Extra- and Intrahepatic Portal Hypertension without Cirrhosis (Hepatoportal Sclerosis) *

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WHEN portal hypertension occurs in the absence of cirrhosis, extrahepatic portal venous bed block is most often indicated etiologically. Ablation of blood flow through the portal vein is believed to be the dominant pathologic mechanism, while liver architecture and function remain undisturbed.

Cases of unexplained portal hypertension have been reported in which hepatic architecture and function were considered to be normal and in which the portal vein was patent.[4, 7, 8, 16, 22, 28, 30, 36] Information concerning the later assessment of these cases is conspicuously lacking. Occasionally we have also observed cases of this type. Many were considered to be examples of extrahepatic portal hypertension until portal vein patency was established by splenoportal venography, operation or both. When a more critical inquiry was directed toward this group, curious features were identified. Although the usual mode of initial presentation was unheralded variceal bleeding, occasionally it was ascites. Whereas function and gross and histologic appearance of the liver could be interpreted as being within normal limits on initial presentation, and whereas most of the patients appeared clinically well after operation, none of these features was necessarily sustained. Most patients later developed abnormal liver tests, some became encephalopathic and a few subsequently died in liver failure. Enigmatically and surprisingly, all of these curious features were duplicated in the patients with classic extrahepatic portal hypertension who were seen during the same period. Patency or occlusion of the portal vein seemed to be the only distinguishing feature. Further in none of these adult cases of extrahepatic portal bed block could a specific causative mechanism for the portal occlusion be identified; specifically, none had sustained any of the processes purported to be etiologic such as omphalitis, peritonitis, pancreatitis, polycythemia or abdominal trauma. In addition, a few patients possibly representing an intermediate stage or a bridge between the two groups have been observed in whom the portal vein was incompletely obliterated by a sclerotic process. In other respects these patients were indistinguishable from the others. Clinical and pathologic details of these three groups of patients are being presented not only because of the clinical interest they evoke, but because of a growing suspicion that they may be variants of the same underlying disease mechanism. We suspect that this underlying mechanism may reside within the portal vein and venules, and have chosen the term hepatoportal sclerosis to describe this disease process.

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Material

This study includes 36 adult patients with portal hypertension whose livers were initially considered to be functionally and architecturally within normal limits. They were selected from patients operated upon for portal hypertension during the last 18 years at the Los Angeles County Hospital and from the private practice of the authors. They have been separated into three groups for the purpose only of initial comparison. Group I (13 patients) represent those with extrahepatic portal vein occlusion. Group II (6 patients) represent those with sclerotic, incomplete obliteration of the portal vein. Group III (17 patients) are those whose portal vein was widely patent. The status of the portal vein was established in all patients by means of splenoportal venography, operation or necropsy.

Many of the patients in Group III, those with an open portal vein, were obtained by reviewing the wedge biopsies of the liver in all patients who had had a portacaval shunt. Some of these patients who had a suspiciously normal appearing biopsy were excluded if the size of the biopsy specimen was insufficient to preclude the possibility that it might have represented only a segment from within a large hepatic nodule. Similar cases with noncirrhotic appearing biopsies were excluded if the operating surgeon described the gross appearance of the liver as being nodular. Three patients with segmental splenic vein occlusion due to chronic pancreatitis were also excluded since their established etiology and marked difference in management requirements separate them from all other cases of portal hypertension.

In Table 1 the gross clinical data are summarized and in Table 2 a more detailed, individual compilation is provided on the 38 patients. The mean age was 43 years with a range from 17 to 74. Distribution by sex was nearly equal. Chronic alcoholism was present in only two of the entire group, Cases 5 and 15. Two thirds are currently alive, one to 18 years after initial presentation. Of 12 deaths, seven were due to hepatic failure, three to exsanguination and two were postoperative fatalities. Approximately one third developed ascites and an equal number subsequently became encephalopathic. There was no important correlation between the initial presence of ascites and the subsequent development of encephalopathy; only four of those with ascites later became encephalopathic.

The degree of ascites was variable. In two, Cases 10 and 36, moderate ascites was present only at necropsy. In six, Cases 5, 9, 14, 24, 32 and 35, tense ascites occurred at some time prior to operation. In the remainder, ascites of 500 to 1,000 ml. was noted at operation. With the exception of the two patients in whom terminal ascites occurred, only three patients had persistent postoperative ascites. All three were members of Group I (extrahepatic portal hypertension) and in none was portal hypertension relieved by the surgical procedure. Two of these, Cases 5 and 9, are dead. The third, Case 1, currently has only minimal

TABLE 1. *Extra- and Intrahepatic Portal Hypertension without Cirrhosis (Hepatoportal Sclerosis). Summary of Clinical Data*

	Total	Group I	Group II	Group III
Number of cases	36	13	6	17
Age—mean (range)	43 (17-74)	38 (17-73)	47 (30-74)	52 (29-71)
Sex—male/female	17/19	6/7	4/2	7/10
Ascites	13	5	2	6
Encephalopathy	12	3	0	9
Deaths (hepatic failure)	12 (7)	4 (2)	1	7 (5)

TABLE 2. *Clinical Details of 36 Patients*

Case No.	Sex	Presentation: Age	Presentation: Manifestation	Age 1st Hemorr.	At Presentation: Hepatomegaly	Splenomegaly	Ascites	C-B Murmur	Bilirubin (mg. %)	Alb./Glob. (Gm. %)	Prothrombin (%)	BSP (% at 30 min.)	WHVP (mm. Hg)	HBF (mL./min.)
Group I. Portal Vein Totally Occluded														
1	F	46	G. I. Hem.	46	0	+	+	0	0.7	3.1/3.0	26	16	2	1080
2	M	40	G. I. Hem.	40	0	0	+	0	0.8	2.5/2.8	75	20	3	1450
3	M	15	Splenomegaly	17	0	+	0	0	0.7	4.4/3.5	80	5	3	1130
4	M	18	G. I. Hem.	18	0	+	0	0	1.2	4.2/2.1	80	10	—	—
5	F	56	G. I. Hem.	56	0	+	+	0	norm.	4.9/1.7	125	10	2	—
6	F	38	Splenomegaly	41	0	+	0	0	0.5	3.7/2.5	100	26	15	1080
7	F	58	G. I. Hem.	58	+	0	0	0	0.4	3.3/3.6	108	14	—	—
8	M	10	Splenomegaly	20	0	+	0	0	1.2	2.9/2.3	85	7	7	430
9	M	21	G. I. Hem.	21	+	+	+	0	2.2	4.1/3.9	100	11	21 cm.*	—
10	F	52	G. I. Hem.	52	0	+	0	0	1.0	4.1/2.4	105	10	2	—
11	F	40	Splenomegaly	41	+	+	0	0	0.6	3.2/3.6	70	14	—	—
12	M	73	G. I. Hem.	73	0	+	0	0	0.6	3.1/2.2	70	23	3	1150
13	F	17	G. I. Hem.	17	0	+	0	+	norm.	4.3/3.0	50	4*	—	—
Group II. Portal Vein Partially Occluded														
14	F	33	G. I. Hem.	33	0	+	+	0	—	2.6/2.6	114	—	—	—
15	M	30	G. I. Hem.	30	+	+	0	0	0.8	3.6/4.3	87	8	—	—
16	M	54	G. I. Hem.	54	0	+	0	0	norm.	4.8/3.0	100	2*	elev.	—
17	M	58	G. I. Hem.	58	0	+	+	0	0.9	3.5/2.3	65	7*	—	—
18	F	74	G. I. Hem.	74	+	+	0	0	0.2	3.3/3.2	70	16	—	—
19	M	35	G. I. Hem.	35	0	+	0	0	0.3	4.1/1.5	43	3*	—	—
Group III. Portal Vein Patent														
20	M	46	G. I. Hem.	46	0	+	0	0	—	3.8/3.4	47	tr.*	—	—
21	M	71	G. I. Hem.	71	+	+	+	0	0.7	3.9/3.0	58	19*	7	1140
22	F	61	G. I. Hem.	61	+	+	0	0	1.8	3.5/?	100	25*	—	—
23	F	46	G. I. Hem.	46	0	+	+	0	0.4	4.1/3.6	—	10*	—	—
24	F	53	G. I. Hem.	53	+	+	+	0	—	3.6/3.6	—	5*	—	—
25	M	53	Splenomegaly	—	+	+	0	+	2.9	4.1/2.3	80	16*	—	—
26	F	36	G. I. Hem.	36	0	+	0	0	0.5	3.9/3.8	75	10*	3	—
27	F	36	G. I. Hem.	36	0	+	0	+	—	4.4/1.7	89	2*	—	—
28	F	50	G. I. Hem.	50	+	+	0	+	1.2	4.4/1.7	100	8	—	—
29	M	29	G. I. Hem.	29	+	+	0	0	1.2	3.0/3.2	80	—	—	—
30	F	66	G. I. Hem.	66	0	+	0	0	0.8	3.5/2.3	92	19*	—	—
31	M	59	G. I. Hem.	59	0	0	0	+	0.8	4.0/1.8	33×	45×	—	—
32	F	44	Ascites	46	+	+	+	0	0.9	3.2/2.6	100	27*	—	—
33	M	49	G. I. Hem.	49	0	+	0	0	—	3.8/3.7	100	25	—	—
34	F	56	G. I. Hem.	56	0	+	0	0	0.7	3.1/3.3	60	19	7	705
35	F	64	Ascites	—	+	+	+	0	0.8	3.5/1.5	35	15*	—	—
36	M	70	G. I. Hem.	70	0	+	0	0	0.5	4.7/2.8	60	10	4*	645*

* 45 minute BSP.
** 60 minute BSP.
× During acute bleeding.
* Postoperative.
* Water.
≠ PC = portacaval shunt; SR = splenorenal shunt; S = splenectomy; Ex = exploration; MS = make-shift shunt; CI-M = Clatworthy-Marion shunt; VL = varical ligation; T = Tanner gastric transection; EG = segmental esophagogastrectomy with colonic interposition; Tr = splenic transposition.

ascites, but a continued duiretic program is necessary to maintain this status.

The degree of encephalopathy was also variable. In five patients, Cases 5, 9, 22, 24 and 32, it occurred terminally only, and in Case 5 it was in association with gastrointestinal bleeding. In Case 25, encephalopathy was intermittent, but progressive, and finally was terminated by death due to hepatic failure 3 years after operation. In Case 36, encephalopathy was severe and incapacitating and led 2 years after portacaval shunt to operative colonic exclusion in an effort to curb its severity. This patient failed to survive the second operation. In the remainder, encephalopathy has been

with Portal Hypertension without Cirrhosis

Operation		Last Assessment					
Age	Type	Age	Bilirubin (mg. %)	Alb./Glob. (Gm. %)	Prothrombin (%)	BSP (% at 30 min.)	Comments
				Group I. *Portal Vein Totally Occluded*			
46 & 47	Ex, MS	48	0.6	3.9/2.8	88	—	Alive; ascites; one *minor* hemorrhage; no encephalopathy.
43	SR	49	1.0	3.8/5.0	59	23	Alive & well; no bleeding, encephalopathy or ascites.
15 & 17	S, Cl-M	20	—	—	—	—	Alive; presumably well; no bleeding.
19	S, VL	20	—	4.2/2.1	80	10	Dead; exsanguination.
62	S, VL	66	2.1	3.8/3.3	50	—	Dead; hepatic failure and hemorrhage.
38 to 44	S, Ex, T, EG	51	0.4	3.7/4.6	90	13	Alive; no bleeding, ascites or encephalopathy. Nutritional problem.
—	—	61	—	3.8/4.6	—	16	Alive; one hemorrhage; no ascites or encephalopathy.
20	SR	25	0.7	3.2/3.1	115	14	Alive & well; no bleeding, encephalopathy or ascites.
23 & 37	S, EG	38	—	2.3/4.4	69	7**	Dead; hepatic failure and inanition.
58 & 59	S, T	62	0.1	3.2/2.8	19	—	Dead; exsanguination; had ascites.
41 to 43	Ex, Cl-M, Tr	46	1.8	3.1/4.9	60	43	Alive & well; no bleeding, encephalopathy or ascites.
73	SR	75	0.8	3.9/4.2	65	31	Alive; periodic encephalopathy; no bleeding or ascites.
17	SR	20	—	3.6/2.8	76	9*	Alive & well; fetor; no bleeding, ascites or encephalopathy.
				Group II. *Portal Vein Partially Occluded*			
40	PC*	40	—	—	—	—	Dead one mo. post-op.; exsanguination; PC shunt occluded.
31	PC	33	0.7	3.1/5.2	59	31	Alive & well; fetor; no encephalopathy, bleeding or ascites.
54 & 56	S, PC	68	1.6	3.6/3.0	53	15	Alive; severe Parkinson's; no bleeding or ascites.
61	PC	63	1.9	3.0/2.5	35	12*	Alive & well; no encephalopathy, bleeding or ascites.
75	PC	81	—	3.6/3.5	—	25	Alive & well; no encephalopathy, bleeding, ascites.
37	SR	47	—	3.5/2.9	88	20	Alive & well; no encephalopathy, bleeding, ascites.
				Group III. *Portal Vein Patent*			
47	PC	65	1.8	4.1/2.9	46	29	Alive; encephalopathy 15 years postop.; no bleeding, ascites.
71	PC	75	0.4	3.3/3.7	50	22	Alive; mild encephalopathy; fetor; no bleeding or ascites.
61	PC	63	—	—	—	—	Dead; hepatic failure.
46	PC	59	—	—	—	—	Alive; Parkinson's; no encephalopathy or bleeding.
54	PC	56	—	—	—	—	Dead; hepatic failure.
53	PC	56	—	—	—	—	Dead; severe encephalopathy; hepatic failure.
38	SR	44	0.4	4.5/3.4	75	23	Alive; not recently examined.
36 and 49	S, PC	51	1.1	4.3/3.8	150	15	Alive & well; fetor; no bleeding, encephalopathy or ascites.
50	PC	54	1.6	3.6/2.1	54	30	Alive; mild encephalopathy; no bleeding or ascites.
—	—	29	—	—	—	—	Dead; exsanguination; also had glomerulonephritis.
66	PC	69	—	—	—	—	Alive & well; no encephalopathy, ascites.
59	PC	66	1.9	3.8/3.3	31	36	Alive; mild encephalopathy; fetor; no bleeding or ascites.
47	PC	51	2.6	1.2/7.3	31	—	Dead; hepatic failure.
51	SR	59	1.6	2.8/3.4	100	42	Alive & well; no encephalopathy, bleeding or ascites.
56	S	57	0.7	3.0/4.4	62	—	Alive; fetor; mild encephalopathy; no ascites or bleeding.
64	PC	64	—	—	—	—	Dead; postoperative peritonitis.
70	PC	72	1.4	2.3/3.0	48	36	Dead; postop. colon exclusion; severe encephalopathy. No bleeding.

intermittent and generally either easily controlled or self limiting. All of these had had a portacaval shunt and were members of Group III, except Case 12 who was in Group I and had a splenorenal shunt. One patient, Case 20, did not become encephalopathic until 15 years after his portacaval shunt. Periods of lethargy and confusion lasting about 3 days at a time have continued in this patient over the last 3 years. The ages of those who developed periodic encephalopathy ranged from 47 to 73 years with a mean of 60 years, an age greater than the mean for the group as a whole.

Minimal hepatomegaly was often detected. However, hepatomegaly of greater than one fingerbreadth extension below the costal margin was noted in only four patients, and in three of these the enlargement was but two fingerbreadths. In contrast, splenomegaly was usually present and the degree of splenic enlargement seemed greater than that usually presented with cirrhosis. Portal pressure recorded at op-

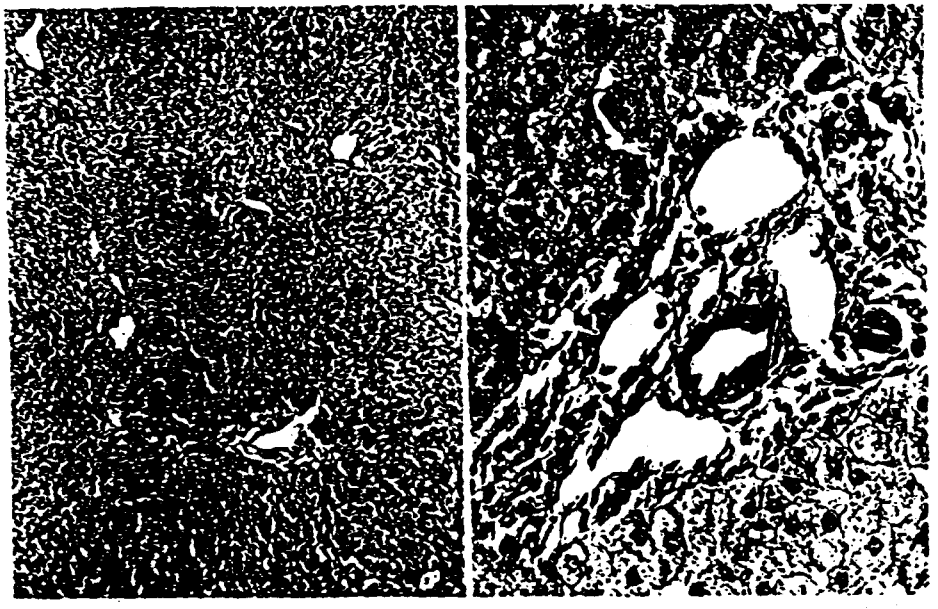

FIG. 1. Case 5. The operative liver biopsy. (Left) Low power showing widening of the portal areas and dilation of at least one hepatic vein. Nodular regeneration and septal fibrosis are not seen. (Right) High power of portal area which shows several thin-walled vascular spaces and two arteriolar radicals. The limiting plate is intact.

eration was not different, on the average, from other types of portal hypertension. Leukopenia and thrombocytopenia appeared to be more frequent and more severe than that usually associated with cirrhosis. The four patients in Group III in whom an epigastric venous bruit was present could probably be classified as typical examples of Cruveilhier-Baumgarten disease.[3] However, a patent umbilical venous connection to the left portal branch was not proved in any of them.

As will be noted in Table 2, hemodynamic studies as represented by wedged hepatic vein pressure (WHVP) and hepatic blood flow (HBF) were determined in only a few patients, and most of these were in Group I. The WHVP in two patients, Cases 9 and 16, was measured in other hospitals; the values reported were 21 cm. of saline and "elevated," respectively. In neither was the wedged position verified by contrast material injection;[24] their validity may be questioned. In the remaining 12 cases studied, hepatic vein catheterization was carried out by one of the authors. In all but one patient the WHVP was within accepted normal limits. In the one exception, Case 6, it was moderately elevated to 15 mm. Hg. HBF, with the exception of a normal value in Case 2, was consistently below mean normal limits. In a single patient (Case 8) it was markedly reduced.

Selected Illustrative Cases

Case 5. A 62-year-old white woman, a chronic alcoholic, provided a history of four episodes of gastrointestinal bleeding over the preceeding 6 years. Two months earlier marked ascites had occurred and paracentesis yielded "two gallons of fluid."

Examination disclosed a liver palpable two fingerbreadths and a spleen palpable three fingerbreadths below the costal margin. There was mild

ascites. No stigmata of cirrhosis were evident. Laboratory data were: serum bilirubin normal, serum albumin 4.9 and serum globulin 1.7 Gm./100 ml. (Howe method), prothrombin 125%, and bromsulfalein retention 10% in 30 minutes (5 mg./Kg.). On hepatic vein catheterization the WHVP was normal; HBF was not measured. Varices were demonstrated by x-ray examination.

At operation the liver appeared normal, the spleen was markedly enlarged and there were about 200 ml. of ascitic fluid. Portal venography with contrast material injected into both the spleen and a superior mesenteric venous radical demonstrated occlusion of all of the major portal venous tributaries including the portal vein. Portal pressure was measured as 36 and 47 cm. saline in two collateral veins. Splenectomy and transesophageal ligation of varices were performed.

Microscopic examination of the operative liver biopsy showed widened portal areas containing dilated, thin-walled vascular spaces (Fig. 1). Central veins were dilated and appeared increased in number when related to the number of portal areas. Nodular regeneration and septal fibrosis were absent. Histologically the spleen demonstrated dilated sinusoids with minimally thickened sinusoidal walls. Hemosiderin was absent and endothelial proliferation was not significant. Scattered Malpighian structures had prominent germinal centers without fibroadenie.

During the following 4 years, varical bleeding recurred on three occasions. Mild to moderate ascites persisted. On her last admission for a rather minor hemorrhage, moderate encephalopathy progressed to deep coma. Within a few days she recovered from coma and became alert. One week later, encephalopathy recurred and she died a few days later in hepatic coma. There had been no recurrence of hemorrhage with the second and terminal episode of encephalopathy. Laboratory data on the final admission were: serum bilirubin 2.1 mg./100 ml., serum albumin 3.8 and serum globulin 3.3 Gm./100 ml. and prothrombin 50%.

At necropsy the body was well developed and nourished and anicteric. There were 1,500 ml. of straw-colored ascitic fluid. The liver was firm and shrunken with an accentuated lobular pattern and weighed 1,025 Gm. There were no regenerative nodules; the surface was smooth. The portal vein within the liver and for 3 cm. proximal to the porta hepatis was patent. Proximal to this site the portal, splenic and superior mesenteric veins were sclerotic, totally occluded and hardly identifiable. There were several, small, thin-walled vascular structures around the sclerotic area. The esophagus had tortuous, dilated submucosal veins. There was a 2.0 by 0.4 cm. ulcer in the second portion of the duodenum. Bloody fluid was present in the stomach and colon.

Histologically the liver showed a striking change from that observed four years before (Fig. 2). There was an extensive arachnoid pattern of fibrosis extending from portal areas which destroyed the limiting plates and often connected adjacent portal areas. Clumps of liver cells appeared entrapped by the fibrous process, but there were no regenerative nodules. Bile stasis was prominent in the centrolobular canaliculi and there was some cholangiolar proliferation. Some of the interlobular ducts had periductal lamellar fibrosis. The prominent portal arterioles and angiomatous spaces observed 4 years previously were no longer apparent.

Case 36. A 70-year-old white man was admitted for his first and only major gastrointestinal hemorrhage. There was nothing of significance obtained from his past history and he was not alcoholic.

Examination disclosed splenomegaly as the only positive finding. There were no stigmata of cirrhosis and the liver was not palpable. Laboratory data were: serum bilirubin 0.5 mg./100 ml., serum albumin 4.7 and serum globulin 2.8 Gm./100 ml., prothrombin 60% and bromsulfalein retention 10% in 30 minutes (3 mg./Kg.). Large varices were demonstrated by x-ray and esophagoscopy. Massive intraperitoneal hemorrhage following an attempted and unsuccessful percutaneous splenoportagram necessitated emergency operation and additional hemodynamic studies were obviated.

At operation the liver was normal in gross appearance and the portal vein was enlarged, tense and patent. There was a large amount of intraperitoneal blood which arose from a 2-cm. laceration of the spleen. The laceration was temporarily tamponaded and an end to side portacaval shunt was done. Portal pressure was reduced from 40 to 15 cm. saline. Bleeding from the splenic laceration had ceased after completion of the shunt so the spleen was not removed.

Microscopic examination of the operative liver biopsy disclosed neither nodularity nor increased fibrosis (Fig. 3 A). The central vein radicals were increased in number and some were quite dilated. Some portal areas were enlarged and contained thickened arterioles and slightly dilated venous structures. Some of the parenchymal cells seemed slightly swollen. The appearance of the biopsy as a whole could readily be classed as normal.

For the first 2 days postoperatively, the patient was comatose. Subsequently his early postoperative course was uneventful. Hepatic vein catheterization done a few months after operation

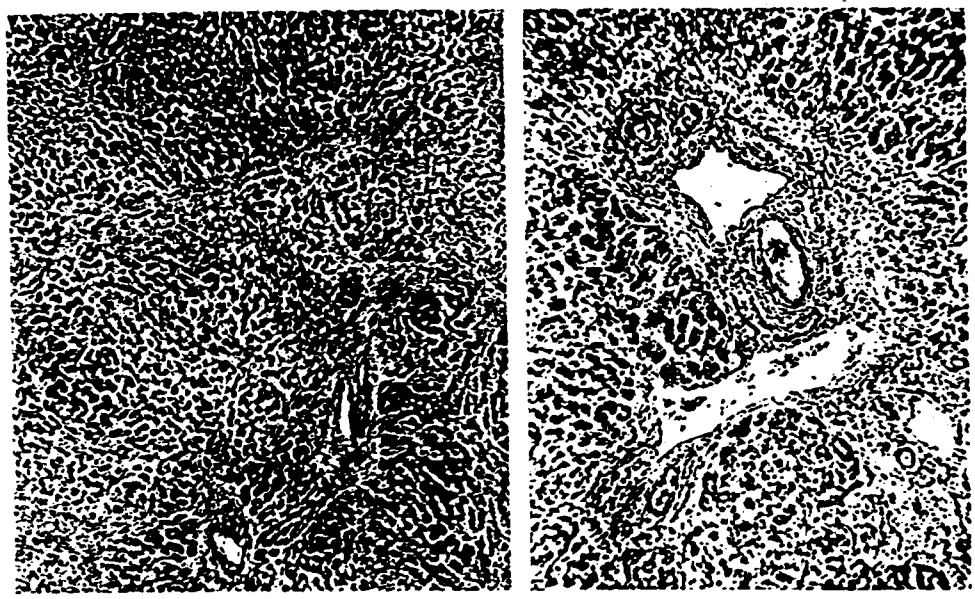

FIG. 2. Case 5. Necropsy sections 4 years after operation. A. (Left) Low power of liver showing extensive arachnoid fibrosis with destruction of the limiting plate of the portal areas but without nodular regeneration. The previously noted angiomatous change is no longer present. B. (Right) A major portal area with extensive fibrosis. In the center of the field is a portal vein radical with lamellar fibrosis or sclerosis.

FIG. 2C. Section of extrahepatic portion of the portal vein showing disruption of muscular layer by fibrosis and marked subendothelial sclerosis.

disclosed a WHVP which was slightly elevated; HBF was 645 ml. per minute.

Not long after operation, periodic encephalopathy developed. This complication progressed until its degree became incapacitating. Hoping to reduce its severity, operative colonic exclusion was performed 2 years after his portacaval shunt. The patient failed to survive this operation and died on the ninth postoperative day in hepatic failure. There had been no recurrence of varical bleeding. Laboratory data obtained just prior to the second operation was: serum bilirubin 1.4 mg./100 ml., serum albumin 2.3 and serum globulin 3.0 Gm./100 ml., prothrombin 48% and bromsulfalein retention 36% in 30 minutes (5 mg./Kg.).

At necropsy the body was anicteric, well developed and well nourished. There were approximately 150 ml. of opaque, foul ascitic fluid. A fibrinous exudate covered a small perforation at the site of the ileosigmoidostomy. The liver, weighing 800 Gm., was greatly reduced in size, rubbery and firm. The parenchyma was mottled with an accentuated lobular pattern but without nodularity. The biliary tract was normal. The portacaval anastomosis was patent. The spleen weighed 570 Gm. and was soft without prominent architectural markings.

Microscopically the liver showed a striking in-

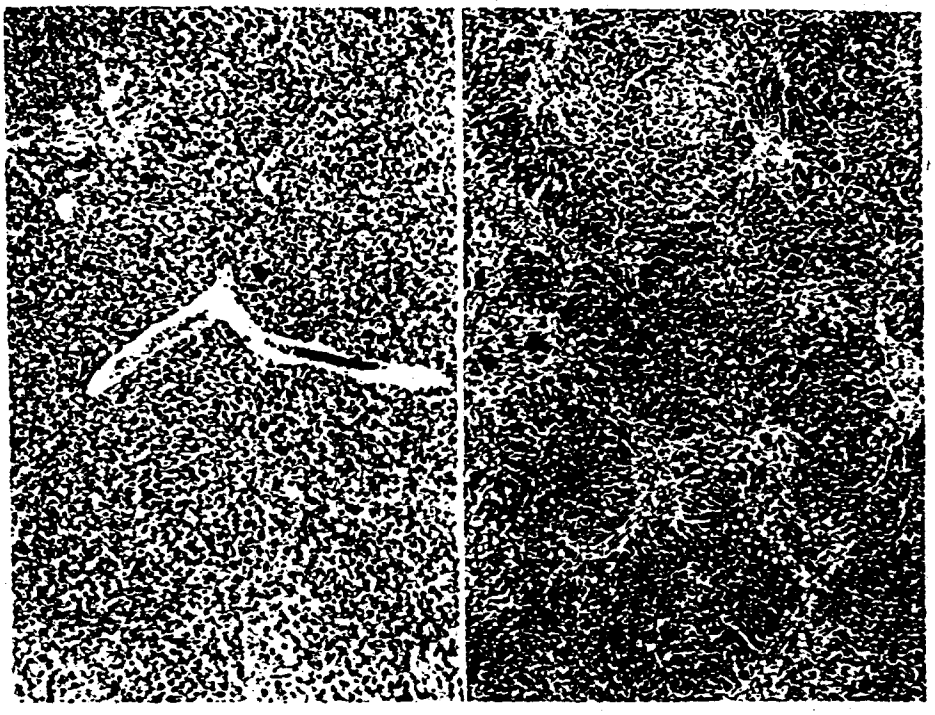

FIG. 3. Case 36. (Left) Low power of operative liver biopsy showing the absence of significant fibrosis and the close approximation of portal and central vein areas. In the center is a prominent central vein. Some liver cells appear swollen. (Right) Low power of necropsy section of liver 2 years after operation which shows extensive fibrosis *spreading from* portal areas with disruption of the *limiting* plate.

crease in fibrosis with arachnoid collagenous fibers extending from the portal areas in a haphazard fashion (Fig. 3 B). Nodular regeneration was absent. In some of the scarified portal regions there were increased numbers of lymphocytes and cholangioles. The vascular elements were no longer accentuated as they had been in the biopsy specimen 2 years previously. The spleen demonstrated mildly dilated sinusoids with proliferation of the lining cells, but their walls were not unusually thickened and there was no deposition of hemosiderin. Lymphoid tissue was atrophic. In some areas there was a nodular configuration of the sinusoids approximating the size of Malpighian corpuscles but not demonstrating penicilliary arteries.

Case 26. A 38-year-old white woman, nonalcoholic, had her first gastrointestinal hemorrhage 2 years previously and her second on this hospital admission. There were no other significant details in her past history.

Examination disclosed splenomegaly as the only positive finding. There were no stigmata of cirrhosis and no ascites. Laboratory data were: serum bilirubin 0.5 mg./100 ml., serum albumin 3.9 and serum globulin 3.8 Gm./100 ml., prothrombin 75% and bromsulfalein retention less than 10% in 30 minutes (5 mg./Kg.). Large varices were demonstrable on x-ray and esophagoscopy. On hepatic vein catheterization the WHVP was normal; HBF was not determined.

At operation the liver appeared normal while the spleen was greatly enlarged (Fig. 4 A). There was no ascites. Operative splenoportal venography demonstrated patency of the portal vein (Fig. 4 B). The portal vein was dissected free sufficiently to permit taking a direct portal pressure which was 39 cm. saline. A splenectomy and splenorenal shunt were done. Post shunt pressure was 15 cm. saline.

Microscopic examination of the liver biopsy disclosed no evidence of septal fibrosis or nodular re-

FIG. 4. Case 26 (Left) Operative photograph which shows an essentially normal appearing liver and a markedly enlarged spleen. (Right) Operative splenoportal venogram which shows a patent portal vein and coronary vein collateral.

generation. The hepatic veins were disproportionately numerous and appeared dilated (Fig. 5 A). Many of the portal structures were diminutively small, others were enlarged with dilated vascular spaces and with marked perivascular and periductal fibrosis (Fig. 5 B). The spleen weighed 780 Gm. Microscopically it showed dilated sinusoids with thickened walls. Only slight endothelial proliferation and very little fibrosis existed. There were no germinal centers and the lymphoid structures did not present adenomatous vascular transformation.

Six months later mesenteric venous occlusion necessitated the resection of 6 feet of small bowel. Six years have elapsed since operation and while the patient is known to be alive and to be presumably well, she refuses to return for evaluation. Her last clinic visit was three years after operation at

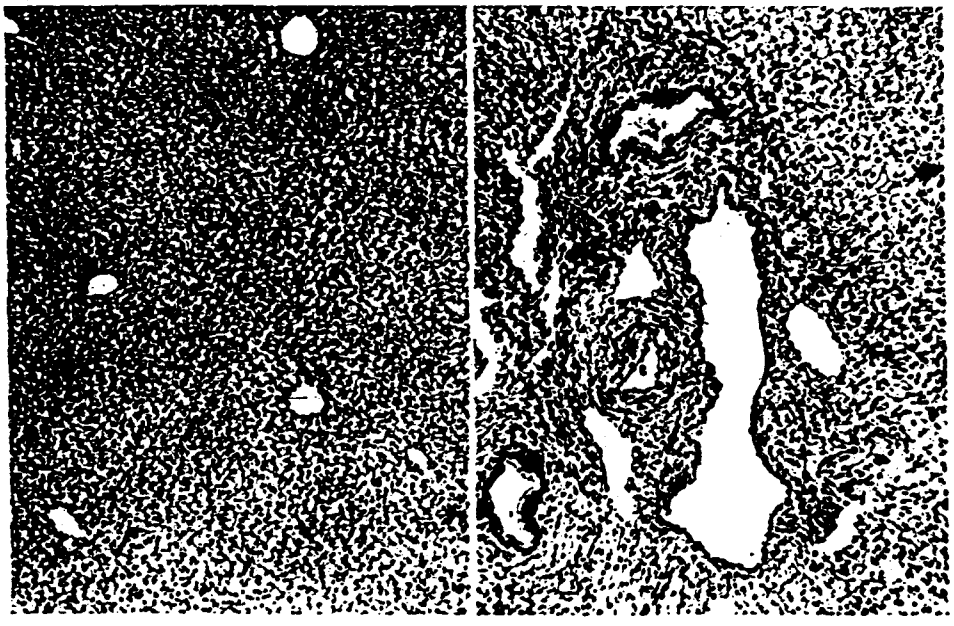

FIG. 5. Case 26. The operative liver biopsy. (Left) Low power showing multiple dilated hepatic outflow tracts in close approximation. Septal fibrosis and nodularity are not present. (Right) High power of an enlarged portal area with increased numbers of vascular channels and periductal fibrosis. Note the eccentric sclerosis in the largest portal vein radical in the center of the field.

h time she was clinically well without encalopathy, ascites or recurrence of varical leeding. Her laboratory data at that time were: erum bilirubin 0.4 mg./100 ml., serum albumin .5 and serum globulin 3.4 Gm./100 ml., prorombin 75%, and bromsulfalein retention 23% 1 30 minutes (5 mg./Kg.).

Case 17. A 61-year-old man, non-alcoholic, had is first gastrointestinal hemorrhage at 58 years of ge and his second on this hospital admission. There were no other significant details in his past istory.

Examination disclosed splenomegaly and mild scites. The liver was not palpable and there were o stigmata of cirrhosis. Laboratory data were: erum bilirubin 0.9 mg./100 ml., serum albumin 3.5 and serum globulin 2.3 Gm./100 ml., prohrombin 65%, and bromsulfalein retention 7% in 45 minutes (5 mg./Kg.). Varices were demonstrated by x-ray examination.

At operation the liver was normal in size, color and contour. Its edge was sharp (Fig. 6 A). The only gross abnormality was the presence of a fine trabecular network over the liver surface; there was no nodularity. The spleen was significantly enlarged and there were approximately 300 ml. of ascitic fluid present. Operative splenoportal venography demonstrated either the effect of portal streaming or partial occlusion of the portal vein (Fig. 6 B). The latter was proved to exist. The partial portal vein occlusion was due to a very adherent sclerotic process that extended from the ta hepatis to the origin of the portal vein and luded the vein by about 60% (Fig. 6 C). A cleavage plane existed and it was removed cleanly, leaving a smooth appearing intimal surface. End-to-side portacaval shunt was done which reduced portal pressure from 47 to 20 cm. saline.

Microscopic examination of the liver biopsy showed an almost normal architectural arrangement. The central veins were unusually prominent. Many portal areas were enlarged and contained thickened vessels. Histologically the material excised from the extrahepatic portal vein (Fig. 7 A) demonstrated a collagenous pattern with an intact and smooth endothelial lining. Its appearance was not unlike that of the phlebosclerotic process within the portal areas of the liver (Fig. 7 B).

Postoperatively he has remained well. There is no encephalopathy or ascites and there has been no further bleeding during the 27 months since operation. His current laboratory data are: serum bilirubin 1.9 mg./100 ml., serum albumin 3.0 and serum globulin 2.5 Gm./100 ml., prothrombin 35%, and bromsulfalein retention 12% in 45 minutes (5 mg./Kg.).

Discussion

All of these patients presented as examples of portal hypertension with established varices. All but two bled from esophogogastric varices and in 29 this was the initial manifestation of disease. Clinical features

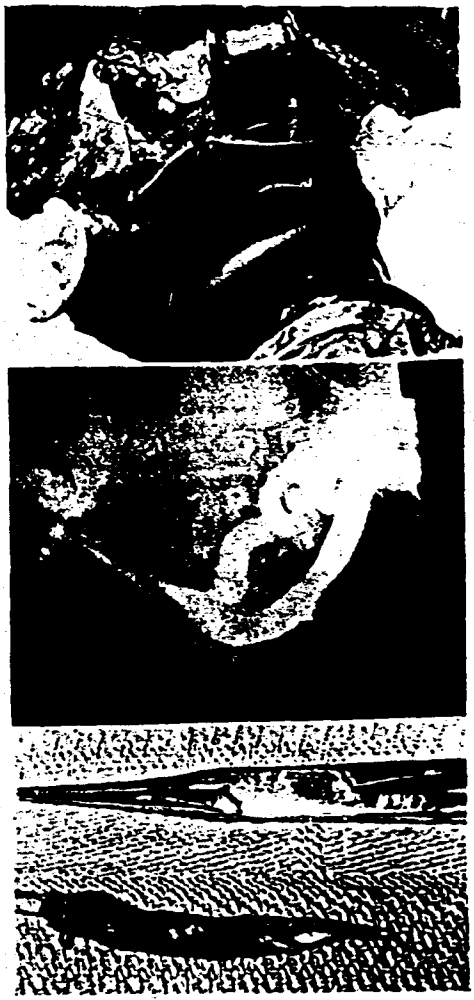

FIG. 6. Case 17. (Top) Operative photograph which shows the sharp edge of the essentially normal-appearing liver. The fine trabecular network over the surface of the liver is discernable. (Center) The operative splenoportal venogram showing partial occlusion of the portal vein. (Bottom) The sclerotic material removed from the lumen of the portal vein.

ith cirrhosis who never develop compli- lated vascular spaces and frequently more

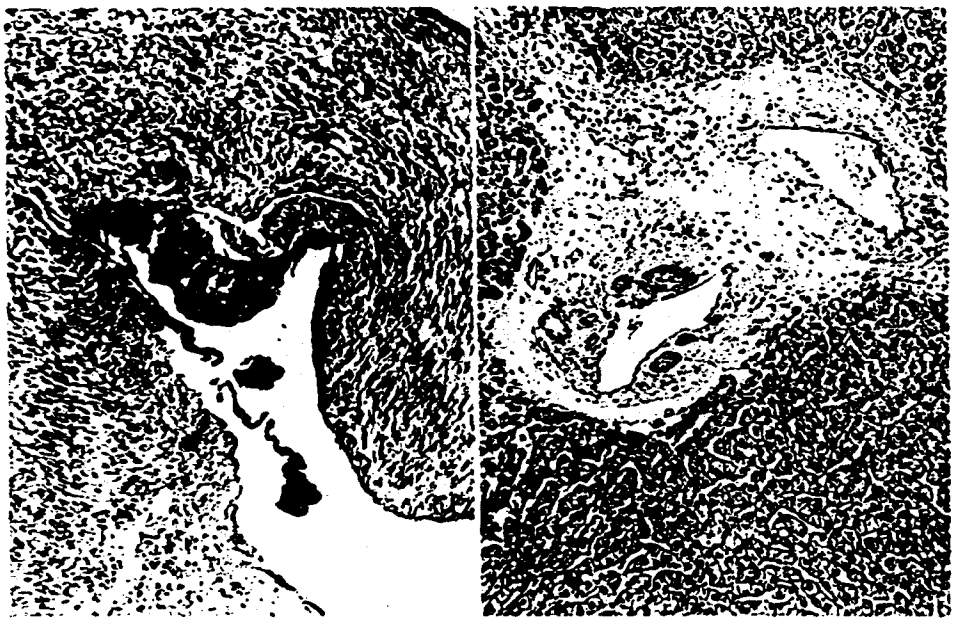

FIG. 7. Case 17. (Left) Cross-section of the sclerotic material, shown in Fig. 6 C, that was excised from the lumen of the portal vein. The material is collagenous without hemosiderin or calcium deposition. There is an intact endothelial lining. (Right) Section of a portal area within the liver showing a similar phlebosclerotic process to that seen in the extrahepatic portal vein.

or complications of hypersplenism or so-called splenic anemia were not obvious although leukopenia and thrombocytopenia were present in two thirds of the patients. Ascites and encephalopathy, although somewhat more common in the group with a patent portal vein, were observed in an appreciable number of those with extrahepatic portal vein occlusion. Others have also noted the occasional association of ascites with extrahepatic portal hypertension.[1, 3, 8, 9, 21] The mechanism by which ascites developed in these patients is even more obscure than it is in cirrhosis. One report recently has called attention to the not infrequent occurrence of abnormal liver function tests and encephalopathy in extrahepatic occlusion.[25] This report suggests further that these abnormal liver tests develop in proportion to aging and that such abnormalities are rarely seen in children. Although not included in this report, we have observed an appreciable number of children with extrahepatic portal hypertension who had abnormal liver tests and ascites.[15]

During the years covered by this review, we have operated upon almost 400 patients with portal hypertension. The 36 patients presented here thus account for almost 10 per cent of the whole. It would, however, be incorrect to assume that this disease actually represents 10 per cent of all our cases of portal hypertension. The great majority of patients with varical bleeding that we see have cirrhosis associated with alcoholism. Most do not survive their hemorrhage to receive operation and many that do survive prove to be unreliable and fail to return for surgical therapy. The nonalcoholic patients, in contrast, are generally reliable; most survive their hemorrhage and return for follow-up treatment. In addition there are a large number of patients

with cirrhosis who never develop complications of portal hypertension. The correct incidence of the disease here presented probably is closer to 2 or 3 per cent of our cases with portal hypertension.

Pathology

Morphologically the livers of patients from the three groups (occluded, partially occluded and patent portal vein) were grossly and histologically indistinguishable. At the initial operation, the livers were essentially normal. The color was a normal red to mahogany-brown; the surface was smooth or occasionally traversed by a fine, lacy, fish-net trabecular pattern. Rarely the surface was mildly irregular, but it was never nodular. The inferior edge was sharp in most, slightly blunted in a few. Although a few were mildly enlarged, the gross configuration was normal in all. Invariably there was a slight, but definite, increase in firmness. The liver edge could not be as easily folded back on itself; it was not as supple or flexible as normal. Sutures used to approximate the edges after a wedge biopsy were unlikely to cut through.

On the initial liver biopsy, histologic deviations from normal were subtle. There were no fibrous septae or regenerative nodules. Nevertheless the lobular arrangement was insidiously deranged. There were often several dilated vascular spaces, presumably hepatic veins, in a single lobule and many were quite close to the portal regions. Two or three portal areas were closely spaced in one area, yet in another they were widely separated. Scattered irregularly throughout the parenchyma were portal areas greatly enlarged by the deposition of perivascular and periductal collagen. In these areas the limiting plate was intact and the collagen was sharply delineated from parenchymal cells. In smaller portal triads this limiting plate was partially disrupted. Within these abnormal portal triads there were usually several dilated vascular spaces and frequently more than one arterial branch. Frequently the portal vein radicals were significantly thickened or sclerotic and occasionally they were differentiated from the arterial branches with difficulty. Cholangiolar proliferation was notably absent.

The material which partially occluded the portal vein in those patients in Group II was indistinguishable from that responsible for the complete portal vein obliteration of patients in Group I who were examined at necropsy. The thickened material was placed eccentrically and there was a notable absence of hemosiderin, calcium or a lamellar pattern. The material closely resembled atherosclerotic deposits in major arteries except that it contained no lipid.

In the few patients, subsequently examined at necropsy who died in hepatic failure 2 or more years after initial presentation, there was a striking change in hepatic architecture. The liver was shrunken, firm and somewhat irregular, but it was not nodular. Weight ranged from 700 to 1,000 Gm. Histologically the limiting plates of the portal areas were disrupted by an arachnoid pattern of fibrosis which had the appearance of sweeping through the hepatic parenchyma entrapping segments or clumps of liver cells. The dilated and proliferated vascular spaces, seen originally, had disappeared. Regenerative nodules were still not apparent.

Splenomegaly was a consistent feature and its degree was greater than that usually encountered in association with cirrhosis; the spleen weight averaged 673 Gm. for the eight patients in which this information was available, in contrast to an average of 309 Gm. for 88 cirrhotic patients examined at necropsy. Microscopically the sinusoids were dilated and their walls thickened, but the vascular change of "fibroadenie" described by Banti was not apparent.

Nature of the Occlusive Process in the Portal Vein

For years disagreement has existed concerning the nature of the portal vein occlusive process in extrahepatic portal hypertension. Is this secondary thrombosis or primary phlebosclerosis? Evidence has been marshalled on both sides and it would appear that those supporting thrombosis have been most convincing.[11-13, 18-20, 31, 39] It is appreciated that the differentiation is difficult to make. Nevertheless we have been impressed by certain features and present these in support of this concept of phlebosclerosis. In some patients in Group III, those with a patent vein, there was eccentric thickening of the portal vein wall, usually on its posterior aspect. Admittedly the portal vein wall is thickened in nearly all instances of portal hypertension regardless of its nature, but this area of eccentric thickening was localized and distinct and was 2 to 4 mm. in depth. It was firmly adherent to the vein wall and its inner or intimal surface was smooth. It is difficult to conceive that this could be thrombosis; it is not unlike intimal thickening in arterial atherosclerosis. We are inclined to think that the patients in Group II, those with partial occlusion of the portal vein, represent an extension of this process. In those in whom an endophlebectomy was done the sclerotic material was very firmly adherent and the plane of dissection was not readily identified. This aspect is strikingly different from those patients with cirrhosis who have obvious thrombosis within the portal vein. Five or six patients with this latter process have had thrombectomy and subsequent portacaval shunt performed. In all the thrombectomy was accomplished with surprising ease; the plane of dissection was immediately identified, adherance to portal vein wall was much less intense and histologically there was no doubt that the removed material represented an organized thrombus. It could be argued that the difference between the two was a manifestation only of age; and perhaps this is true. However one final feature merits consideration in this question. In many of the patients from all three groups there was, histologically, distinct and impressive concentric thickening of the peripheral portal vein radicals within the liver. This must be sclerosis; its presence indicates that an identical process may occur in the extrahepatic portion of the portal vein.

If the existence of phlebosclerosis is accepted, it is then interesting to speculate whether it has preceded or followed portal hypertension. Intrahepatic, presinusoidal, portal venule resistance as a result of phlebosclerosis conceivably could induce portal hypertension in a manner similar to schistosomiasis[34] or to experimental injection of silica particles.[27]

Conversely it is perhaps easier to conceive of phlebosclerosis developing as a secondary process, that is, developing in response to portal stasis and hypertension.[13] This hypothesis, however, is not supported by the venous findings in the far more common form of portal hypertension due to cirrhosis. In cirrhosis, symmetrical thickening of the extrahepatic portal vein wall occurs, but we have not seen eccentric phlebosclerosis (or thickening). Also if phlebosclerosis is a secondary phenomenon we are left with no explanation for the presumed intrahepatic vascular block.

Unquestionably there exist other types of portal vein obstruction which lead to portal hypertension. A localized stricture or area of portal vein stenosis probably on a congenial basis has been reported.[6, 26, 29, 29, 38] Congenital stenosis of the entire portal vein has been encountered;[32] and perhaps its congenital absence has occurred. Although compression from without the portal vein due to neoplasia has been reported[38] we have not seen such a lesion which induced varical bleeding. All of the

above mechanisms are undoubtedly unusual causes of portal hypertension.

Mechanism of Portal Hypertension

As implied before, the hemodynamic alterations responsible for portal hypertension in these patients remain obscure. For one reason or another we have been repeatedly thwarted in obtaining complete hemodynamic data in our patients in Group III, those with a patent portal vein. Wedged hepatic vein pressure was normal in the three such patients catheterized and hepatic blood flow was reduced in the two patients in whom it was measured. A large experience with an apparently similar disease has been had by the Nagoya group in Japan.[19] In their patients WHVP and HBF were not elevated. These data are identical to those obtained in Group I patients, those with extrahepatic portal hypertension. It is difficult to accept the hypothesis of increased splanchnic arterial inflow as the sole mechanism responsible for the portal hypertension in those patients with an open portal vein. If this were the case, hepatic blood flow and cardiac output should be greatly increased.[23] Arteriovenous shunting as a cause encounters the same theoretical argument.[17, 23, 27] Although not apparent histologically, it is difficult to escape the belief that vascular obstruction within the liver must exist. This obstructive mechanism for elevation of portal pressure is in greater consonance with the currently available hemodynamic data. If the elevation of WHVP which is usually seen in cirrhosis correctly implicates a sinusoidal or postsinusoidal location of hepatic vascular block,[23] then the block in the cases under current consideration should be presinusoidal. Normal WHVP has been reported with portal hypertension in a number of different liver diseases, so that it would be wrong to place a patient in the category that we are describing on the basis of this finding alone.

Semantic Considerations

Are some of these patients representative of those studied by Banti? Those most suspect for such a designation would be the few who died later in hepatic failure and in whom necropsy disclosed a shrunken, firm, fibrotic liver. If this be the case then it must be assumed that Banti was liberal in his use of the label cirrhosis. This error is understandable; it was not too long ago that "international criteria" were established for the pathologic designation of cirrhosis. Today many pathologists would label our few late cases with extensive fibrosis as cirrhosis. However none demonstrated regenerative nodules and by the criteria of today they were not cirrhotic. Though on an historic basis, *Banti's syndrome* might be an acceptable description, we are reluctant to recommend the reintroduction of a term which has been responsible for so much confusion in the past. While in recent years we have used this label among ourselves, it is probably preferable to let the sleeping Banti lie.

It would be pleasing to have a short descriptive label for this disease which would fulfill semantic requirements, rather than to employ an unwieldy group of words which describe a negative aspect as in the title of this article. Hepatoportal sclerosis would fulfill this role as well as any term when related to our current knowledge of this process. Sclerosis signifies firmness or hardness; the portal areas within the liver and the portal vein outside the liver are those afflicted by sclerosis.

On the other hand it is somewhat presumptuous to attempt to label a disease about which so little is understood. For that matter, is but a single disease entity represented by these 36 patients? We only suspect and have been intrigued by the possibility that this may be the case. In blind exercise we have never been able to separate histologically the three groups. Additionally there is little to clinically dif-

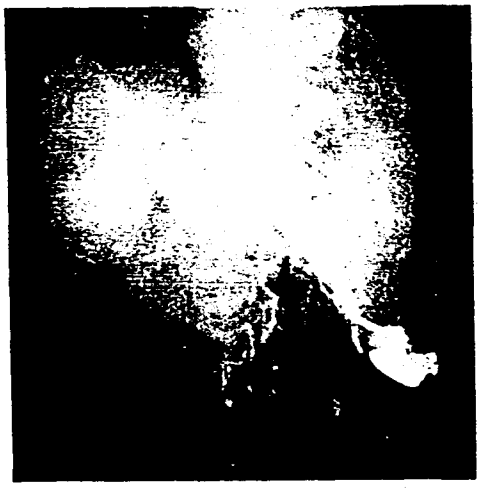

FIG. 8. Case 34. The operative splenoportal venogram which on "second look" demonstrates a widely patent portal vein. It had been previously overlooked because of its lack of contrast and because of being partially obscured by a huge, tortuous collateral.

FIG. 9. Case 19. The operative splenoportal venogram which demonstrates almost complete occlusion of about the mid-point of the portal vein. Formerly classified as an example of extrahepatic portal hypertension, it now is placed in Group II, those patients with partial portal vein occlusion.

ferentiate them; mean age is not too divergent and age range is essentially the same; incidence of ascites and encephalopathy is similar; initial and later liver function tests are identical; and about an equal percentage have died in hepatic failure. Further evidence for this similarity may be marshalled. Cases 16 and 27 had splenectomy performed elsewhere; their postoperative diagnosis was extrahepatic portal hypertension. Both were later proved to have a patent portal vein. Case 34 is especially noteworthy. At operation the liver was grossly normal and a hard, rod-shaped structure believed to be a thrombosed portal vein was presumably palpated in the hepatoduodenal ligament. These features, plus what must have been but a perfunctory glance at the wet x-ray film of the operative splenoportogram, led to a diagnosis of extrahepatic portal hypertension which was continued for 3 years until the current review prompted a "second look" at the splenoportogram. The portal vein was unquestionably widely patent but was partially obscured by a huge, tortuous collateral (Fig. 8). Case 19 has been used for 10 years in student teachings as an example of extrahepatic portal hypertension. Perhaps he should continue to be so classified, but in this study we felt compelled to place him in Group II (Fig. 9). Of additional interest is that periodically during these 10 years his liver tests have been more abnormal during three episodes of small bowel adhesive obstruction than those listed in Table 2 which are current. These laboratory results were puzzling since we thought during these years that liver function in portal occlusion remained normal. Case 5, although alcoholic and with documented previous tense ascites, clearly proved to be an example of extrahepatic portal bed block with what would be accepted as a normal liver on initial presentation to us. Four years later when necropsy followed death due primarily to hepatic failure, the portal vein within the liver and for 3 cm. proximal to the porta hepatis was patent. Proximal to this site

the portal, splenic and superior mesenteric veins were sclerotic and totally occluded. Six years before we first saw her and 10 years prior to death, she had her first gastrointestinal hemorrhage, presumably (but not proved) from esophagogastric varices. Can it be assumed reliably that her portal vein was occluded at that time? And finally what was the status of the portal vein in Cases 3, 6, 9 and 10 at their initial splenectomy? Because the portal vein was obliterated at the time they presented themselves to us does not prove that it was so before their splenectomy. Splenectomy alone, in cases of portal hypertension, notoriously provokes splenic and portal vein occlusion and this sequence could conceivably be accentuated if some degree of portal and splenic phlebosclerosis was coexistent.

In his last contribution in 1910, Banti described 50 patients personally observed.[14] "The characteristic lesions are in the spleen, liver, and almost always in the splenic vein and portal vein." He called the venous lesion "chronic sclerotic endophlebitis." When related to the patients presented here by us, it seems strange that Banti did not describe a single case of complete portal or splenic vein occlusion.

Summary and Conclusions

Thirty-six adult patients with portal hypertension, but without cirrhosis, have been analyzed. One third had classic extrahepatic portal hypertension with total occlusion of the portal vein. A few had partial occlusion of the portal vein and one half had a widely patent portal vein. Although the liver has been considered to be normal in extrahepatic portal hypertension, we believe that a distinct histologic lesion exists. Furthermore this same lesion is identifiable in those patients with a partially occluded or a widely patent portal vein. We suspect that all three types have the same underlying etiologic mechanism and that this mechanism is phlebosclerosis of the intrahepatic and extrahepatic portal vein and venules.

The gross and microscopic hepatic morphology and the clinical features and course were essentially the same for all of the patients. About one third had ascites and an equal number became encephalopathic. Liver function tests, which were essentially normal early, became abnormal later.

If recurrent variceal hemorrhage was eliminated, most patients in all three groups appeared clinically well. A few in each group, however, did not follow this course and had a steady deterioration in liver function. Seven of the 12 who are dead, died in hepatic failure. In those in whom necropsy was performed, a marked extension of the initial pathologic process in the liver was noted. It was grossly shrunken and firm but not nodular; microscopically there was extensive, arachnoid fibrosis which had replaced much of the parenchyma.

Acknowledgment

Our appreciation is expressed to Dr. Arthur C. Pattison who kindly permitted the inclusion of four of his private patients in this study.

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Discussion

Dr. Charles Gardner Child III (Ann Arbor, Mich.): I rise to make three points: one, an expression of appreciation to Dr. Mikkelsen for focusing our attention on these patients who appear sporadically in almost all series of patients with portal hypertension. We have all recognized them, usually by ones and by twos; I am amazed that Dr. Mikkelsen could find so many in his experience. I can not help wondering what their basic problem really is.

I think my second point is one of distress at having once again to consider Banti's disease. I would recall to you that in Dr. Banti's original description he pointed out that these were young people, originally with normal livers who went on

to develop big spleens, sometimes ascites and die the death of cirrhotic patients with portal hypertension.

The third comment I would make is to document very briefly three patients in our experience with the picture Dr. Mikkelsen has outlined. In these we have done end-to-side portacaval shunts. If their livers were truly normal they should have gone on and died with the picture of the Eck fistula dog. Dr. McDermott and I—and others—have performed end-to-side portacaval shunts in patients with normal livers in association with resections for pancreaticoduodenal cancer. They invariably presented the Eck-fistula-Pavlov-meat intoxication syndrome. The three patients with normal livers, portal hypertension and varices in whom we did end-to-side portacaval shunts have gone on and behaved just as individuals with cirrhosis in whom the conventional end-to-side portacaval shunt was performed.

I am sure there is an additional dimension here that substantiates Dr. Mikkelsen's conception that these are not normal livers. On the other hand, it is very hard for me to persuade my friends in pathology to give me much of a diagnosis other than a normal liver. I congratulate Dr. Mikkelsen on being able to identify these microscopic changes and calling them to our attention. I can assure you a good many of us are going to go back and review some of our previous liver biopsies.

Dr. W. Dean Warren (Miami): I would like to call your attention to one problem that exists in this very interesting group of patients.

We have been interested in the syndrome of portal deprivation after portacaval shunts in animals with a normal liver and normal liver blood flow. As you know these animals do not tolerate portacaval shunt well and usually succumb within a few months.

In the few humans who have been shunted with a normal liver and a normal, unoccluded portal vein, the postoperative course generally has been quite unsatisfactory.

Now you will notice, from Dr. Mikkelsen's figures, that the group of patients having patent portacaval veins demonstrated a very high incidence of portal encephalopathy, and a very high incidence of hepatic failure in the fairly early postoperative course, despite preoperative normal or near-normal hepatic function tests.

We believe that in most such instances the patient has a normal or near-normal liver blood flow. A portacaval shunt will immediately and dramatically reduce the estimated hepatic blood flow to roughly 50 per cent of normal. If portacaval shunting is done in this type of patient I believe a high incidence of these very severe complications is inevitable.

I would therefore like to make two pleas: first, that more hemodynamic data be obtained on the patients. We have had just one such patient; she had a normal liver blood flow. Second, if operation is required, a nonshunting procedure is to be preferred in general. As you know, the bleeding can be controlled fairly well in this type of patient. I believe that this will lessen the chance of delayed motility or supply markedly.

Dr. William W. L. Glenn (New Haven): The occurrence of portal hypertension and bleeding esophageal varices in the absence of both intrahepatic and extrahepatic obstruction has been recognized for some time. But we are indebted to Drs. Mikkelsen, Reynolds and Peters for their excellent report of their remarkably broad experience with this unusual condition.

The cause of portal hypertension in patients without obvious venous obstruction remains obscure. Undoubtedly, as the authors point out, there are pathologic changes in the livers, but they are by no means typical of cirrhosis. In some of these cases these changes might account for the increased resistance to flow of blood in the hepatic venous radicles. In others, portal hypertension may be due, as the authors have demonstrated, to a partial occlusion of the portal vein caused by phlebosclerosis. There remain, however, a few patients with no demonstrable lesion of the liver or the vein to account for the increase in vascular resistance.

Since the blood pressure within the portal system depends on the volume of, as well as on the resistance to, blood flow, it is reasonable to suppose that certain cases of otherwise unexplained portal hypertension may result from abnormalities of *flow* through an otherwise normal splenoportal axis. Such was the situation, we believed, in four cases of portal hypertension without portal obstruction that we reported in collaboration with Drs. Tisdale and Klatskin.

After failure to demonstrate the factors responsible for portal hypertension in our four patients, we were led to conjecture that either an increase in blood flow in the portal system or functional changes, such as an increase in venous tone, was the cause of the hypertension.

The liver biopsies in these patients were normal —or nearly normal—at the time of operation and before, and in two of the patients 2 and 4 years postoperatively. Theoretically, an increase in the volume of blood entering the portal vein—or entering the portal system—may lead to sustained portal hypertension.

Practically, this concept is proved by the demonstration of portal hypertension and its consequences in some patients with arteriovenous fistulas involving the splenoportal axis.

I would like to ask the authors if they have made any direct observations on blood flow in the portal vein in their cases, and also, do they have any opinion as to the role of venous tone as the cause of increased resistance to flow through the portal system.

Dr. Richard M. Peters (Chapel Hill): I merely want to ask a question very similar to Dr. Glenn's. Were any cardiac outputs measured in

these patients? It may well be that the reason they will not tolerate a shunt procedure is that the blood flow through the liver is low. If one found that they did not have the elevation in cardiac output which most cirrhotics do, one would expect that their liver would not tolerate a shunting procedure.

DR. LOUIS M. ROUSSELOT (New York): I reiterate Gardner Child's belief—not belief but statement—as to the paucity of these cases, and we would also like to add that same note.

This group of cases is extremely rare. I suspect there is some geographic variation on this. The Italians see a considerable number of these cases. We have not seen nearly as many in the East.

I would also like to add an historic note in support of the New Haven group's contention that this may be primarily a functional derangement with these anatomic changes developing later in many of these cases.

Essex, over 30 years ago at the Mayo Clinic, postulated a state of chronic vasospasm in the—either in the sinusoidal or presinusoidal area, and he was able to produce experimentally a state of temporary portal hypertension, using some ascaris extract.

This is an extremely interesting group of cases and I agree with the author that the surgical management should be one of very selective distinction and not necessarily total portal bed decompression.

DR. WILLIAM P. MIKKELSEN (Closing): Unfortunately, we have been repeatedly thwarted in our efforts to obtain good hemodynamic data on this group of patients. In the 12 patients so studied, hepatic blood flow has been reduced consistently and wedged hepatic vein pressure has been normal. This has been true for those with an open as well as those with an occluded portal vein. Unfortunately, cardiac output has not been measured. In a few patients from each of the three groups, plasma volume, red cell mass and whole blood volume recently have been measured. In all patients studied these values have been elevated above normal, just as they are in cirrhosis. The implication of this fact is thus far occult.

Dr. Rousselot must be correct when he suggests that there may be geographic differences in the incidence of this disease. For example, nearly half of the patients with portal hypertension seen by the Nagoya group in Japan are representatives of this or a similar category.

It would be wrong to leave the impression that all of these patients do poorly. Actually, most do well. We have several patients who are alive and well without encephalopathy ten and more years after a portacaval shunt.

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