CLASSIFICATION AND TREATMENT OF PORTAL HYPERTENSION

HAJIME IMANAGA, SADAHIRO YAMAMOTO, MITSUO ISHIGURO, JIRO OWA, RYUGO IMAMURA, HAJIME HIRANO, KATSUMI ROKUO, FUJIHIKO ANDO, FUJIO SUZUKI, TOYOHISA ARAI, ATSUYOSHI DOI, YASUHISA YOKOYAMA, TAKESHI MIZUTANI, AND MASASHI SAWADA

2nd Department of Surgery, Nagoya University School of Medicine
(*Director: Prof. Hajime Imanaga*)

INTRODUCTION

In portal hypertension, ascites, esophageal varices, and splenomegaly are the main clinical manifestations which require treatment. However, although these pathologic signs are based on one common cause, *i.e.*, elevated portal vein pressure, their occurrence varies from case to case; that is, some cases show only ascites, and others esophageal varices and splenomegaly.

Since Whipple, Rousselot, *et al.*[1)2)] evolved the concept of portal hypertension and classified them into extrahepatic and intrahepatic portal hypertension, this concept has been the basis of treatment adopted by surgeons.

Up to the present, we have undertaken surgical treatment on 250 cases of portal hypertension, with 101 cases of end-to-side portacaval anastomosis. Our detailed observations on these cases, however, have often been met with difficulties in interpreting their clinical manifestations, if we resort to the conventional classification of this syndrome, based on morphological alterations of the liver.

In extrahepatic portal hypertension, the mechanism of circulatory disturbances causing this hypertensive state is quite obvious and is correlated well with the resulting clinical manifestations.

However, the problems lie in the intrahepatic group. As the number of cases increased, questions rose why in some cases esophageal varices and splenomegaly are the main symptoms, and why in other cases merely ascites, or ascites combined with esophageal varices and splenomegaly occur. Since 1958, on the basis of studies on intrahepatic circulatory disturbances we have tried to analyse the cause of these differences in the clinical signs of portal hypertension. As a result, it was assumed that the cause of these different manifestations lay in the site of obstruction of the portal circulation, *i.e.*, in the state of intraphepatic circulation. In other words, it was speculated that the cause of these differences lies on whether portal circulation is obstructed at the site of the intrahepatic portal veins, or of the intrahepatic hepatic veins.[3)4)5)6)]

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Therefore, in 1960, the following classification of portal hypertension was suggested.[7][8]

Group I. Extrahepatic portal vein obstruction
Group II. Intrahepatic portal vein obstruction
Group III. Intrahepatic hepatic vein obstruction
Subgroup 1. Intrahepatic obstruction of the hepatic vein
Subgroup 2. Intrahepatic obstruction of the hepatic and portal veins
Group IV. Extrahepatic hepatic vein obstruction

Here, those in the intrahepatic groups complicated by portal vein thrombosis are eliminated from Group I and classified as Group II and Group III, respectively. The clinical characteristics of each group are illustrated in the attached Table 1.

TABLE 1. Characteristics of Portal Hypertension

		No. of cases	Esophag. varices	Spleno-megaly	Ascites	Liver function	WHVP	H.B.F. H.A. : P.V.	H.B.F. after P.C.A.	Liver histology
I. Extrahep. obst. portal vein		11	+	+	−	Normal	Normal			Normal, or caverno-matous
II. Intrahep. obst. portal vein		96	+	+	−	Normal	Normal	80 : 20	No reduction	Normal, fibrosis, or shistosomiasis
III. Intrahep. obst.	1. Hepatic vein	65	−	−	+	Poor	High	50 : 50	Marked reduction	Cirrhosis A (Nagayo)
	2. Hepatic and portal vein	69	+	+	+	Moderate	High	70 : 30	Slight reduction	Cirrhosis B (Nagayo)
IV. Extrahep. obst. hepatic vein		9	+	+	+	Modarate				Congestive cirrhosis

This classification has not only enabled us to interpret the variations in the symptomatology of portal hypertension, but also has provided a rationale in selecting a suitable treatment for each group.

In this paper, we are going to analyse results of our studies of portal hypertension in order to explain the theoretical reason why the above-mentioned classification has been proposed, and to suggest suitable treatment for each group.

1. Portal vein pressure (PVP) and wedged hepatic vein pressure (WHVP)

PVP was determined in every patient who underwent a laparotomy and WHVP[9] was meausred in 80 cases of our series. Repeated examinations of these patients revealed that there were two types of patients in the intrahepatic group (Fig. 1). Namely, in some cases both PVP and WHVP were elevated, while others showed almost normal WHVP with markedly elavated PVP, although their liver biopsy specimens showed no cirrhotic change. These findings not only disproved the conventional concept of WHVP that WHVP is an indirect

estimate of PVP, and also seemed to indicate that WHVP would reflect an intrahepatic pressure, *i.e.*, intra-sinusoidal pressure by damming back the blood from the hepatic artery and the portal vein.

Therefore, these clinical experiences induced us to assume that these cases of portal hypertension with normal WHVP, where the portal trunk remained patent, should be classified into a different category from the conventional "intrahepatic" which had been regarded *en bloc* as portal hypertension due to cirrhosis of the liver; thus, the former constitutes Group II and the latter Group III. In other words, Group II is characterized by normal WHVP, and Group III by elevated WHVP.

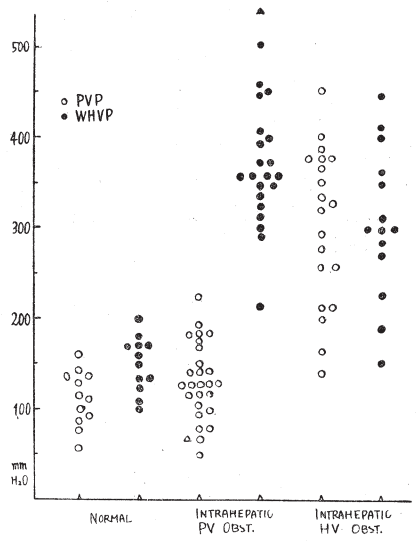

FIG. 1. WHVP and PVP in portal hypertension.

2. Hepatic blood flow and hepatic vascular resistance

For determination of hepatic blood flow, BSP method[10] has been employed in most instances. Occasionally, when hepatic catheterization was impossible, Au^{198} method described by Vetter, *et al.*[11] was performed. However, in our experience, total hepatic blood flow, hepatic blood flow per unit body surface (M^2), or per unit body weight (Kg) failed to establish diagnostic patterns in each group, but a decreasing trend in the blood flow was noticed in Group III (Fig. 2).

However, hepatic vascular resistance according to Reynolds' formula[12] showed fairly significant differences in each group. As indicated in Fig. 3, Group II remains within normal limit, whereas Group III showed elevated resistance. It should be noted that Subgroup 1 of Group III, *i.e.*, those only with ascites gave higher values than Subgroup 2, *i.e.*, those with ascites and esophageal varices. This difference between the subgroups will be discussed later.

Although preoperative determination of hepatic blood flow failed to show definite characteristics in each group, comparison of the values before and after end-to-side portacaval anastomosis demon-

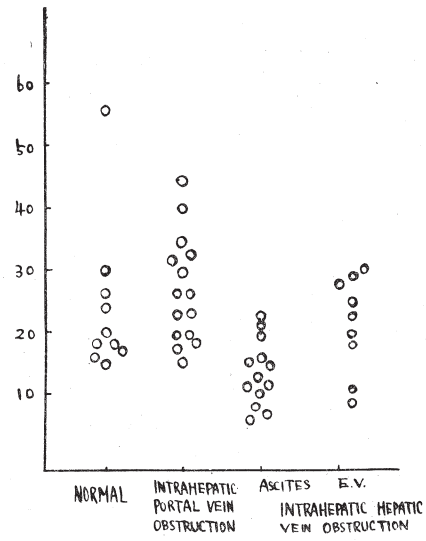

FIG. 2. Estimated hepatic blood flow BSP method (ml/min./kg).

strated well noticeable differences among the cases. As is shown in Fig. 4, in Group II this operation brought about little decrease in hepatic blood flow, but rather an increase in some cases. On the contrary, in every patient of Group III the blood flow was reduced after the operation. Furthermore, differences between the two subgroups were noticed; the postoperative decrease in the blood flow being greater in Subgroup 1 than Subgroup 2.

These findings indicate that in those with less postoperative decrease, a considerable amount of portal blood bypasses the liver already before the operation by way of formerly established collaterals, *e.g.*, esophageal varices. It should also be pointed out that this preoperative natural

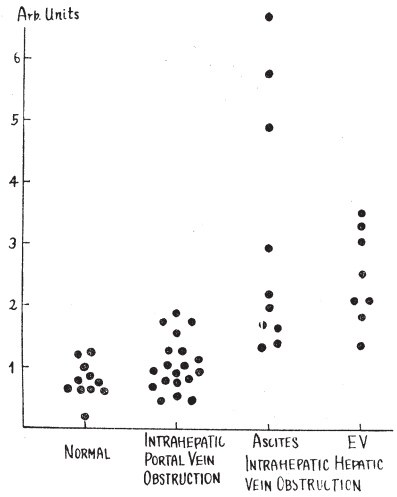

FIG. 3. Hepatic vascular resistance.

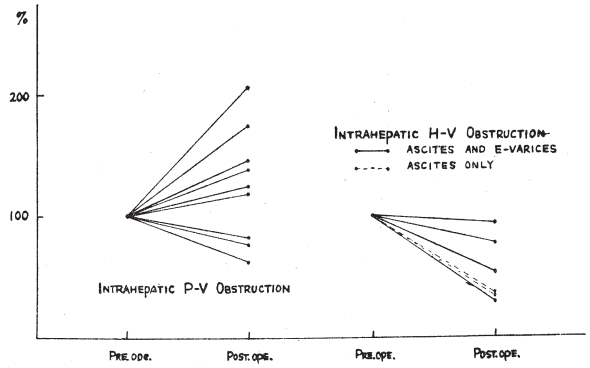

FIG. 4. Hepatic blood flow before and after end-to-side portacaval anastomosis (percent of preoperative value).

shunting of portal blood directly reflects the postoperative prognosis of patients who undergo portacaval anastomosis. Our clinical experiences in more than 100 cases of this operation ascertained this fact (Fig. 5).

3. Simultaneous, separate measurement of hepatic arterial flow and portal blood flow

Previously Ueda[13] introduced a method to measure separately hepatic arterial and portal venous flows. However, according to our experience, it is often difficult, especially in patients with portal hypertension, to divide one from the other by analysing a curve obtained by Ueda's method. Therefore, in 1960 the procedure as illustrated in Fig. 6 was performed at our clinic.[14] Since this procedure is rather toilsome for routine practice we have employed it in

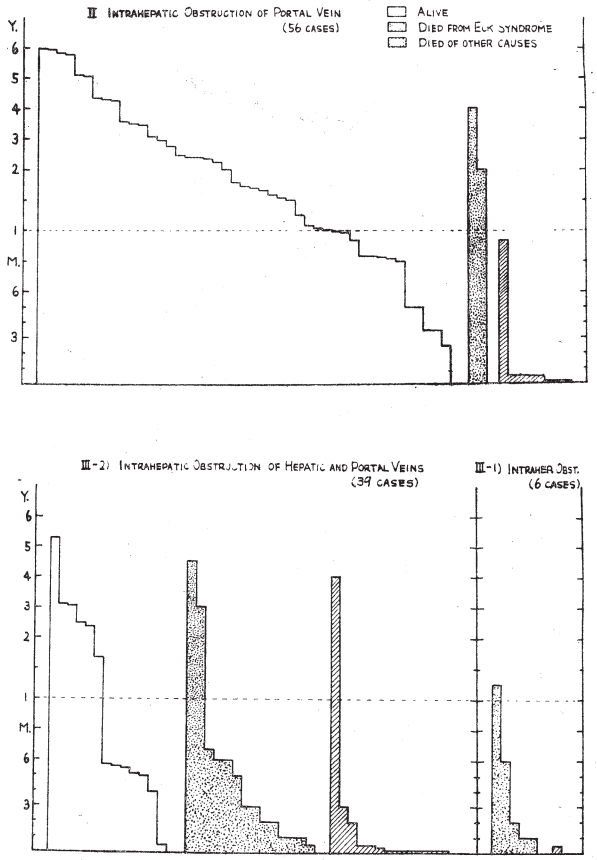

FIG. 5. Prognosis of 101 cases of portacaval anastomosis.

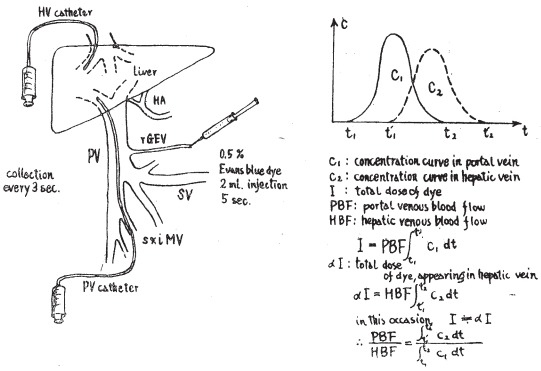

FIG. 6. Method and formula of separation of the portal venous and hepatic arterial blood flows.

only 10 cases, including 2 control patients with gastric ulcer, 3 patients of Group II, and 5 of Group III. In Fig. 7 are shown the results obtained, and the differences in the ratio, portal venous flow versus hepatic arterial flow, are characteristically demonstrated.

4. Interpretation of the results: basis of the classification

In Group II, PVP is raised, whereas WHVP and hepatic vascular resistance remained at the normal level. This seems to indicate that in this group there exists some intrahepatic obstruction to portal inflow and this results in a compensatory increase of arterial blood flowing into the liver. In Fig. 7, this reversion of the ratio "arterial versus portal" of this group is clearly demonstrated. Therefore, it is assumed that the circulatory disturbance in Group II lies at the presinusoidal region of the intrahepatic portal veins, and that hepatic arterial-hepatic venous circuits via hepatic sinusoids are well maintained at almost normal condition. However, an increase in hepatic blood flow after portacaval anastomosis can not yet be explained clearly, although the following speculation may be made that arterial blood might flow into the region of the sinusoids which had hitherto received portal blood, because we have found several autopsy cases where the isolated portal vein remained patent after portacaval anastomosis had been performed.

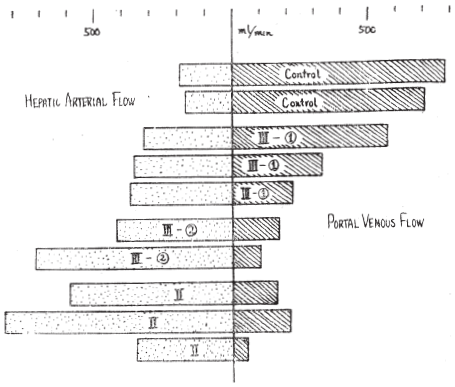

FIG. 7. Separation of portal venous and hepatic arterial blood flow.

On the other hand, in Group III, the elevated WHVP, increased hepatic vascular resistance, and other above-mentioned findings may suggest that the location of obstruction exists in the postsinusoidal site. Therefore the blood from both the hepatic artery and the portal vein remains stagnant within the liver, more precisely in the hepatic sinusoids, and this results in producing fluid transudation from the surface of the liver through lymphatic channels, finally leading to ascites formation. These alterations in hepatic hemodynamics are typically manifested in Subgoup 1, namely liver cirrhosis only with ascites.

However, in Subgroup 2, *i.e.*, cirrhosis with ascites, splenomegaly and esophageal varices, it is assumed that obstruction of blood flow extends to the presinusoidal portal veins, and that this portal obstruction tends to decrease the portal inflow to the liver (Fig. 7) and to form hepatofugal, porto-systemic collaterals which facilitate the absorption of ascites from the peritoneal cavity. Clinically, as shown in Fig. 8, ascitic patients in Subgroup 2 responded well to diuretic treatment, but the patients in Subgroup 1 hardly responded. In addition, there is often encountered in clinics ascites retension which is reduced as the esophageal varices become apparent.

However, mechanisms producing splenomegaly can not be explained only

by the congestive theory and other factors should be added to interpret the etiology in future studies.

5. Intrahepatic circulation and histology of the liver

In order to study the relationship between intrahepatic circulatory disturbances and histological alterations of the liver, 96 cases of Group II and 50 cases of Group III were examined.

As illustrated in Table 2, no cirrhotic change could be observed in Group II. The shape and arrangement of hepatic cells and of hepatic acini were almost normal, accompanied by localized fibrosis in Glisson's sheath, or in other words, periportal fibrosis of various degrees. In some cases, walls of the portal venules were thickened and their intravascular lumina were found to be narrowed, or at its extreme, completely obliterated. The central veins, on the other hand, remained intact.

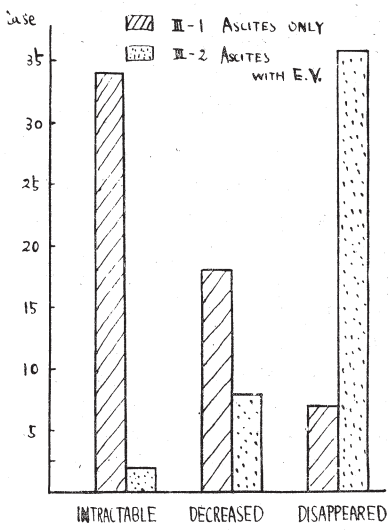

FIG. 8. Ascites in intrahepatic obstruction of hepatic vein.

TABLE 2. Histological Findings of Intrahepatic Portal Vein Obstruction

Etiology	Schistosomiasis	Not identified		
No. of cases	6	90		
		Fibrosis		
		None	Mild	Moderate
		18%	35%	46%

On the contrary, Group III was characterized by cirrhotic changes, exclusively of postnecrotic cirrhosis. Furthermore, adopting the classification of liver cirrhosis proposed by Nagayo-Mitamura,[15)16)] it was ascertained that more than one half of the patients in Subgroup 1 were of the A type, whereas most of those in Subgroup 2 were B type, as illustrated in Table 3.

TABLE 3. Correlation of Histologic Classification of Liver Cirrhosis to Two Types of Portal Hypertension

Nagayo-Mitamura→ / Imanaga↓	Case	A	Mixed	B
1. Intrahepatic obst. of hepatic vein (Ascites only)	19	11 (58%)	5 (27%)	3 (15%)
2. Intrahepatic obst. of hepatic and portal veins (Ascites with Esophageal varices, Splenomegaly)	31	3 (10%)	7 (22%)	21 (68%)

6. Treatment of portal hypertension: its rationale from the view point of the proposed classification

In Table 4, methods of treatment are summarized.

TABLE 4. Surgical Treatment of Portal Hypertension

		Surgical treatment
I. Extrahepatic obstruction of portal vein		Splenorenal anastomosis, proximal gastrectomy, omentonephropexy, splenectomy
II. Intrahepatic obstruction of portal vein		Portacaval anastomosis, splenectomy
III. Intrahepatic obstruction	1. Hepatic vein	Omentonephropexy
	2. Hepatic and portal veins	Portacaval anastomosis, splenectomy, proximal gastrectomy, omentonephropexy
IV. Extrahepatic obstruction of hepatic vein		Proximal gastrectomy, omentosternal implantation

a) Treatment of Group I: Extrahepatic portal vein obstruction

This type of portal hypertension is rarely encountered in clinics. In our series, it constituted only less than 5 per cent of all cases.

In this group esophageal varices and splenomegaly should be treated. For the former, splenorenal anastomosis can be suggested, if the splenic vein remains patent. However if this anastomosis is impossible or fails, as has often been the case, proximal gastrectomy,[17] combining omentonephropexy[3] (subcapsular wrapping of the left kidney with the greater omentum) may be recommended. The latter procedure aims to decompress the elavated portal vein pressure by way of the collaterals, formed in the adhension that this operation will cause, and finally to prevent recurrence of the varices.

Hyperchromic anemia due to splenomegaly can be corrected by splenectomy in all cases.

b) Treatment of Group II: Intrahepatic portal vein obstruction

It has been widely acknowledged by many investigators that portacaval anastomosis is the operation of choice for bleeding esophageal varices. However, its postoperative complications, namely Eck syndrome and increasing hepatic impairment, have made us wary of selecting this operation for any patient with esophageal varices. However, according to our increasing experiences with this operation, patients of this group showed fairly good post-operative courses, in contrast to those of Group III (Fig. 5); namely occurrence of Eck syndrome and resulting death seen in the former group are less frequent than in the latter.

Therefore, we are of the opinion that portacaval anastomosis should be employed for esophageal varices in Group II, even in the sense of a prophylatic measure against bleeding.

As to splenomegaly and the resulting anemia, some investigators reported that satisfactory portal decompression by means of portacaval anastomosis will relieve the congestive state of the spleen and this normalizes the hematologic findings.[17] However, our detailed investigation of these cases revealed that the anemia could not be corrected merely by portal decompression, though the spleen decreased in size, but in some cases, on the contrary, the anemia was augmented within two months after the operation. On the other hand, it was ascertained that these patients showed almost unexceptional, marked recovery after the enlarged spleen was removed. Therefore, we believe that splenectomy should be performed for patients with splenomegaly, even if portacaval anastomosis has brought about satisfactory portal decompression.

In this connection, it should be emphasized that portacaval anastomosis must precede splenectomy, because we have encountered several autopsy cases in which thrombosis was formed in the remaining splenic vein and extended into the portal trunk.[3] This thrombosis is considered not only to increase the danger of bleeding from esophageal varices, but also to make successive portacaval anastomosis impossible.

c) Treatment of Group III: Intrahepatic hepatic vein obstruction

In this group, ascites, esophageal varices and splenomegaly require treatment.

As for the treatment of ascites of Subgroup 1, our experiences in clinical and experimental studies induced us to believe that establishment of portosystemic collateral circuits should be attempted in the first place, in order to augment the absorption of ascites from the peritoneal cavity; otherwise this ascites remains "intractable". For this purpose, portacaval anastomosis is apparently most effective. However, as explained before, this operation can not be recommended for patients of Subgroup 1, because postoperative hepatic impairment is fatal in these cases (Fig. 5). Therefore, it seems most rational to create satisfactory collaterals by employing an adhension procedure, *e.g.*, omentonephropexy, and to enhance the effect of electrolyte diuretics in these patients.

Recently some have claimed that side-to-side portacaval anastomosis is favorable in treating ascitic patients.[18][19] However, our studies on dogs in which the subphrenic hepatic veins were constricted,[20] revealed that side-to-side anastomosis caused a reverse flow through the proximal portal vein, and that this reverse flow passed through the liver without having been metabolically used.[21] Therefore, we are now of the opinion that side-to-side portacaval anastomosis will aggravate further the hepatic impairment by depriving the liver of efficient blood from the hepatic artery, to a greater extent than end-to-side type of the anastomosis.

In Subgroup 2, ascites usually is combined with esophageal varices. As illustrated in Fig. 8, most of the patients of this group responded well to diuretic treatment. However, if a satisfactory result can not be obtained by simple administration of diuretics, procedures to promote the hepatofugal collateralization should be attempted in order to stimulate diuresis.

The next target of treatment in Subgroup 2 is esophageal varices. As

mentioned before, portacaval anastomosis is believed to be most effective for relieving the danger of bleeding from the varices. However, in 39 cases of this group where this anastomosis was performed, 10 cases survived for more than one year, but the remaining 24 patients died of Eck syndrome within a year (Fig. 5). These clinical experiences indicate that, even though the postoperative reduction of hepatic blood flow is less severe in this group than Subgroup 1, the impairment of intrahepatic blood circulation tends to aggravate the postoperative condition of patients. Therefore, here arises a problem, whether a portacaval anastomosis should be attempted in order to relieve patients from the fatal bleeding of varices, or other procecures which are usually less effective in treating the varices, but in which postoperative complications are less frequent, should be employed. At present, however, this needs further studies. As the latter procedure, proximal gastrectomy, combining omentonephropexy has been performed in our clinic and considerably good results have been obtained.

As for splenomegaly in this group, splenectomy must be done to improve the hematologic findings. But, if the patients manifest hyperchromic, macrocytic anemia, splenectomy will not correct the anemia, because this hematologic sign is cosidered to be due to some untoward effects of impaired hepatic function.

d) Treatment of Group IV: Extrahepatic hepatic vein obstruction

This group corresponds to what has been termed Budd-Chiari's[22] syndrome. Our clinical experiences revealed that in all cases thrombosis extended from the hepatic veins to the inferior vena cava, and that they manifested ascites, splenomegaly, and esophageal varices.

It is assumed that ascites may be attributed to the obstructive mechanism in the hepatic venous region, but the damming effect of this obstruction in producing the remaining two manifestations is still a question, which needs furthre studies.

On considering ways of treatment of this group, it should be remembered that almost all of the patients manifest not only portal hypertension, but also an elevation of the inferior caval pressure. Therefore, these procedures to connect the portal system to the superior caval region should be attempted. For this purpose, an implantation of the greater omentum into the bone marrow of the sterunm[3] has been perfomed in some cases of this group. Adding to these collateralizing measures, proximal gastrectomy has also been performed in order to remove esophageal varices. However, the results are not too favorable and hence, further attempts should be made in order to cure these patients.

Recently Kimura[23] reported a few cases with membranous obstruction of the inferior vena cava just below the diaphragm, which were successfully removed by digital membranotomy via the right atrium. However, these particular cases have not been encountered at our clinic.

Besides, if the patients manifest hypochromic anemia, the spleen must be removed, as has already been discussed.

SUMMARY

Portal hypertension produces different signs, depending on whether the etiologic obstruction is in the portal vein or the hepatic vein, and whether the obstruction is extrahepatic or intrahepatic.

Therefore, all therapeutic procedures should take such differences into consideration.

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