THE EFFECTS OF RETROGRADE PORTAL VENOUS FLOW FOLLOWING SIDE-TO-SIDE PORTACAVAL ANASTOMOSIS: A COMPARISON WITH END-TO-SIDE SHUNTS *

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Reversal of blood flow in the portal vein has been demonstrated in a few patients with Laennec's cirrhosis (1, 2). This circulatory abnormality is probably uncommon and occurs only when the disease has distorted vascular pathways so that outflow resistance through the hepatic veins exceeds that existing through the portal venous channels. Retrograde flow in the hepatic branch of the portal vein following side-to-side portacaval anastomosis has been more consistently demonstrated in man (1, 2) and experimental animals (3). Reversal of flow in the portal vein, whether it occurs in an occasional patient with portal cirrhosis or, more commonly, following side-to-side portacaval anastomosis, implies that the entire inflow of blood to the liver is through the hepatic artery; this leaves two routes available for the egress of blood—the usual circulatory pathways out the hepatic veins and by retrograde flow out the portal vein. The hepatic artery is also the only blood supply to the liver following an end-to-side portacaval anastomosis; however, because no flow is possible from the liver out the ligated portal vein, all of the arterial inflow passes through the liver lobule and leaves via the hepatic veins. The important difference between end-to-side shunts on the one hand, and both portal cirrhosis and side-to-side anastomosis on the other, is that the increment of blood flowing out the portal vein would occur at the expense of circulation through the hepatic veins. This condition would be of no concern, or might even be advantageous, if the pathways between the hepatic artery and portal vein carried the blood through the hepatic sinusoids. However, if communications between these vessels occurred at the presinusoidal level, perfusion of the liver lobule might be impaired and cause hepatocellular ischemia.

The purposes of this study were twofold: first, to study some of the functional aspects of retrograde portal venous blood flow in dogs following surgical side-to-side portacaval anastomosis; and second, to compare the effects of side-to-side with end-to-side types of anastomoses in the otherwise normal dog.

MATERIALS

Successful experiments were performed on 26 mongrel dogs divided into three groups. Group 1 consisted of 13 dogs (nos. 1–13) studied from two different aspects designed to evaluate the effects of side-to-side portacaval anastomoses. In 8 splenectomized dogs (nos. 1–8) studied 1 to 12 months after a side-to-side shunt the experimental preparation shown in Figure 1 was used. Under pentobarbital anesthesia, cardiac catheters (no. 8 or 9F) were passed via both external jugular veins into a branch of the hepatic vein (HV) and the inferior vena cava (IVC). A laparotomy was performed, the anastomosis visualized, and under manual guidance the IVC catheter was placed 3 to 5 cm cephalad to the shunt. Another catheter (no. 6 or 7F), passed via the femoral vein and guided through the shunt, was directed toward the liver and left in the portal vein 4 to 5 cm from the liver (PV_H, the subscript refers to the hepatic side of the shunt). A polyethylene catheter (PD 90) was inserted into a distal mesenteric vein near the intestine and passed proximally until it could be felt in the portal vein 5 to 7 cm above the shunt (PV_G, the subscript refers to the gut side of the anastomosis). Finally, the femoral artery (FA) and vein (FV) were cannulated.

The direction of flow through the anastomosis in 6 dogs (nos. 1–6) was determined by regional indicator dilution studies. Indocyanine green (4) was injected into the FV, PV_H and PV_G catheters while blood was sampled from either the IVC or HV catheter with a Harvard constant speed withdrawal apparatus.[1] Time-

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[1] Dover, Mass.

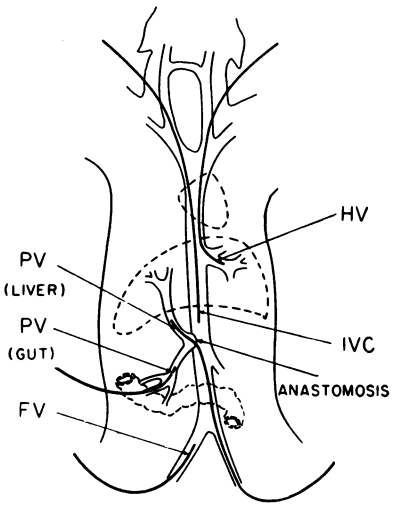

FIG. 1. SCHEMATIC REPRESENTATION OF AN EXPERIMENTAL ANIMAL AFTER A SIDE-TO-SIDE PORTACAVAL ANASTOMOSIS. The positions of the sampling and injecting catheters are shown. Abbreviations are given in the text.

concentration curves were detected with a Colson cuvet densitometer [2] and inscribed on a Varian G-10 recorder.[3]

After establishing that retrograde flow occurred in the PV_H segment of the portal vein, the experiment was amended to evaluate its effects on hepatic metabolism. In 5 dogs (nos. 4–8) a priming dose of 1 to 3 mg per kg of sulfobromophthalein (BSP) was followed by a sustaining infusion of 0.06 to 0.10 mg per kg per minute into the FV through a Bowman constant speed infusion pump.[4] After 30 minutes, two or three successive 10-minute simultaneous blood samples were obtained from the FA, HV and PV_H cannulas. Dog 13 was studied intact and then had a laparotomy to allow aspiration of blood from PV_H with a syringe so only single sample comparisons are reported. Plasma BSP concentration was determined in duplicate by the method of Gaebler (5). Heparinized blood was obtained anaerobically from the same sites and the PV_G cannula in Dogs 4–8, and from the FA and HV in Dogs 9–13 for determination of oxygen content by the manometric method of Van Slyke and Neill (6). Oxygen capacity was measured in the arterial sample; percentage saturation at all collection sites was related to the single capacity measurement after ensuring that hemoglobins and hematocrits were the same in all samples (if not, appropriate corrections were made).

Group 2 consisted of 7 dogs in each of which a splenectomy and end-to-side portacaval anastomosis were performed 1 to 12 months prior to final study. Oxygen and BSP determinations were the same as in group 1 animals with the exception that PV_H samples were unobtainable because the liver limb of the PV is obliterated in end-to-side shunts. Total hepatic blood flow was calculated by the method of Bradley, Ingelfinger, Bradley and Curry (7), using an assumed plasma volume of 90 ml per kg and the uncorrected arterial hematocrit. There were no problems regarding the direction of blood flow following end-to-side shunts so indicator dilution studies were not performed.

Group 3 consisted of 6 dogs in each of which no portacaval shunt had been performed. Each had a laparotomy so that a complete set of samples could be obtained as in group 2 dogs.

RESULTS

Directional flow studies (group 1; Dogs 1–6). The proper position of the HV catheter was ascertained in each dog by injecting indocyanine green into the FV while withdrawing blood from the HV through the cuvet. If the catheter was not far enough into the HV, the slightest reflux of dye from the IVC could be easily detected by the prompt inscription of a curve with a sharp upstroke; a low, flat and much delayed curve, seen with a correctly placed catheter, indicated that the dye had made its appearance following passage through the lungs and had arrived at the liver via the systemic circulation and hepatic artery. Indocyanine green was injected into the portal vein on the intestinal side of the anastomosis (PV_G) while sampling from the HV. In no instance was dye recovered from the HV, indicating the complete diversion of the intestinal portal venous drainage into the IVC. This was confirmed by injecting dye through the PV_G cannula while

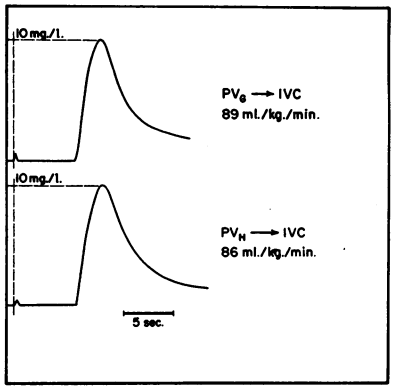

FIG. 2. SIMILARITY IN SUCCESSIVE INDICATOR DILUTION CURVES AS RECORDED FROM THE IVC CEPHALAD TO THE SHUNT OPENING AFTER PV_H AND PV_G INJECTIONS OF 1.25 MG INDOCYANINE GREEN. The catheter delay from the time of injection (the vertical spike) is 3.8 seconds. Abbreviations are given in the text.

[2] Elyria, Ohio.
[3] Palo Alto, Calif.
[4] Brooklyn, N. Y.

sampling from the IVC cephalad to the anastomotic site; an early sharp dye curve (Figure 2) indicated blood flow through the shunt.

When dye was injected into the portal vein on the hepatic side of the anastomosis (PV_H), no early appearing dye was recorded at the HV, in all animals but two. In these two dogs large volumes of dye (5 ml instead of 1 ml) were injected rapidly, causing a transient rise in PV_H pressure. Using smaller (1 ml) volumes or a slower rate of injection resulted in successively lower curves until no dye was recorded at the HV, as shown in Figure 3. These curves demonstrate that the preferred direction of flow in the PV_H is from the liver out through the shunt to the IVC. When the pressure is raised in the PV_H the flow away from the liver can be temporarily reversed and blood will pass through to the HV. However, reversal of the retrograde flow in the PV_H was probably facilitated by the presence of the catheter passing through the shunt which narrows the orifice and increases resistance to flow out the anastomosis. It is conceivable that the flow of some dye from the PV_H into the liver might escape detection because extraction of indocyanine green will take place in a single passage through the sinusoids (8). However, curves were always promptly recorded from the IVC following PV_H injection and occasionally were quantitatively similar to curves obtained after PV_G injection (Figure 2). Barring problems from streamline blood flow (see below), this indicates that the same flow was being measured and should thereby account for all the dye injected.

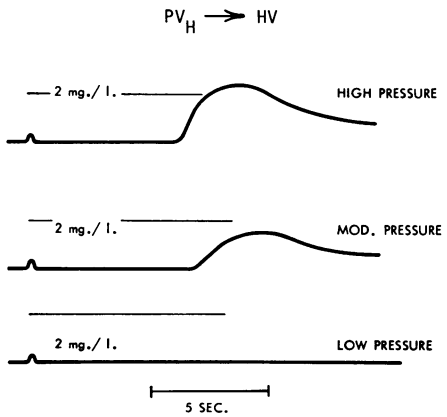

FIG. 3. INDICATOR DILUTION CURVES RECORDED FROM THE HV FOLLOWING PV_H INJECTION. The preferred retrograde portal venous flow (away from the HV) can be reversed by using high injection pressures. The amount of dye used and the catheter delay are the same as those given in Figure 2.

In most animals, however, sampling at the IVC following injections into the FV, PV_G and PV_H yielded grossly different curves. This means that either there is streamline flow and incomplete mixing of dye and blood or diversion of dye away from the sampling site. For reasons given above, it is felt that PV_G and PV_H blood flow is through the anastomosis and the curves should have similar areas; the failure to record identical curves indicates streamlining of blood flow. In two animals, dye was recovered in blood sampled from the IVC 2 to 3 cm caudad to the shunt opening following PV_H injection; this is best accounted for by a jet effect of the large blood flow from the liver traveling a few centimeters retrograde in the IVC.

Functional effectiveness of the retrograde portal venous flow (group 1). After the demonstration that retrograde flow occurred in the portal vein in dogs, studies were performed in ten dogs (nos. 4–13) to evaluate the functional significance of this blood flow. The results of oxygen and BSP analyses are presented in Tables I and II. There was greater extraction of BSP and oxygen in the blood flowing out the HV than out the PV_H. However, it was noteworthy that there was invariably some uptake of oxygen and BSP in PV_H, indicating that this blood had passed functioning hepatic cells and was being utilized. All five of the animals showed relatively the same division of function with evidence that the fraction of total hepatic inflow leaving the liver via the HV was being utilized to a greater degree than the outflow via PV_H. In order to decide if some of the results found in Dogs 4–8 were induced in part by the effects of the laparotomy which was performed to allow portal venous sampling, Dogs 9–13 were studied with only HV catheterizations and without abdominal surgery. No PV_H samples could be obtained, but the same large arterial-hepatic venous oxygen differences and BSP extractions were noted as in Dogs 4–8 that had had a laparotomy; therefore, the data on Dogs 4–8 were not considered to have been influenced by the collection methods.

Arterial oxygen saturation (FA_{O_2}). The mean FA_{O_2} for ten side-to-side, seven end-to-side, and

TABLE I

Oxygenation data in intact and laparotomized dogs after side-to-side portacaval anastomosis and splenectomy *

Dog no.	Wt	Hct	FA			HV		PV_H		PV_G		A-HV	A-PV_H
			Cap.	Cont.	Sat.	Cont.	Sat.	Cont.	Sat.	Cont.	Sat.		
	kg	%	*vol %*		%	*vol %*	%	*vol %*	%	*vol %*	%	*vol %*	
						A. Laparotomy							
4	22.8	40.0	18.0	16.2	90	6.4	35	13.1	73			9.8	3.1
5	17.0	39.2	17.5	16.0	91	7.0	40	14.0	80	10.2	58	9.0	2.0
6	20.4	37.8	17.3	15.4	89	8.8	51	11.8	68	13.2	76	6.6	3.6
7	20.0	37.5	16.8	15.4	92	5.0	30	11.5	68	12.4	74	10.4	3.9
8	17.8	46.2	21.4	18.6	87	7.0	33	14.7	69	12.9	60	11.6	3.9
						B. Intact							
9	17.1	34.5	16.0	14.6	91	6.6	41					8.0	
10	20.6	47.6	21.8	18.9	87	8.5	39					10.4	
11	15.7	35.3	15.6	13.4	86	5.8	37					7.6	
12	15.4	29.3	13.1	11.0	84	4.4	33					6.6	
13	17.7	44.6	21.1	19.5	92	8.5	40					11.0	
Mean		39.2			88.9		37.9		71.6		67.0	9.10	3.30
SEM		1.79			0.89		1.83		2.25		3.97	0.573	0.361

* Abbreviations: Hct, arterial hematocrit; FA, femoral artery; HV, hepatic vein; PV_H, portal vein, hepatic limb; PV_G, portal vein, gut limb; A-HV, arterial-hepatic vein oxygen difference; A-PV_H, arterial-portal vein (hepatic limb) oxygen difference; Cap., oxygen capacity; Cont., oxygen content; Sat., oxygen saturation; SEM, standard error of the mean.

six control dogs was 88.9, 90.0 and 88.8 per cent, respectively. These and the oxygen data given below are from single sample determinations in each dog. The lower than normal levels undoubtedly reflect the respiratory effects of the anesthesia and the duration of the experiment. No difference was encountered between the three groups of animals, as shown in Tables I and III.

TABLE II

Mean plasma sulfobromophthalein (BSP) values, two successive 10-minute samples, in group 1 dogs studied with laparotomy following side-to-side portacaval anastomosis *

Dog no.	FA	HV	PV_H	A-HV	A-PV_H	Cl_{BSP}
	mg %	*mg %*	*mg %*	%	%	*ml/min*
4	4.42	1.96	3.74	56	15	49
5	4.30	3.50	3.84	19	11	25
6	4.62	3.82	3.90	17	16	31
7	2.48	1.46	2.06	41	17	60
8	3.36	2.66	2.98	21	11	32
13†	3.36	2.42	2.96	28	12	41
Mean				29.3	13.7	39.7
SEM				6.24	1.29	5.33

* Abbreviations: A-HV extr., arterial-hepatic vein BSP extraction (FA-HV/FA × 100); A-PV_H extr., arterial-portal vein BSP extraction (FA-PV_H/FA × 100); Cl_{BSP}, BSP clearance (BSP removal rate/arterial BSP concentration). For other abbreviations, see footnote to Table I.
† Single samples only.

Hepatic vein oxygen saturation (HV_{O_2}). HV_{O_2} differed significantly between the three groups (Tables I and III). The mean values were: ten side-to-side dogs, 37.9 per cent (compared with controls $p < 0.001$, compared with end-to-side $p < 0.005$); seven end-to-side dogs, 55.6 per cent (compared with controls $p < 0.05$); and six controls, 66.2 per cent.

Arterial-hepatic venous oxygen difference ($FA–HV_{O_2}$). The virtually constant FA_{O_2} and the changing HV_{O_2} were reflected in a progressive widening of the $FA–HV_{O_2}$ between the six controls, seven end-to-side and ten side-to-side dogs; the mean values for these groups are 4.62, 6.24 and 9.10 vol per cent, respectively. These differ from one another at the same level of significance indicated above under HV_{O_2}.

Portal venous oxygen saturation (PV_{O_2}). The PV_{O_2} was higher in the six control animals (77.3 per cent) than PVG_{O_2} in five side-to-side dogs (67.1 per cent) and PV_{O_2} in four end-to-side dogs (72.0 per cent). The differences between these values were not statistically significant.

Hematocrits. A wide variation in hematocrits within all three groups was encountered (Tables I and II). The mean values in the ten side-to-side dogs (39.2 mm) and seven end-to-side dogs

TABLE III

Oxygenation data from end-to-side anastomosis and control animals *

Dog no.	Wt	Hct	FA			HV		PV		A-HV
			Cap.	Cont.	Sat.	Cont.	Sat.	Cont.	Sat.	
	kg	%	*vol %*		%	*vol %*	%	*vol %*	%	*vol %*
Group 2: End-to-side portacaval anastomosis										
14	24.1	45.7	20.9	19.5	93	14.9	71	16.8	80	4.6
15	19.8	39.6	18.7	16.2	86	10.5	56	13.3	71	5.7
16	21.7	46.2	22.2	19.5	88	14.6	65	16.3	73	4.9
17	18.0	47.7	21.9	19.5	89	11.5	52	13.9	64	8.0
18	17.5	27.5	13.0	11.3	87	3.4	26			7.9
19	18.7	43.6	19.8	18.2	92	10.6	53			7.8
20	16.7	38.0	16.8	15.9	95	11.1	66			4.8
Mean		41.2			90.0		55.6		72.0	6.24
SEM		2.65			1.24		5.58		2.58	0.596
Group 3: Control										
21	17.8	54.8	24.6	22.2	90	17.1	70	20.7	84	5.1
22	17.7	42.0	17.9	15.2	85	9.7	54	10.4	58	5.5
23	21.1	46.3	21.0	19.3	92	16.4	78	18.4	87	2.9
24	21.0	40.8	19.1	16.7	88	12.1	63	15.6	82	4.7
25	15.1	48.6	21.9	20.6	94	16.1	74	17.0	78	4.5
26	15.1	42.5	19.2	16.2	84	11.2	58	14.1	75	5.0
Mean		45.8			88.8		66.2		77.3	4.62
SEM		2.15			1.59		3.71		4.27	0.373

* The abbreviations are the same as noted in Table I. The three animals in group 2 without PV data did not have laparotomies.

(41.2 mm) were both lower than the mean value for the six controls (45.8 mm), but only the side-to-side difference was significant ($p < 0.05$).

Sulfobromophthalein studies. Considerable variation occurred in arterial plasma BSP levels when a constant prime (3 mg per kg) and sustaining infusion (0.10 mg per kg per minute) were used. Values in both groups of shunted animals, especially side-to-side dogs, tended to be higher than the controls, so eventually less BSP was given to these animals (1 mg per kg prime and 0.06 mg per kg per minute sustaining). All animals receiving BSP had an extraction greater than 10 per cent at plasma levels above 1 mg per 100 ml. The difference in arterial values precludes comparison of BSP extraction ratios. Mean plasma BSP clearance values (removal rate/arterial concentration) were 39.7 ml per minute for side-to-side, 61.4 ml per minute for end-to-end, and 81.2 ml per minute for control animals (Tables II and IV). Although there is a statistically significant difference between end-to-side and side-to-side dogs ($p < 0.05$), part of this discrepancy may be due to the higher arterial plasma BSP concentrations in the side-to-side animals and therefore does not necessarily reflect reduced hepatic func-

TABLE IV

Mean plasma sulfobromophthalein (BSP) values, two successive 10-minute samples, in end-to-side and control dogs with resultant estimated hepatic blood flow, percentage extraction and BSP clearance *

Dog no.	FA	HV	EHBF	EHBF	A-HV	Cl_{BSP}
	mg %		*ml/min*	*ml/kg/min*	%	*ml/min*
Group 2: End-to-side portacaval anastomosis						
14	2.60	1.68	369	15.3	35	68
15	3.80	2.50	293	14.8	34	55
16	2.14	1.32	213	9.8	38	44
17	1.64	1.00	227	12.6	39	44
18†	1.44	0.80	278	15.9	44	78
19†	3.31	2.68	509	27.2	19	51
20†	0.90	0.56	424	25.4	38	90
Mean				13.13		61.4
SEM				2.460		6.14
Group 3: Control						
21	2.26	1.22	404	22.7	46	84
22	2.04	1.38	428	24.2	32	74
23	1.02	0.64	580	27.5	37	110
24	2.00	1.31	479	22.8	35	92
25	1.42	0.84	350	23.2	41	70
26	1.48	0.78	269	17.8	47	57
Mean				23.03		81.2
SEM				1.277		7.57

* EHBF, estimated hepatic blood flow. For other abbreviations, see Tables I and II.
† Dogs studied without laparotomy.

tion. Total estimated hepatic blood flow (EHBF) could be calculated for the six controls and seven end-to-side dogs (Table IV); however, EHBF could not be measured in side-to-side dogs from available data because it is not known what fraction of the total amount of BSP arriving at the liver is distributed to the two exit pathways. There was a significant difference in mean EHBF between the six control dogs (23.0 ml per kg per minute) and the four laparotomized end-to-side dogs (Dogs 14–17, 13.1 ml per kg per minute). The control EHBF values are lower than those commonly encountered in the laboratory (mean, 39 ml per kg per minute). Part of this variation may be from the splenectomy and part due to the abdominal procedure; evidence for the latter is shown by the three end-to-side dogs (nos. 19–21) studied without laparotomies that had higher EHBF values than the other animals in their group (Table IV).

Other results. Barring technical difficulties from the shunt procedure itself, more problems were experienced in the postoperative management of side-to-side then end-to-side dogs; side-to-side animals recovered from surgery slowly, ate poorly and often lost weight. Although we have maintained side-to-side dogs in apparent good health for more than a year, six of them died prior to study for unexplained reasons. Only two end-to-side animals died under similar circumstances. Liver function studies were not done, but a lower BSP clearance was found in side-to-side dogs. The more severe anemia, intolerance of subsequent procedures, and fragility of the animals, suggest a greater hepatic disturbance induced by the side-to-side than end-to-side types of anastomosis.

DISCUSSION

This study substantiates previous observations that retrograde flow in the PV_H occurs following side-to-side portacaval anastomosis (1–3). The original investigations, in patients with portal cirrhosis at or shortly after side-to-side anastomosis, indicated that retrograde portal venous flow occurred, but its quantitative and metabolic aspects were not measured (1, 2). Long and Lombardo (3), using direct measures of flow in normal dogs following side-to-side shunts, revealed that outflow through the PV_H accounted for 70 per cent of the hepatic arterial inflow; however, the functional effectiveness of the portal venous circulation was not analyzed. The large volume of blood flowing retrograde in the PV under these conditions is readily explained by the creation of a new pathway to the IVC offering less resistance than does flow through the usual channels via the HV. When the PV is available as an outflow vessel, hepatic arterial blood, after arriving in the liver, may leave through two routes with different resistances to flow: *1*) through the sinusoids and the hepatic veins, and *2*) through the lower resistance communications to the PV; the latter pathway is preferentially utilized in the dog.

The principal purpose of the present study was to determine if the blood flowing retrograde in the PV_H had been effectively utilized by the liver. The results show clearly that there was invariably some extraction of oxygen and of sulfobromophthalein in the portal venous effluent. The low PV_H extractions might reflect either poor tissue uptake or high blood flow; the data do not distinguish between these possibilities. However, the hepatic venous outflow was invariably more efficiently utilized than was blood leaving through the PV_H. It is of interest that evidence of appreciable function was demonstrated in the portal venous outflow and it can be concluded that at least part of this blood passed by parenchymal liver cells.

In the normal dog following side-to-side portacaval anastomosis, the volume-capacity of existing presinusoidal arterial-portal venous communications would determine how much blood reaches the sinusoids. Although ample anastomoses between hepatic arterial and portal venous channels have been demonstrated, their precise location(s) remains controversial. It was felt by Mall (9) and by Olds and Stafford (10) that the communications occurred within the liver lobule at the periphery of the sinusoids. However, subsequent injection and transillumination studies have revealed a more liberal network at the presinusoidal level (11, 12). Figure 4 shows a schematic representation of the microanatomy of the hepatic lobule. In the normal mammal, hepatic arterial blood may communicate with the portal venous circulation within the sinusoids and by presinusoidal connections with interlobular branches of the PV. The many anastomoses be-

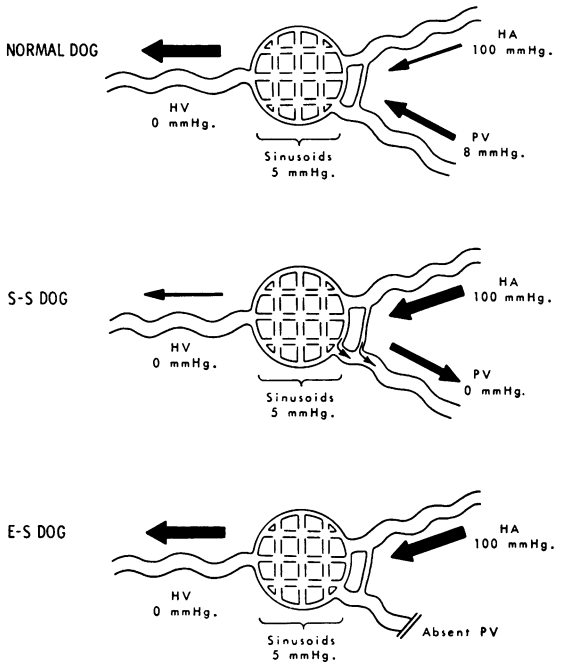

FIG. 4. SCHEMATIC REPRESENTATION OF INTRAHEPATIC BLOOD FLOW IN THE NORMAL DOG AND AFTER SIDE-TO-SIDE OR END-TO-SIDE PORTACAVAL ANASTOMOSIS. The thickness of the arrows indicates the relative magnitude of flow. The significance of the alterations is discussed in the text.

tween the HA and PV before or at the periphery of the sinusoids would offer immediate access of hepatic arterial blood to the portal venous circulation. The appreciable evidence of hepatocellular activity in the blood flowing out the PV is best explained by assuming that the interlobular hepatic arterial-portal venous communications cannot accommodate the entire inflow and that some arterial blood arrives at the liver lobule. Once this occurs, Elias (13) demonstrated that even though branches of the HA and PV meet at the periphery of the hepatic sinusoids, the inflows are separated by a streaming effect within the arterial circulation which serves to force blood toward the center of the lobule. In the same paper Elias (13) reported, and later strongly emphasized (14), arterial branches that open into the sinusoids as far into the lobule as two-thirds of the distance to the central vein. Both the "morphologically peripheral, yet physiologically central, arterial supply" (13) and the intralobular arterial communications enable a portion of the arterial blood to flow through the sinusoids to the HV and the remainder of the lobular inflow to depart via the PV where it joins with the presinusoidal "shunted" portion. There is no low resistance pathway to the IVC following end-to-side anastomosis; therefore, thorough perfusion of the lobule is maintained (Figure 4).

Without knowing the exact amount of blood distributed to the two exit pathways, it is impossible to state whether total liver function is impaired. It is possible that the excessive outflow through the PV_H occurs at the expense of adequate circulation to the center of the liver lobule. The very low HV_{O_2} indicates poor perfusion, hence large oxygen and BSP extraction, of the cells surrounding the central vein. Although the amount of ischemia necessary to interfere with hepatic cellular metabolism is unknown, it seems likely that optimal activity will be jeopardized in the oxygen environment existing after a side-to-side shunt. Poor hepatocellular function would explain why animals with side-to-side shunts are more anemic, have lower BSP clearances and clinically are more fragile than animals with end-to-side shunts.

A comparable marked reduction in HV_{O_2} was not noted in Warren and Muller's (2) studies on patients with liver disease after side-to-side anastomosis. Our own studies (15) in three patients tended to confirm these observations and, in addition, in two of our patients there was greater extraction of BSP and oxygen evident in the PV_H than in the HV outflow. However, one of the subjects had an A-HV_{O_2} difference of 9.9 vol per cent and has not done well clinically following surgery; this may be due to progression of his underlying liver disease or may reflect inadequate sinusoidal perfusion following the shunting procedure. These reports (2, 15) indicate variations within the available patient data, and usually a contrast is found between the findings following side-to-side anastomosis in humans with liver disease and in normal dogs. The most likely explanation for these data lies within the distorted parenchymal architecture of Laennec's cirrhosis, which can affect the portal venous radicles or sinusoids to a different degree. Obstructive scarring either in branches of the portal vein or in the sinusoids would impede outflow through one channel and facilitate it through the other. It seems reasonable to conclude that, although most patients with Laennec's cirrhosis are benefited by a side-to-side anastomosis, the previously nor-

mal dog suffers some impairment of adequate perfusion of the central portion of the liver lobule with resulting liabilities.

SUMMARY

Hemodynamic and metabolic studies were performed on 13 dogs following side-to-side portacaval anastomosis. Directional flow studies indicated that the proximal portal vein no longer carried blood toward the liver but served as an outflow vessel. Available evidence indicates that hepatic arterial inflow communicates extensively with portal venous blood by presinusoidal and intralobular anastomoses; following a side-to-side shunt these vessels afford a low resistance pathway to the inferior vena cava which bypasses the hepatic veins.

The metabolic effectiveness of the outflow in the portal vein was compared with that in the hepatic veins. There was invariably uptake of oxygen and sulfobromophthalein (BSP) in the portal venous effluent; however, in no instance was the evidence of metabolic efficiency as great in the portal vein as it was in the hepatic veins. Moreover, it appeared that retrograde flow out the portal vein occurred at the expense of adequate perfusion of the center of the liver lobule. The resultant low hepatic venous oxygen content reflected central lobular ischemia which could impair hepatocellular function; this mechanism was felt to be responsible for the lower BSP clearance, greater anemia and poorer survival following side-to-side shunts when compared with end-to-side anastomoses.

Findings from comparable studies in human patients with liver cirrhosis and side-to-side shunt are usually different from those in the dog. It is concluded that portacaval shunts in otherwise normal dogs do not accurately reflect the consequences of similar anastomoses in patients with Laennec's cirrhosis.

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REFERENCES

1. Longmire, W. P., Jr., Mulder, D. G., Mahoney, P. S., and Mellinkoff, S. W. Side-to-side portacaval anastomosis for portal hypertension. Ann. Surg. 1958, **147**, 881.
2. Warren, W. D., and Muller, W. H., Jr. A clarification of some hemodynamic changes in cirrhosis and their surgical significance. Ann. Surg. 1959, **150**, 413.
3. Long, R. T. L., and Lombardo, C. R. Hemodynamic observations on the hepatic circulation: Modifications produced by portacaval shunting. J. clin. Invest. 1959, **38**, 1021.
4. Fox, I. J., and Wood, E. H. Applications of dilution curves recorded from the right side of the heart or venous circulation with the aid of a new indicator dye. Proc. Mayo Clin. 1957, **32**, 541.
5. Gaebler, O. H. Determination of bromsulphalein in normal, turbid, hemolyzed, or icteric serums. Amer. J. clin. Path. 1945, **15**, 452.
6. Van Slyke, D. D., and Neill, J. M. The determination of gases in blood and other solutions by vacuum extraction and manometric measurements. I. J. biol. Chem. 1924, **61**, 523.
7. Bradley, S. E., Ingelfinger, F. J., Bradley, G. P., Curry, J. J. The estimation of hepatic blood flow in man. J. clin. Invest. 1945, **24**, 890.
8. Murray, J. F., Rafferty, J., and Maddox, R. Measurement of hepatic blood flow in dogs by the indicator dilution technic using indocyanine green. Clin. Res. 1959, **7**, 71.
9. Mall, F. P. A study of the structural unit of the liver. Amer. J. Anat. 1906, **5**, 227.
10. Olds, J. M., and Stafford, E. S. On the manner of anastomosis of the hepatic and portal circulations. Bull. Johns Hopk. Hosp. 1930, **47**, 176.
11. Wakim, K. G., and Mann, F. C. The intrahepatic circulation of blood. Anat. Rec. 1942, **82**, 233.
12. Seneviratne, R. D. Physiological and pathological responses in the blood-vessels of the liver. Quart. J. exp. Physiol. 1949, **35**, 77.
13. Elias, H. A re-examination of the structure of the mammalian liver. II. The hepatic lobule and its relations to the vascular and biliary systems. Amer. J. Anat. 1949, **85**, 379.
14. Elias, M. H. Morphology of the liver *in* Liver Injury: Transactions of the Eleventh Conference, F. W. Hoffbauer, Ed. New York, Josiah Macy Jr. Foundation, 1952, p. 111.
15. Mulder, D. G., and Murray, J. F. An evaluation of the side-to-side portacaval anastomosis. Surg. Forum 1960, **11**, 278.