmunds, 1915), and

../Mall

Mall (1892) has demonstrated that the portal vein may contract on stimulating the splanchnic nerves. Direct mechanical stimulation of the splenic and portal veins in cats and dogs induces localized spasm of these vessels which may last as long as two hours (Tait and Cashin,1925).

No distension of the splenic vein during the injection of diodone into the spleen has been observed. Severe spasm of this vein has occurred at death (fig.25). This appearance was not the result of a diminished blood flow through the spleen as the vessel contracted suddenly, and the other veins were not diminished in size. Milder degrees of splenic vein contraction may occur in dogs during the injection of dye into the spleen. Contraction of the portal vein has not been observed. 70% diodone is an irritating solution, but it is unlikely that it irritates the splenic vein and causes spasm, as the latter has been absent in the venograms on humans and in the great majority of those on dogs. It is possible that impulses via the splanchnic nerves induce the vasospasm when the dog is too lightly anaesthetized. Whatever, the cause there is no doubt that contraction of the splenic vein can occur in the living dog.

4. THE FILLING DEFECT AT THE ENTRANCE OF THE SUPERIOR MESENTERIC VEIN

A filling defect is almost constantly present where the superior mesenteric vein joins the splenic (figs. 13, 16 to 19, 28). It appears to be due to the inflow of blood from the superior mesenteric, which displaces the diodone upwards in the portal vein. This shows the tendency of the portal blood to form separate streams. The filling defect does not extend more than

../one to two

one to two cm. along the portal vein; it is obliterated as the dye mixes with the mesenteric blood.

Such a filling defect in the portal venogram has not been reported by other observers. Its presence appears to be of importance. It is a good indication that the dynamics in the portal system are not disturbed by the intrasplenic injection of dye. When diodone is administered directly into a vein of the portal system, the dynamics can be altered with greater ease, and this probably explains the failure of other workers to observe this defect. It can be pointed out that Franklin and Janker (1937) actually noticed distension of the veins of the portal system on injecting the dye directly into the portal tributaries. It is possible that a large amount of dye given rapidly into the spleen will disturb the portal mechanics, when the filling defect will be absent. If such an injection is made in the presence of intrahepatic portal obstruction, a reflux of dye into the superior mesenteric vein may occur (fig. 32). This reflux extends only a few centimetres, as the dye flows against the mesenteric stream (the superior mesenteric vein does not take part in the formation of a collateral circulation and the direction of its blood flow is never reversed). It is doubtful whether the reflux of dye indicates a backflow of blood; when portal stasis occurs in the presence of portal obstruction, the diodone, which is heavier than blood, will gravitate into the superior mesenteric vein. Whatever the mechanism of this reflux, its presence suggests that there is severe obstruction to the portal flow of blood.

../The backflow

The backflow into the superior mesenteric vein is also seen at death (fig. 25). The circulation through the intestines, and therefore the flow in the superior mesenteric vein, stops. The result is that the dye easily flows into this vein.

5. STREAMLINING OF THE BLOOD IN THE PORTAL VEIN

"Streamlines" is the term used by hydraulic engineers for separate streams in a moving body of water, for example, when two rivers meet their streams may remain separate for long distances. Streamlining occurs in the inferior vena cava, below the renal (Franklin and McLachlin, 1936) and above the hepatic veins (Daniel and Prichard, 1951 a).

A review of the literature shows that the majority of experimental observations indicate that streamlining also occurs in the portal vein. In 1901 Sérège injected India ink particles into the splenic vein of dogs and noticed that they were carried to the left lobe of the liver. He suggested that blood from the spleen sticks to the left side of the portal vein and goes to the left lobe of the liver, whereas the mesenteric blood flows along the right half of the portal vein to the right lobe. By employing the same method a number of workers have confirmed his results: Barlett and his co-workers (1914) stated that the physical character of India ink was foreign to the blood. They used an olive oil emulsion, which was also tried, but found to be unsatisfactory, by Copher and Dick (1928; Dick 1928). The latter workers injected a solution of trypan blue into different veins of the portal system. The dye stained the left lobe of the liver when administered into the left gastric and splenic veins, the right lobe when injected

../into the

into the pancreatico-duodenal, jejunal and superior mesenteric veins, and both lobes were stained when the inferior mesenteric vein was injected. They also studied the transilluminated portal vein during administration of the trypan blue, and confirmed the suggestion of Sérège that the blood in the portal vein is streamlined.

When the inferior mesenteric vein was injected the dye flowed along the centre of the portal vein.

The results of Copher and Dick were confirmed by Hahn and his colleagues (1945), who injected radio-active phosphorus into the splenic and superior mesenteric veins and determined the radio-activity of different parts of the liver. By using the dye method, Seneviratne (1949) also demonstrated the presence of streamlining in the portal vein. A method that was more physiological than injecting substances into the veins of the portal system, was employed by Barlett and his co-workers (1914). Copper sulphate was administered into the intestine of dogs at various levels. The copper that was absorbed from the stomach, duodenum and upper jejunum, was deposited in the left lobe of the liver; that from the lower jejunum, ileum and first part of the colon, was deposited in the right lobe.

The observations mentioned above were all made on dogs. Some workers were unable to confirm them (Brissaut and Bauer, 1909; Gilbert and Villaret, 1909). Observations on humans have been few. Barlett and his colleagues (1914) studied the records of 1000 autopsies; there was no evidence of streamlining in the cases with intestinal lesions that had spread to the liver. However, Moore and Bridenbaugh (1951), who obtained portal venograms on humans at operation, noticed evidence of

../streamlining

streamlining in the portal vein. Leger and his co-workers (1951 b), using the same method, were unable to confirm this observation.

From this historical survey it appears that the presence of streamlining in the portal vein has been established in the dog, but not in man. The portal venogram described in this thesis, has proved a good method of investigating portal streamlining, as, apparently, it does not disturb the physiological flow in the portal system. Streamlining was seen in a small number of the experiments only (figs. 14 and 28), and the results were not uniform. A number of factors appear responsible for these variable results:

(1) The Anatomical Disposition of the Tributaries of the Portal Vein

The angle at which the superior mesenteric vein meets the splenic is about 90° in man (Douglass et al, 1950) and 45° in dogs (Copher and Dick, 1928). The more acute this angle, the more likely are the streams to remain separate in the portal vein. There will, therefore, be a greater tendency for the streams to mix in man. Variations in the size of this angle will explain the inconstant results.

(2) The Volume and the Rate of Blood Flow

The greater the velocity of the blood in the splenic vein, the greater will be its tendency to mix with the mesenteric blood. The velocity, however, cannot explain variable results, as it is fairly constant.

The smaller the volume of blood flowing through the splenic vein, the more likely it is to be displaced by the mesenteric flow to the left side of the portal

../vein

vein. The splenic blood flow is relatively smaller in the dog than in man (Feil and Forward, 1922; Burton-Opitz, 1909); streamlining, therefore, is more likely to occur in the dog. If a great amount of dye is rapidly injected, it is unlikely that separate streams will be observed in the portal vein. The rate of injection may explain variable results.

(3) Variations in the Vascular Tone of the Portal Vein and its Branches.

Dick (1928) has stated that this may influence streamlining in the portal vein. Variations in the tone will affect the volume and rate of blood flowing in the splenic and superior mesenteric veins, and, therefore, also the tendency to form separate streams in the portal vein.

(4) The Posture of the Subject

Changes in posture have no obvious effect on the presence of streamlining in dogs (Copher and Dick, 1928). However, it is possible that posture may influence streamlining by altering the angle between the splenic and superior mesenteric veins, especially in humans in the erect position.

(5) The Viscosity of the Blood

The greater the viscosity of the fluids, the sharper will the streams be separated (Barlett et al, 1914; Dick, 1928). The viscosity of 70% diodone is greater than that of blood, but the dye becomes so diluted in the splenic vein, that this cannot be an important factor. 70% diodone, being heavier than blood, tends to gravitate to dependent parts. It is possible

../that this

that this may occur in the portal vein and so obscure any evidence of separate streams. This can also explain the flow of diodone along the right side of the portal vein (fig. 27).

(6) The Distance of the Flow

The streams in the portal vein tend to remain separate for a distance of 10 cm. (Barlett et al, 1914). Therefore, the longer the portal vein, the more likely is the portal blood to mix. This has an important bearing on the distribution of blood to the liver. Streamlining may be evident in the peripheral part of the portal vein but absent at the hilum. Mixing of blood is more likely to occur in the longer portal vein of man than in the dog. This may explain the greater concentration of dye in the left lobe of the liver in dogs, and in the right lobe in man, as was shown by the venograms that demonstrated the liver vessels clearly (figure 14; figures 16 and 20).

Occasionally a large volume of blood may enter the portal vein through the left gastric vein. This may displace the splenic blood to the centre (fig.30) or to the right side of the portal vein (fig. 27).

It has been pointed out that many factors may influence streamlining of the portal blood. These factors are not constant, and the extent to which the streams mix in the portal vein probably changes continually. The portal venogram, obtained by injecting, without great force, small amounts of dye into the spleen, appears to be the best method of demonstrating these physiological changes.

../It can be

It can be concluded that streamlining is usually present in the portal vein of dogs, and sometimes in that of man. Its degree apparently varies in the same subject under different physiological conditions. The two streams in the portal vein supply the corresponding lobes of the liver in the dog, but in man they mix before the portal vein divides at the hilum.

6. THE DIRECTION OF THE BLOOD FLOW IN THE PORTAL SYSTEM

The portal venogram is a useful method to study the direction of the blood flow in the portal system. In the presence of severe portal obstruction, the normal direction towards the liver changes, and the blood flows from the splenic and portal veins to the left gastric (figs. 29 and 31), inferior mesenteric (fig.31), gastro-epiploic and short gastric veins (fig.34). Whether some blood still flows towards the liver in the portal vein, will depend on the severity of the obstruction.

In addition to these normal anastomoses that are opened up in the presence of portal obstruction, new vessels are formed. They may develop round the block in the portal vein (fig. 37) or at the spleen (figs. 35, 36 and 41). A striking feature has been the rapidity with which these new vessels form in the dog; they may become prominent within a few weeks and are easily demonstrated by the portal venogram. A collateral circulation may develop round the exteriorized spleen in the absence of portal obstruction. This has made total ligation of the portal vein a safe procedure in dogs with exteriorized spleens.

../The change

The change in the direction of the blood flow when portal obstruction is present, depends on a raised portal pressure. With a greater pressure gradient between the portal and systemic veins, existent anastomoses are opened up and new ones are formed. Therefore, although the portal pressure is not related to the volume of blood flow, it regulates the direction of flow in the portal system. It can be concluded that when the portal venogram shows up veins other than the splenic and portal, some degree of portal obstruction is present.

This method of demonstrating the portal system will show the patency of an Eck fistula (fig.38). The diodone that enters the inferior vena cava also demonstrates the presence of streamlining in this vein (Franklin and McLachlin, 1936; Daniel and Prichard, 1951 a).

7. THE ADVANTAGES AND DISADVANTAGES OF THE PORTAL VENOGRAM OBTAINED BY THE INTRASPLENIC INJECTION OF DIODONE

ADVANTAGES:

These can be summarized as follows:

1) It is an ideal method to study the rate and direction of the blood flow in the splenic and portal veins; it also demonstrates the presence of collateral vessels.

2) It appears to be a good method for studying the presence of streamlining in the portal vein.

3) The normal dynamics of the portal system are not disturbed by it.

4) A general anaesthetic is not required, nor is a laparotomy

5) It appears a safe method that is applicable to humans with enlarged spleens; the presence of portal hypertension as well as the site of obstruction can be diagnosed.

../Disadvantages

DISADVANTAGES:

These are summarized as follows:

1) This method does not measure the volume of the portal blood flow.

2) In the absence of portal obstruction only the splenic and portal veins, and not the whole portal system, are shown.

3) It has not been possible to inject human spleens of normal size without exposing them at operation.

4) The injection may traumatize the spleen. However, this has not occurred and it is unlikely that the needle will tear the spleen if the procedure is done with reasonable care. A small area of haemorrhage is produced in the substance of the spleen, at the site of the injection. This is absorbed within 15 to 20 days (Abeatici and Campi, 1951). It is possible that infection of such a haematoma may occur.

5) The left lung may be traumatized when the spleen is injected trans-thoracically. One patient had a small haemoptysis immediately after the injection had been given. However, the trans-thoracic approach to the spleen is the only reliable one in man.

6) Hypersensitivity reactions to diodone may occur; they have not been observed in the series of experiments reported in this thesis.

C H A P T E R V 1

THE BLOOD PRESSURE IN THE PORTAL VEIN

The literature on the pressure in the portal vein has been reviewed in Chapter 11. For the purpose of this thesis observations on the portal pressure were made on six dogs. The results will now be discussed.

THE NORMAL PRESSURE IN THE PORTAL VEIN

The normal pressure, as measured in anaesthetized dogs at laparotomy, was fairly constant, ranging between 10.0 and 12.5 cm. 3.8% sodium citrate solution. When it was measured at the end of several experimental procedures on the portal system, it was 0.5 to 1.0 cm. higher than at the beginning. This small difference is not significant. The pressure in the splenic vein appeared the same as that in the portal. All the pressures were read at the level of the portal vein, which is also the level of the hepatic pedicle. This probably explains the constancy of the results and it indicates that the zero-level from which the pressure is read, must be constant.

The portal pressure is measured best by inserting a polythene catheter into the portal vein, through a branch of the portal system. A needle inserted into the portal vein is easily displaced and is likely to traumatize it. These observations on the normal portal pressure are well within the limits mentioned by other workers,

../but they

but they show a greater constancy than the reported results, probably because the readings were made under identical conditions in the different dogs. If results are to be reliable, the normal pressure in the portal vein should show small variations only. It has been noted that many factors control the portal pressure. The constancy of these results indicates how perfect this control is.

THE PORTAL PRESSURE ON OCCLUDING THE PORTAL VEIN AT THE HILUM OF THE LIVER

Occlusion of the portal vein at its entrance into the liver raises the portal pressure to between 60 and 90 cm. 3.8% sodium citrate. This observation confirms the results of previous workers (Bayliss and Starling, 1894 a; Manwaring et al, 1923; Feldberg et al, 1928; Auvert, 1950 - Table XV). The rise, which commences 5 to 10 seconds after occlusion, reaches its maximum in one to two minutes. Once the top level has been reached the pressure remains constant.

Variations in the top level depend on the aortic blood pressure and on the adaptability of the portal system. The maximum pressure reached almost equals the blood pressure in the splenic and mesenteric arteries, indicating that the splanchnic vascular resistance is low during occlusion of the portal vein. A rise to the same extent is not seen on occluding other veins in the body and it is probable that the low splanchnic resistance is due to the blood flow through the spleen.

The gradual rise over a period of one to two

../minutes

minutes in the presence of a portal flow of 200 to 375 cc. per minute, indicates that the portal system, to some extent, adapts itself to the increase in blood volume.

THE PORTAL PRESSURE ON OCCLUDING THE INFERIOR VENA CAVA ABOVE THE LIVER.

It is difficult to occlude the hepatic veins in the dog. Simonds and Brandes (1925) have described a method but whether it is effective is doubtful. Occlusion of the inferior vena cava above the liver obstructs the outflow of blood from the hepatic veins, but does not occlude them completely. However, the rise in portal pressure, which reaches a level of 22 to 35 cm. 3.8% sodium citrate solution, corresponds to the findings of other workers (Bayliss and Starling, 1894 a; Manwaring et al, 1923; Simonds and Brandes, 1925). The pressure in the inferior vena cava rose from five and seven cm. sodium citrate, respectively to 19 and 29 cm. in two dogs; in each the portal pressure was 6 cm. higher. This suggests that with an hepatic pressure gradient of 6 cm., the blood flow in the portal vein is not diminished when the inferior vena cava is occluded above the liver; the direction of flow in the inferior vena cava must be reversed, the blood flowing through collateral veins. Vessels between the liver surface and diaphragm may also help to bypass the obstruction; the liver may prevent a greater rise in portal pressure by accommodating part of the back pressure.

The portal pressure on occluding the inferior vena cava rises at the same rate on hilar obstruction of the portal vein; there is also a 5 to 10 second delay before it starts to rise. The former shows that the liver does not accommodate much blood; the latter

../indicates

indicates that pressure changes are readily transferred from the hepatic veins to the portal. This suggests that the hepatic vascular resistance is low and that the portal pressure is readily influenced by pressure changes in the hepatic veins, inferior vena cava and right auricle.

The portal pressure remains the same if, in addition, the hepatic artery is occluded; this shows the comparatively small volume flow in the hepatic artery.

THE PRESSURE IN THE PORTAL VEIN ON OCCLUDING THE HEPATIC ARTERY.

There was a drop of 0.5 to 2.0 cm. sodium citrate in portal pressure on occluding the hepatic artery in three experiments, in two the pressure rose and in the sixth there was no change. The changes in pressure are not significant. These observations do not confirm the findings of previous workers, who observed a significant fall in portal pressure on hepatic artery occlusion (Jaure, 1932; Rienhoff, 1951). This discrepancy must be the result of technical errors and more observations are needed.

THE PRESSURE ON OCCLUDING THE PORTAL VEIN PERIPHERALLY.

McMichael (1932), apparently, is the only worker who has observed the effect of peripheral occlusion of the portal vein on the portal pressure. He noticed, in cats, that the pressure fell from 10 to 6 cm. 5% sodium citrate. No observations on dogs have been reported.

The observations reported in this thesis, showed a fall in portal pressure on peripheral occlusion of the portal vein in five out of six dogs. In three dogs the pressure fell 6 to 7 cm. and in two, 1 to 1.5 cm. sodium citrate. Technical errors may explain these different results, but the striking feature is that, although the

../blood flow

blood flow into the portal vein is completely obstructed, the pressure distal to the obstruction does not drop to zero. This corresponds to McMichael's findings, and it may be explained by the following factors.

(1) The cystic and accessory pancreatic veins open into the portal vein near the hilum of the liver, and the inflow of blood from them may prevent the pressure from falling to zero. However, it is unlikely that the amount of blood that flows through these small vessels can keep the pressure elevated when the portal vein has been occluded peripherally.

(2) A more likely explanation is that the blood flowing through the hepatic artery is shunted from the liver, back into the portal vein. However, on obstructing the hepatic artery after the portal vein has been occluded, there is no additional fall in portal pressure. This has also been observed by McMichael. Therefore, the inflow of blood from the hepatic artery is not the factor which keeps the pressure raised.

(3) It is possible that a high vascular tone in the hepatic veins may obstruct the outflow of blood from the liver, thus preventing the portal pressure from falling to zero; but it is most unlikely that this will maintain the portal pressure at the high level observed.

(4) The most likely explanation is that the pressure in the inferior vena cava is transferred across the hepatic sinusoids, to the portal vein. It has been noted that pressure changes in the inferior vena cava and hepatic veins are readily reflected in the portal pressure. The

../latter

latter on occluding the portal vein peripherally, probably indicates the pressure in the hepatic veins. Further work needs to be done and it will be interesting to observe the effect on the portal pressure of obstructing the inferior vena cava above the liver, after the portal vein has been occluded on its intestinal side. This has not yet been done.

THE PORTAL PRESSURE DURING THE INJECTION OF 20 CC. SALINE INTO THE SPLEEN

The portal venograms obtained by injecting 20 cc. diodone into the spleen, show that the dynamics in the portal vein are not disturbed by the injection. This has been confirmed by the absence of elevation of the portal pressure on injecting rapidly 20 cc. saline into the spleen, an observation which is also suggested by the experiments of Carnot and his co-workers (1932 b). They noticed that there was no significant rise in pressure on increasing the portal flow by 230 cc. per minute. It can be concluded that the portal pressure is not raised when 20 cc. saline is injected into the spleen; it is likely that the same applies to the injection of 20 cc 70% diodone.

VARIATIONS IN THE PORTAL PRESSURE WITH RESPIRATION

Various workers have reported a rise in portal pressure on inspiration and a fall on expiration (Schmid, 1909; Feldberg, 1929; Feldberg et al, 1928; McMichael, 1932). The observations made in this thesis show that when the portal pressure falls from a high level to normal, it does so during expiration, remaining stationary during inspiration. This corresponds to the results of the

../above mentioned

above mentioned workers. Franklin and Janker (1937), using serial X-ray photography after thorotrast had been injected into the portal system, noticed a back-flow of blood into the hepatic veins during expiration. This reflux of hepatic venous blood will tend to raise the portal pressure during expiration. This, therefore, is not the mechanism by which respiration affects the pressure in the portal vein. The increase in intra-abdominal pressure on descent of the diaphragm during inspiration is not responsible for the rise in pressure, as the latter also occurs when the abdomen is open. However, the movements of the diaphragm probably cause the pressure changes; the greater the diaphragmatic excursions, the greater have been the fluctuations in portal pressure. On inspiration, the diaphragm may compress the vessels of the portal system directly, raising the pressure; or it may compress the liver or rotate it on the inferior vena cava, thereby obstructing the portal outflow. Whatever the mechanism, the movements of the diaphragm appear responsible for the pressure changes during respiration.

It can be concluded that the dynamics of the portal circulation can be studied by observing the portal pressure, but no conclusion on the volume flow in the portal system can be reached.

C H A P T E R V l l

THE CIRCULATION THROUGH THE SPLENIC PULP AND THE BEHAVIOUR OF DIODONE IN THE SPLEEN

THE VASCULAR STRUCTURE OF THE SPLEEN (FIG.44, PAGE 137)

The spleen has a connective tissue capsule from which trabeculae penetrate its substance, dividing it into segments. In the dog the capsule and trabeculae are rich in smooth muscle fibres. These are absent in the capsule of the human spleen, but are found in small groups in its trabeculae, which are rich in elastic fibres. (Maximow and Bloom, 1947).

The branches of the splenic artery, after having pierced the capsule, run in the trabeculae. When an artery reaches the size of 0.2 mm. it leaves the trabecula, while its tunica adventitia becomes replaced by a sheath of lymphatic tissue, which gives rise to Malphigian follicles. Capillaries from the artery supply the lymph follicle. The artery breaks up into two to four straight branches - the penicilli of Ruysch. The proximal parts of the penicilli form the arteries of the pulp, which are approximately 0.6 to 0.7 cm. long (Maximow and Bloom, 1947). They become the sheathed arteries of Schweigger-Seidel (1863), from which the arterial capillaries, having a length of 60 to 90μ and a diameter of 10μ, arise.

The venous drainage of the spleen starts in the venous sinuses of the pulp. These sinuses are from 12

../to 40

to 40μ in diameter and occupy a large amount of the pulp space. They are lined by macrophage cells and encircled by reticular fibres. They open into the intralobular veins (Mall, 1902); the latter drain into the interlobular veins in the trabeculae. Robinson (1930) traced the veins of the cat's spleen backwards from the hilum. They enter the spleen through trabeculae in which they run. On piercing the capsule a vein loses its tunica adventitia and media, being supported in the trabecula by muscle and connective tissue. Intralobular veins are lined by a single layer of endothelial cells in direct contact with the pulp cells, and have numerous stomata in their walls.

According to Mall (1902), the blood flow through the spleen is controlled by the arterial pressure, the elasticity of the reticulum and the muscle of the trabeculae. He states that the latter keeps the veins from collapsing when the spleen contracts, enabling the blood to be squeezed out. The arterial pressure fills the organ with blood and the elasticity of the reticulum aids contraction. He also mentions that the arterial pressure can maintain the circulation through the spleen, but contraction of the organ is necessary to empty the pulp spaces of blood. This was also pointed out by Tait and Cashin (1925). However, muscle is practically absent in the human spleen, which, probably, is not able to contract, and its size is controlled by its blood flow only (Ravenna, 1940). Summarizing, the main factor that regulates the blood flow through the spleen appears to be the pressure gradient between the splenic artery and vein. The elastic tissue of the

../reticulum

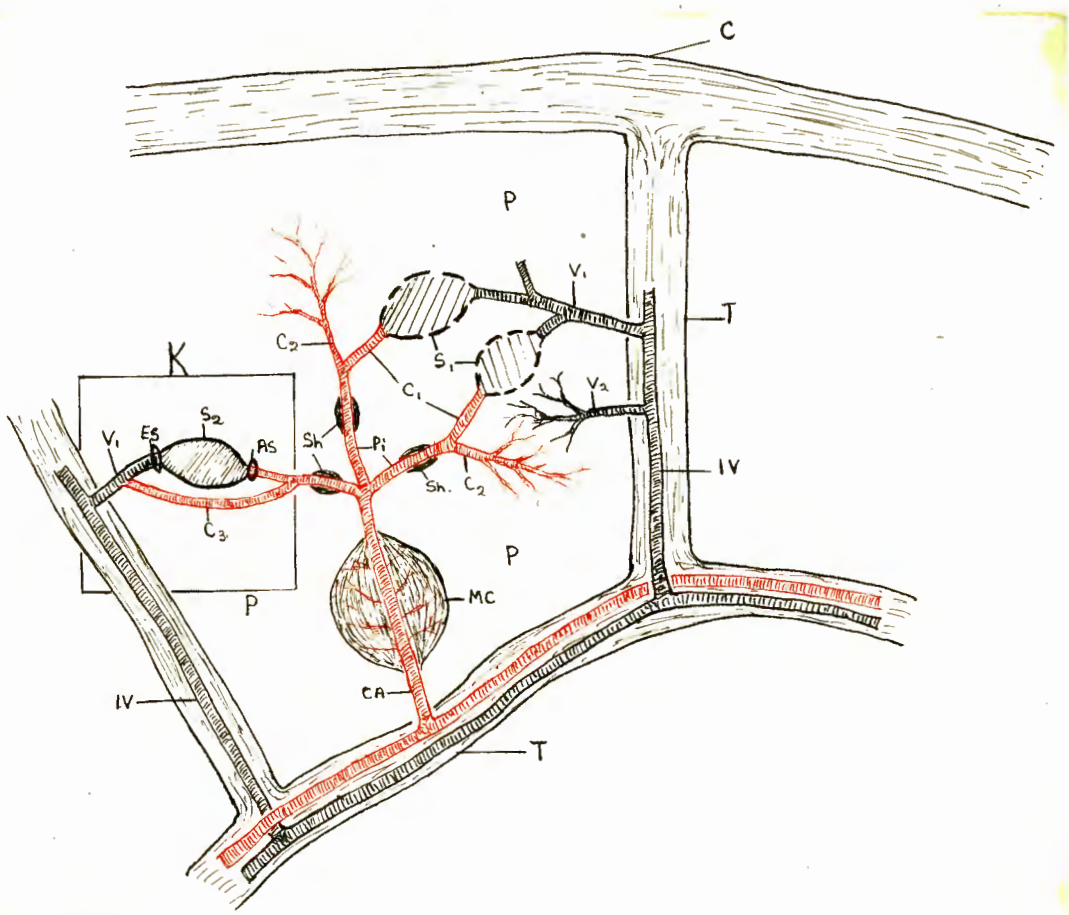


Fig. 44 Diagram of the blood flow through the spleen, showing the commonly accepted theory of the "combined" type of circulation. In the square (K) the "divided" circulation of Knisely is demonstrated.

AS : Afferent sphincter
C : Capsule
C1 : Capillary opening into sinus
C2 : Capillary opening into pulp
C3 : Pulp cord capillary
CA : Central artery
ES : Efferent sphincter
IV : Interlobular vein
MC : Malpighian corpuscle
P : Pulp
Pi : Penicilli
S1 : Venous sinus with fenestrated wall
S2 : Venous sinus with intact wall
Sh : Sheath of Schweigger-Seidel
T : Trabecula.
V1 : Intralobular vein draining sinus
V2: Intralobular vein draining pulp.

reticulum enables the organ to accommodate extra blood and probably helps to squeeze blood out when the inflow is diminished. The muscle present in the human spleen plays no role in controlling its blood flow, but in the dog it enables the organ to contract and dilate rhythmically, thus aiding the blood flow through it (Barcroft, 1926).

THE SEGMENTAL NATURE OF THE SPLEEN.

The spleen is supplied by the splanchnic nerves. When these are stimulated in cats and dogs, the whole organ contracts (Tait and Cashin, 1925). When a single branch of the splenic nerve, arising from the coeliac plexus, is stimulated, a sharply circumscribed portion of the spleen contracts. Tait and Cashin (1925) also noticed that the same happens when a branch of the splenic artery and its accompanying nerve fibre are stimulated. The localized contraction is bandlike and the segments do not overlap. These workers defined up to 13 such zones in the dog's spleen, and when India ink was injected through a branch of the splenic artery or vein, the same segmental distribution of dye was shown. These zones in the spleens of cats and dogs correspond to the branches of the splenic artery, and they appear to be arterial and venous units, which, each with a nerve supply of its own, are separated by the splenic trabeculae. The muscular arteries supplying these lobes are end-arteries (Cohnheim, 1872), and are capable of contracting, shutting off greater and smaller parts of the spleen from the circulation (Von Herrath, 1935).

The distribution of diodone when injected into the spleen of the dog confirms the observations of Tait

../and Cashin

and Cashin. It does not diffuse through the pulp, but remains localized to the lobe into which it has been injected. From here it is drained by a single vein. When the dye is injected into a trabecula, it may flow into more than one segment, thus accounting for more than one vein filled with dye, as observed in some venograms. It is also possible that, when the diodone is forcefully injected, it may rupture across trabeculae into other compartments, demonstrating the veins draining them.

That the human spleen is also divided into segments that can function independently, is suggested by its anatomical structure, but has not been proved. However, when diodone is injected into the human spleen, it behaves in exactly the same way as in the dog. It can, therefore, be concluded that the spleen of man also consists of lobes, which can function as independent units, each having a nerve and blood supply of its own.

A reflux of dye from the splenic hilum into branches draining the non-injected part of the spleen, has been observed in some of the venograms of both dogs and humans (fig.s 16 and 31). Compared with the backflow into the superior mesenteric vein, this reflux occurs in the absence of portal obstruction. It may be 5 to 8 cm. long but does not extend into the splenic substance. The denseness of its shadow shows that the dye is not much diluted. It is possible that this reflux occurs against the normal blood flow. However, the extent to, and the ease with which the diodone flows backwards, as well as its density, suggest a diminished blood flow in the veins draining the non-injected parts of the spleen. That segments of the spleen can be shut off from their vascular supply by spasm of the

../branches

branches of the splenic artery, has been suggested by Von Herrath (1935). The segmental nature of the venous drainage of the spleen may be a normal physiological occurrence. The reflux of dye into the tributaries of the splenic vein is confirmatory evidence that, in man and dog, the spleen is divided into segments which can function independly.

A REVIEW OF THE LITERATURE ON THE CIRCULATION THROUGH THE SPLENIC PULP

Ever since Billroth described the venous sinuses of the spleen in 1860 the nature of the circulation through the pulp has been a subject of discussion. Many workers have brought forward evidence that the blood leaves the normal vascular channels and is poured into the pulp of the spleen. In this "open" circulation the blood passes from the sheathed capillaries, through the pulp into the venous sinuses and intralobular veins, entering them through stomata in their walls. Other investigators have shown that the circulation through the spleen is a "closed" one, that is, the blood never leaves the normal vascular channels, passing directly from the capillaries to the venous sinuses and intralobular veins. Only plasma passes through the sinus walls, and the presence of red blood cells in the splenic pulp, shown histologically, is explained as an artifact resulting from the preparation of the sections.

The Theory of the "Open" Circulation

This was advanced by Billroth in 1860. Two years later Stieda (1862) discovered that material injected through the splenic artery filled the pulp and that it was not possible to perfuse the spleen backwards through the splenic vein. Muller (1865) studied the spleens of

../different species

different species and noticed erythrocytes in the pulp which he regarded as a natural channel for the flow of blood. There was a free communication between the veins, and material injected into one escaped through the others. In 1901 Weidenrich injected avian erythrocytes intravenously into dogs and rabbits. He discovered the avian cells in the splenic pulp immediately after the injection; later they appeared in the splenic sinuses as well. He concluded that the capillaries opened into the pulp, but he also observed direct communications between the capillaries and splenic sinuses. These observations were confirmed by Mall (1902), who noticed that numerous red cells were present in the pulp when the spleen was dilated; when it was contracted very few red cells were visible outside the splenic sinuses. Mall wrote as follows: "Recent researches upon the blood vessels of the spleen prove definitely that the arterial capillaries communicate quite freely with the pulp spaces, but there is still a difference of opinion regarding the presence of distinct channels, independent of the pulp spaces, connecting the arterial capillaries with the venous sinuses". He stressed the lobular structure of the spleen and concluded that he had been unable to "gather any good evidence in favour of some closed capillaries".

In 1926 Krumbaar stated that the blood might travel directly from the arteries, through the pulp, to the veins and not necessarily to the sinuses; stigmata were present in the walls of the veins. In the same year Robinson (1926) observed that the intralobular veins had incomplete walls. By injecting stained gelatine into the

.../splenic artery

splenic artery of different species, he confirmed Mall's view on the lobular structure of the spleen, and observed that the capillaries passed through the ellipsoids into the pulp. He, therefore, concluded that the circulation through the spleen was an "open" one. In a later paper (Robinson, 1930) he mentioned that the venous sinuses drained the pulp spaces and that the blood was forced into the veins by contraction of the spleen. He did not find direct communications between arteries and veins. His observations were made on cats and the author indicated that his conclusions did not necessarily apply to the spleens of man and dogs.

McNee (1931; 1932) stated that the pulp spaces were the reservoirs of the spleen, consisting of a network of reticulum and abundant blood vessels. The blood flowed from the pulp through stigmata in the walls of the veins. The author suggested that the circulation through the spleen was "open" in fishes, "closed" in reptiles, and in other species "combined", that is, the splenic arterioles, after having passed through the ellipsoids, opened into the perforated sinuses from which the pulp was filled. Quoting Barcroft's work (1923-24) on the reservoir function of the spleen, as confirmatory evidence, McNee concluded that the pulp stored blood when the spleen was relaxed; when it contracted, blood was forced through the holes in the walls of the veins. A direct circulation from the capillaries to the sinuses was always going on.

Contrary to the observations of Robinson (1930), Nisimaru and Steggerda (1932) were able to perfuse the spleen of cats backwards through the splenic vein, at a

../pressure of

pressure of 40 to 50 mm Hg. They mentioned that the capillaries opened directly into the splenic pulp.

The Theory of the "Closed" Circulation

A number of workers have suggested that the blood does not leave the vascular channels in the spleen. Key (1861) stated that the splenic pulp was a widely ramified network of capillaries, through which the blood flowed. However, Schweigger-Seidel (1863) showed that the pulp consisted of a connective tissue framework which was filled with lymph; the blood flowed directly from the arteries to the veins. Sokoloff (1888), who tied the splenic veins of rabbits, dogs and cats, noticed that the sinuses, and not the pulp, were stuffed with erythrocytes when the spleen was engorged. He mentioned that the sinus wall acted as a permeable membrane with the blood flowing from the capillaries to the sinuses directly. With these observations, Kalenkiewicz (1892), Wicklein (1888) and Panski (1890) agreed. The conclusion that the blood flow through the spleen was a "closed" one, was also reached by Helly (1902) and by Thoma (1924). The latter author pointed out that the sinus walls were permeable, allowing plasma, filtered out through the capillary walls, to be re-absorbed. By using silver stains and examining spleens histologically, Snook (1944) also concluded that the splenic circulation was a "closed" one.

The theory of the "closed" circulation, however, has been convincingly disproved by the protagonists of the "open" circulation, and it is not accepted in standard textbooks of Physiology (Maximow and Bloom, 1947; Schafer, 1938; Samson-Wright, 1940; Evans, 1941; Best and Taylor, 1946).

../At present

At present the main problem appears to be how the blood reaches the pulp spaces: it may pass from the capillaries to the venous sinuses, and then through holes in their walls into the pulp, being drained by the intralobular veins; or it may flow directly from the capillaries into the pulp spaces, being drained by both the venous sinuses and the veins.

The Theory of the "Divided" Circulation

In 1936 Knisely (1936 a and b) reported his studies on the circulation in living mammalian spleens. He transilluminated and studied microscopically the exposed spleens of mice, rats and cats. The penicilli and venous sinuses were easily visible and he observed that the artery of the Malphigian body divided into 3 to 7 branches, each giving off 2 to 4 penicilli, which branched into, and were interconnected by, capillaries. He observed two different vessel systems connecting the arterioles and venules:

(1) The venous sinuses

(2) Long "pulp cord capillaries". No capillaries were seen to open directly into the pulp and the author stated that "in the living unstimulated spleen the vascular system consists of a series of completely interconnected, preformed, lined channels". Sphincters were present at the afferent and efferent ends of the venous sinuses, and the ellipsoids (sheaths of Schweigger-Seidel) also had a sphincteric function. Contrary to all previous observations he saw no pores in the sinus walls. The plasma, which was separated from the red cells in the sinuses, filtered through their walls into the pulp. The sinuses underwent cyclic changes, which comprised stages of filtration and filling, storage, emptying and conduction of blood.

Different sinuses passed through different stages at the same time. The red cells were stored in the sinuses and the plasma was absorbed from the pulp by the venules and venous ends of the capillaries. The circulation through the pulp cord capillaries was necessary for nourishment.

In the second paper (Knisely, 1936 b) he pointed out that the walls of the venous sinuses were thin and easily ruptured, accounting for the presence in the pulp of material injected through the splenic vein. He observed that on direct mechanical stimulation of the spleen and at death the Schweigger-Seidel sheaths contracted and the erythrocytes passed from the sinuses into the pulp. This was a pathological response to trauma and accounted for the presence of red cells in the pulp in histological preparations of the spleen. Knisely also stated that the ampulla of Thoma (1895) was actually a venous sinus in the storage phase.

That the sinus functioned as a filter, separating the erythrocytes and the plasma, was also suggested by Björkman (1947), who injected a rice starch suspension intravenously into rabbits and noticed that the larger grain particles occupied the sinuses and the smaller ones the pulp. He concluded that the theory of the "open" circulation was false and that the presence of erythrocytes in the pulp was an agonal occurrence. The plasma which passed through the sinus walls, was forced back into circulation through the fenestrated walls of the smaller veins.

Knisely's method was employed by MacKenzie and

../his co-workers

his co-workers (1941) on the spleens of mice, rats, cats, guinea pigs and rabbits. They bathed the exposed spleen in saline at a constant temperature and took great care that it remained stationary during observation. These authors were unable to confirm the findings of Knisely. The capillaries opened into the pulp by means of funnel shaped dilatations - the ampullae of Thoma, which were 15μ in length and 6 to 12μ in diameter. The pulp spaces separated the capillaries from the venous sinuses, which originated in the meshes of the pulp and were lined by pulp cells at their origin. The sinuses and intralobular veins were interconnected and their walls were fenestrated. From these observations the authors concluded that the circulation through the spleen was only an "open" one, with the interstices of the pulp the only connection between the arterial and venous systems.

MacKenzie and his colleagues observed that erythrocytes traversed the inter-vascular zone of the pulp quickly, entering the sinuses and veins through their stomata. During its passage through the pulp the blood was concentrated. They did not observe the sphincters described by Knisely, nor the different phases of the sinuses, which appeared to have a purely passive drainage function. The blood flow through isolated areas of the spleen were controlled by arterial vasoconstriction, and that through the whole organ by its contraction and relaxation. The unit of erythrocyte storage appeared to be the pulp space and not the venous sinus, and when the spleen contracted, the pulp was

../emptied

emptied of red blood cells. The authors pointed out that in the contracted spleen the blood was conveyed directly from the capillaries to the sinuses, without any lateral trickling in the pulp, thus giving the impression of a "closed" circulation.

The experiments of MacKenzie and his colleagues were most carefully done and cast doubt on the conclusions reached by Knisely and Björkman. The most likely theory seems to be that the splenic circulation is an "open" one when the spleen is dilated; when it is contracted, blood is short circuited from the capillaries to the venous sinuses through endothelial lined channels (these have been observed by the great majority of workers). This is the "combined" type of splenic circulation which is accepted in many standard textbooks of physiology (Best and Taylor, 1946; Evans, 1941; Schafer, 1938; Maximow and Bloom, 1947 - Fig. 44). Samson-Wright (1940) points out that the practical difference as regard the termination of the arterioles is slight, because the stomata in the walls of the venules permit red blood cells to pass in and out, making intimate contact with the cells of the pulp.

THE RELATION OF THE INTRASPLENIC INJECTION OF DIODONE TO THE CIRCULATION THROUGH THE SPLENIC PULP

It has been noted that whenndiodone is injected into the spleen, it immediately leaves the pulp in large amounts (20 cc. diodone takes 10 to 20 seconds to leave the spleen). This has been a constant finding in man and in dogs and it is confirmatory evidence that the circulation through the spleen is an open one (This also

../applies to

applies to the enlarged spleen in humans with cirrhosis of the liver). It is impossible that the dye can pass so rapidly, and in such great quantities, into the veins if their walls (or those of the sinuses) were not fenestrated. A small amount of dye may be injected directly into the venous sinuses but most of it must fill the pulp spaces.

The behaviour of dye in the spleen does not indicate whether the blood flows from the arterioles, through the venous sinuses, to the pulp spaces and thence to the intralobular veins, or whether it reaches the pulp directly from the arterioles, to enter both the sinuses and the intralobular veins. However, it indicates that the veins, and probably also the sinuses, drain the pulp directly through stomata in their walls. It would be interesting to study the behaviour of dye in the contracted spleen, when the pulp spaces are, presumably, shut off from the circulation. This has not yet been done.

STAINING OF THE SPLEEN BY DIODONE

It has been observed that the spleen presents, radiologically, a typical honeycombed appearance at the site of diodone injection (figs. 21, 39 and 40). This staining of the splenic substance remains for a period of ten minutes to 24 hours. It may possibly result from the absorption of the dye by the reticulo-endothelial cells, but its features suggest that the diodone stains the connective tissue framework of the pulp. From here it is slowly absorbed into the blood stream or removed by macrophages. It can be concluded that, although most of the diodone enters the venous sinuses and veins

../immediately

immediately after its administration, a small amount, which is only slowly removed, remains in the connective tissue of the pulp.

C H A P T E R V l l l

THE INTRAHEPATIC CIRCULATION AS DEMONSTRATED BY THE PORTAL VENOGRAM, AND SUGGESTIONS FOR FUTURE WORK

THE INTRAHEPATIC CIRCULATION

A number of workers have attempted to demonstrate the intrahepatic circulation radiologically. Rappaport (1951) catheterized the hepatic veins of dogs and injected radio-opaque material into them. He was able to show the finer tributaries of the hepatic veins radiologically. Other workers have tried, without much success, to demonstrate the portal branches in the liver by injecting thorotrast or diodone into branches of the portal system (Moore and Bridenbaugh 1950, 1951; Leger et al, 1951 b; Santy and Marion, 1951). Child and his colleagues (1951) observed the smaller branches of the portal vein in the liver of man by injecting 40 cc of 35% diodone into the superior mesenteric vein. In cases of cirrhosis the small intrahepatic portal branches were less well filled, and the main branches of smaller calibre than in normal controls. Daniel and Prichard (1951 a and b) in their angiographic studies on the portal system of different animals, clearly demonstrated the finer intrahepatic portal branches.

The portal venograms obtained by Abeatici and Campi (1951) and Leger and his co-workers (1951 b), by injecting diodone into the spleens of dogs and man

../respectively

respectively, did not show the smaller portal branches in the liver. That it is possible to demonstrate these vessels by injecting diodone into the spleen is shown by some of the venograms in this thesis (fig.s 16, 20, 24, 29 and 32 in man and figs. 13, 15 and 19 in dogs). However, the smaller vessels are clearly visible in only a few venograms, and no conclusions on the pattern of the intrahepatic portal branches can be reached. (The vessels appear to be fewer, coarser and further apart in humans with cirrhosis - figs. 24 and 30 than in the normal - fig. 16). Further work must be done and the normal pattern of the portal branches determined in dogs and man. It may be possible to demonstrate space occupying lesions in the liver.

Research workers have also attempted to demonstrate the intrahepatic branches of the hepatic artery radiologically. Daniel and Prichard (1951 a) injected a radio-opaque dye into the aorta of animals, but it became too diluted. Bierman and his co-workers (1951) canalized the hepatic artery in humans and injected diodone into it. Only the larger intrahepatic branches were visible radiologically. In the experiments reported in this thesis five attempts to catheterize the hepatic artery in dogs failed. Aortograms, obtained by injecting diodone at the level of the coeliac axis, showed the hepatic artery but not its intrahepatic branches (figs.42 and 43). However, it should be possible to canalize the hepatic artery in dogs and further experimental work is required.

The observations of Daniel and Prichard (1951 a and b) on the transhepatic circulation time in animals, have

../been mentioned

been mentioned. No attempt to estimate this time has been made in the experiments recorded in this thesis, but it has been shown that the diodone can be traced across the liver vessels into the inferior vena cava (figs. 13 to 15). It will, therefore, be possible to study the transhepatic circulation time by injecting diodone into the spleen, and the dynamics in the portal system will not be disturbed.

SUGGESTIONS FOR FUTURE WORK

The following suggestions, some of which have been mentioned already, can be made:

(1) The pattern of the liver vessels should be studied by injecting diodone into the spleen and into the hepatic artery. It will be most useful to demonstrate the intrahepatic portal branches in man, and with the correct technique, the injection of a normal sized spleen may become a practical procedure.

(2) The behaviour of diodone when injected into the contracted spleen of dogs should be studied. Splenic contraction may be induced by adrenaline, stimulation of the splanchnic nerves or haemorrhage. The behaviour of the dye may indicate whether the splenic circulation becomes a "closed" one when the organ contracts.

(3) The sizes of the portal vessels are demonstrated by the venograms. The effects of chemical agents on their vasomotor tone can be studied by injecting these agents systemically, or mixed with the diodone into the spleen; the latter constitutes an intraportal injection. The density of the dye in the vessels will give some idea of

../the volume flow

the volume flow, and any change in the rate of flow can also be observed.

(4) It has been shown that dogs in "irreversible" haemorrhagic shock, may recover if arterial blood is transfused into the portal system (Fine et al, 1947; Cohn and Parsons, 1950). An intrasplenic transfusion of arterial blood will probably have the same effect; this should be investigated. The blood can be administered through a polythene catheter inserted into the spleen.

S U M M A R Y

SUMMARY

1) The literature on the volume flow in the portal vein has been reviewed. From this review the following conclusions can be made:

(a) The volume flow varies from 200 to 375 cc. per minute in dogs and from 800 to 1200 cc. per minute in man.

(b) The portal vein supplies 60 to 85% of the total hepatic flow but the hepatic arterial blood is more important in maintaining liver function.

(c) The portal flow is controlled by the arterio-venous pressure difference in the splanchnic vessels, and, to a lesser extent, by the tone of the intrahepatic portal branches.

(d) Normal variations in the portal flow may occur and a pulse is present in the portal vein.

(e) A partial reciprocal relationship exists between the flows in the hepatic artery and in the portal vein.

(f) There is no relationship between the volume flow in the portal vein and the portal pressure.

(g) The intrahepatic portal branches are under vaso-motor control, being constricted by adrenaline and by impulses along the splanchnic nerves.

2) A review of the literature on the blood pressure in the portal system indicates that the pressure varies from 7 to 20 cm. water in man, as well as in dogs and other animals. It is the same in the tributaries of the portal vein. The

../height

height of the portal pressure mainly depends on the tone of the portal branches in the liver. This tone is under nervous and hormonal control.

3) Personal observations on the portal pressure have been made in 6 dogs. It has been shown that the pressure is fairly constant (10.0 to 12.5 cm. sodium citrate above the level of the hepatic pedicle) under constant experimental conditions.

4) On occluding the portal vein at the hilum of the liver the portal pressure rises to a level approaching the blood pressure in the splenic and mesenteric arteries.

5) On occluding the inferior vena cava above the liver the portal pressure increases to a level twice normal.

6) Pressure changes in the inferior vena cava and hepatic veins are readily transferred across the hepatic sinusoids to the portal vein.

7) On occluding the portal vein on its intestinal side the portal pressure does not fall to zero. It is maintained at a level below normal, not by the hepatic arterial flow or pressure, but probably by the transference of pressure from the inferior vena cava, across the hepatic sinusoids , to the portal vein.

8) The injection of 20 cc saline into the spleen does not affect the portal pressure.

9) The pressure rises on inspiration and falls on expiration. These changes with respiration appear to be the result of diaphragmatic movements.

10) The anatomy of the portal system in man and in dog is described, and the more common variations are indicated.

11) A method of demonstrating the splenic and portal veins

../radiologically

radiologically by injecting 20 cc. 70% diodone into the spleen, is described. This method has been applied to 5 dogs with exteriorized spleens and to 12 humans. In the latter the procedure is done under local anaesthesia. The diodone commences leaving the spleen the moment the injection is started. It leaves it quickly (within 10 to 20 seconds) and in large amounts, thus producing a "bolus effect" in the splenic and portal veins. This procedure appears to be a useful method of studying the portal circulation.

12) It demonstrates the sizes of the splenic and portal veins and indicates, to some extent, the relative amounts of blood flowing in the branches of the portal system.

13) The rate of portal blood flow can be measured and it appears to be 15 to 25 cm. per second in both man and dog.

14) This method has shown that spasm of the splenic vein may occur.

15) A constant "filling defect" is present where the superior mesenteric flow meets the splenic. This defect probably indicates that the intrasplenic injection of 20 cc dye does not disturb the dynamics of the portal circulation.

16) In the presence of portal obstruction this method may indicate the site of obstruction. In addition, collateral veins are filled with dye, the splenic vein is tortuous, the portal vein is dilated and a reflux of dye may occur into the superior mesenteric vein.

../changes

Changes in the direction of blood flow are shown.

17) The method described can demonstrate the patency of a porta-caval anastomosis in man and dog.

18) The effects of drugs on the rate of blood flow and on the tone of the portal vein and its branches, can be studied by this method.

19) The literature on streamlining in the portal vein has been reviewed. Its presence appears established in the dog but not in man.

20) The portal venogram obtained by injecting diodone into the spleen appears to be a good method for investigating streamlining in the portal vein, as, apparently, it does not disturb the physiological flow.

21) The presence of portal streamlining in man and dog depends on a number of factors. Of these the most important are the anatomical disposition of the veins, the volume and velocity of blood flow in the portal tributaries and the posture of the subject. These factors are not constant and the extent to which the streams mix in the portal vein probably changes continually.

22) The streams in the longer portal vein of man are more liable to flow together than in the dog. The splenic blood flows mainly to the left lobe of the liver in the dog, but to both lobes in man.

23) The method of injecting diodone directly into the spleen appears to be safe and no ill effects have resulted in man or dog.

../ An intrasplenic

24) An intrasplenic haematoma is produced by the injection. It is absorbed within 15 to 20 days.

25) Attempts to inject a normal sized human spleen, not exposed at operation, have failed.

26) The vascular anatomy of the spleen has been described. That the spleen of both man and dog is divided into segments or lobes that can function, as independent units, is suggested by the intrasplenic behaviour of diodone. The dye does not diffuse through the organ and leaves it only by the veins draining the injected segments.

27) A short review of the literature on the circulation through the splenic pulp has been given. From this review it appears that the circulation is a "combined" one: it is "open" when the spleen is relaxed and "closed" when it is contracted. The amount of diodone and the rate with which it leaves the spleen suggest the presence of an "open" circulation.

28) Further work on the behaviour of dye in the contracted spleen should be done.

29) A small amount of diodone remains in the spleen, staining the connective tissue of the pulp. It is slowly absorbed within 24 hours.

30) It is possible to demonstrate radiologically the intrahepatic portal branches by injecting 70% diodone into the spleen. The transhepatic circulation can also be studied; further work is required.

31) The intrahepatic portal branches appear to be fewer, coarser and further apart in cirrhosis of the liver.

A P P E N D I X

1. Method of Placing the Dog's Spleen Subcutaneously

2. Reprint of a Reported Case of Splenic Vein Thrombosis.

APPENDIX 1

EXTERIORIZATION OF THE SPLEEN IN THE DOG - A METHOD OF PLACING THE SPLEEN SUBCUTANEOUSLY ON THE ABDOMINAL WALL.

THE OPERATION

Pre-operatively, the animal is starved for twenty four hours and the abdomen is shaved.

Anaesthetic: Atropine, grs. 1/100th, is administered intravenously and the anaesthetic is induced with intravenous pentothal. Oxygen, nitrous oxide and ether with a Boyle's apparatus, or air and ether with an Oxford vaporizer, are then administered through an intratracheal tube.

Technique: The dog lies on its back, tilted 30° towards the right side. Under aseptic conditions an incision, extending outwards from the rectus muscle, is made six inches long and two inches below and parallel to the left costal margin. The skin and superficial fascia, after having been incised, are undermined for 3 to 4 inches round the wound. This can be done without much bleeding - a few vessels from the lower intercostal arteries may require ligation. The muscles and peritoneum are then incised in the line of the skin incision.

The spleen is gently delivered into the wound and folded double so that its two poles lie together, pointing postero-laterally. It has a long mesentery and can easily be delivered. However, at its lower pole the mesentery may be short, requiring division. The peritoneum and transversalis muscle are closed round the splenic pedicle with a continuous catgut suture, taking

A P P E N D I X 2

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SPLENIC VENOGRAPHY

DEMONSTRATION OF THE PORTAL CIRCULATION WITH DIODONE

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THE anastomoses now used for the relief of portal hypertension depend for their success on exact localisation of the obstruction.

Several indirect methods of estimating the pressure in the portal system have been suggested—e.g., the rate of absorption of acetylene (Henning et al. 1950) or dyes (Souidan 1950) from the intestinal tract—but only after opening the abdomen has the surgeon been able to look for the obstruction, either by multiple venous-pressure readings (Blakemore and Lord 1945, Blalock 1947) or by the injection of diodone into the splenic vein or its tributaries (Whipple 1945). These manipulations prolong the operation undesirably and demand considerable team organisation.

We describe here a method by which the splenic vein and part of the portal circulation can be examined before operation, and the site of obstruction demonstrated in cases of portal hypertension.

METHOD

The patient is fasted and given a mild hypnotic to allay apprehension. He is placed supine on an X-ray table. The skin over the splenic area is cleaned, and the tissues in the 9th intercostal space are infiltrated with a local anæsthetic. A small lumbar-puncture needle is attached to a syringe containing 20 ml. of 70% diodone heated to body-temperature. The patient is told to hold his breath; the needle is pushed medially, and slightly posteriorly, through the 9th intercostal space into the spleen, the engagement of the organ being usually distinctly felt; and the dye is rapidly injected. The X-ray exposure is made towards the end, but before the completion, of the injection.

RESULTS AND APPLICATIONS

This procedure has now been applied in eleven cases without untoward incident. The spleen was palpable in

all of them. Two of them subsequently came to operation, and no tear or other gross lesion of the spleen was found. On one occasion the patient could not hold his breath, but no harm resulted. The intraperitoneal injection of diodone produces no reaction in animals and is apparently also harmless in man.

A radiogram from a case with normal portal circulation is shown in fig. 1. The " filling defect " or dilution of the dye at the junction of the splenic and superior mesenteric veins is clearly seen.

Some interesting features of the physiology of the spleen have emerged during the development of this method :

(1) The great rapidity with which the diodone leaves the spleen (2 seconds or less) supports the conception of an " open " splenic circulation (MacKenzie et al. 1941) and opposes the " closed " circulation hypothesis of Knisely (1936).

(2) The diodone does not diffuse throughout the splenic pulp. The spleen seems to work in distinct compartments draining into the splenic vein near the hilus (Douglass et al. 1950).

(3) Fig. 1 and similar radiograms taken during the preliminary experimental work on dogs throw doubt on the idea of " stream-lining " in the portal blood-flow; the radio-opaque material fills the whole liver and can certainly be seen in the right lobe in fig. 1. This confirms the findings of Daniel and Prichard (1951), who showed that ' Thorotrast ' injected into a branch of the superior mesenteric vein in different laboratory animals perfused the whole liver.

Several clinical applications of this simple method suggest themselves. The demonstration of the intrahepatic circulation may be of diagnostic significance in obscure hepatomegaly. The patency of a portocaval anastomosis may be demonstrated. (This has been done experimentally in dogs, but no opportunity has yet arisen in man.) The main value, however, will be in portal hypertension, in which the splenic venogram differentiates between intrahepatic and extrahepatic obstructions and may thus be the deciding factor in the treatment to be adopted, as in the following illustrative case.

CASE-RECORD

A Nyasaland Bantu male, aged 29, presented with a history of two attacks of malaria, the first 15 and the second 5 years previously. Three months before admission he had two small hæmatemeses a week apart, but at the time no lesion in his stomach or his duodenum was detected by radiography. Two more hæmatemeses occurred, the last 10 days before admission.

On examination he was pale (hæmatocrit 15%) and his enlarged smooth firm non-tender spleen was felt 3 in. below the costal margin.

Radiography now revealed a normal œsophagus, but there was considerable hypertrophy of the mucosa at the cardiac end of the stomach.

Fig. 1—Splenic venogram showing diodone in splenic vein and portal vein in a case in which the portal circulation was normal. Note filling defect at junction of splenic vein with superior mesenteric vein.

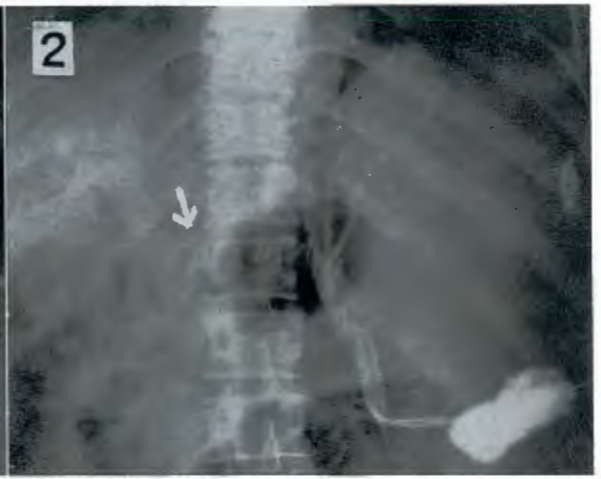

Fig. 2—Splenic venogram in a case of thrombosis of splenic vein, showing complete absence of radio-opaque material from splenic vein, but diodone passing through anastomosing left gastric and short gastric veins to portal vein.

Splenic venography (fig. 2) showed complete obstruction of the splenic vein, with the radio-opaque material reaching the portal vein via anastomosing short gastric and left gastric veins.

Liver-function tests gave slightly abnormal values.

Operation was therefore at first deferred, but a month after admission profuse hæmatemesis recurred and an emergency splenectomy was carried out. At operation the thrombosis of the splenic vein and the gross dilatation of the gastric veins were confirmed.

Biopsy.—The histological appearance of the spleen was that of portal hypertension, and a specimen of the liver showed degeneration of liver cells, atrophy of cells with pigmentation, pigment within Kupffer cells, hyperplasia of cells, minimal fibrosis, and bile-duct proliferation. From the specimen neither postnecrotic fibrosis nor cirrhosis of the liver could be diagnosed.

Postoperative recovery was uneventful, and there has been no further hæmatemesis; but three months after the splenectomy the liver-function tests still gave abnormal results; so the ultimate prognosis must remain in doubt.

In this case the splenic venogram indicated clearly what the surgeon could expect to find at operation: obstruction of the splenic vein and dilatation of the gastric veins, including the submucosal veins (the "hypertrophied mucosa" of the radiologist), but no œsophageal varices, because the gastric veins drained back into the portal circulation. These predictions were confirmed.

SUMMARY

A method is described for the visual demonstration of the splenic and part of the portal circulation by the injection of radio-opaque material into the spleen without laparotomy.

Several uses of the method are indicated, and its value is shown in a case of thrombosis of the splenic vein.

Our thanks are due to Dr. L. Mirvish and Mr. G. Sacks for permission to publish this case.

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care not to obstruct the splenic vessels. (The opening after suture should admit a finger; if the splenic vein is obstructed, the spleen becomes congested, making closure of the skin difficult). By taking the same precautions, the internal and external oblique muscles are sutured with interrupted catgut sutures. Next the skin flaps are brought together over the spleen with many kaldermic sutures (the tension is equally distributed if closely placed sutures are used). Further undermining will ease the tension if the skin flaps are too tight. The dead space round the spleen should not be drained as infection may follow. A fairly tight abdominal binder is applied and this is covered by elastoplast. The procedure takes about thirty minutes.

Post-Operatively: it is advisable to administer penicillin to prevent infection of the dead space round the spleen. The wound is usually soundly healed at the end of fourteen days, when the stitches are removed.

Advantages:

The main advantages of this method as compared with that of Barcroft (1927), are as follows:

(1) There is no discharge of serum from the wound as occurs with the spleen outside the skin, and frequent dressings are not necessary.

(2) The risk of sepsis is diminished and primary healing usually occurs.

(3) The spleen is less likely to be traumatized. The completely exteriorized spleen, being insensitive, is often injured, and a dog may even eat is own spleen.

(4) The subcutaneous spleen can be injected easily by fixing it between the fingers.

(5) Fibrosis of the capsule and trabeculae and shrinking of the spleen in size, are not as prominent as in the completly exteriorized spleen.

Disadvantages:

The disadvantages of this method are:

(1) The raw surface between the spleen and skin leads to the formation of an extensive collateral circulation. However, the main blood flow remains through the splenic vessels.

(2) The spleen cannot be inspected and changes in its size, although palpable, cannot be observed accurately.

(3) A hernia may develop through the incision. However, this may also occur after the spleen has been exteriorized completely.

(4) The spleen may recede into the abdomen, due to a faulty operative technique.

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