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NON-CIRRHOTIC PORTAL FIBROSIS WITH PORTAL HYPERTENSION : A NEW SYNDROME.

Part I.

CLINICAL AND FUNCTION STUDIES AND RESULTS OF OPERATIONS.

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INTRODUCTION

IN recent years, a number of reports have appeared in the literature where large splenomegaly with portal hypertension was associated with relatively minor changes in the liver. Although the detailed pattern of this syndrome has not been properly set out in any of the publications, it seems that many authors have been conscious that such a syndrome exists in many widely separated countries of the world. Cook *et al.* (1963) from Hong Kong reporting on what they called 'Cryptogenic splenomegaly' mentioned that 'in a proportion of cases, scarring in the liver may be minimal or absent. In such cases, the liver is usually enlarged and histological examination shows infiltration of sinusoids and not infrequently of the periportal tissue by round cells, dominantly plasma cells and lymphocytes'. Basu (1958) and Basu and Aikat (1963) in their paper and monograph on 'Tropical Splenomegaly' discussed about one of the patterns of liver changes where there was evidence of 'hepatitis with scarring but without any cirrhosis'. Leather (1961) studied 47 cases of gross splenomegaly in Uganda, Africa. In large majority of these cases, the intrasplenic pressure was much above normal. Forty one cases were studied histologically. Five cases had undoubted cirrhosis of the liver. In 7 cases, there were smaller degrees of portal fibrosis and in the remaining 29, there was infiltration of the sinusoids with lymphocytes, macrophages and plasma cells with minimal fibrosis around portal tracts. Tisdale *et al.* (1959), from U.S.A., described 4 cases in which portal hypertension and bleeding oesophageal varices were present in the absence of both intrahepatic and extrahepatic obstruction of the portal vein.

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They postulated that increase in portal blood flow may have led to the development of portal hypertension in these cases. Similar reports about 'Idiopathic' portal hypertension have been published by Walker (1959) from England. Hunt (1954), also from England, studied the splenic outflow in a number of cases of 'essential' portal hypertension and discussed about the possibility of excessive volume of splenic effluent being responsible for portal hypertension in the absence of demonstrable obstruction.

Imanaga *et al.* (1962) reporting from Japan, also came across a number of cases of portal hypertension which did not have extrahepatic obstruction and where the liver histology did not show definite cirrhosis. In India, Ramalingaswamy *et al.* (1962) and Wig (1966) described what they called 'Type III splenomegalic cirrhosis' where splenomegaly of many years duration was associated with severe portal hypertension. Histology of liver in this type was normal or indicative of nonspecific and mild abnormality. They were doubtful if type III cases should be included in the group of 'Cirrhosis'. It is clear, therefore, that there exists a group of cases in whom severe portal hypertension and splenomegaly may exist in the absence of definite cirrhotic changes in the liver or extrahepatic portal venous system obstruction.

Materials and Methods.

During the last few years, we have come across 25 such cases and have studied them in great detail. The study included clinical, biochemical, radiological and haemodynamic investigations in addition to needle biopsies of the liver prior to operation. At operation, the morphology of the liver was seen and recorded by photography. Generous wedge and needle biopsies were taken. Appropriate shunt operations were performed. Post-operatively, over a course of months or years, the cases were followed clinically and the liver function and the liver structure were studied biochemically and by repeat biopsies.

Observations.

Total incidence.—These 25 cases form part of 150 cases of portal hypertension operated on by one of us (A.K.B.) between 1959 and 1966. The incidence of the disease as seen by us may be said to be about 17 per cent of all the portal hypertension cases.

Age and sex incidence.—The age group of the 25 patients studied varied between 13 and 47 years. The average age was 31·2 years. The cases were divided into the following age groups (Table 1) :—

Table I.

Year	Cases
11—20	6
21—30	8
31—40	7
41—50	4
Total ..	25

Average age of the group was 29·8 years (±12·4).

This age incidence conforms to the general pattern of the cirrhotic population in our overall series of cases, where 80 per cent of the cases also were between 11 and

40 years of age (Basu *et al.*, 1966). Seven cases were females and 18 were males, giving a ratio of 1 : 2·6 F : M.

Signs and symptoms :

Haemorrhagic episodes.—The most important presenting symptom was repeated episodes of massive haemorrhages. Twenty three of the 25 cases were admitted to the hospital because of recurrent haemorrhages. The intensity and the frequency of the haemorrhagic complications are listed in Table II :—

TABLE II

Intensity and frequency of haemorrhagic episodes.

3 plus (very severe and recurrent episodes)	6 cases
2 plus (moderately severe and recurrent episodes)	15 „
1 plus (one or two instances of severe haemorrhage)	2 „
Haemorrhage not severe	2 „
Total	25 cases.

It would be seen that severe haemorrhagic complication constitutes the most important single symptom which brings these patients to the attention of doctors. This complication is usually both severe and recurrent. As compared to other allied pathological states in the liver and portal venous system, viz. cirrhosis and extrahepatic portal vein obstruction, the incidence of haemorrhagic complication is even more marked in this group of cases (Table III):—

TABLE III

Comparison of haemorrhagic episodes in 3 group of cases.

	Portal fibrosis (Average of 25 cases)	Extrahepatic obstruction (Average of 38 cases)	Cirrhosis (Average of 45 cases)
Incidence	90·5 per cent	76·5 per cent	50·0 per cent
Haematemesis (Average per patient)	4·6	4·4	1·7
Duration from onset of haemorrhage to admission in Hospital Average :	3·1 years	5·1 years	2·4 years

It is obvious that the portal fibrosis cases bleed more severely and frequently than the other 2 types of cases. As compared to extrahepatic obstruction group, this difference may not be statistically significant but, compared to the cirrhotic group, the difference is striking. Another interesting fact is that the bleeding episodes are tolerated fairly well in this group of cases. This will be apparent from the occurrence of the large number of haemorrhagic episodes (average 4·6) before the patient presents himself for attention to the hospital. In this respect, this group of cases behave very similarly to the extrahepatic group and quite unlike the cirrhotic group where the haemorrhagic complications are tolerated poorly.

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Splenomegaly.—Apart from haemorrhage, the second most important presenting feature was the large splenomegaly. Average size of the spleen in 23 cases was 4 fingers enlarged below the left costal margin. The details of the degree of splenic enlargement are given in Table IV :—

TABLE IV

Splenic enlargement.

	Case
More than 6 fingers	4
4—6 fingers	10
2—4 fingers	8
Less than 2 fingers	1
	23

In 2 cases splenectomy had been performed previously.

However, it cannot be said that the splenic enlargement in this group of cases is very much different from the cirrhotic or the extrahepatic obstruction group in our series. Large splenic enlargement is a characteristic and common findirg in cirrhotic cases found in this geographical area (Basu *et al.*, 1966). The relative degrees of the splenic enlargement as found in the 3 groups of cases are given in Table V :—

TABLE V

Degree of splenomegaly.

	Portal fibrosis	Extrahepatic obstruction	Cirrhosis
Splenomegaly	10 cm (± 5·1)	7.8 cm (± 3·4)	8·5 cm (± 3·6)

Hepatomegaly.—Compared to splenomegaly, enlargement of the liver was much less. It was palpable in 10 cases and not palpable in 15 cases. The degree of enlargement varied between 1 finger and 4 fingers below the right costal margin. The liver felt firm on palpation ; its margin was rounded and the surface was felt to be generally smooth. The details of the macroscopic anatomy of the liver will be described later during the operative findings, but even pre-operatively, distinction could be drawn between the liver as found in our cirrhotic cases as compared to the portal fibrosis cases. Very few cases of liver were clinically palpable in the cirrhotic group and those that were palpable were generally found to be bossy and nodular on the surface. These features were markedly different from the findings in the portal fibrosis group.

Other physical findings.—Apart from haemorrhagic episodes, large splenomegaly and the associated manifestations of hypersplenic syndrome, such as moderate anaemia and general weakness, other evidences or stigmata of cirrhosis of liver, were singularly absent. However, 5 patients had ascites. In 2 of these cases, the ascites was significant in amount and in the other 3, it was moderate to slight. Five cases gave history of jaundice sometime in the past but only one case presented with jaundice in the hospital. However, this patient was diagnosed to be suffering from congenital familial haemolytic anaemia and the jaundice was ascribed to that cause.

Investigations :

Liver-function.—The liver-function studies included estimation of serum albumin and globulin, serum bilirubin, alkaline phosphatase, prothrombin time, zinc sulphate and thymol-turbidity tests, transaminase studies (SGOT and SGPT) and 45 minutes retention of BSP. None of these tests in isolation could give an accurate estimate of the state of liver function but reliance was placed more on the absolute value of serum albumin and on BSP retention.

Approximate average figures of the important liver function studies in the 25 cases are listed in Table VI :—

TABLE VI.

Serum albumin	3·5 g. per cent	(± ·69)
Serum globulin	3·8 ,,	(± ·59)
Serum bilirubin (total)	1·08 mg. per cent	(± 2·1)
BSP test (45′ retention)	10·6 per cent	(± 5·6)
Alk. phosphates (Bodansky)	2·8	(± ·63)
S G.O.T.	76·3 units	(± 62·0)
S.G.P.T.	45·8 units	(± 28·8)
Prothrombin time	4·1 secs	(± 3·0)

On the whole, it can be said that the overall liver function of the portal fibrosis group, as found pre-operatively, was substantially better than in the cirrhotic group of cases. The absolute average value of serum albumin was 3·5 g. per cent as compared to 3·1 g. per cent in the cirrhotic cases and globulin was 3·8 g. per cent as compared to 4·3 g. per cent in the cirrhotic group. The values of serum bilirubin similarly showed better figures in the fibrosis cases. The most important and striking distinction was found in the values of BSP retention tests. In this Laboratory, control values of 45 minutes BSP retention showed the mean figure of 4·4 per cent with standard deviation of ±3·0 per cent. In the portal fibrosis group, the mean retention in 25 cases was 10·6 per cent (± 5.6 per cent), whereas in the cirrhotic group (mean of 24 cases) mean retention was 19·3 per cent (±9·7 per cent). This difference is statistically significant ($P < 0.005$). It appeared to us, therefore, that 45 minutes BSP retention test could be utilized as a screening test to differentiate between portal scarring and cirrhotic cases prior to operation and histological studies (Boyer and Basu, 1966).

Haematological status.—The haematological status of the group of cases did not reveal anything significant except showing moderate amount of anaemia. The average findings are shown in Table VII :—

TABLE VII.

Hb	10·2 g. per cent	(± 4·2)
Haematocrit	32·0 per cent	(± 6·5)
White cell count	3730/cmm.	(± 1·425)
Platelet count	144,000/cmm.	(± 48,500)
Reticulocytes	2·2 per cent	(± 1·82 per cent)
Bone marrow	Erythroid hyperplasia.	

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Patient	E.H.B.F
K.D.	1426 ml/mi
S.M.	1187 ,,
K.K.	1267 ,,
N.B.G.	1610 ,,
B.B.G.	—
V.B.	—
S.M.	—
J. J.	784 ,,
S.K.B.	1030 ,,
R.R.	1515 ,,
P.N.K.	1305 ,,
B.S.	1055 ,,
B.C.D.	1610 ,,
S.N.N.	1000 ,,
R.V.H.	975 ,,

The average value

W.H.V.P.
S.P.
E.H.B.F.
H.V.R.

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W.H.V.P.
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Haemodynamic studies.—Detailed haemodynamic studies with the help of hepatic venous catheterization were performed on 15 patients of the fibrotic group. These included estimation of the wedged hepatic venous pressure (W.H.V.P.), splenic pressure (S.P.), estimated hepatic blood flow (E.H.B.F.) (Bradley *et al.*, 1945) and hepatic vascular resistance (H.V.R.). The details are presented in Table VIII :—

TABLE VIII.

Haemodynamic data in the portal fibrosis group.

Patient	E.H.B.F.	W.H.V.P.	S.P.	H.V.R.	Degree of fibrosis
K.D.	1426 ml/min.	8·0 mm. Hg.	—	0·56 units	1 plus
S.M.	1187 ,,	11·0 ,,	—	0·93 ,,	—
K.K.	1267 ,,	18·0 ,,	—	1·42 ,,	—
N.B.G.	1610 ,,	8·0 ,,	—	4·9 ,,	1 plus
B.B.G.	—	7·0 ,,	—	—	2 plus
V.B.	—	9·0 ,,	—	—	1 plus
S.M.	—	—	33·0	—	3 plus
J. J.	784 ,,	—	14·0	—	3 plus
S.K.B.	1030 ,,	—	23·0	—	1 plus
R.R.	1515 ,,	14·0 ,,	—	0·92 ,,	4 plus
P.N.K.	1305 ,,	24·0 ,,	24·0	1·84 ,,	2 plus
B.S.	1055 ,,	21·0 ,,	27·5	1·99 ,,	1 plus
B.C.D.	1610 ,,	11·5 ,,	16·0	0·71 ,,	½ plus
S.N.N.	1000 ,,	19·5 ,,	19·5	1·94 ,,	2 plus
R.V.H.	975 ,,	11·0 ,,	29·5	1·1 ,,	2 plus

The average values obtained are given in Table IX :—

TABLE IX.

W.H.V.P.	— 13·5 mm. Hg.	(± 5·5)
S.P.	23·3 mm. Hg.	(± 6·2)
E.H.B.F.	1230 ml./min.	(± 2·61)
H.V.R.	1·19 units	(± 0·56)

In our Laboratory, normal values of the above data as obtained in 8 control patients are shown in Table X :—

TABLE X.

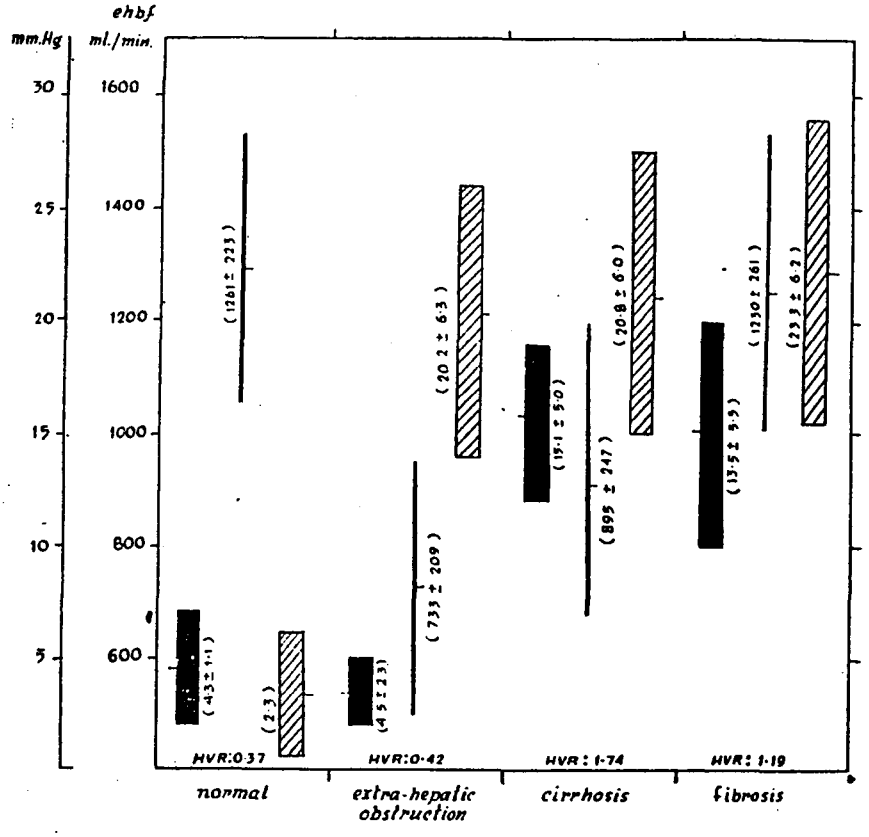
W.H.V.P.	— 4·3 mm. Hg.	(± 1·1)
S.P.	2·3 mm. Hg.	(2 cases)
E.H.B.F.	1261 ml./min.	(± 223)
H.V.R.	0·37 units	(± 0·10)

It appears clear, therefore, that haemodynamically portal fibrosis cases exhibit considerable rise of post-sinusoidal hepatic resistance but the hepatic blood flow remains more or less the same as in normal cases. Comparison of similar data in a group of 22 cirrhotic cases and 16 cases of extrahepatic obstruction showed (Graph 1) considerable differences. In the cirrhotic group, the mean flow was 895 ml./min. (± 247) and

in extrahepatic obstruction 733 ml./min. (±209). The mean W.H.V.P. in the 2 groups of cases were 15·1 mm. Hg. (±5·0) and 4·5 mm. Hg. (±2·3) respectively. It can be concluded, therefore, that patients with cirrhosis had the highest post sinusoidal resistance with considerably reduced blood flow and the portal fibrosis cases had the second highest post-sinusoidal resistance with little or no reduction of hepatid blood flow (Boyer and Basu, 1966).

GRAPH 1.

Comparative study of haemadynamic data in portal fibrosis, cirrhosis of liver and extrahepatic obstruction group of cases.



Splenic pressure. (mm. Hg.)
Wedged hepatic venous pressure. (mm. Hg.)
ehbf: Estimated hepatic blood flow. (ml./min)
HVR: Hepatic vascular resistance (units).
Figures in parentheses indicate mean values.

Oesophageal varices.– oesophageal mucosa. This representation of the cases degree of varicosity as seen under 4 categories, viz., 0 different cases :—

0
+
++
+++

When the varicosity w patic obstruction group, it varicosity.

Splenoportal venograp were studied in some detail

(1) The splenic vein large splenomegaly (Plate X

(2) The portal vein evidence of irregularity of intraluminal thrombus (Pl

(3) Large sized colla present. In many cases, t (Plate XXVII, Fig. 3).

(4) The distribution a interesting. In the large n showed a truncated appe Moreover, there was signif branches of the portal vein Fig. 4). This was designat bution of the intrahepatic t dichotomous type of divisi up to the periphery (Plate from that seen in cases o show characteristic 'sweep Fig 6) (Basu, 1962). The had been noted previously (Basu, 1958) but its relati until now.

Oesophageal varices.—Almost all the cases exhibited marked varicosity of the oesophageal mucosa. This finding is in conformity with the most important clinical representation of the cases, viz., severe and recurrent haemorrhagic episodes. The degree of varicosity as seen in barium swallow studies of the oesophagus was specified under 4 categories, viz., 0 to 3 plus. Table XI gives the degree of varicosity in the different cases :—

TABLE XI.

Degree of varicosity.

0	
+	10 cases
++	12 „
+++	3 „
	25 cases.

When the varicosity was compared to that found in the cirrhotic and the extrahepatic obstruction group, it was found that the portal fibrosis cases showed maximum varicosity.

Splenoportal venography.—The venographic pattern of the portal fibrosis cases were studied in some detail and revealed interesting and distinctive findings.

(1) The splenic vein was markedly dilated and tortuous in conformity with the large splenomegaly (Plate XXVI, Fig. 1).

(2) The portal vein was also hugely dilated. In a number of cases, there was evidence of irregularity of the portal vein and filling defects indicating presence of intraluminal thrombus (Plate XXVI, Fig. 2).

(3) Large sized collaterals involving the left gastric or the short gastric veins were present. In many cases, the collateral veins outlined the varices in the oesophagus (Plate XXVII, Fig. 3).

(4) The distribution and arrangement of the intrahepatic redicles were extremely interesting. In the large majority of the cases, the large branches of the portal vein showed a truncated appearance soon after their entry into the hepatic hilum. Moreover, there was significant disparity between the large sized main intrahepatic branches of the portal vein and tributaries of the first or the second order (Plate XXVII, Fig. 4). This was designated as a 'cut off' pattern and was in contrast with the distribution of the intrahepatic tributaries in a normal case where they show a characteristic dichotomous type of division and gradual diminution in the size of the tributaries up to the periphery (Plate XXVIII, Fig 5). The arrangement was also quite different from that seen in cases of post-necrotic cirrhosis, where the intrahepatic branches show characteristic 'sweeps' indicating presence of large sized nodules (Plate XXVIII, Fig 6) (Basu, 1962). The 'truncated' and 'cut off" pattern of the intrahepatic branches had been noted previously and had been described by us as 'withered tree' appearance (Basu, 1958) but its relationship to the portal fibrosis group had not been realized until now.

We tried to ascertain the degree of the 'cut off' appearance by grading such appearances up to 4 grades (0, 1 plus, 2 plus and 3 plus) of severity. The degree of grading depended upon the distance at which the smallest intrahepatic branch were clearly seen from the bifurcation of the portal vein. The details are given in Table XII.

TABLE XII.

Degree of 'cut off' appearance of the intrahepatic branches.

0	1 case
+	6 cases
++	15 cases
+++	1 case
Total ..	23 cases

In 2 cases, the venograms were inconclusive.

Operative findings :

Appearance of the liver.—At operation, the liver presented a characteristic appearance in nearly all the cases so much so that a very good estimate of the histological state could be made at this time. The surface of the liver was generally smooth (Plate XXIX, Fig 7). In a few cases, it was finaly granular (Plate XXIX, Fig 8) and in only 2 instances were there few nodules dispersed at some distance from each other. The overall appearance, however, was quite different from that of a normal liver. The shine of the normal liver had been lost ; in many cases there were areas of whitish looking scars on the surface. The texture of the liver had also been markedly altered. It was firm in consistency and inelastic. When cut with scissors (during taking of the wedge biopsy), bleeding was very small in amount and stitches did not have any tendency to cut through the liver.

The portal vein was generally thick walled, dilated and hypertrophied. This became more evident when the vein was sectioned for performing the portacaval shunt. The contrast between the thick walled portal vein and the thin wall of the inferior vena cava was very marked. In a number of instances, the intima of the vein showed evidence of sclerosis. In a few cases, plaque-like thickening was present in the posterior wall of the vein. In 4 cases, intramural thrombus was present within the lumen of the vein. This had to be dissected cleanly from the intima before anastomosis.

Histopathology.—Details of the histopathological changes are presented in Part II of this paper.

The histopathological changes were studied on the basis of a generous wedge biopsy taken at the time of operation. In many cases, pre-operative needle biopsies were also available. Further, a needle biopsy was taken from the depth of the liver at the time of operation in a large number of cases. The histopathological changes were reviewed on numerous occasions by the histopathological and the clinical groups jointly and the same slide was often reviewed a number of times. After mutual discussion, agreement on the status of the histopathological changes in each slide was reached. The main features of the histopathological changes were periportal scarring and

FIG. 1. Dilated and tortu

FIG. 2.

FIG. 1. Dilated and tortuous splenic vein in a case of portal fibrosis with large splenomegaly.

FIG. 2. Dilated portal vein with suggestion of filling defect.

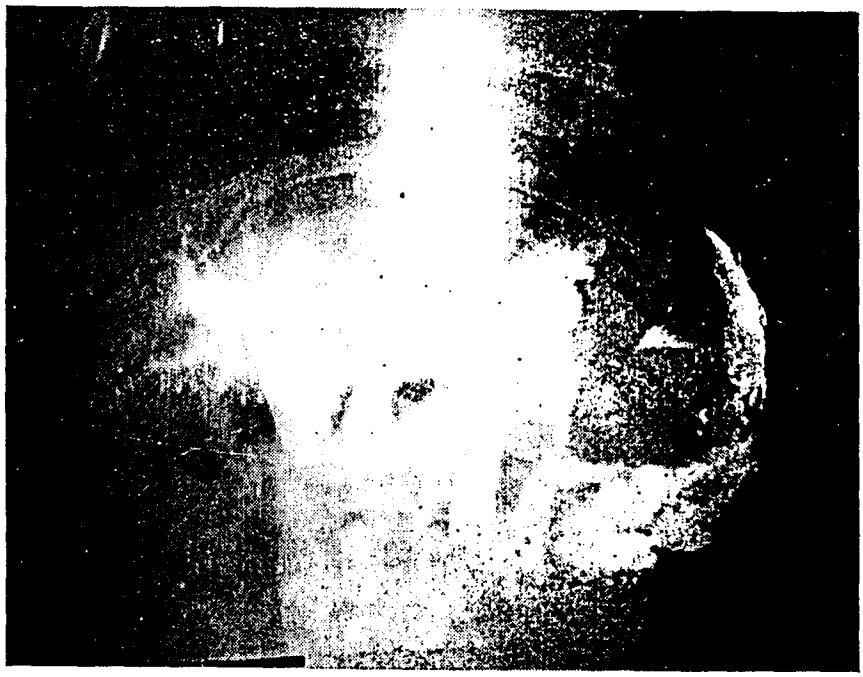


FIG. 3. Oesophageal collaterals outlining the varices in the oesophagus.

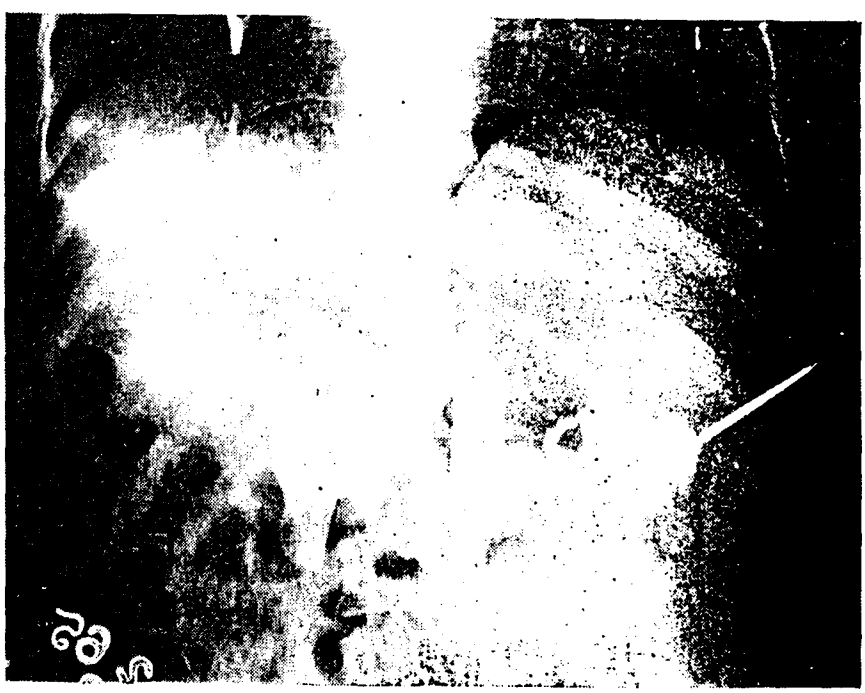


FIG. 4. 'Cut off' pattern of the intrahepatic radicles.

FIG. 5. Normal pat
intrahepati

FIG. 6. 'Sweeping'

PLATE XXVII.

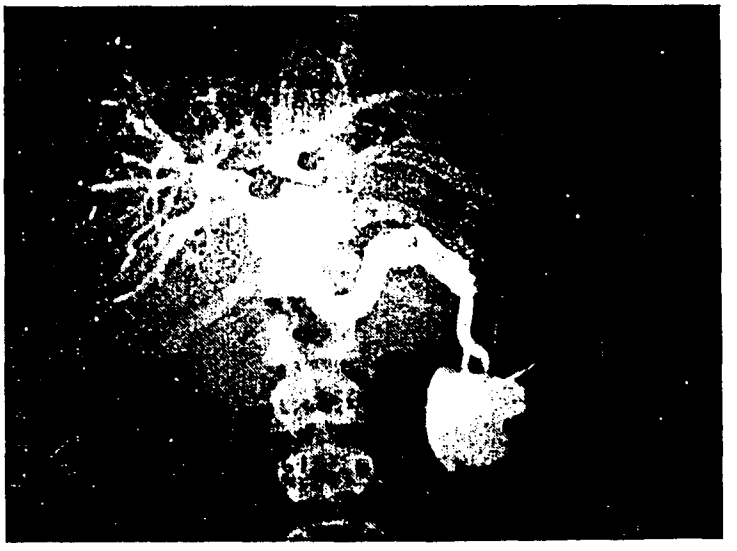


FIG. 5. Normal pattern of the intrahepatic radicles showing gradual diminution in size of the intrahepatic radicles.

FIG. 6. 'Sweeping' arrangements of the intrahepatic radicles in cases of post-necrotic cirrhosis

FIG. 7. Generally smooth appearance of the surface of the liver.

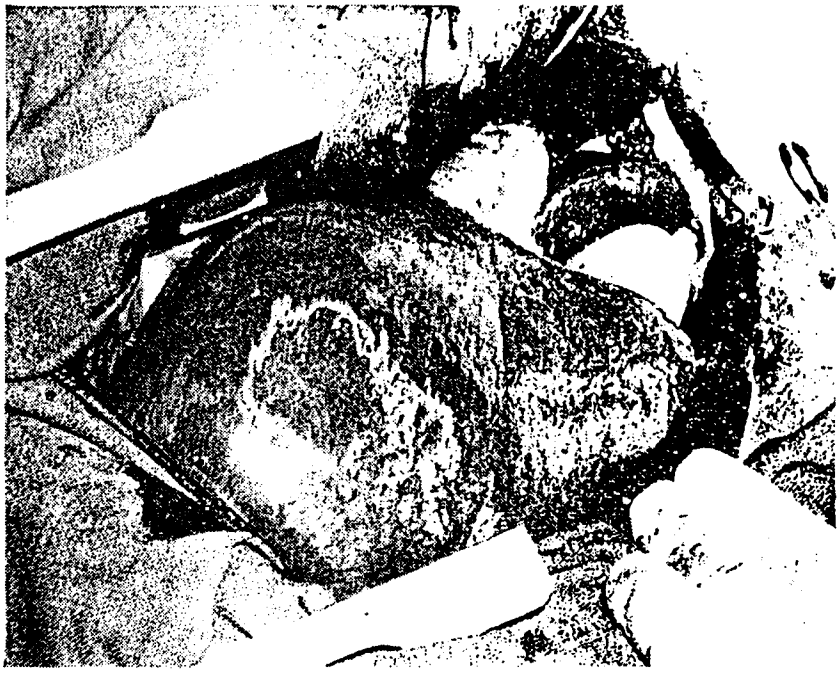


FIG. 8. The liver surface shows finely granular appearance.

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7 cases

In addition, autopsy
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patients for as long a tim
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Less than 6 mont
Between 6 month
Between 1 year a
Between 2 years
Between 3 years
Between 4 years
Between 5 years
Between 6 years

Three patients died
Another patient died 9 mo
due to the failure of the

infiltration with round cells, formation of septæ extending for varying distances into the parenchyma and joining together of adjacent portal tracts by condensation of reticulin.

In 7 cases, repeat needle biopsies of the liver were available from patients who had portacaval shunt operation. The interval of time between the operation and the repeat biopsy is given in Table XIII :—

TABLE XIII.

Case.	Time.
2	9 months after operation
1	1 year after operation
2	2 years after operation
1	2½ years after operation
1	3 years after operation
7 cases	

In addition, autopsy studies were available in 2 cases—in one case of post-operative death (15 days after operation) and in another case who died in the follow-up period (9 months after operation). The details of the autopsy material are presented in Part II of the paper.

In general, it can be said that the follow-up histological study in the biopsy material available did not show progression to cirrhosis in any of the cases. The pattern of periportal scarring, formation of septæ and trabeculation was more or less the same as in the pre-operative study. In only one case, the degree of scarring was seen to be more intense than in the pre-operative slide. In many of the follow-up slides, there was evidence of fatty changes in the liver cells. This was thought to be due to protein deprivation of the patients in the post-operative period.

Post-operative follow up.—Considerable effort was made to follow up all the patients for as long a time as possible. The time interval between the operation and maximum follow up period is set up in Table XIV :—

TABLE XIV.

Duration of post-operative follow up.

Less than 6 months	..	1 case
Between 6 months and 1 year	..	5 cases
Between 1 year and 2 years	..	5 cases
Between 2 years and 3 years	..	4 cases
Between 3 years and 4 years	..	3 cases
Between 4 years and 5 years	..	2 cases
Between 5 years and 6 years	..	1 case
Between 6 years and 8 years	..	1 case
	Total ..	22 cases

Three patients died after operation. Two patients died shortly after operation. Another patient died 9 months after operation. The death of the 1st two patients was due to the failure of the shunt to function efficiently in the immediate post-operative

period. The patients bled repeatedly and went into hepatic failure. In the third case, the immediate reaction of the patient following operation was excellent and the patient who was fairly sick before operation, did extremely well and was discharged in good condition 3 weeks after operation. However, 7 months after operation, he came back with deep jaundice and, in spite of all treatment, did not respond well. The jaundice persisted and the patient developed intermittent encephalopathy and died 9 months after operation. Autopsy study was available in 2 cases and has been described in Part II of this paper.

Studies conducted in the follow up period included estimation of general health ; and incidence of haemorrhagic episodes (if any) ; liver function studies and repeat liver biopsy studies in a number of cases. The general health of the patients remained fairly satisfactory except for the usual stigmata of post-porta caval shunt syndrome. These included certain amount of lethargy and facial and ankle oedema. Recurrence of haemorrhagic episode occurred in only one case 1 year after operation. Liver-function studies showed generally satisfactory results. The mean value of post-operative albumin level was 3.83 g. per cent (average 12 cases) compared to 3.5 g. per cent before operation. Post-operative liver biopsy studies did not show progress to cirrhotic changes and except for one case, the degree of fibrosis was more or less the same as before the operation. On the whole, therefore, it can be said that these patients of portal fibrosis behaved fairly well in the post-operative period over a period extending to 8 years. If we compare the follow up status of the portal fibrosis cases with that of the cirrhotic and the extrahepatic obstruction cases in our series, we get interesting information. Table XV gives certain interesting follow up data amongst the 3 groups of patients.

TABLE XV.

Follow up data of the shunt surgery patients.

	Portal fibrosis. (25 pts).	Extrahepatic obstruction. (18 pts).	Cirrhosis. (32 pts).
Operative mortality, per cent	8	11	25
Total mortality to date (follow up 6 months to 7 years), per cent	12	16·6	47 (40 in 1st year)
Incidence haemorrhage in survivals	1/22	1/15	1/17
Incidence of encephalopathy in survivals	10/22 (1 plus only)	2/15 (1 plus only)	8/17 (1 to 4 plus)
Follow up range	6 months to 8 years	6 months to 8 years	1 year to 8 years)

DISCUSSION.

It appears to us that these cases of portal fibrosis which are associated with severe portal hypertension, repeated haemorrhagic episodes, large splenomegaly and fairly good liver function should be separated from cases of 'true' cirrhosis of the liver and should form a separate clinical entity. They could explain many of the cases of so-called 'idiopathic' portal hypertension and 'tropical' or 'cryptogenic' splenomegaly. These cases tolerate haemorrhagic crises well. It seems reasonable to think that the better

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It is also clear that the portal fibrosis cases have better prognosis after the shunt procedure than the cirrhotic cases. The cirrhotic cases have increased operative mortality. In addition, many of them died in the 1st year after operation. This period constitutes the most dangerous time for them (Basu *et al.*, 1966). The total mortality including operative and long term follow up mortality (47 per cent) is significantly higher than in the fibrosis group (12 per cent). The severity of the encephalopathic symptoms is also greater in the cirrhotic than in the fibrosis group. In many respects, the fibrosis group behaves more akin to the extrahepatic obstruction group. This is understandable, because the liver function and structure is generally satisfactory in these 2 groups and their main symptom is repeated haemorrhagic complication from portal hypertension. The apparently good results that have been reported in some of the cirrhosis series following portacaval shunt operations are possibly because of the inclusion of all such cases in the series.

The important question to decide is the etiopathogenesis of the disease group. Two possibilities arise. They may be looked upon as a pre-cirrhotic process in the liver where the brunt of the disease has fallen on the area around the portal tracts leading to periportal infiltration and fibrosis but not extending very much to the parenchyma of the liver and development of classical cirrhosis. This interpretation would fit in with the generally satisfactory liver-function studies and post-shunt behavioural pattern of the patients. It would also be in conformity with the markedly thickened walls of the portal vein. However, the fact that repeat liver biopsy studies even after 3 years showed little or no progression to true cirrhosis goes against this postulate.

The other possibility is that the disease is due to primary phlebosclerosis involving the extra and intrahepatic branches of the portal vein and that the histopathological changes in the liver are consequent on such abnormalities in the vein wall. Mikkelsen *et al.* (1965) reported 36 apparently similar types of cases which they designated as 'Hepatoportal sclerosis'. In 13 of these cases, there was complete extrahepatic obstruction, in 6 there was partial portal venous block and in 17 the portal vein was apparently normal. The histopathological findings in the above cases were not extensively reported and differed, to some extent, from what has been described in our series. These authors make the point that intraluminal phlebosclerosis was possibly the etiologic basis of the disease and differentiated between portal vein thrombosis and portal vein phlebosclerosis.

In our series of cases, the portal vein was definitely thickened and hypertrophied almost in every case. However, definite evidence of sclerosis of the vein wall with presence of plaques was recorded at the time of operation only in a small number of cases. Intraluminal thrombus was present in 4 cases.

In reporting this series, we have taken care to exclude those cases which, on venographic appearances, undoubtedly belonged to the type of extrahepatic obstruction. Detailed analysis of liver histology in this latter group of cases was made in order to compare the findings with those of the portal fibrosis group.

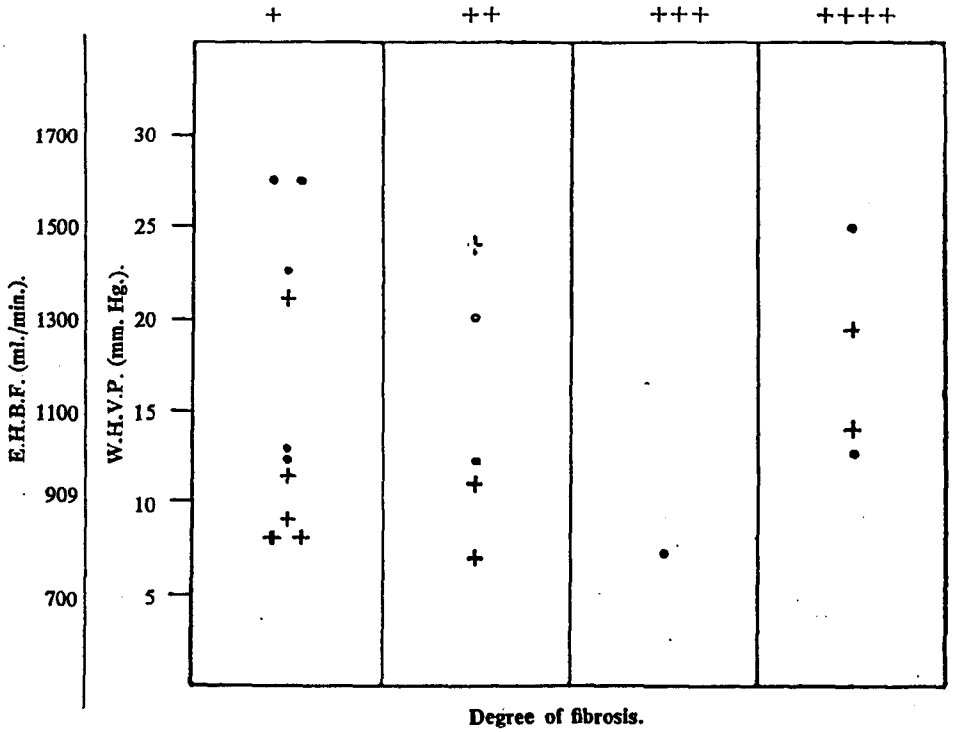
Study of the liver histology in 19 such cases of extrahepatic obstruction revealed that except in one case, scarring was generally absent or, if present, was minimal

in degree. Similarly, 'trabeculation' and formation of 'septæ' were also generally absent. The appearances, on the whole, were markedly different from what is seen in the portal fibrosis group.

Haemodynamic studies performed in a limited number of portal fibrosis cases in our series revealed moderate rise of wedged hepatic venous pressure indicating increased post-sinusoidal resistance but little reduction of estimated hepatic blood flow. These findings again go against the concept of pre-sinusoidal block caused by phlebosclerosis as being responsible for portal hypertension. In the series reported by Mikkelsen *et al.* (*loc. cit.*), haemodynamic data were available in only few cases. Their findings showed normal W.H.V.P. and reduced hepatic blood flow. However, these cases were mostly those where the portal vein was totally occluded and they cannot be strictly correlated with the series reported here. Correlation of the rise of the wedged hepatic venous pressure and estimated hepatic blood flow with the degree of fibrosis in our cases (Graph 2) failed to show any definite relationship between them. For example, in case No. 22, the W.H.V.P. was 19·5 mm. Hg., the E.H.B.F. was 1000 ml./min. and the degree of fibrosis was considered 4 plus, whereas in case No. 12, the W.H.V.P. was 24·0 mm. Hg. and the E.H.B.F. was 1305 ml./min. and the degree of fibrosis was 2 plus.

GRAPH 2.

Correlation of the W.H.V.P. and E.H.B.F. with the degree of fibrosis.



Degree of fibrosis.

W.H.V.P. : Wedged hepatic venous pressure : +
E.H.B.F. : Estimated hepatic blood flow : •

It seems clear, therefore, that while the concept of primary phlebosclerosis as the etiogenic agent responsible for the disease is attractive and reasonable, further well-documented data are necessary before we would be in a position to give a positive opinion on the subject.

The other great point of interest is about the geographical distribution of the disease. Rousselot (1965), in the discussion on Mikkelsen's (*loc. cit.*) paper made the interesting comment that there is geographical variation about the incidence of the disease. He said that the Italians saw a considerable number of such cases and that they (Rousselot) had not seen nearly as many as in the East. This observation is reinforced by the large number of similar cases reported from Japan (Imanaga *et al.*, *loc. cit.*) and by the current emergence of great interest in the disease in India and reports of large number of cases from several centres in the country (Wig, *loc. cit.* ; Aikat, 1966). It also fits in with similar types of cases which were reported from Hong Kong and from several areas in the African subcontinent. Many of the cases of so-called 'tropical' splenomegaly (Basu and Aikat, *loc. cit.*) with apparently normal looking liver would fit in with this syndrome. Whether this syndrome is predominantly an Eastern disease or not cannot be decided for certain at present but the existing balance of evidence points to its greater prevalence in this part of the world.

Summary and Conclusion.

1. A review of 25 cases of portal hypertension with massive and recurrent haemorrhages and large splenomegaly has been presented. The haemorrhagic complications were well borne. Hepatomegaly was not prominent. Liver-function studies were generally satisfactory and hepatic catheterization revealed raised wedged hepatic venous pressure with almost normal hepatic blood flow. Splenoportovenography was characteristic with a 'cut off' or 'withered tree' appearance of the peripheral intrahepatic portal venous radicles. The liver surface was smooth or slightly granular and firm at operation. The portal vein was thickened and sclerosed with occasional thrombi. Histopathological study of the liver showed periportal scarring and trabeculation with generally undisturbed parenchyma. The patients tolerated the operative procedure well and remained in good health during the follow up period extending up to 8 years. Liver function did not deteriorate during this period and repeat liver biopsy did not show progress to cirrhosis.

2. It seems to us that this syndrome of portal fibrosis causing portal hypertension should be separated from frank cirrhosis of the liver or true extrahepatic obstruction. The syndrome might explain many of the hitherto unrecognized cases of 'idiopathic' portal hypertension or 'cryptogenic' or 'tropical' splenomegaly.

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