THE BUDD-CHIARI SYNDROME

A Study of Diagnosis, Haemodynamics and Treatment.

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for the Degree of Doctor of Medicine

in the University of Cape Town.

PREFACE

Symptomatic occlusion of the hepatic veins is a rare condition caused by tumour or thrombus arising either locally or by extension from the inferior vena cava. It is usually called the Budd-Chiari syndrome. The etiology remains unknown in over two-thirds of the patients. Its rarity and interest has led to a large number of individual case reports. 322 instances of symptomatic hepatic vein occlusion have been reported, of which 184 are single case publications. There are only six series of more than five cases (Nishikawa, 1910; Corinini and Oberson, 1937; Palmer, 1954; Parker, 1959; Gibson, 1960; Safouh and Shehata, 1965) and these have been largely drawn from autopsy records, although Palmer (1954) described seven patients seen during life.

The clinical and pathological features of hepatic vein occlusion have been described in a number of papers (Hess, 1905; Thompson and Turnbull, 1912; Armstrong and Carnes, 1944; Kelsey and Comfort, 1945; Thompson, 1947; Parker, 1959; Gibson, 1960) during the one hundred and twenty years since the publication of Budd's treatise. However, accurate diagnosis has generally relied on autopsy, and detailed investigations have seldom been performed. Consequently, little is known of the roentgenographic and haemodynamic features. The diagnosis of liver disease has been revolutionized by such special techniques as percutaneous liver

biopsy, portal pressure measurements, isotope scanning and selective arteriography and venography.

This study describes six patients with the Budd-Chiari syndrome in whom these methods have been applied to establish the diagnosis, to ascertain the underlying cause and to assess the possibility of surgical intervention. Special attention has been given to hepatic venography and hepatography. The vascular pattern in the Budd-Chiari syndrome has been compared with that in normals and in patients with other diseases of the liver. Diagnostic features have been determined and an attempt made to evaluate compensatory changes in the lymphatic drainage and venous blood supply following hepatic vein obstruction. Alterations in portal dynamics have also been recorded. The clinical course has been followed and the effect of treatment assessed in each patient. Finally, the literature has been reviewed with particular reference to the diagnosis and treatment of hepatic vein thrombosis.

The studies reported in this thesis were carried out during the tenure of a Research Fellowship in the Royal Free Hospital School of Medicine, and they were supported by a grant from the William Shepherd Bequest to the Royal Free Hospital.

The special radiological procedures, haemodynamic studies, isotope investigations and laboratory work were personally performed with the exception of the scintillation scans, coeliac axis arteriograms and the other individual tests acknowledged overleaf.

ACKNOWLEDGEMENTS

I am especially grateful to Professor Sheila Sherlock for allowing me to supervise and investigate the patients in this study. Dr. W.B. Young kindly made available to me facilities in the Radiology Department.

I wish to thank Dr. L. Kreel for the coeliac axis arteriograms, Drs. A.S. Tavill and E.A. Jones for the scintiscans and measurements of albumin synthesis, Mr. H. Williams for the PVP (I-131) excretion and Dr. J.G. Walker for carrying out hepatic vein catheterization in one case. Dr. B. Seniwaratne gave valuable advice on diuretic therapy and arranged the daily electrolyte estimations. Drs. P. Scheuer and M. Petrelli reported on the liver biopsies and autopsies. The erythropoeitin assay was performed by Dr. Pennington of the London Hospital. The illustrations were prepared by Mr. Gibson and the Staff of the Photographic Department of The Royal Free Hospital.

SYNOPSIS

Symptomatic occlusion of the hepatic veins is a rare condition. Clinical diagnosis has been difficult in the past and the disease is frequently unsuspected until autopsy. Detailed investigations have seldom been performed. This study describes the use of modern investigative techniques including liver biopsy, portal pressure measurements, hepatic venography, hepatography, arteriography and scintiscanning in the Budd-Chiari syndrome during life. These methods have been applied to establish the diagnosis, ascertain the underlying cause, reach an understanding of the compensatory vascular changes and assess the possibility of surgical intervention. The results are discussed and the entire literature on the Budd-Chiari syndrome reviewed.

Six patients were studied, 3 with polycythaemia and 3 with hepatic vein occlusion of unknown cause. Serial liver function tests in these cases were compared with others in the literature. Liver biopsies regularly demonstrated the centrizonal changes of hepatic venous occlusion.

Hepatic venography and hepatography were carried out in the Budd-Chiari syndrome and in normals and patients with other diseases of the liver for comparison. Radiographic confirmation pf the diagnosis was made in each case. A typical pattern was described on hepatic venography for the first time. The main

hepatic veins were narrowed or occluded. In the adjacent area of liver there was a network of tortuous collateral vessels. The hepatic vein catheter could not be advanced the usual distance and the normal features of hepatic venograms were absent.

Injection of contrast material into the hepatic parenchyma (Hepatography) showed prolonged opacification of the hepatic veins compared with normals and patients with cirrhosis. The position and extent of the hepatic vein occlusions were determined by a combination of hepatography and hepatic venography.

A widespread collateral circulation was evident radiographically. Interlobular, intralobar and interlobar vessels were shown to bypass the obstruction. Collation of the data from this investigation, animal experiments and other human studies revealed the importance of these diversionary channels within the liver in relieving the congestion caused by hepatic vein thrombosis. Increased lymph flow does not seem to play an important compensatory role in the Budd-Chiari syndrome.

Isotope scans showed activity over the central zone of the liver but there was absent or decreased uptake in lobes drained by occluded veins. The abnormalities on hepatic arteriograms seem to be caused by lobular congestion following

hepatic venous occlusion. Contrast radiography demonstrated compression of the cava by the engorged liver.

Pressure studies were made in the hepatic vein in each case and their value in the differential diagnosis was assessed. The effect of paracentesis on hepatic haemodynamics was investigated by measurements of portal pressure, hepatic blood flow and systemic vascular changes.

An approach to the diagnosis of the Budd-Chiari syndrome was evolved from these investigations. Surgical treatment was analysed in 23 reported cases, and the value of a modern diuretic regimen in controlling fluid retention was discussed.

CONTENTS

CHAPTER 1

HISTORICAL INTRODUCTION

Like many eponyms, that associated with occlusion of the hepatic veins is disputed. It is strange that a physician was reputed to have first described the pathology (Budd, 1845) and that the clinical features were attributed to a pathologist (Chiari, 1899). The papers of Lambron (1842) and Frerichs (1861) take chronological precedence over the contributions of Budd and Chiari.

Attention was first drawn to hepatic vein thrombosis by Budd's textbook, "Diseases of the liver", published in 1845. Budd observed the association between intrahepatic abscesses and inflammation of the hepatic veins. In his words, "the abscess touching the thin coat of the vein sets up inflammation on its inner surface. The canal of the vein becomes closed at that point, and all the branches that feed it, even back to their capillary divisions, become subsequently, and in consequence, choked with fibrin and coagulated blood". He described two further cases with similar pathology: a patient of Dr. James Russell of Birmingham who died in 1836 after an amputation, and that of M. Lambron, first published in the Archives Generales of June 1842. The latter was probably caused by a neoplastic ulcer of the stomach.

None of these patients, however, would now be classified as the Budd-Chiari syndrome. Today, this title is reserved for symptomatic occlusion of the hepatic veins, and the pathological lesions in these patients seem to have been incidental findings at autopsy.

The first adequate clinical description of hepatic venous thrombosis was recorded by Frerichs in 1861. He reported the case of a woman of 38 years who had abdominal pain, ascites, slight jaundice and oedema of the lower half of the body. Chiari's paper did not appear for another 38 years.

Chiari (1899) is widely regarded as having introduced the concept of primary inflammation of the hepatic veins. This, too, had been put forward earlier. Hess (1905) quotes the inaugural address of Lange (1886) who suggested that thrombosis in the hepatic veins might be the sequel to a primary phlebitis.

Chiari, however, extended and developed this theme, and he described 3 patients with stenosis or obliteration of the ostia of the hepatic veins due to intimal thickening. He commented as follows:_ "These three cases of obliterating phlebitis of the hepatic veins have much in common. In all there was inflammation in the wall of the veins, which, with the exception of the first case, affected exclusively the intima; even in the first case the adventitia was affected to a lesser extent. The process therefore represented an endophlebitis. The phlebitis was localised in all three cases in

the same manner, i.e., in the proximal* end of the hepatic vein, although in the third case there was some peripheral extension. There was always a definite tendency to obliteration, and in many cases complete obliteration. In every case it was an entirely independent process, unconnected with changes in the surrounding parts, and was also not secondary to a preceding thrombosis. The results of this phlebitis obliterans showed themselves in all three cases in the same manner, namely: congestion, hyperaemia, atrophy and induration of the liver, with congestion of the portal veins and a resulting fatal ascites.

In accordance with what has been said, I do not hesitate to say that this independent phlebitis obliterans of the main trunk of the hepatic vein is a disease sui generis."

Chiari's report also contained 7 cases of hepatic vein thrombosis which were secondary to an intrahepatic lesion such as a carcinoma. He suggested that there was a clear distinction between the patients in whom there was ostial occlusion which resulted from circulating "irritants" and patients with an underlying hepatic disorder. Some authors have continued to use the terms "Chiari's Disease" and the

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*proximal is used by Chiari to refer to the end nearest the heart. This is contrary to the current anatomical nomenclature with regard to veins which is used elsewhere in the text.

"Budd-Chiari Syndrome" to separate these conditions. Gibson (1960) made a strong plea for retaining this classification but, as Parker (1959) has pointed out, all the anatomical features can be explained by thrombosis alone, although an initial endophlebitis cannot be excluded on morphological grounds. Further, there is no clear division of patients according to the site of thrombosis. None of Parker's cases had ostial occlusion alone. There was always a substantial involvement elsewhere in the hepatic veins. Most of the ideopathic cases in the literature have also had more proximally situated lesions. Because of this, it is current usage to employ "Budd-Chiari syndrome" as the title for symptomatic hepatic vein occlusion from any cause, although obstructive thrombosis which is limited to the sublobular and central veins comes under the heading of veno-occlusive disease and is a different entity. The term "Chiari's disease" is no longer in vogue.

Since this first, thorough review by Chiari (1899), with its careful illustrations, there have been several noteworthy publications which dissect the pathological details. Before considering the different approaches and concepts of these authors, it is relevant to single out the report of Willcocks (1896) for special mention, because it was the first correct diagnosis of the

Budd-Chiari syndrome during life. He presented the case record of a child of one year and ten months in whom there was sudden onset of abdominal distension and liver enlargement. In his own words, "The extreme varicosity of the veins over the front of the chest and abdomen, and the absence of any oedema of the legs, led to the diagnosis being entertained that there was obstruction of the inferior vena cava. The presence of ascites pointed to the obstruction being probably situated in the neighbourhood of the fossa on the posterior aspect of the liver, at the point of emergence of the hepatic veins. The post mortem examination confirmed this view".

In 1905, Hess published an excellent review to draw attention, in the United States, to a disease he believed was being overlooked, clinically and at post-mortem. Hess had studied in Prague and the case he described was from the General Hospital in that city. He supplied a tabular synopsis of all the cases he could trace. There were twenty-three of them, of whom five had come from Chiari's clinic.

One of the features he noted in his own case was the relative enlargement of the spigelian or caudate lobe which projected downwards like a tumour mass. The same observation was made by several subsequent authors and has been discussed in some detail

(see Chapter 5) (Nishikawa, 1918; Caroli et al., 1958; Burgeon and Guntz, 1959; Parker, 1959; Gibson, 1960).

German authors, following Chiari's lead, have throughout plumped for endophlebitis as the underlying cause of the thrombosis. This hypothesis was disputed in 1912 by Thompson and Turnbull in a good account of two personal cases. They believed that the histology was not in keeping with a pure endophlebitis and that the condition was basically thrombotic in nature. The ostium of the hepatic vein was the area most frequently obstructed and "the orifice of the veins is the site which on a priori grounds appears to be the site of election for thrombosis". They dismissed the view of Penkert (1902) that there is a congenital basis and invoked Gee's (1871) argument that as the ductus venosus was closed the hepatic veins must have been patent at birth. Further, as recently pointed out by Ludwick et al. (1965), since the hepatic veins and hepatic portion of the inferior vena cava have a common origin, a developmental abnormality involving failure of fusion would not occur at this site.

In addition to their contribution on pathogenesis, Thompson and Turnbull (1912) gave a detailed description of the gross lesions. They drew attention to two clinical types which were illustrated by their two patients. In one, the manifestations appear gradually,

usually with epigastric pain before abdominal swelling. In the second variety, symptoms develop with great rapidity and death may occur in a few days. This classification has been adopted by later authors but, as Parker (1959) pointed out, the acute presentation is uncommon and constitutes only 20 per cent of reported cases.

During the next forty years the rarity and interest of hepatic vein thrombosis led to several reviews and many individual case reports, but there was no substantial advance in knowledge of the causes, pathology and clinical features. A comprehensive account of the gross lesions in 9 personal cases was reported by Nishikawa (1918), and a detailed description of the microscopical appearances was given by Coronini and Oberson (1937). A beautifully written pathological report contributed by Turnbull in the paper by Hutchison and Simpson (1930) is worthy of special mention.

The rarity of the Budd-Chiari syndrome is indicated by statistics compiled over the years. Only 4 cases of symptomatic disease were found in a search of autopsy records in a 30-year period at the Mayo Clinic (Kelsey and Comford, 1939). In the Stanford University Department of Pathology, there was an incidence of 0.04 per cent (Armstrong and Carnes, 1944), and in the Bernhard

Baron Institute of the London Hospital, an incidence of 0.061 per cent in 29,720 autopsies (Parker, 1959). More than 100 cases of the Budd-Chiari syndrome had been recorded by 1947 (Thompson, 1947) and in 1959 (Parker, 1959) a detailed study of the literature accounted for 164 cases. A personal assessment up till 1966 amounted to 322 reports.*

The diagnosis of the Budd-Chiari syndrome has seldom been made during life. Thompson's review in 1947 is distinguished by the inclusion of two personal cases which were recognised before death. The first was a miner of 31 years of age who had sudden severe pain in the abdomen followed by abdominal swelling. Thirty-one litres of fluid, containing 1.0 gm per cent of protein were removed from the abdomen. He died in hepatic coma after a few days. The second case was a girl of 2 years who had an attack of cyanosis and vomiting from which she recovered. A month later abdominal pain and swelling occurred. There were dilated abdominal wall veins, ascites and a large liver. Peritoneal fluid was removed on two occasions. She died fourteen

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*Personal assessment. Most of the cases were confirmed at autopsy. But living patients were included if there was sufficient clinical information to make a definite diagnosis. Individual cases are referred to in the bibliography by a figure in parenthesis after the page references. This figure indicates the number of cases reported in that particular publication.

weeks after admission to hospital.

Few of the earlier case reports indicate clearly whether the diagnosis was considered before death. Thompson (1947) believed this had been achieved in 10 patients in addition to his own. Recent publications have shown an increasing awareness of the condition. In the last decade, the Budd-Chiari syndrome has been suspected during life in 39 out of 80 patients in whom adequate clinical details were recorded (personal assessment).

Although there have been several excellent reviews of symptomatic hepatic vein thrombosis, Parker (1959) has written the only detailed analysis of the incidence of individual symptoms, signs and pathological features. He reviewed the entire literature from Budd (1845) up to 1958 (excepting publications in Russian), and contributed the largest personal series of 15 cases. These were all extracted from autopsy records. He found 236 reports of hepatic vein occlusion but based this analysis on 164 cases in which there was evidence of hepatic vein occlusion during life and in which the diagnosis was confirmed at autopsy.

He showed that hepatic vein occlusion may present in one of five ways. In about 75 per cent of cases there is a subacute or chronic illness dominated by severe ascites. Sudden complete

obstruction to hepatic outflow may lead to an acute abdominal emergency, and in 4 per cent of patients to death in a few hours. Symptoms due to inferior vena caval occlusion precede clinical liver involvement in 16 per cent. Five patients presented with a haematemesis. Rarely, cachexia and pain from a primary hepatoma are the main features.

It is well known that ascites, hepatomegaly and abdominal pain dominate the clinical picture. Parker's figures confirm these findings but, surprisingly, show that there was no peritoneal fluid in 7 per cent, that there was clinical absence of liver enlargement in 30 per cent and that pain occurred in only half the cases. A third of patients had jaundice or splenomegaly.

Most of the cases proved fatal and Parker concluded that once symptoms appeared recovery never occurred. In the light of more recent reports, including the present study, death is not invariable and occasional cases may have a long survival although full resolution of the pathology is improbable (Palmer, 1954; Burger et al., 1961; Parkinson and Miller, 1961; Tapie et al., 1961; Leger et al., 1964; Schreiber and Gonzales, 1967; Cases 2 and 3).

Like previous writers, Parker was concerned mainly with pathological details, but he differed in eschewing hypothesis for factual analysis. Although nearly half the ideopathic cases

had occlusion of the hepatic vein ostia, he showed that proximal lesions were frequent and that sometimes the ostia were spared. His findings have largely scotched the persisting belief that obstruction at the ostia is a distinct entity. Perhaps the most interesting part of his paper is the catalogue of causes. The etiology was established with reasonable certainty in 49 of the 164 patients. Polycythaemia vera, hypernephromata and tumours of the inferior vena cava were most commonly encountered.

Coming shortly after Parker's comprehensive account, Gibson's paper (Gibson, 1960) has been largely overshadowed. Apart from 11 new cases, his main contribution was a discussion of the clinical features in relation to the pathological evolution. He put forward evidence to show that there is a symptomless period during which the occlusions are present while their effects are compensated. However, this concept was not new. Hutchison and Simpson (1930) concluded that "the degree of collateral circulation depends upon the amount of obstruction in the hepatic veins, or in the vena cava at or above the junction of the hepatic veins. If the collateral circulation is adequate there may be no signs of disease, or at least no ascites, but sooner or later in most cases it breaks down". Gibson suggested there were several mechanisms which help limit the hepatic congestion. There is intrinsic regulation of liver blood flow which may reduce the hepatic arterial

supply and there may be deviation of venous blood into portosystemic shunts. The caudate lobe has an autonomous venous drainage and is often greatly enlarged in the Budd-Chiari syndrome presumably because blood is shunted through from the right and left lobes. Lymphatics might also play a role and in several cases the lymphatics in the portal tract and hepatoduodenal ligament were dilated.

Gibson (1960) also made much of the difference between Chiari's disease and the Budd-Chiari syndrome which Parker's (1959) evidence had already rejected.

However, neither Gibson nor Parker gave much attention to the role of special investigations in the diagnosis of hepatic vein thrombosis. Indeed, throughout the one hundred and twenty years since the publication of Budd's treatise, reviews have followed a similar pattern of dissection and analysis of the clinical and pathological features. Parker (1959) devoted four lines and a small table to laboratory tests in a paper of thirty-three pages, and Gibson (1960) who was concerned mainly with pathogenesis and histology, contributed a short paragraph on liver function. In a recent textbook of gastroenterology (Jones, 1965), there is a brief account of liver function tests and a passing mention given to contrast radiography. There have been occasional reports of special diagnostic procedures and of medical and surgical treatment of the Budd-Chiari syndrome, but no critical review of diagnostic methods or treatment

has appeared.

On account of its rarity, the Budd-Chiari syndrome seldom presents where there are facilities to examine the problem intensively. The following study arose from a unique opportunity to investigate personally six patients with symptomatic hepatic vein thrombosis using modern diagnostic techniques.

CHAPTER 2

CLINICAL FEATURES IN SIX CASES OF THE BUDD-CHIARI SYNDROME

CASE 1

In 1958 a thirty-eight year old toolmaker suffered a thrombosis in the left leg. Two years later he was seen at the National Hospital, Queen Square for giddy spells. No abnormality was found. In 1962 he experienced intermittent right upper quadrant abdominal pain and dizziness. In September he was admitted to hospital with abdominal pain, jaundice and dark urine. On examination at that time he was flushed and plethoric with telangiectasiae on the face, neck and chest. The liver was 6 cm enlarged. Investigations showed a haemoglobin of 19.9 gm per 100 ml, haematocrit 65 per cent, total white count 15,000 per cu mm and platelets 295,000 per cu mm. Polycythaemia vera was diagnosed, and he was treated with 5 millicuries of radioactive phosphorus (P-32) intravenously, and venesection at four-monthly intervals. Cirrhosis was suspected on account of liver enlargement, spider naevi and abnormal liver function tests. Liver biopsy was refused and a barium swallow showed no varices.

He remained fairly well after discharge from hospital but in March, 1963 and on several subsequent occasions he had severe epigastric pain. The serum bilirubin and alkaline phosphatase remained slightly elevated (Table 3.4). In 1964 he had episodes

TABLE 2.1

CLINICAL SUMMARY OF SIX PATIENTS WITH BUDD-CHIARI SYNDROME

Case	sex and age	Presentation	Underlying pathology	Confirmation of diagnosis	Fate	Duration from initial symptoms: Years
1	M 45	Dizziness	Polycythaemia vera	Autopsy	Died, peritonitis	1
2	F 46	Ascites	Polycythaemia vera	Biopsy, Hepatic venography	Alive, well	2.5
3	F 43	Ascites	Polycythaemia vera	Biopsy, Hepatic venography	Alive, well	2.5
4	M 29	Ascites	Unknown	Autopsy	Died, Hepatic coma	1
5	F 44	Menorrhagia	Unknown	Biopsy, Hepatic venography	Alive, well	2.5
6	F 53	Ascites	Unknown	Autopsy	Died, Hepatic coma	2

of thrombophlebitis in both legs and an enlarged spleen was detected. During the following year ankle oedema developed, followed by ascites and clinical jaundice.

In 1965, when first seen there was obvious weight loss, facial plethora, numerous spider angiomata, jaundice, ankle oedema, ascites and hepatosplenomegaly. The haemocrit was 59 per cent, leucocyte count 18,000 per cu mm, platelet count 388,000 per cu mm and red cell volume 56 ml per Kg (Tables 4.2 and 4.3). Liver function tests were compatible with hepatocellular damage (Table 3.4). A barium swallow showed oesophageal varices. Caval obstruction was suspected on account of prominent collateral veins flowing upwards over the abdomen and the loins (Fig. 2.1). Radiography showed side-to-side narrowing of the hepatic portion of the inferior vena cava (Fig. 8.3). Hepatic venography demonstrated a narrow right hepatic vein and arising from it an unusual network pattern of fine vessels (Fig. 5.11). He was treated with a low sodium diet, lasix, spironolactone and potassium supplements. Body weight fell by 35 lbs to 130 lbs. There was considerable diminution of ascites and leg oedema.

Severe upper abdominal pain required his re-admission to hospital on several occasions. No duodenal or gastric lesions were seen on further barium examinations. His general condition gradually deteriorated. In August, 1965 signs of hepatic

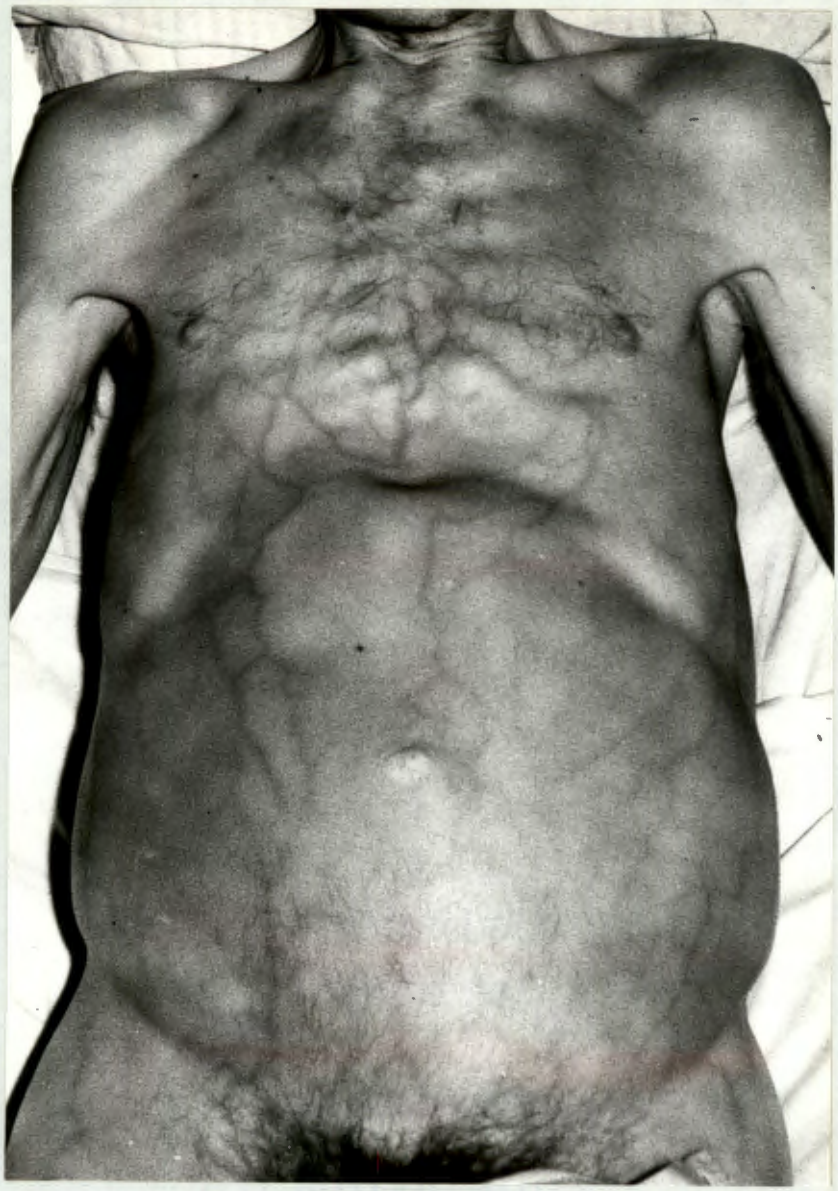

Fig: 2.1 CASE 1

Infra-red photograph showing abnormal veins over the trunk and abdomen. Contrast radiography of the inferior vena cava demonstrated narrowing at the upper end (fig. 8.3), but no organic stenosis was visible at autopsy.

encephalopathy appeared. For about a week he had behaved strangely. On admisskon he looked ill. Hepatic foetor and a flapping tremor were present. These responded transiently to reduction of dietary protein, cessation of diuretics, and administration of purgatives and oral neomycin. On 1st September, he complained of severe upper abdominal pain which was controlled with analgesics. There was no tenderness or guarding. The blood pressure fell and his condition deteriorated. He died on 3rd September.

At autopsy, there was old thrombotic occlusion of medium-sized hepatic veins. The liver was enlarged (2065 gm) and the surface finely granular. Sectioning showed intensely congested areas with intervening yellowish brown parenchyma. Scarred remnants of medium-sized hepatic veins were identified, and others contained organised thrombus. Segments of veins showed recanalization. Microscopically, central veins were dilated, and there was prominent central congestion and fibrosis. The intrahepatic segment of the inferior vena cava was narrow owing to compression by the enlarged liver. There were thrombosed oesophageal varices and splenomegaly. A perforated duodenal ulcer was sealed by fibrous and pancreatic tissue. The peritoneal cavity contained five litres of greenish yellow fluid. This was not related to the ulcer and was probably a terminal event.

CASE 2

In September, 1965 this forty-six year old housewife noticed slight abdominal distension which resolved following treatment with oral diuretics. Tense ascites developed six weeks later and three litres of abdominal fluid were removed at the local hospital. There was no pain. The peritoneal fluid rapidly re-accumulated and her legs became swollen.

When seen in December, 1965 she complained of tiredness and abdominal discomfort. She had previously been in good health and had travelled widely in Africa and South America. There was no history of toxic drugs, transfusions or past jaundice. Before the onset of swelling she had lost 7 lbs in weight. She was in poor general condition. There was muscle wasting and slight jaundice. The tongue and oral mucosa were plum-coloured but there was no obvious plethora. Gross ascites was present and the liver was tender and enlarged. There were no collateral veins. No venous hum or arterial murmur was present. Leg oedema extended to both knees; pelvic examination was normal. The blood pressure was 130/80 mm Hg, the jugular venous pressure was normal and the jugular veins filled on abdominal compression. The apex beat was not displaced. The heart sounds were normal and there were no murmurs. Bilateral pleural effusions were detected.

The haemocrit was 7 per cent, leucocyte count 26,800 per cu mm

(neutrophils 23,850), platelet count 290,000 per cu mm and the red cell volume 48 ml per Kg (Table 4.4). The neutrophil alkaline phosphatase was 186 (normal 15-75). Liver function tests were consistent with hepatocellular dysfunction (Table 3.5). The ascitic fluid contained no malignant cells. Serum erythropoietin assay was normal. Apart from ascites, there was no clinical evidence of portal hypertension; the spleen was not felt and a barium swallow did not show varices. However, wedged hepatic vein pressure was elevated (Table 7.1) and right atrial pressure was normal. Hepatic venography showed partial occlusion of the right and left hepatic veins and filling of collateral vessels (Figs. 5.17 through 5.19).

The combination of panmyelosis, increased red cell mass and high leucocyte alkaline phosphatase score was characteristic of polycythaemia vera. No cause of secondary polycythaemia was found. The ascites and liver enlargement followed thrombosis of the hepatic veins which resulted from the underlying myeloproliferative disease. The diagnosis of the Budd-Chiari syndrome could not be histologically confirmed because the low thrombotest precluded liver biopsy. She was treated with intravenous heparin, venesection of three litres of whole blood and 5 millicuries (P-32), intravenously. Fluid retention responded to sodium restriction and oral lasix. Catheterization of the inferior vena cava for venesection was

complicated by a staphylococcal septicaemia. The organism was cultured from the blood and from the catheter, and the infection was successfully treated with crystalline penicillin. Venesection reduced the haematocrit to 59 per cent.

There was a marked improvement in her general condition. In July, 1966 she was admitted to hospital for re-assessment of the polycythaemia and liver function. The haematocrit was 52 per cent and the white cell and platelet counts were normal (Table 4.4). The serum albumin had increased to 4.0 gm per 100 ml. Liver biopsy confirmed the diagnosis of the Budd-Chiari syndrome, centrilobular congestion being prominent with fibrosis and slight necrosis. Fluid retention remained under control. However, in September during a holiday in Italy, ascites recurred. This was successfully treated with ethacrynic acid, spironolactone and potassium supplements. She remained well when last seen in November, 1966.

CASE 3

In November, 1965 a 43-year old housewife noticed abdominal distension which increased over the following two months. Ankle oedema appeared. She had previously enjoyed good health. At the local hospital a swelling was noted in the right upper quadrant

of the abdomen. Cholecystography and intravenous pyelography were normal, and a barium meal showed a deformity of the stomach due to liver enlargement. The abdominal swelling and oedema increased during December. Laparotomy was carried out in January. There was a large congested liver, splenomegaly, dilatation of the portal vein and congestion of the jejunum and proximal ileum. Liver biopsy showed intense centrilobular congestion with patent central veins. After the operation, the ascites re-accumulated and the haematocrit rapidly rose to 59 per cent.

When first seen in February, 1966 she was well apart from the tense ascites which precluded palpation of abdominal organs. There was no history of drugs, excessive alcohol ingestion or jaundiced contacts. At the age of 15 years she had infective hepatitis. On examination, there was no clinical jaundice and there were no stigmata of chronic liver disease. Slight sacral oedema was present. The cardiovascular system was normal. There was a healing abdominal wound. After paracentesis, an enlarged, firm, non-tender left lobe of liver was felt. The spleen was not palpable. There were no masses, bruits or collateral vessels. The haematocrit was 62 per cent, leucocyte count 13,000 per cu mm (11,180 neutrophils), platelet count 550,000 per cu mm and red cell volume 44.5 ml per Kg (Table 4.5).

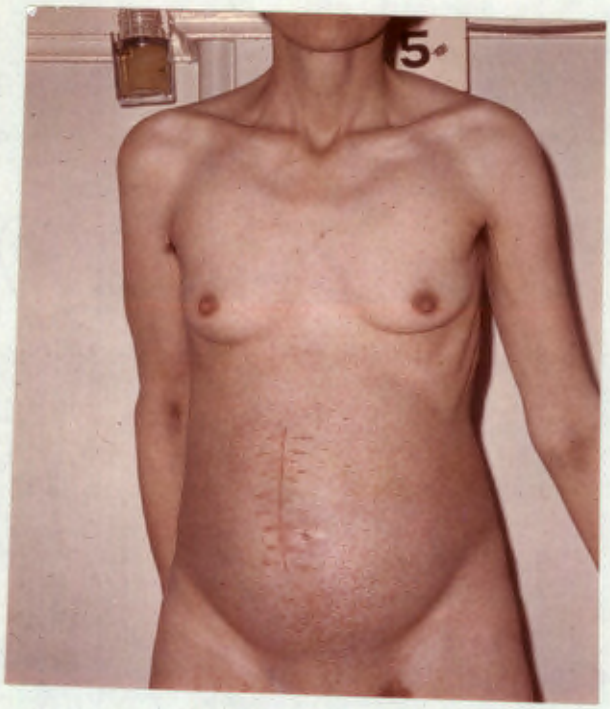

Fig: 2.2 **CASE 3**

Clinical photograph of a patient with the Budd-Chiari syndrome. The distended abdomen, laparotomy scar and drug rash are visible.

Serum albumin and thrombotest were low, but other liver function tests were normal (Table 3.6). The ascitic fluid was free from malignant cells. Contrast radiography showed a patent inferior vena cava (Fig. 8.5). In the absence of cardiac disease, the combination of hepatomegaly, ascites, centrilobular congestion of the liver and a patent cava, was presumptive evidence of hepatic vein thrombosis. Hepatic venography confirmed this diagnosis (Fig. 5.15). Panmyelosis and a high red cell mass pointed to polycythaemia vera as the underlying cause.

Polycythaemia was initially treated with venesection of 2 litres of blood which reduced the haematocrit from 62 to 46 per cent. She received 6 millicuries of intravenous radioactive phosphorus (P-32). A severe allergic reaction consisting of nausea, exfoliative dermatitis and photophobia followed therapy with oral lasix (Fig. 2.2). Fluid retention was controlled by salt restriction and ethacrynic acid 125 mg daily. On discharge, the haematocrit was 43 per cent; leucocyte and platelet counts were also normal.

In September, 1966 ascites recurred and a paracentesis was performed at the local hospital. Diuretic requirements were re-assessed and satisfactory regimen was established. When last seen in November, 1966 she was well and the fluid retention remained under control.

CASE 4

This 29-year old school teacher was unwell for many years with chronic otitis media, sinusitis and bronchiectasis. Several nasal polyps were removed surgically and a Caldwell-Luc operation was carried out. In 1964, after a haematemesis, a duodenal ulcer was shown radiologically. There was no recurrence. He began to feel tired and listless in May, 1965. Two months later he noticed stiffness of the knees and ankles but there was no redness or joint swelling. Ankle and abdominal swelling started in August, 1965 and was followed in a month by anorexia, dark urine and pale stools. He was admitted to hospital in September. There was slight jaundice, gross sacites, sacral and leg oedema and moderate splenomegaly. The serum albumin was low and the bilirubin was slightly raised. Thrombocytopaenia and anaemia were present (Table 4.6). There was no response to diuretics. After paracentesis, the liver was felt 7 cm below the costal margin. Laparotomy revealed only a large, congested liver. The operative liver biopsy showed intense centrizonal congestion.

When first seen in October, 1965 he was wasted and in poor general condition. There was no history of excessive alcohol ingestion, drugs or hepatitis. Stigmata of chronic liver disease were absent. Jaundice was slight, the abdomen was distended with fluid, the liver edge was just palpable and the spleen extended

4 cm below the costal margin. The blood pressure was normal and there were no signs of cardiac failure. Coarse crepitations= and rhonchi were heard over the right mid and lower zones of the chest. Biochemical tests were consistent with moderate hepatocellular dysfunction (Table 3.7). Hepatic venography showed narrowed and occluded hepatic veins (Fig. 5.13). The splenic vein was thrombosed (Fig. 6.1). An underlying cause could not be established. There was no evidence of polycythaemia (Table 4.6) and no malignant cells were found in the ascitic fluid. Amyloid was not present in a gum biopsy nor in the operative liver biopsy. The bone marrow was hypercellular and the reiculoendothelial elements were prominent. A bone biopsy was normal. Evidence for a myeloproliferative disorder was uncertain.

Fluid retention was controlled by salt restriction, 260 mg of lasix daily, and potassium supplements. Ampicillin was given for a chest infection. He remained unwell though he was later able to reduce the dose of diuretic. In March, 1966, there was no detectable ascites. He gradually became tired and irritable. In April, the ascites re-accumulated. After increasing the lasix, he developed severe cramps and was admitted to hospital. His general condition was poor. There was increased skin pigmentation, jaundice, tremor, ascites and firm hepatomegaly.

Distended veins ran upwards over the abdomen. Liver function had deteriorated. On account of his general state and disturbed serum electrolytes, all diuretics were stopped. After four days he developed severe back pain unrelieved by a small ascitic tap. He died the next morning.

The autopsy showed bilateral bronchiectasis and emphysema. The liver was enlarged and congested (Fig. 2.3). The main hepatic veins were patent but lobular and sublobular veins were found to be narrowed or occluded by organised thrombus and surrounded by fibrous tissue. The cut surface showed an exaggerated nutmeg pattern and there were bright yellow areas up to 0.5 cm in diameter. Microscopy showed severe congestion, slight fibrosis and massive loss of centrilobular liver cells (Fig. 2.4). There was no cirrhosis. No tumour was found and the bone marrow and lymph nodes were normal. There were dilated veins in the lower half of the oesophagus. The spleen was very large and weighed 720 gm. The portal vein and inferior vena cava were normal, but the splenic vein was occluded by an organized thrombus. No cause was found for occlusion of the splenic and hepatic veins.

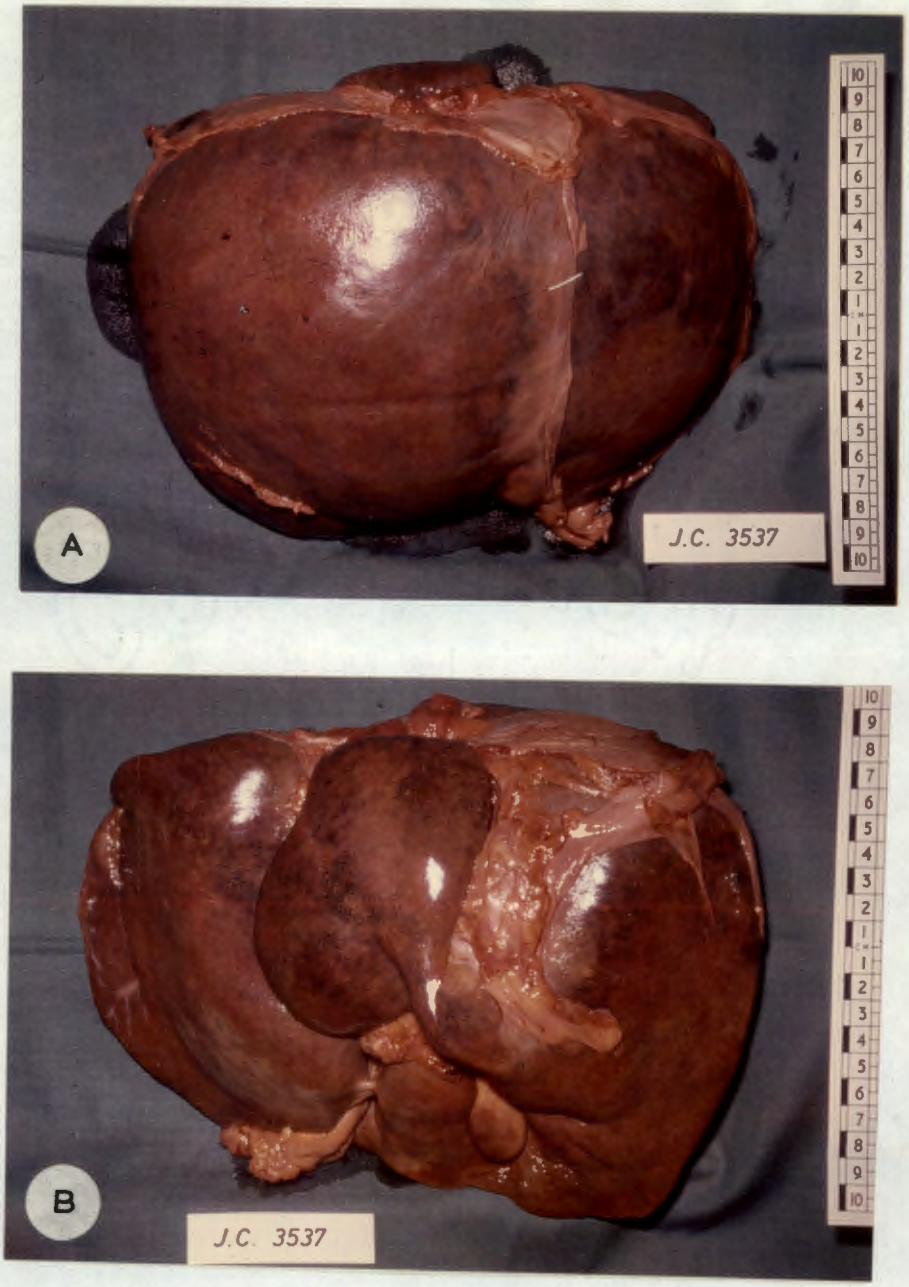

Fig: 2.3 **CASE 4**

Autopsy specimens of the liver in the Budd-Chiari syndrome showing anterior (A) and posterior (B) aspects. The liver weighed 2930 g. and was a deep brownish-red colour with yellow mottled areas mainly over the left lobe. The caudate lobe was prominent. There was equal enlargement of the other lobes.

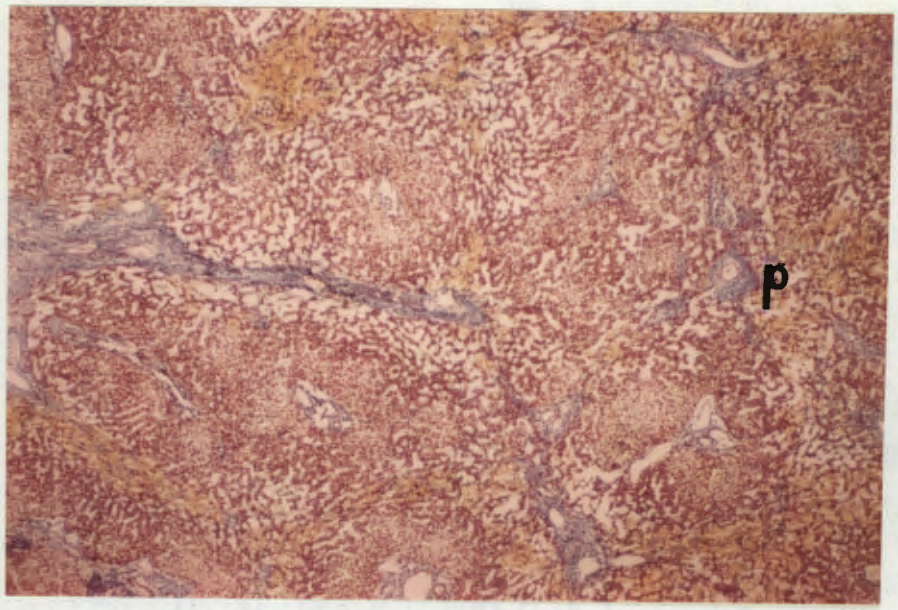

Fig: 2.4 CASE 4

The liver in the Budd-Chiari syndrome. There is congestion, haemorrhage and centrilobular necrosis. Cells near the portal tracts (P) are spared. Trichrome stain x 30.

CASE 5

In October, 1965 this forty-four year old gown machinist was admitted to hospital for investigation of menorrhagia. She had suffered from bronchial asthma for 20 years and from April to August, 1965 had received prednisone following an attack of status asthmaticus. She was found to have a large, firm liver. A barium swallow showed no varices and liver function tests were unhelpful. A hepatic tumour was suspected. At laparotomy the liver was uniformly reddish-blue in colour. No tumour was found but there was a fibroid uterus. The spleen was not enlarged. A small volume of ascites was present which increased rapidly after the operation. An operative liver biopsy showed intense centrilobular congestion, haemorrhage and disappearance of parenchymal cells.

She was first seen in December, 1965. There was no history of jaundice. She bruised easily but had not bled from the nose or gums. Her general condition was poor and the mucous membranes were pale. There was no jaundicem spider naevi, liver palms or parotid gland enlargement. The blood pressure, pulse, jugular venous pressure and heart were normal. No abnormal signs were present on auscultation of the chest. Tense ascites precluded palpation of the abdominal organs. Pelvic examination was normal.

There was leg oedema and tenderness over a thrombosed superficial calf vein. Liver function tests were abnormal (Table 3.8). The haematocrit was 33 per cent and the red cells were microcytic and hypochromic. Radiography showed the inferior vena cava to be patent but narrowed in the hepatic portion (Fig. 8.7). A catheter could be passed only 1 cm along a left hepatic vein (Fig. 5.16). Free hepatic vein and inferior vena caval pressures were raised due to the tense ascites (Table 7.1). Hepatic venography confirmed occlusion of the hepatic veins. Hepatic scanning and coeliac axis arteriography failed to demonstrate an underlying cause.

The ascites was dispelled with salt restriction and lasix 120 mg daily. The enlarged left lobe of the liver became palpable. The anaemia responded to oral iron. She returned to work, and ascites was easily controlled with diuretics. She was again admitted to hospital in May 1966 for routine re-assessment. Her general condition had greatly improved. There was no anaemia or jaundice. Marked hepatic foetor was present but there was no mental impairment, coarse tremor or abnormal neurological signs. Ascites was well controlled. The enlarged, left lobe of the liver could be easily palpated through an incisional hernia; it was hard with a finely nodular surface. The spleen tip was felt. There was no ankle oedema. Liver function had improved (Table 3.8).

While in hospital she developed herpes zoster of the 5th and 6th thoracic segments for which no cause was found. Her progress continued satisfactorily and when last seen in October, 1966 she was well and the ascites was controlled with lasix, 80 mg, and spironolactone, 200 mg daily.

CASE 6

In March, 1964 this 53-year old housewife had nausea, vomiting and severe pain in the right upper quadrant of the abdomen. She had been investigated for similar symptoms 6 years previously but no abnormality was detected. Jaundice appeared after 3 weeks and she was found to have ascites. The liver and spleen were impalpable. A cholecystogram showed poor filling of the gall bladder, and liver function tests suggested an intrahepatic lesion. At laparotomy there was an enlarged liver, and the gall bladder was opaque but no stones were felt. No other abnormality was present. The operative liver biopsy was reported as normal. The ascites increased and cytology of the fluid was thought to show malignant cells. After a course of thiotepa injections, intraperitoneally and intravenously, she progressively improved. Ascites, oedema and jaundice resolved. A year later she was well and able to carry out household tasks. In December, 1965 there

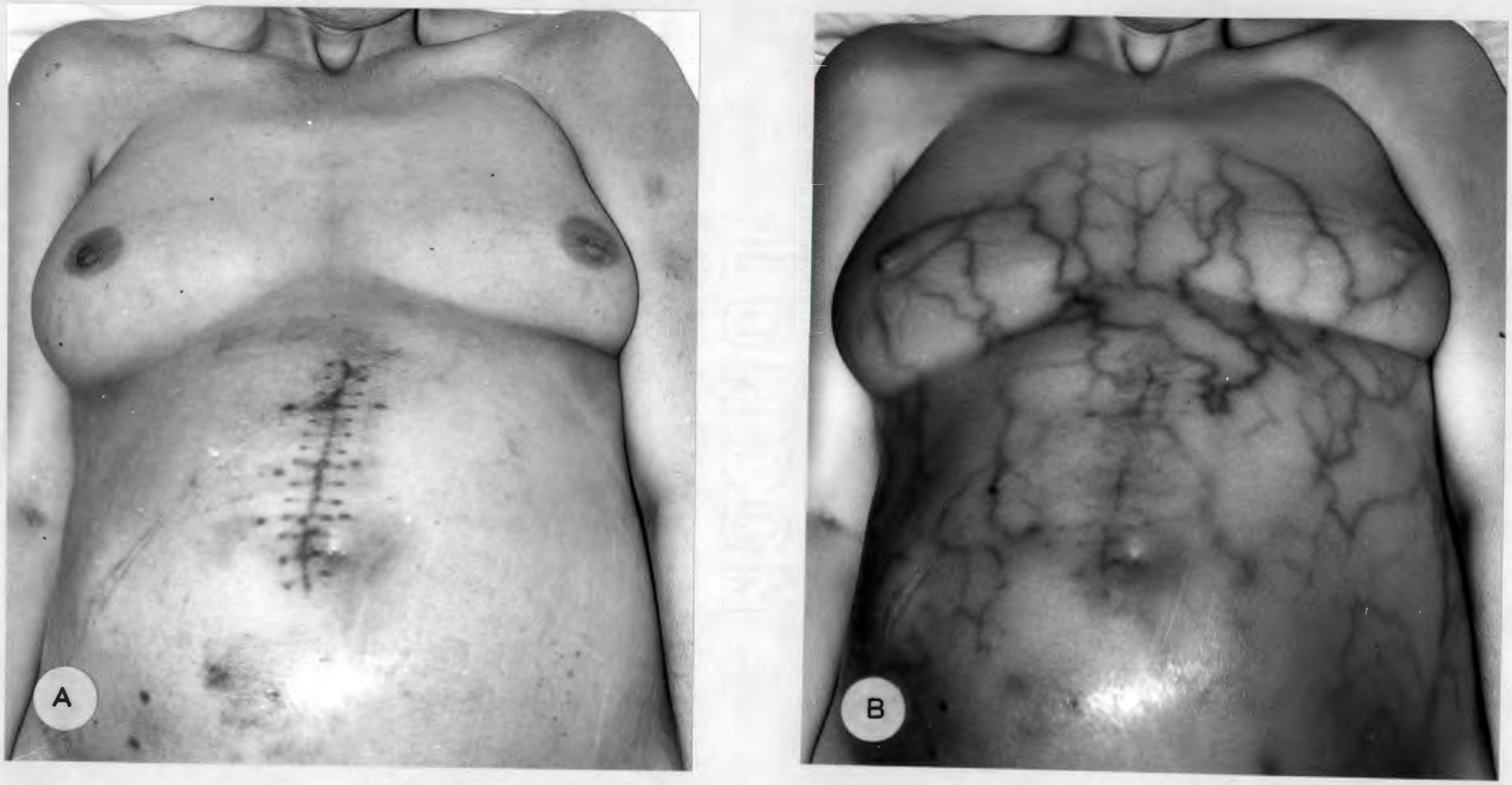

Fig: 2.5 CASE 6

The Budd-Chiari syndrome. The value of infra-red photography is demonstrated. There are dilated veins over the chest and abdomen. Complete occlusion of the inferior vena cava was shown by radiography (fig. 8,9) and later at autopsy (fig. 2.7). Normal film, A; infra-red film, B.

was a recurrence of fluid retention and jaundice. Liver function tests suggested hepatocellular disease. Portal vein thrombosis and a collateral circulation were shown on splenicvenography. Cells from the ascitic fluid were again considered malignant and in February, 1966 another laparotomy was done. There were no abnormalities apart from a large, firm liver and bloodstained ascites. She was treated with lasix but ascites returned and further paracenteses were carried out.

When first seen a month later her main complaints were abdominal discomfort and dyspnoea due to tense sacites. Repeated nose bleeds were troublesome. The menopause was in 1954 and there has been no subsequent menstruation. She was wasted, anaemic and slightly icteric. A coarse tremor and hepatic foetor were present but there were no spider naevi or palmar erythema. The muscles of the chest and arms were wasted. There was normal female hair distribution. Sdveral bruises were seen on the limbs and abdomen. The jugular venous pressure was raised and the cardiac apex was displaced upwards to the second left intercostal space. The heart sounds and blood pressure were normal. Massive ascites precluded palpation of the abdominal organs. Sacral oedema was absent. Large dilated veins coursed upwards over the front and back of the trunk (Fig. 2.5). Pelvic dxamination was normal, and the legs were oedematous. The lung bases were dull due to ascites.

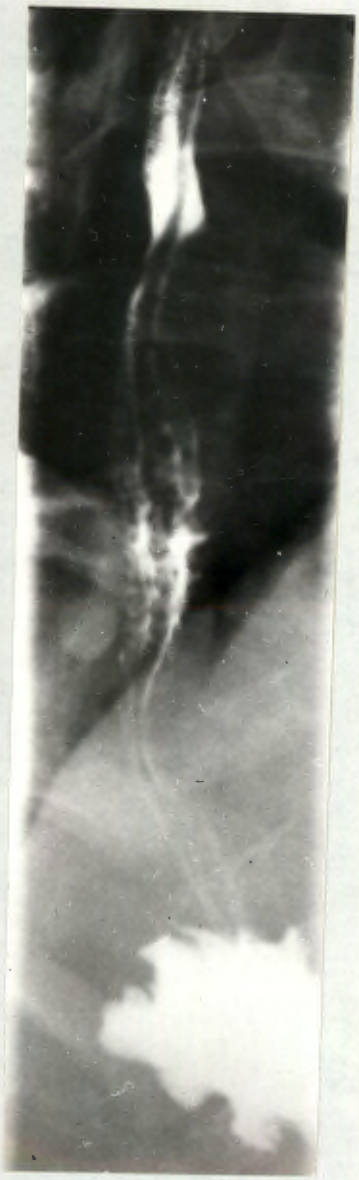

Fig: 2.6 **CASE 6**

Budd-Chiari syndrome. Barium swallow showing oesophageal varices.

There were no abnormal neurological signs.

Liver function was moderately impaired (Table 3.9). The serum bilirubin was 3.5 mg per 100 ml, alkaline phosphatase 22 KA units per 100 ml, aspartate transaminase 23 i.u. per litre and serum albumin 2.8 gm per 100 ml. Oesophageal varices were shown radiologically (Fig. 2.6). Malignant cells were not found in the peritoneal fluid. Electrocardiographs showed reduced voltage and non-specific T wave changes. Routine urinalysis and intravenous pyelography were normal. On review of the liver biopsies of 1964 and 1966, there was intense centrilobular congestion with obliteration and fibrosis of central veins (Fig. 2.9). Contrast radiography showed occlusion of the inferior vena cava by a thrombus. This involved the area of the hepatic vein ostia (Figs. 8.8 and 8.9), and it was not possible to pass the catheter into the hepatic veins. Right ventricular end-diastolic pressure was normal. An intensive effort was made to find the underlying cause of the thrombosis. Peripheral blood films and bone marrow showed no evidence of a primary haematological disorder. Abnormalities on a liver scan (Fig. 6.11) and a selective coeliac axis arteriogram (Fig. 6.5) were interpreted as due to the effects of hepatic vein occlusion.

There was a gradual deterioration in her condition from the time of admission. Treatment with diuretics was followed by

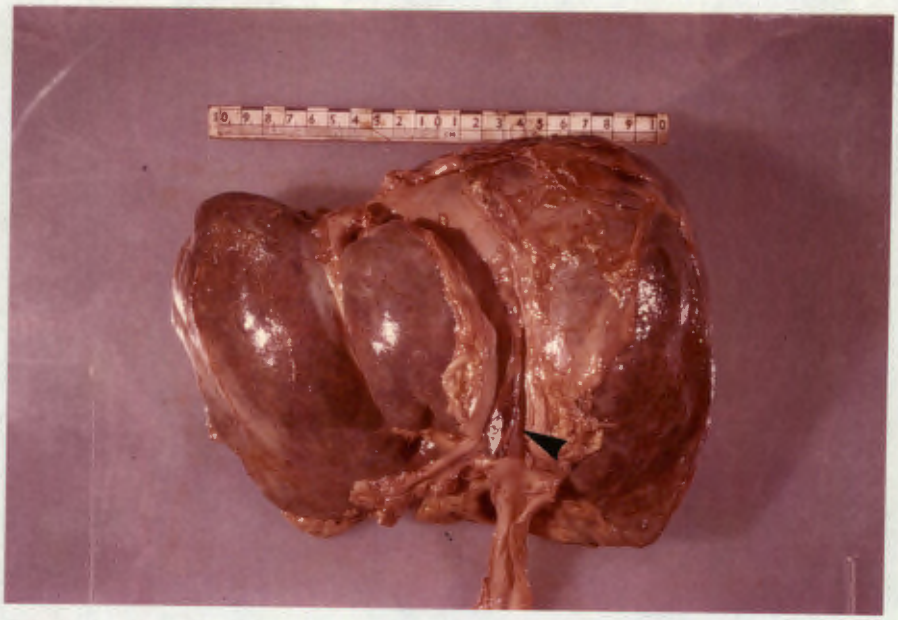

Fig: 2.7 CASE 6

Budd-Chiari syndrome. The liver is large and weighed 2100 g. The hepatic segment of the inferior vena cava has been opened. It is partly occluded by a thrombus (arrow) which starts at the level of the renal vein and extends up to but does not occlude the hepatic veins. The hepatic veins are separately thrombosed. The caudate lobe is prominent.

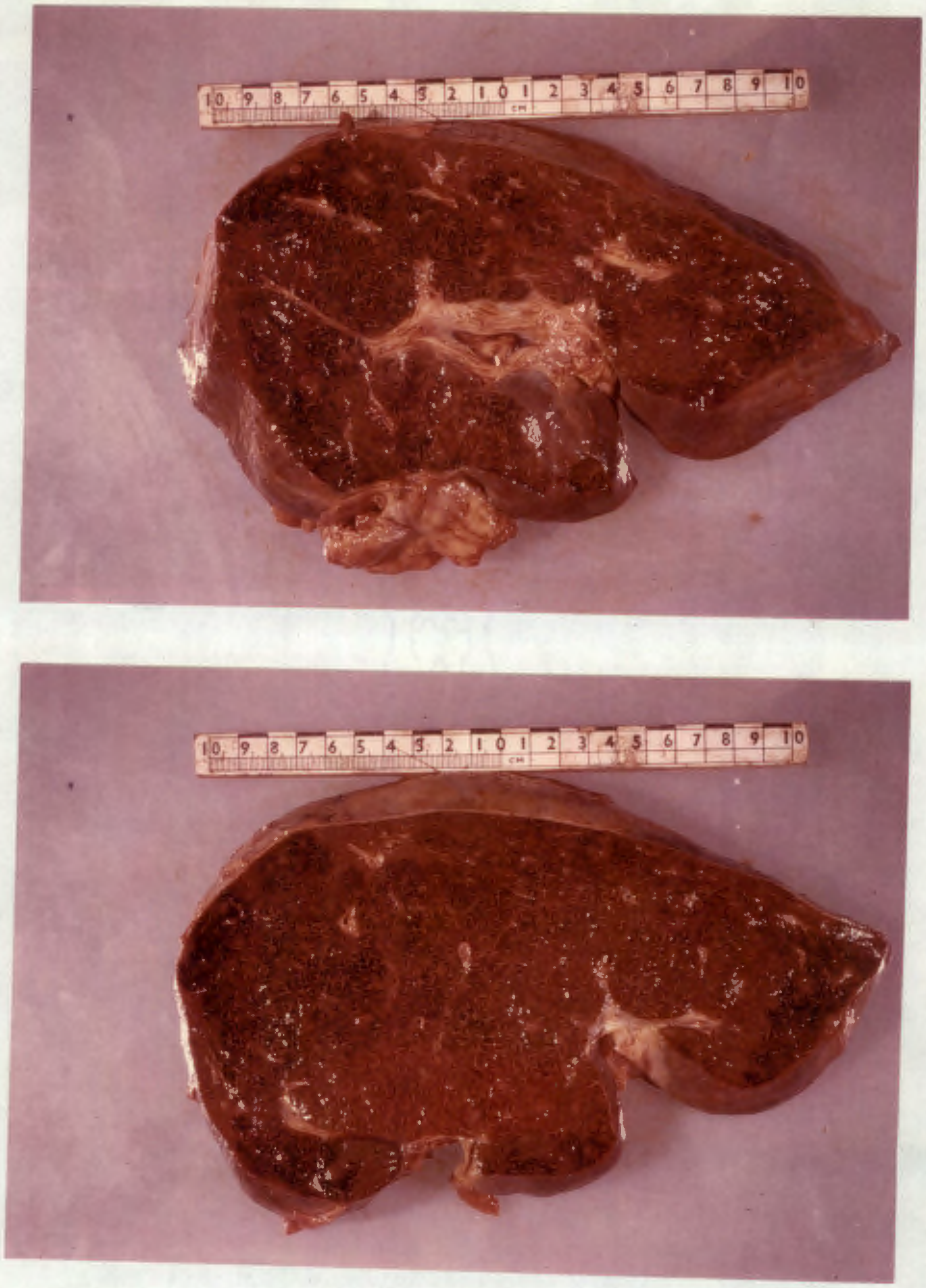

Fig: 2.8 CASE 6

Budd-Chiari syndrome. Cut surfaces of the liver show gross congestion with an exaggerated nutmeg pattern. There is no cirrhosis and no tumour. The scarred remnants of hepatic veins are seen.

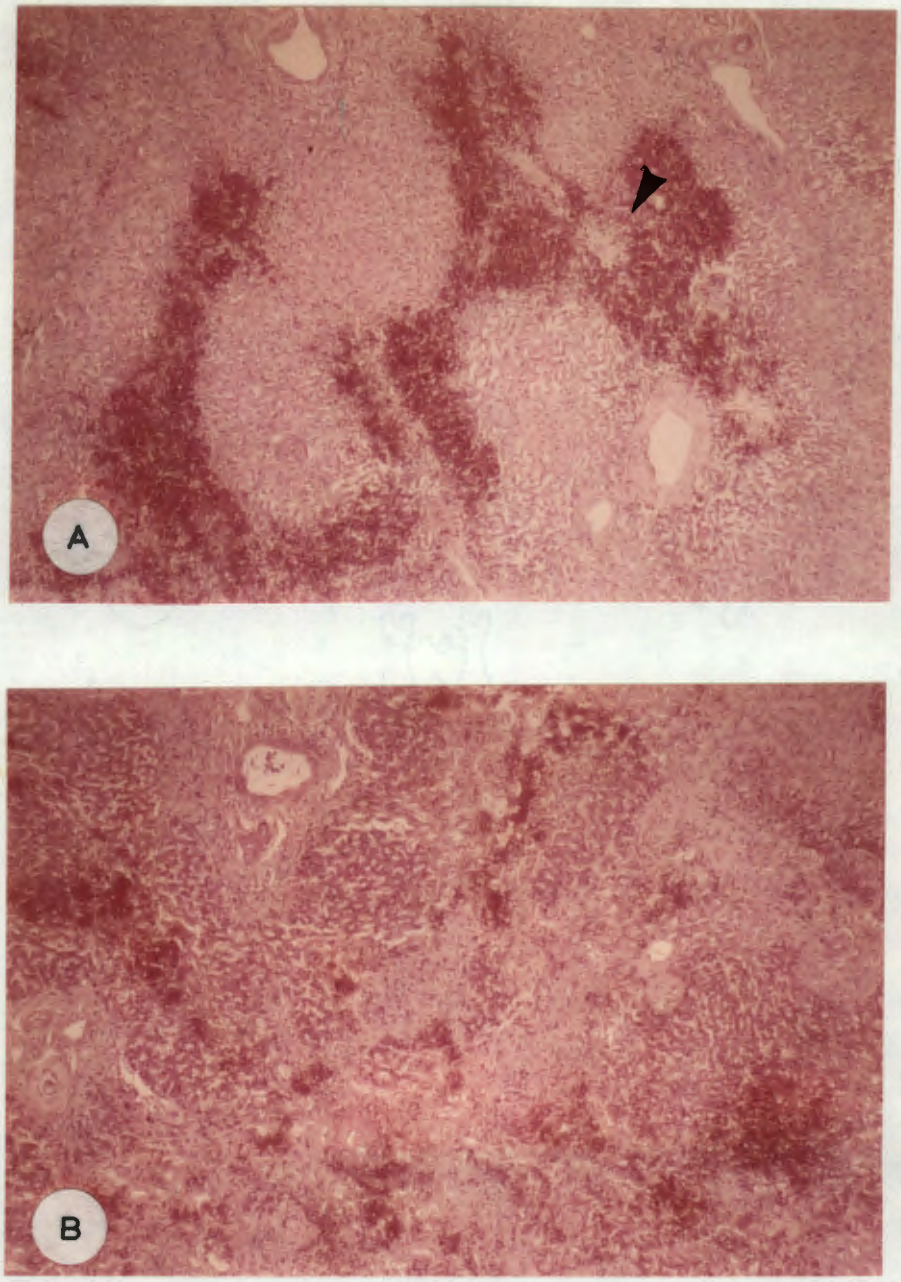

Fig: 2.9 CASE 6

The liver in the Budd-Chiari syndrome. There is severe centrilobular congestion, and very little normal tissue remains. Haemorrhages are widespread especially around central veins (arrow). Stained H. and E.
Magnification: A. x 30; B. x 60.

vomiting and electrolyte disorders (Table 10.4), and small volumes of ascitic fluid were removed on several occasions to relieve the tension. A few days before she died, there was profuse prupura due to thrombocytoplenia. On 14th May she became drowsy, passed into coma and died the following day.

An autopsy confirmed the findings during life. There was thrombus in the inferior vena cava extending from the level of the renal veins to the hepatic veins but not occluding their ostia (Fig. 2.7). The hepatic veins were separately involved and were represented by organised thrombus and fibrous strands (Fig. 2.8). The left hepatic vein was partially patent near the entrance to the cava. The cut section of the liver showed intense centrizonal congestion with very little normal tissue remaining. Histology showed a similar picture to the operative biopsy of 1966 (Fig. 2.9). The portal vein was completely occluded by thrombus. The spleen was slightly enlarged and the splenic vein was narrow but patent. No tumour was found and no cause could be established for the widespread thrombosis.

CHAPTER 3

LIVER FUNCTION IN THE BUDD-CHIARI SYNDROME

Only in the last decade have tests of liver function in the Budd-Chiari syndrome been regularly reported. During the hundred years after the publication of Budd's description, physicians and pathologists were mainly concerned with the anatomy, histology and clinical features. Diagnosis and treatment received scant attention. Thompson (1947) was able to find only five reports referring to tests of hepatic function and none of these are currently in vogue (Sohval, 1938; Kahn and Spring, 1940; Goldstein, 1931). Thompson (1947), himself, recorded only serum proteins in one of his two cases. In the most extensive clinical and pathological review to date (Parker, 1959), it is recorded that, "liver function tests, performed in a minority of cases, indicated a mild or moderate impairment of hepatic function". Results obtained in sixteen patients (including three of the author's) were set out in a table. In a recent textbook of gastroenterology, Jones (1965) commented that liver function studies had not been recorded in many instances of the Budd-Chiari syndrome. He noted that an increase in serum alkaline phosphatase and bromsulphthalein retention might be present, but there was no critical review.

In this chapter, serial tests of liver function in six patients are recorded and compared with others recently reported. The

synthesis rate of albumin, albumin loss into the gut, and the diagnostic value of the level of protein in the ascitic fluid were also investigated.

METHODS

Liver function tests were determined by standard procedures in the routine laboratory of the hospital. Albumin synthesis was measured directly by McFarlane's sodium (C-14) carbonate method as described by Tavill et al. (1967), which is valid for metabolically unsteady states. Protein leakage into the bowel was assessed by intravenous injection of polyvinyl pyrolidone labelled, with 10 microcuries of I-131 and all the faeces were collected for five days (Dawson et al., 1961).

RESULTS (Tables 3.1, and 3.4 through 3.9)

LIVER FUNCTION TESTS:

Although deep jaundice was not observed there was a moderate increase in serum bilirubin in the three patients who died. Of these, cases 1 and 6 were icteric on first presenting, and in the latter there was a steady rise from 3.5 mg to 8.0 mg per 100 ml. In case 4 the serum bilirubin increased to 5 mg per 100 ml shortly before death. In cases 2 and 5 bilirubin levels fluctuated up to 3.0 mg per 100 ml, but in case 3 they remained within normal limits.

Serum alkaline phosphatase was abnormal in all patients, and

showed a marked increase in three (Cases 1, 4 and 5). The patient (Case 5) with the highest initial alkaline phosphatase showed the best progress but this was accompanied by a gradual fall from 90 KA units to 15 KA units. Two patients (Cases 1 and 4) with consistently high values died.

The aspartate transaminase showed intermittent, slight elevation in all patients but there was no relationship with the clinical status. The highest reading was 51 i.u. per litre. The thrombotest was moderately reduced over-all, but there was no association, individually or as a group, with clinical progress. Bromsulphthalein retention was notably increased in two out of three patients in whom it was measured.

ALBUMIN STUDIES:

Serum albumin was initially reduced in five patients, and case 1 developed hypoalbuminanaemia before he died. In the survivors (Cases 2, 3 and 5), serum albumin gradually rose to normal levels. Serum globulin was often increased but there was special trend.

The protein content of the ascitic fluid varied widely, though levels were remarkably constant in individual patients. There was no direct relationship between serum albumin and protein in the ascitic fluid. In fact, the highest serum albumin (Case 1) occurred with the lowest ascitic protein of 0.9 gm per 100 ml.

TABLE 3.1

BIOCHEMICAL VALUES AT THE TIME OF PRESENTATION

Test	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Total bilirubin mg/100 ml.	5.2	1.2	0.5	1.8	0.8	3.5
Aspartate transaminase i.u. per L.	37	19	12	35	25	23
Alkaline phosphatase. King Armstrong units	42	18	16	30	90	22
Albumin Gm/100 ml.	3.7	2.6	2.8	3.1	3.3	2.8
Globulin Gm/100 ml.	4.3	2.4	2.1	1.8	3.6	3.2
Ascitic fluid protein Gm/100 ml.	0.9	1.2	2.8	2.0	2.5	1.6
Bromsulphthalein retention at 45 min. per cent	-	59	30	-	7	-
Thrombotest	17(13)*	12	71	100	80	38

*Prothrombin time in seconds (control in parenthesis)

TABLE 3.2

BIOCHEMICAL VALUES IN 50 CASES* OF THE BUDD-CHIARI SYNDROME

Test	Number of Estimations	Range	Mean
Total bilirubin mg/100 ml.	45	0.2 - 17.0	2.5
Alkaline phosphatase King-Armstrong	14	5 - 26	15
Bodansky units/100 ml.	15	2.5 - 18.4	8.1
Serum albumin gm/100 ml.	36	1.7 - 5.2	3.5
Prothrombin per cent	28	10 - 100	57
BSP retention per cent	23	4 - 93	23
Ascitic fluid protein gm/100 ml.	24	1.1 - 4.8	2.5

*(Bronte-Stewart and Goetz, 1952; Jonas and Lawrence, 1954; Brink and Botha, 1955; Fitzgerald et al., 1956; Abell, 1957; Carolietal, 1958; Case Records of the Massachusetts General Hospital, 1958; Ninov, 1958; Edwards et al., 1959; Ryvarden, 1959; Catinat et al., 1960; Cole, 1960, Gattas and Hall, 1960; Harland et al., 1960; Burger et al., 1961; Frank and Peckholz, 1961; Hernandes and Rojas, 1961; Leblond et al., 1961; Parkinson and Miller, 1961; Zebro et al., 1961; Beaird and Scofield, 1962; Clinco-Pathological Conference of Barnes Bospital, 1962; Erlik et al., 1962; Wohlgemuth and Mueller, 1962; Gagne and Bertrand, 1963; Ohara et al., 1963; Serban et al., 1963; Bruno and Ober, 1964; Clinico-Pathological Conference, 1964; Nicoloff et al., 1964; Strotmeyer, 1964; Ticholov and Usunov, 1964; Zalm and Moore, 1964; Bonnette et al., 1965; Case Records of the Massachusetts General Hospitalm 1965; Clinico-Pathologucal Conference, 1965; Ludwick et al., 1965; Norris, 1965; Chomette et al., 1966; Eguchi et al., 1966; Ecker et al., 1966; Hales and Scatliff, 1966; Hoffbauer, 1966; Becker and Moser, 1967; Clauvel et al., 1967; Schrieber and Gonzalez, 1967.)

TABLE 3.3

ALBUMIN SYNTHESIS STUDIES IN CASE 3

Test	Before venesection	After venesection
Serum albumin Gm. per 100 ml.	3.1	3.0
Plasma volume ml.	2436	2885
Intravascular albumin pool Gm.	75.5	86.6
Fractional synthesis rate. Per cent of i.v. pool $24\ hr.^{-1}$	8.6	4.3
Absolute synthesis rate Gm. $24\ hr.^{-1}$	6.5	3.7
mg. $Kg.^{-1}\ 24\ hr.^{-1}$	108	64

On the other hand, the highest ascitic protein of 2.8 gm per 100 ml was associated with a serum albumin of the same value (Case 3). The protein content of the ascites was less than 2.0 gm per 100 ml in cases 1, 2 and 6.

Albumin syntheses rates were determined in Case 3 before and after venesection of 2 litres of whole blood. Fractional and absolute synthesis rates were initially below the normal range, and they fell after the venesection although the intravascular albumin pool increased by 11 grams (Table 3.3).

Faecal radioactivity was normal (less than 2 per cent) in three patients (Cases 2, 5 and 6) after they had received an intravenous injection of I-131 polyvinyl pyrrolidone.

DISCUSSION

Liver function test results in this study were similar to those in fifty recent case reports of the Budd-Chiari syndrome (Table 3.2). There is usually moderate hepatocellular dysfunction, evidenced by slight elevation of bilirubin and serum transaminases, and depression of serum albumin and prothrombin. The most abnormal tests were bromsulphthalein retention and serum alkaline phosphatase. In a few patients, tests of liver function were normal (Bruno and Ober, 1964; Cox et al., 1966).

Serum alkaline phosphatase was on average lower in the patients from the literature. In the Budd-Chiari syndrome, as in primary

hepatoma, the alkaline phosphatase level may be substantially elevated in the absence of jaundice. Normal values are occasionally found. As in other forms of hepatocellular disease, bilirubin often rises in stressful situations such as haematemesis and surgicaloperations. Abnormal serum bilirubin levels, especially rising values, did not augur well. This was well illustrated by my six cases.

Bromsulphthalein retention was the most consistent abnormality in liver function. None of the present series and only one out of twenty-three from the literature were normal. In twenty out of a combined total of twenty-six estimations, bromsulphthalein retention was greater than three times the normal. Very high values, up to 93 per cent, have been recorded (Caroli et al., 1958). As hepatocellular function is only moderately impaired, the increased bromsulphthalein retention is probably due to a reduction in hepatic blood flow or to intrahepatic shunting through abnormal vessels. Allen et al. (1958) showed that occlusion of the hepatic veins in dogs rapidly caused bromsulphthalein retention of 10 to 70 per cent, which suggests a vascular rather than a hepatocellular mechanism.

A high content of protein in the ascitic fluid is believed to be a constant feature of hepatic vein thrombosis. This view has been fostered by the high protein values found in the ascites after experimental ligation of the hepatic veins (Allen et al., 1958). But both this series and reported cases show that there are many

patients with an ascitic protein content of less than 2.0 gm per 100 ml. In this study, the ascitic fluid protein was 2.0 gm per 100 ml or less in four of the six cases, whereas the mean level from the literature was 2.5 gm per 100 ml, and there were six out of twenty-four cases with 2.0 gm per 100 ml or less.

The polyvinyl pyrrolidone test was carried out in three patients with the Budd-Chiari syndrome to determine whether there was a leakage of protein into the gut. This was prompted by reports of protein-losing enteropathy in constrictive pericarditis (Peterson and Hestrup, 1963), and in veno-occlusive disease of the liver (Wolff, 1961), two other conditions in which hepatic outflow is obstructed. The normal result is not altogether surprising. In constrictive pericarditis, the protein loss is probably due to the high systemic venous pressure which interferes with lymphatic drainage into the inferior vena cava and not to the portal hypertension. In hepatic cirrhosis, portal hypertension does not cause gastro-intestinal protein loss (Dawson et al., 1961).

The depression of albumin synthesis was of the same order as in cirrhosis (Tavill et al., 1967). The failure to increase the rate of synthesis after venesection is in keeping with the findings of Tavill et al. (1967), who showed that the production of albumin is not regulated by its plasma concentration or the pool size. In fact, the synthesis rate of albumin fell after venesection, and there is no convincing reason. It is conceivable that the specific

activity time curve of C-14 urea which is used to calculate the albumin synthesis rate could have been affected by impaired release of urea from the congested liver.

Serial tests of liver function have not been recorded in many instances of the Budd-Chiari syndrome (Case records of the Massachussets General Hospital, 1958; Gattas and Hall, 1960; Parkinson, 1961; Beaird and Scofield, 1962; Erlik et al., 1962; Gagne and Bertrand, 1963; Ohara et al., 1963; Eguchi et al., 1966; Hales and Scatliff, 1966; Hoffbauer, 1966). Of special interest are the reports of six patients who underwent surgical procedures (Chapter 10). In three, a prosthesis was inserted to bypass an obstruction in the suprahepatic portion of the inferior vena cava; in two, a portosystemic shunt was constructed; and, in one, the hepatic artery was ligated.

Hales and Scatliff (1966) described a patient who survived for thirteen years after clinical signs suggesting inferior vena caval obstruction. Liver function tests were followed for four years. Bromsulphthalein retention, alkaline phosphatase and serum albumin showed no significant change during this period. Bilirubin rose steadily from 0.5 mg to 1.8 mg per 100 ml, and the prothrombin time fell from 90 to 64 per cent. Death occurred shortly after a caval bypass procedure.

Ohara et al. (1963) successfully placed a Dacron prosthesis

between the proximal vena cava and the right atrium. The patient was alive four months after the operation. Bromsulphthalein retention showed no change, at one and at four months, from the pre-operative figure of 35 per cent. The alkaline phosphatase was 12.1 units (Sinohara-Johnes) one month after the bypass, and 5.3 units three months later. Eguchi et al. (1966) anastomosed a Teflon graft end-to-side from the abdominal to the thoracic inferior cava. There was no change in the biochemistry.

CASE OF EGUCHI ET AL., 1966

Tests	Before bypass	4 months after bypass
Bilirubin mg per 100 ml	1.4	1.6
Alkaline phosphatase Bessey-Loury units	2.5	2.6
Bromsulphthalein per cent retention	15	15

A twenty-two year old woman with polychthaemia was recorded by Fitzgerald et al. (1956). After treatment with P-32, the bromsulphthalein retention fell from 70 to 15 per cent. A splenorenal anastomosis was performed on account of portal hypertension. Seven months later the liver function tests showed moderate improvement (no figures given). The prothrombin time, which was

45 per cent pre-operatively reached 100 per cent fourteen months after the operation.

The best documented case is that of Erlik et al. (1962). a side-to-side portocaval anastomosis was done for hepatic vein occlusion of unknown cause. Serial biochemical tests are shown in Table 3.10. Liver function deteriorated immediately after surgery. Gradual improvement followed, and by two months to pre-operative values were attained.

Tapie et al. (1961) described a young woman with polycythaemia vera who was treated with anti-coagulants and radio-phosphorous and who underwent hepatic artery ligation. Clinical recovery over 30 months was accompanied by a fall in serum bilirubin to 1.6 mg per 100 ml and a probable improvement in bromsulphthalein retention.

There was no significant improvement in liver function in 3 of the 45 patients who had successful shunts. This might be ascribed to the failure of portocaval, cavo-caval or even cavo-atrial shunts to influence hepatic congestion in view of the persistence of hepatic vein occlusion. However, after the porto-caval shunt (Erlik et al., 1962) and the cavo-atrial shunt (Ohara et al., 1963), serial liver biopsies showed resolution of hepatic congestion (Chapter 10).

The patient of Fitzgerald et al. (1956) who improved after a

spleno-renal shunt, and the patient of Tapie et al. (1961) who recovered after hepatic artery ligation, were also receiving treatment for polycythaemia, and this may have been the important factor. In the present study, two patients with polycythaemia vera, during intensive treatment with anticoagulants and P-32, showed a progressive increase in serum albumin to normal levels (Tables 3.5 and 3.6), but this was not accompanied by improvement in other modalities of liver function. One other report of liver function tests in a patient treated with anticoagulants and P-32 described a slight fall in bilirubin and alkaline phosphatase levels (Parkinson and Miller, 1961).

CONCLUSIONS

The investigations and review in this chapter aimed to determine:-

(a) The value of liver function tests in the diagnosis and prognosis of the Budd-Chiari syndrome.

(b) The value of ascitic fluid protein in the diagnosis of the Budd-Chiari syndrome.

(c) The amount of gastro-intestinal protein loss in the Budd-Chiari syndrome.

(d) The albumin synthesis rate in the Budd-Chiari syndrome.

The conclusions are as follows:-

(a) Moderate hepatocellular dysfunction associated with a high bromsulphthalein retention and/or elevated serum alkaline phosphatase in the absence of jaundice, should suggest the possibility of the Budd-Chiari syndrome in unusual cases of liver disease.

A raised serum bilirubin, especially a progressive increase, usually indicated a poor outlook. The initial serum albumin was not of prognostic import, but serial tests were often a good guide to the clinical course. However, the prothrombin time, bromsulphthalein retention and alkaline phosphatase, which were the most frequently abnormal tests, were not of prognostic value. Liver function did not change significantly after successful surgical shunts, but there was some improvement in four cases after treatment of the underlying polycythaemia.

(b) The ascitic fluid protein is not invariably high. Levels below 2 gm per 100 ml are often seen. This test is therefore of less value than is reputed.

(c) There was no gastro-intestinal protein loss as measured by the polyvinylpyrrolidone (I-131) test.

(d) Albumin synthesis was reduced, in one patient, to levels seen in hepatic cirrhosis.

TABLE 3.4

CASE 1

SERIAL TESTS OF LIVER FUNCTION

Test	1962	1963	1964	1965 1/1	1965 1/2	1965 17/2	1965 1/3	1965 20/3	1965 5/4	1965 26/4	1965 24/5	1965 5/7	1965 26/7	1965 17/8	1965 23/8	1965 31/8
Total bilirubin mg/100 ml.	3.0			3.2	5.2	5.0	4.5	4.4	5.0	3.5	2.6	3.9	3.4	2.0	4.0	5.8
Aspartate transaminase i.u./L.					37	14	24	28	33	10	12	14	20	29	34	26
Alkaline phosphatase King-Armstrong Units/100 ml.	18	23	16	24	42	40	54	54	54	36	56	48	40	46	56	56
Albumin Gm/100 ml.	4.1				3.7	3.0	2.4		3.0	3.4		3.1	2.8	3.1	3.1	3.1
Globulin Gm/100 ml.	2.7				4.3	3.7	5.0		4.9	4.9		4.2	4.0	4.6	4.6	4.6
Ascitic fluid protein Gm/100 ml.					1.1	0.9					0.9	0.8				
Prothrombin time seconds					17	20	15	18			17				20	

TABLE 3.5 CASE 2

SERIAL TESTS OF LIVER FUNCTION

Test	1964 14/12	1964 20/12	1964 28/12	1965 3/1	1965 10/1	1965 17/1	1965 25/1	1965 29/1	1965 24/3	1965 16/5	1965 23/6	1965 12/9
Total bilirubin mg/100 ml.	1.2	2.5	1.2	1.4	1.4	1.6	3.0	2.6	1.3	1.1	1.3	2.2
Aspartate transaminase i.u./L.	19	13	9	34	14	28	25			19		11
Alkakine phosphatase King-Armstrong units/100 ml.	18	18	20				14			18	20	33
Albumin Gm/100 ml.	2.6	2.6	2.5	3.1	3.1	3.2	3.9	4.6	3.7	4.0		4.4
Globulin Gm/100 ml.	2.4	2.4	3.0	3.0	2.9	2.4	2.5			2.5		2.7
Ascitic fuild protein Gm/100 ml.	1.2	1.9	1.0									
Prothrombin time seconds	12		11	27	25					28		23

TABLE 3.6

CASE 3

SERIAL TESTS OF LIVER FUNCTION

Test	1966 29/1	1966 7/2	1966 17/2	1966 21/2	1966 11/3	1966 28/4	1966 27/6	1966 12/8	1966 11/10
Total bilirubin mg/100 ml.	0.5	1.0	0.6	0.7	0.5	0.8	1.0	1.0	1.2
Aspartate transaminase i.u./L.	12	15		15	17	13	12	11	8
Alkaline phosphatase King-Armstrong units/100 ml.	16	26	12	18	18	20	14	12	12
Albumin Gm/100 ml.	2.8	3.2	2.9	3.1	3.1	3.5	3.8	3.8	4.1
Globulin Gm/100 ml.	2.1	3.4		2.7	3.5	3.2	3.4	3.0	3.1
Prothrombin time, seconds	71	23	16	10	30		27		45

TABLE 3.7

CASE 4

SERIAL TESTS OF LIVER FUNCTION

Test	1965 29/9	1965 11/10	1965 18/10	1965 25/10	1965 1/11	1965 4/11	1965 8/11	1965 11/11	1965 15/12	1966 3/5	1966 10/5
Total bilirubin mg/100 ml.	1.5	1.8	1.5	1.4	1.8	1.5	1.2	1.3	1.2	2.4	5.0
Aspartate transaminase i.u./L		35	51	29	26	23	30	28	48	50	42
Alkaline phosphatase King-Armstrong units/100 ml.	9	30		31	27		29			33	43
Albumin Gm/100 ml.	2.5	3.1	3.5	2.9	3.8		3.9	3.7	4.9	3.3	
Globulin Gm/100 ml.	2.5	3.8	2.1	2.4	1.8		2.4	2.4	2.0	2.2	
Ascitic fluid protein Gm/100 ml.	2.7		2.0							2.2	
Prothrombin time, seconds	38	100		100		100				42	70

TABLE 3.8

CASE 5

SERIAL TESTS OF LIVER FUNCTION

Test	1965 11/12	1965 20/12	1965 28/12	1966 3/1	1966 10/1	1966 10/3	1966 7/4	1966 17/5	1966 23/6	1966 11/8
Total bilirubin mg/100 ml.	0.8	0.6	0.8	0.6	0.6	1.3	1.8	2.0	1.8	0.5
Aspartate transaminase i.u./L.	25	25	8	23	14	15		22	17	12
Alkaline phosphatase King-Armstrong units/100 ml.	90	56	43	42	22	27		29	23	15
Albumin Gm/100 ml.	3.3	2.9	4.0	3.6	4.3	4.0	4.4	4.2	3.8	4.8
Globulin Gm/100 ml.	3.6	2.6	2.4	3.4	2.7	2.4		2.4		1.7
Prothrombin time, seconds	80							31	48	36

TABLE 3.9

CASE 6

SERIAL TESTS OF LIVER FUNCTION

Test	1966 24/3	1966 4/4	1966 12/4	1966 18/4	1966 21/4	1966 4/5	1966 9/5	1966 13/5
Total bilirubin mg/100 ml.	3.5	4.0	6.0	7.0	7.7	7.5	7.5	8.0
Aspartate transaminase i.u./L.	23		19	18	30	28	25	33
Alkaline phosphatase King-Armstrong units/100 ml.	22	25	18	26	22	23	20	18
Albumin gm/100 ml.	2.8	2.9	2.5	2.3	2.8	2.7	2.7	
Globulin Gm/100 ml.	3.2	3.1	3.4	3.4	3.9	3.1	3.1	
Asciticfluid protein gm/100 ml.	1.6				1.8			
Prothrombin time seconds	38		58	30		48	48	38

TABLE 3.10

LIVER FUNCTION TESTS IN CASE OF ERLIK ET AL.? 1962.

Test	Before operation	days after operation				
		5	10	17	35	60
Total bilirubin mg/100 ml.	0.7	2.2	1.2	1.0	0.9	0.8
Aspartate transaminase i.u./Litre	35	-	38	45	25	30
Alkaline phosphatase Bodansky units/ 100 ml.	4.9	7.5	10.0	12.4	11.2	7.2
Albumin Gm/100 ml.	3.9	3.5	2.6	2.9	3.5	4.0
Globulin Gm/100 ml.	2.1	2.3	3.2	2.7	4.1	3.2

CHAPTER 4

HAEMATOLOGICAL FINDINGS IN THE BUDD-CHIARI SYNDROME

Several blood disorders are known to be associated with the Budd-Chiari syndrome. Leukaemia and sickle cell anaemia have been implicated (Hirsch and Manchester, 1946; Palmer, 1954). But polycythaemia vera is the most frequently diagnosed cause of hepatic vein thrombosis.

In Parker's review (1959) it was reported in 19 of the 54 cases in which a cause for thrombosis was found. The addition of more recent cases and some previously omitted raised the incidence of polycythaemia to 37 out of a total of 322 patients with the Budd-Chiari syndrome (Table 4.1).

RESULTS

Three patients in the present series had polycythaemia vera (Cases 1, 2 and 3). All had a raised haematocrit and an increase of erythrocytes, leucocytes and platelets above the normal (Table 4.2). The diagnosis was confirmed in each case by examination of the bone marrow and by measurement of the red cell mass using the Cr-51 red cell method. Marrow examination showed a panmyelosis, normoblasts and megakaryocytes being mainly affected. The red cell volume was 56.6, 48.0 and 44.5 ml per Kg (in Cases 1, 2 and 3) respectively. Separate measurement of the plasma volume by injection of I-131 - labelled albumin in Cases 2 and 3 gave normal values.

TABLE 4.1

RECORDED CASES OF THE BUDD-CHIARI SYNDROME WITH POLYCYTHAEMIA VERA

YEAR	AUTHOR	RED CELLS Millions per cu. mm.	WHITE CELLS Thousands per cu. mm.	PLATELETS Thousands per cu. mm.	VOLUMES in ml.
1929	Oppenheimer	8.83	34.0	360	-
1930	Baehr and Klemperer	6.00	9.9		-
1932	Ulhorn	8.70	49.7	190	-
1933	Cole	8.80	17.1		-
1937	Norman and Allen	6.03			117 per Kg. (TBV)
1938	MacAlpin and Smith	8.90	8.3		-
1938	Sobval	7.43	29.5	220	65 per Kg. (RCM)
1939	Altschulle and White	6.89	21.0	2,000	
1944	Armstrong and Carnes	6.20	29.3	361	-
1949	Davis et al.	Haemocrit 68 per cent			
1952	Berk	7.20	12.0		-
1953	Burris and Arrowsmith	Haemoglobin 17.9 g./100 ml.			
1953	Kopec et al.	9.81	17.2	177	-
1953	Mandelbaum	8.50	22.7	250	-
1954	Altman and Kuhn	8.00	8.5	160	-
1954	Bobek and Vanek	5.76	11.5	140	-
1955	Brown et al.	7.00	16.0		-
1956	Caroli and Soulier	6.19	13.5	390	-
1956	Fitzgerald et al.	8.70	6.4	500	-
1958	Caroli et al.	7.29	12.8	583	2,100 (RCM)
1959	Alexandridis et al.	6.36	29.0	298	-
1959	Corcos et al.	5.99	4.5	250	1,850 (RCM)
1959	Parker	7.76	21.0		-
1960	Cole	8.00	14.9	448	2,646 (RCM)
1961	Burger et al.	6.50	9.6	420	-
1961	Burger et al.		NO RECORD BEFORE TREATMENT		
1961	Parkinson and Miller	6.08	22.0	576	-
1961	Tapie et al.	6.30	24.0	297	-
1963	Thaler	7.86	40.6	280	-
1963	Ginzler	6.00 - 8.00	NO RECORD BEFORE TREATMENT		
1964	Ticholov and Usunov	5.36	34.5	420	-
1965	Bareis	Haematocrit 70 per cent	28.0	-	56 per Kg. (RCM)
1966	Hoffbauer	6.80	22.3	229	6.100 (TBV)
1967	Clauvel et al.	7.50	13.0	520	2,860 (RCM)
1968	CASE 1 - present study	6.90	17.5	300	56.6 per Kg.
1968	CASE 2 - present study	8.21	26.6	290	48.0 per Kg.
1968	CASE 3 - present study	6.50	13.0	5,500	44.5 per Kg.

TBV, Total blood volume; RCM, Red cell mass.

In Case 2, the leucocyte alkaline phosphatase score was raised to 186. In Case 3, assay of plasma erythropoeitin was normal.

Treatment with radioactive phosphorous (P-32) was given intravenously, and several venesections were performed in each case. In Cases 2 and 3, heparin was given until venesection had substantially reduced the haematocrit. All three patients had symptoms referable to the liver when the polycythaemia was diagnosed but, in Case 1, retrospective evaluation of the history suggests that symptoms of polycythaemia preceded the hepatic disease. In Cases 1 and 2, the presenting features were due to hepatic vein thrombosis.

Treatment was started in 1962 in Case 1, and in 1966 in Cases 2 and 3. The response to treatment is shown in Tables 4.3, 4.4 and 4.5 which present serial haematological values. Control of the polycythaemia was achieved in all patients. Case 1 died of liver failure three years after starting treatment. Cases 2 and 3 showed clinical improvement and were alive and well in July, 1968.

Cases 4, 5 and 6 showed abnormal haematological findings. There was simple iron deficiency in Case 5 which responded to oral iron medication although the reticulocytosis was transitory (Table 4.7). Blood loss was ascribed to the menorrhagia with which she presented. Stool occult blood tests were negative. Bone marrow examination after treatment was normal.

In Case 4, anaemia persisted from the time of presentation to his death. Although the serum iron was initially 15 micrograms per 100 ml, the peripheral blood film was not that of iron deficiency and there was no response to treatment with oral iron. The spleen was palpable. Moderate thrombocytopaenia and an increase of reticulocytes were a constant feature. The red cell mass was 19.4 ml Kg and the half life of the red cells, measured by Cr-51 - labelling, was 15.5 days. Excess counts over the liver and spleen indicated abnormal sequestration in these organs. The loss of Cr-51 in the stools was normal. The Coombs test was negative and no L.E. cells were present. A myeloproliferative disorder was suspected and bone marrow examination showed a slight excess of reticulum and mast cells. However, a bone biopsy was normal. Examination of the bone marrow at autopsy provided no further clue to the cause.

There was persistent anaemia, thrombocytopaenia and a bleeding tendency in Case 6. Profuse purpura appeared several days before death. Bone marrow examination on two occasions showed a paucity of megakaryocytes and platelet buds. There was a normal capillary fragility test. Prothrombin consumption, fibrinolysis and assay of factors V, IX, X and XI and fibrinogen were within the accepted range. The autopsy provided no explanation for the marrow depression.

TABLE 4.2

HAEMATOLOGICAL VALUES AT TIME OF PRESENTATION IN SIX CASES OF THE BUDD-CHIARI SYNDROME

Case	Haema-tocrit per cent	Red cells millions per cu mm	White cells thousands per cu mm	Platelets thousands per cu mm	E.S.R. mm per hour	Reticu-locytes per cent	Red cell mass ml per Kg	Bone marrow examination
1	59	6.90	17.5	300	2	1	56.6	Hyperplasia, most marked in normoblasts
2	73	8.21	26.6	290	1	3.5	48.0	Hyperplasia, most marked in normoblasts
3	62	6.50	13.0	5,500	4	1.5	44.5	Erythroid and megokaryocytic hyperplasia
4	29	-	6.0	56	50	5.8	19.4	Increase in reticulum and mast cells. Normal bone biopsy
5	33	-	10.0	195	30	1.2	-	Normal (after iron therapy)
6	33	-	6.3	83	79	2.0	-	Slight erythroid hyperplasia

DISCUSSION

The presence of a blood disorder in all six cases was unusual. Apart from polycythaemia, haematological abnormalities have not been a frequent occurrence in the Budd-Chiari syndrome, although anaemia has been reported in experimental hepatic vein occlusion (Maetani, 1966).

In cases 4, 5 and 6 there was no evidence to suggest that the abnormal findings were etiologically related to the hepatic vein thrombosis. Iron deficiency in Case 5 was due to symptomatic menorrhagia. In Case 4 the anaemia was associated with a shortened red cell life span. Increased erythrocyte destruction is an almost constant accompaniment of hepatocellular failure, (Chaplin and Mollison, 1953; Cawein et al., 1960) but haemolysis has not been previously reported in hepatic vein thrombosis. Frank haemolysis with persistent anaemia and reticulocytes is seldom seen in liver disease and the reduced red cell lifespan in cirrhosis is largely due to a metabolic abnormality in the cells rather than sequestration by the spleen. Therefore the presence of haemolysis, reticulocytosis and splenic sequestration in Case 4 pointed to a cause other than the liver, but marrow biopsy and the autopsy were unhelpful.

There was also no explanation for the blood disorder in Case 6. Thrombocytopaenia is common in liver disease but purpura seldom

results. The bone marrow in hypersplenism usually shows normal or increased activity and not the scanty megakaryocytes and platelet buds seen in this patient. At the autopsy no cause was found for the marrow depression or the widespread thrombosis.

The presence of polycythaemia vera in Cases 1, 2 and 3 was not surprising as this is the most frequently diagnosed cause of hepatic vein thrombosis. On the other hand, thrombosis of the hepatic veins is a rare complication of polycythaemia vera. Out of a total of 1956 patients with polycythaemia vera reported in 13 papers, 5 developed the Budd-Chiari syndrome, an incidence of only 0.25 per cent (Clauvel et al., 1967).

In cases 4, 5 and 6, the blood disorder was in some way secondary to the liver involvement, whereas polycythaemia was the primary event in the other three patients. The diagnosis of polycythaemia has certainly preceded the hepatic disorder in many instances (Caroli and Soulier, 1956; Fitzgerald et al., 1956; Cole, 1960; Ginzler, 1963), but there has never been a demonstration of hepatic vein thrombosis before the onset of polycythaemia. Symptoms of liver involvement may, however, be the presenting features as they were in Cases 2 and 3.

The presence of an increased haematocrit, red cell count and haemoglobin level are not conclusive for polycythaemia vera. In the Budd-Chiari syndrome, relative polycythaemia may result from haemoconcentration (Gibson, 1960). The absolute increase in red

cell mass in all three cases excluded this possibility. The association of secondary polycythaemia and hepatoma is well known (Brownstein and Ballard, 1966), but tumour was not the cause of polycythaemia in my cases. No tumour was found in Case 1 at autopsy; leucocyte alkaline phosphatase was raised and erythropoeitin assay was normal in Case 2; and panmyelosis was present in all cases, a finding characteristically absent in patients with polycythaemia due to hepatoma. Furthermore, two patients have remained in godd health for 2½ years, an unlikely course for neoplastic liver disease.

It has also been suggested that the anoxic liver in hepatic vein thrombosis may lead to polycythaemia. Oppenheimer (1929) put forward this possibility in the first case in which polycythaemia and hepatic vein thrombosis were described in association. But the burden of clinical and experimental proof is against this conception. Polycythaemia is not induced by hepatic vein occlusion in dogs (Maetani, 1966), and the presence of erythrocytosis in the Budd-Chiari syndrome is accompanied by an increase in all blood elements which is not a feature of secondary polycythaemia.

There seems little doubt that the elevated haematocrit in these and other cases was due to polycythaemia vera. But one problem is unsolved. The average age of polycythaemia patients with the Budd-Chiari syndrome is 39 years compared with an average age of 55 years in uncomplicated polycythaemia vera (Clauvel, 1967).

CONCLUSIONS

The investigations and review in this chapter aimed to determine:-

(a) The type of blood disorder in the six patients with the Budd-Chiari syndrome.

(b) The nature of the polycythaemia associated with the Budd-Chiari syndrome.

(c) The incidence of polycythaemia vera in the Budd-Chiari syndrome.

The conclusions were as follows:-

(a) Cases 1, 2 and 3 had polycythaemia vera. Case 5 had an iron deficiency anaemia. Haemolysis in Case 4 and marrow depression in Case 6 were not satisfactorily explained. They are not likely to have been the result of hepatic vein thrombosis and no primary blood disorder was established.

(b) Relative polycythaemia and secondary causes of polycythaemia. such as hepatoma and hepatic anoxia, have been excluded as causes of the polycythaemia in the patients in this study.

(c) 37 cases of polycythaemia vera have been reported out of a total of 322 patients with the Budd-Chiari syndrome.

TABLE 4.3 CASE 1

SERIAL HAEMATOLOGICAL VALUES

Test	1962 1/2	1965 8/2	1965 10/2	1965 22/2	1965 10/3	1965 24/3	1965 12/4	1965 26/4	1965 11/6	1965 11/6	1965 28/7	1965 16/8
Haemoglobin Gm/100 ml.	19.9	16.2	15.4	14.3	14.5	14.7	15.4	16.2	15.6	14.5	14.3	15.1
Haematocrit per cent	65	59	55	52	50	52	52	55	53			53
White cells thousands/ cu. mm.	15	17.5	17.7	16.7					18.8		18	17.5
Platelets thousands/ cu. mm.	295	300	372		205			130	292	150		260
Reticulocytes per cent		1						2		4		

TABLE 4.4

CASE 2

SERIAL HAEMATOLOGICAL VALUES

Test	1964 13/12	1964 20/12	1964 23/12	1964 28/12	1965 3/1	1965 6/1	1965 10/1	1965 17/1	1965 25/1	1965 24/3	1965 16/5	1965 23/6	1965 12/9
Haemoglobin Gm/100 ml.	22.4	18.6	16.2	13.0	14.1	13.6	14.0	15.1	17.8	13.2	14.0	14.0	14.3
Haematocrit/ cent	73	63	55	47	52	52	52		59		52	52	56
Reticulocytes per cent	3.5	5.8					3.0		1.5		1.0	1.0	
White cells thousands/ cu. mm.	26.8	27.4		30.0	30.0		17.4	11.6			9.0	9.9	12.5
Platelets thousands/ cu. mm.	245				103		149			85	134	79	103

TABLE 4.5

CASE 3

SERIAL HAEMATOLOGICAL VALUES

Test	1966 29/1	1966 2/2.	1966 10/2	1966 12/2	1966 14/2	1966 17/2	1966 21/2	1966 28/2	1966 8/3	1966 14/3	1966 26/3	1966 28/4	1966 28/6..	1966 20/7	1966 17/8	1966 11/10
Haemoglobin Gm/100 ml.	16.2	17.4	15.8	14	12	11.6	12.6	10.8	11.6	12.2	13.1	10.4	11.1	11.5	12.2	12.0
Haematocrit per cent	63	62	54	49	46	43	45	41	42	43	42	40	40	41	41	43
White cells thousands/ cu. mm.	18.2	13	10.8			10.6	9.2	6.5	5.3		2.8	6.0	5.7	7.2		4.0
Platelets thousands/ cu. mm.	219	550	244			84	249	310	139				117	131		211
Reticulocytes per cent	1.6	1.5	1.0				3.5		1.0							

TABLE 4.6

CASE 4

SERIAL HAEMATOLOGICAL VALUES

Test	1965 9/9	1965 11/10	1965 18/10	1965 1/11	1965 4/11	1966 5/5
Haemoglobin Gm/100 ml.	9.6	9.5		10.8	9.7	10.8
Haematocrit per cent		30			29	36
Platelets thousands/ cu. mm.	52	50	36		56	105
Reticulocytes per cent		5.8	6.4	4.8	6.0	1.0

TABLE 4.7 CASE 5

SERIAL HAEMATOLOGICAL VALUES

Test	1965 10/12	1965 28/12	1966 4/1	1966 10/2	1966 10/3	1966 17/5..	1966 23/6	1966 14/7	1966 25/8
Haemoglobin Gm/100 ml.	8.5	10.2	11.6	13.6	11.8	14.3	15.2	13.6	14.0
Haematocrit/ cent	33	40	40		38	49			44
Reticulocytes per cent	1.2	2.0	3.2		1	1			
Platelets thousands/ cu. mm.	195				81	100		105	130

TABLE 4.8

CASE 6

SERIAL HAEMATOLOGICAL VALUES

Test	1965 24/3	1965 4/4	1965 14/4	1965 27/4	1965 5/5	1965 9/5	1965 13/5
Haemoglobin Gm/100 ml.	7.9	9.3	9.7	8.1	5.4	8.9	7.9
Reticulocytes per cent	3.3	3.5	1.0	3.3	2.4	2.5	4
Platelets thousands/ cu. mm.	83	20	44		19		12

CHAPTER 5

RADIOLOGY OF THE HEPATIC VEINS

The pathology in the Budd-Chiari syndrome lies in the hepatic veins. The application of modern techniques which can define abnormalities in this region, is the logical method of reaching a clinical diagnosis. Radiology offers the only certain means of investigating the condition of the hepatic veins during life.

Contrast radiography of the hepatic veins has been approached in two ways. Either a catheter was advanced into the hepatic vein from the inferior vena cava and contrast material injected in a retrograde manner against the normal flow of blood, or a needle was inserted percutaneously through the liver substance and a hepatic vein was directly injected (Bierman et al., 1955).

In a recent attempt to find a more logical technique, Moreno et al. (1963) introduced contrast material into the parenchyma of the liver and radiologically observed the rate and route of flow away from the site of deposition. This method has been called "functional hepatography" and it is superior in many respects to direct percutaneous injection of the hepatic veins. The application of hepatic venography and hepatography to the diagnosis of the Budd-Chiari syndrome is the subject of this chapter.

HEPATIC VENOGRAPHY

In this section, hepatic venography (IVC) studies are described in

five patients with the Budd-Chiari syndrome. In order to understand the methods employed and the results obtained, it is worth while to consider briefly the anatomy of the hepatic veins and the recent development of hepatic venography as a clinical diagnostic technique.

In the embryo, the liver grows out from the entoderm of the gut into a mass of mesoderm called the septum transversum. The veins of the liver develop from the vitelline vessels which become a network of sinusoids at about the fourth week. The distal portion of this network ultimately forms the portal vein, and the proximal portion forms the hepatic veins. Initially, there is a common hepatic vein which also drains the ductus venosus and which is later incorporated in the developing vena cava.

This sequence of events explains the absence of a common hepatic venous channel and the separate entry of the hepatic veins into the inferior vena cava. From the radiological standpoint, this anatomical arrangement creates considerable technical difficulties in examining the entire hepatic venous drainage.

The hepatic veins begin at the central veins of the liver lobules and join to form sublobular veins. The largest vessels are the right, middle and left hepatic veins. The right lobe is drained by three branches, the principal or superior vein and

the middle and the inferior accessory veins. The veins from the right lobe join the right side of the inferior vena cava as it lies in the fossa venae cavae just below the diaphragm. A cardiac catheter which has been introduced via the right atrium into the inferior vena cava, when positioned with its point to the right and anteriorly, will advance downwards into the right hepatic vein. The middle and left veins enter at a slightly higher level usually via a common trunk. There are several smaller veins, draining the caudate lobe and the inferior portion of the right lobe, which open into the inferior vena cava below the main branches. The arrangement of the smaller veins is unpredictable (Elias and Petty, 1952). They assume importance when the main veins are obstructed. Diversion of blood through interlobular anastomoses may convert them into major routes of hepatic outflow (Bourgeon and Guntz, 1959).

There are no valves in the hepatic veins in man. This is fortunate because a cardiac catheter is easily passed to the periphery of the liver where contrast material can be injected, blood samples taken, or venous pressures recorded. The blood flow in the hepatic veins is influenced by the respiratory cycle (Brauer, 1963; Norhagen, 1963), and there may normally be reflux into the hepatic veins during expiration (Norhagen, 1963).

Unlike the portal system which can be opacified by a single injection of contrast material into the portal vein or the spleen,

the hepatic veins have no common trunk. In man, the hepatic veins are best demonstrated radiologically by separate catheterization of each hepatic vein. However, some of the earliest observations were made by injection of contrast material into the inferior vena cava during epigastric compression (Farinas, 1947). Only the proximal portion of the hepatic veins was shown. With the advent of hepatic vein catheterization, successful attempts were made to obtain contrast radiographs by injection directly into the hepatic veins of dogs (Rappaport, 1951). Tori (1953) was able to reproduce this work in man, using a conventional cardiac catheter. Several other workers performed segmental hepatic venograms by introducing the catheter via the brachial or femoral veins (Servello, 1960).

From these studies, it became evident that the position of the catheter in the hepatic veins had considerable influence on the venogram. If the contrast material was injected with the catheter in a peripheral, wedged position, there was retrograde filling of the sinusoids and portal vein radicles. To opacify the hepatic veins, the catheter was withdrawn almost to the entry of the hepatic vein into the inferior vena cava. Nakamura et al. (1959) added to this knowledge by carefully defining the type of radiograph to be expected with the different positions of the catheter.

Later, interest centred on the extent of portal vein filling which could be achieved by wedged injection. Widman et ak, (1961) were able to opacify the entire intrahepatic portal system in dogs. This was also achieved in man, and in some cases the extrahepatic portal-systemic collateral vessels were shown as well (Schlant et al., 1962).

Hepatic venography by these techniques has been used mainly to show the changes in the hepatic and portal veins associated with cirrhosis (Nakamura et al., 1959), hepatoma (Schlant et al., 1963), secondary deposits (Helander et al., 1958), abscesses and cysts (Ruzicka, 1965).

Demonstration of the entire hepatic venous tree requires catheterization of each vein separately. This is tedious and frequently impossible. Isolation of the intrahepatic segment of the cava can be achieved and total hepatic venography performed. Several studies have been made using either balloons or increased endobronchial pressure to halt the flow in the inferior vena cava (Nogveira, 1961; Norhagen, 1963; Rappaport et al., 1964). This technique has not been perfected in man, and it has not been applied in this study.

METHODS

Hepatic vein catheterization was carried out by a standard method (Paton et al., 1953; Leevy and Gliedman, 1958). Radiopaque,

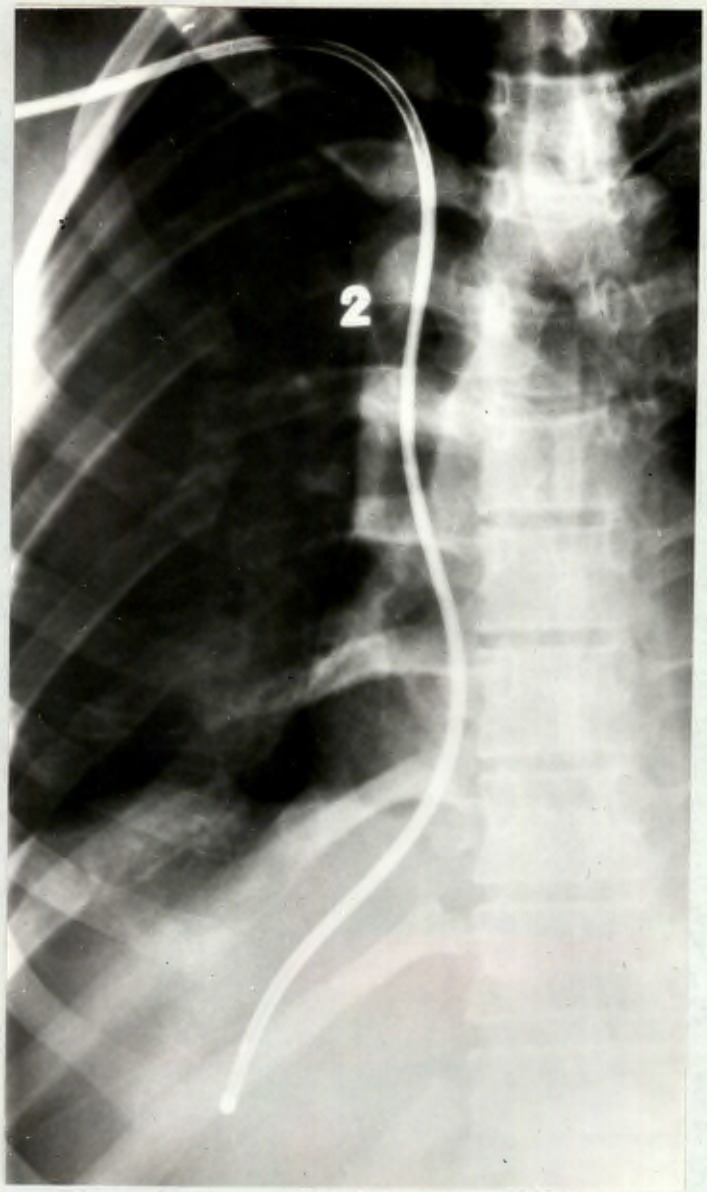

Fig: 5.1

A catheter introduced via a right brachial vein has been advanced through the right atrium into a right hepatic vein.

Cournaud-type Teflon catheters were introduced via a right brachial vein under television fluoroscopy (Fig. 5.1). There was constant cardiac monitoring while the catheter was in the right atrium. Hepatic venography was performed in the free and wedged positions. The wedged position was attained by advancing the hepatic vein catheter until it occluded the vessel. Wedging was confirmed by noting the absence of reflux past the catheter tip after injection of contrast material (Fig. 5.2). After hand injection of 10 - 20 ml of 45 per cent sodium diatrizoate, serial hepatic venograms were taken at one-second intervals using an Elema Schonander automatic cassette changer.

PATIENTS

The hepatic venograms of five patients with the Budd-Chiari syndrome have been compared with the venograms of nineteen patients with other diseases of the liver who were studied by the same radiological method (Table 5.1). In the sixth patient with the Budd-Chiari syndrome, extensive caval thrombosis prevented catheterization of the hepatic veins (Fig. 8.9).

RESULTS

Control Study

Hepatic venography was normal in the patient with portal vein thrombosis and in 6 of the 17 patients with cirrhosis or haemochromatosis. The normal wedged hepatic venograms (Fig. 5.2) showed

TABLE 5.1

HEPATIC VENOGRAMS

Diagnosis	Number studied	Number abnormal	Number illustrated
Budd-Chiari syndrome	5	5	5
Cryptogenic cirrhosis	9	5	4
Alcoholic cirrhosis	5	4	3
Active cirrhosis	1	1	0
Haemachromatosis	2	1	1
Portal vein thrombosis	1	0	0
Sarcoidosis	1	1	1
TOTAL	24	17	14

the catheter tip at the periphery of the liver. There was retrograde filling of portal vein radicles and opacification of an area of parenchyma which drained into hepatic veins of normal calibre. The portal tree had regular branches. The normal free hepatic venograms showed the main hepatic veins and their tributaries tapering evenly towards the periphery (Fig. 5.3).

In cirrhosis, the main abnormality seen in the portal and hepatic venous branches was loss of the regular diminution in size with each successive division. Vessels showed tortuosity and irregularity of branching. A localised filling defect was present in a hepatic vein in one case (Fig. 5.9). An unusual vascular pattern was seen in the patient with hepatic granulomata due to sarcoidosis (Fig. 5.10).

The salient features in individual patients with cirrhosis, haemachromatosis and sarcoidosis are described in the legends to Figures 5.4 to 5.10.

Patients with the Budd-Chiari Syndrome

Hepatic venography in five patients with the Budd-Chiari syndrome showed narrow or occluded main hepatic veins and a characteristic pattern in adjacent vessels. This pattern was composed of tortuous veins of fine calibre which formed a network of spiderweb appearance (Figs. 5.11 to 5.17) and covered an area

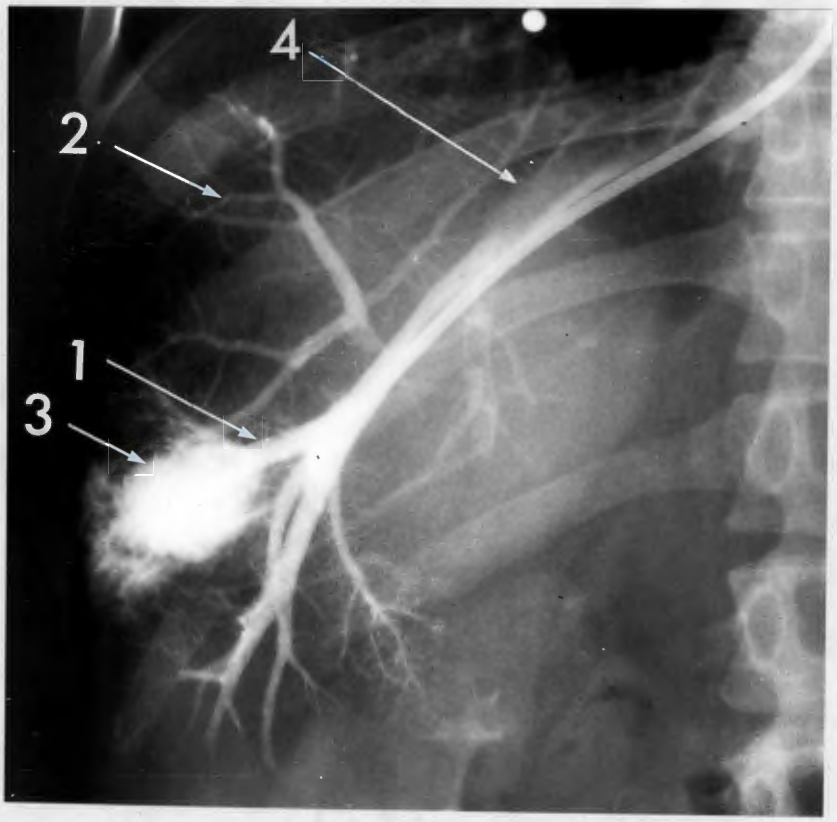

Fig: 5.2

Normal wedged hepatic venogram showing peripheral position of the catheter (1) in a right hepatic vein. There is retrograde filling of portal vein radicles (2), and opacification of an area of parenchyma (3) which drains into a hepatic vein of normal calibre (4). Absence of efflux along the catheter, confirmed the wedged position.

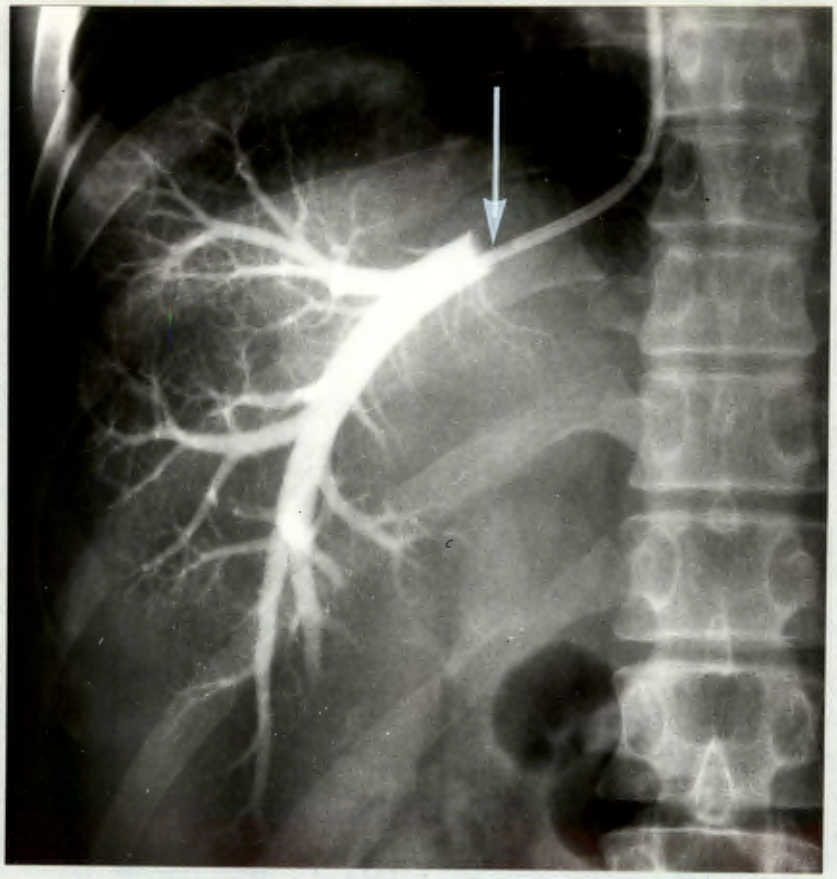

Fig: 5.3

Hepatic venogram showing the right hepatic vein. The catheter is in the free position. The vein is occluded by a balloon (arrow) which is proximal to the tip of the catheter. Although the patient had haemochromatosis, the venogram is within normal limits. Peripheral hepatic venous branches are well shown and they are not distorted.

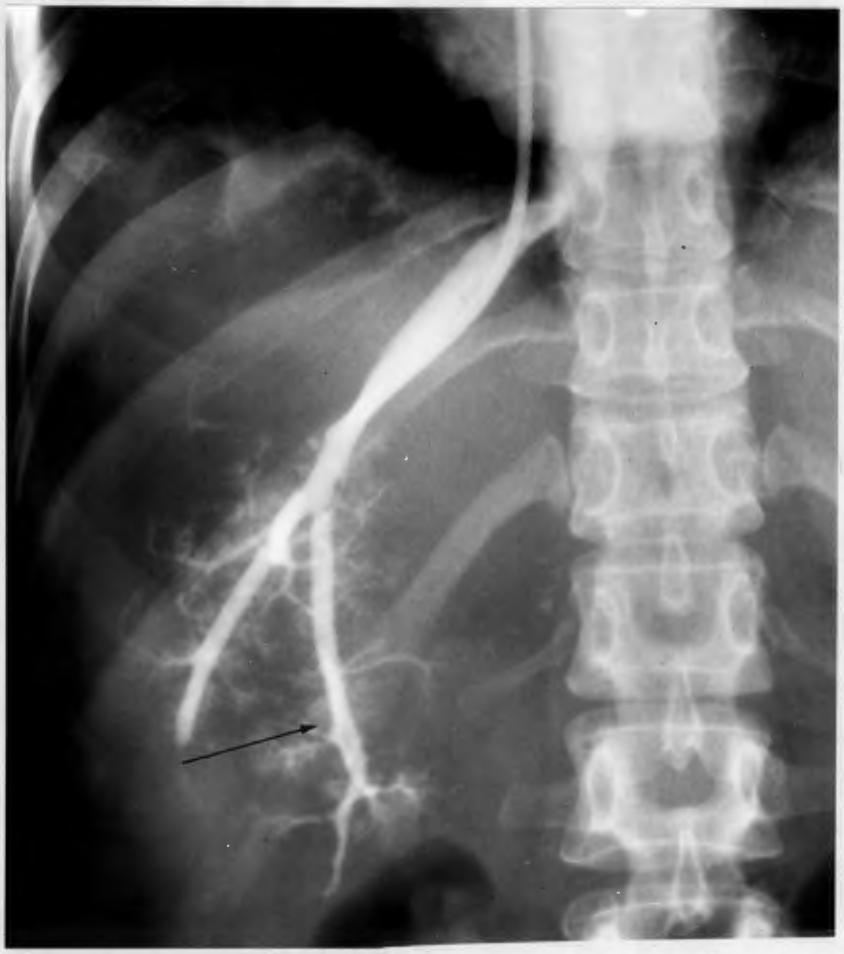

Fig: 5.4

Free hepatic venogram in a patient with cryptogenic cirrhosis. There is no balloon occlusion. Contrast material flows freely from the right hepatic vein into the inferior vena cava and the right atrium. Branches are sparse. There is distortion and narrowing of the small veins. The stippled appearance (arrow) around the veins is due to opacification of the parenchyma and indicates that the hepatic veins have filled back as far as the sinusoids.

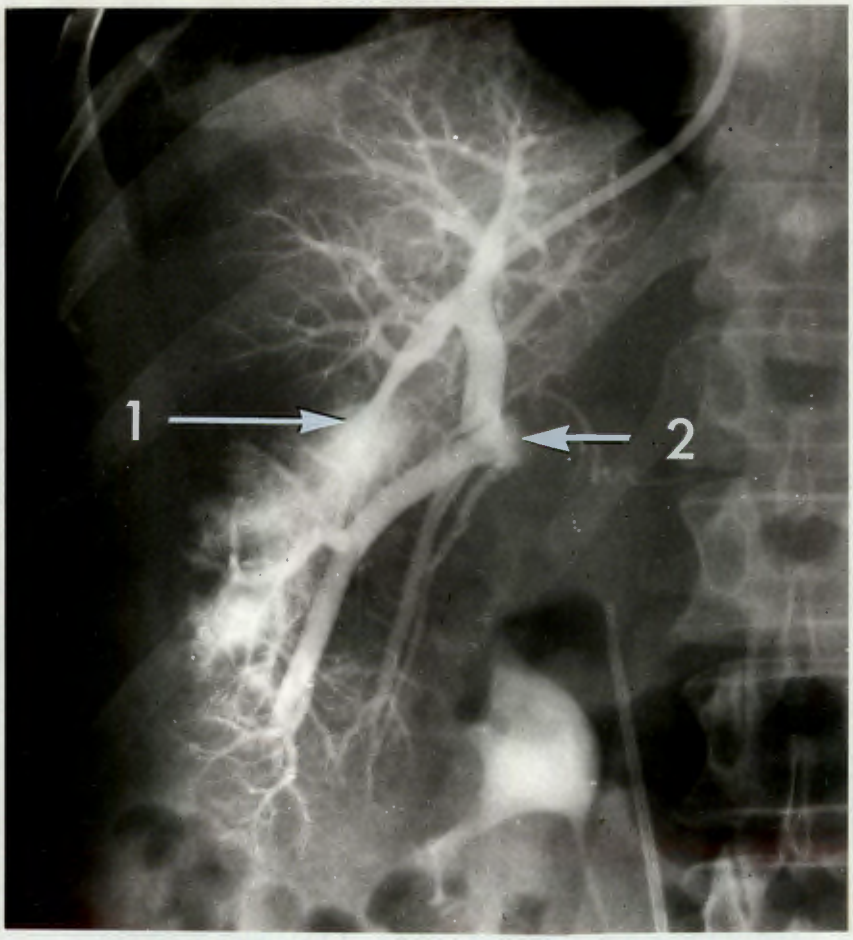

Fig: 5.5

Wedged hepatic venogram in a patient with alcoholic cirrhosis and centrilobular scarring. No hepatic veins have filled. The contrast material has opacified an area of parenchyma (1) and has refluxed into the portal system as far as the bifurcation of the portal vein (2). The left branch of the portal vein is not demonstrated. The portal tree shows some distortion and narrowing consistent with cirrhosis. The scarring around the central veins does not seem to have influenced the venogram.

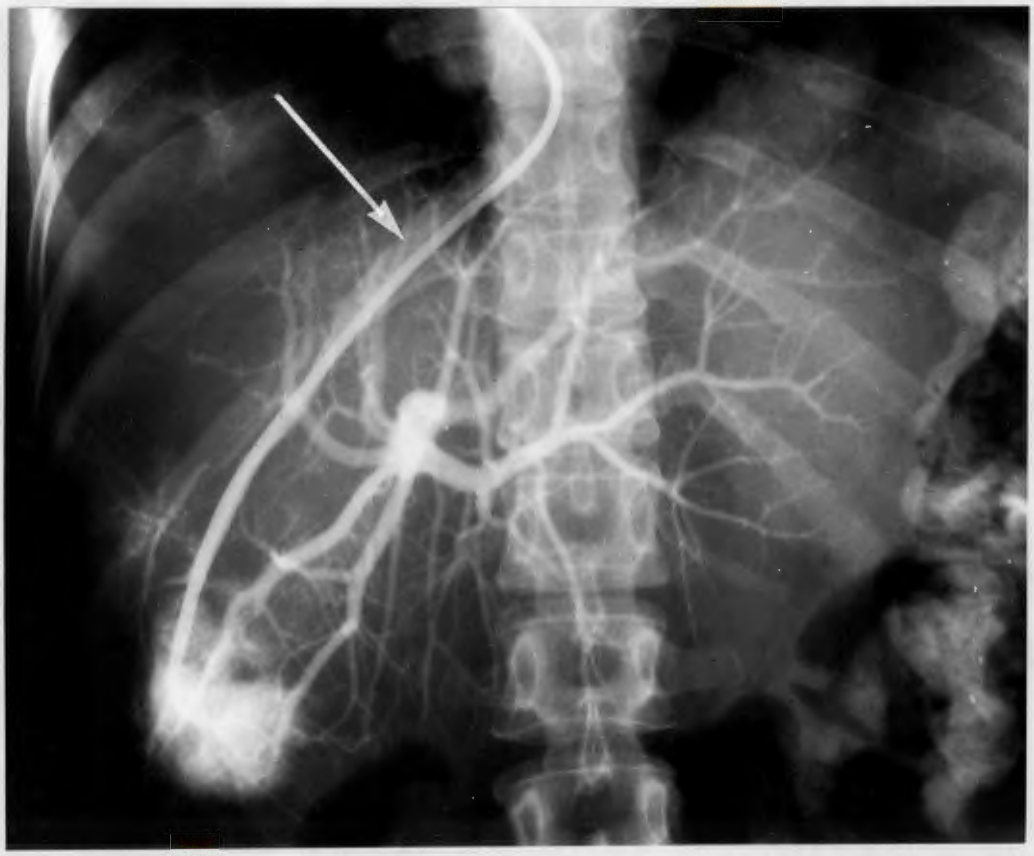

Fig: 5.6

Wedged hepatic venogram in a patient with alcoholic cirrhosis. Reflux of contrast material has opacified the entire intrahepatic portal system. Branches are sparse and narrow, producing the "tree in winter" appearance associated with cirrhosis. One hepatic vein is faintly seen (arrow).

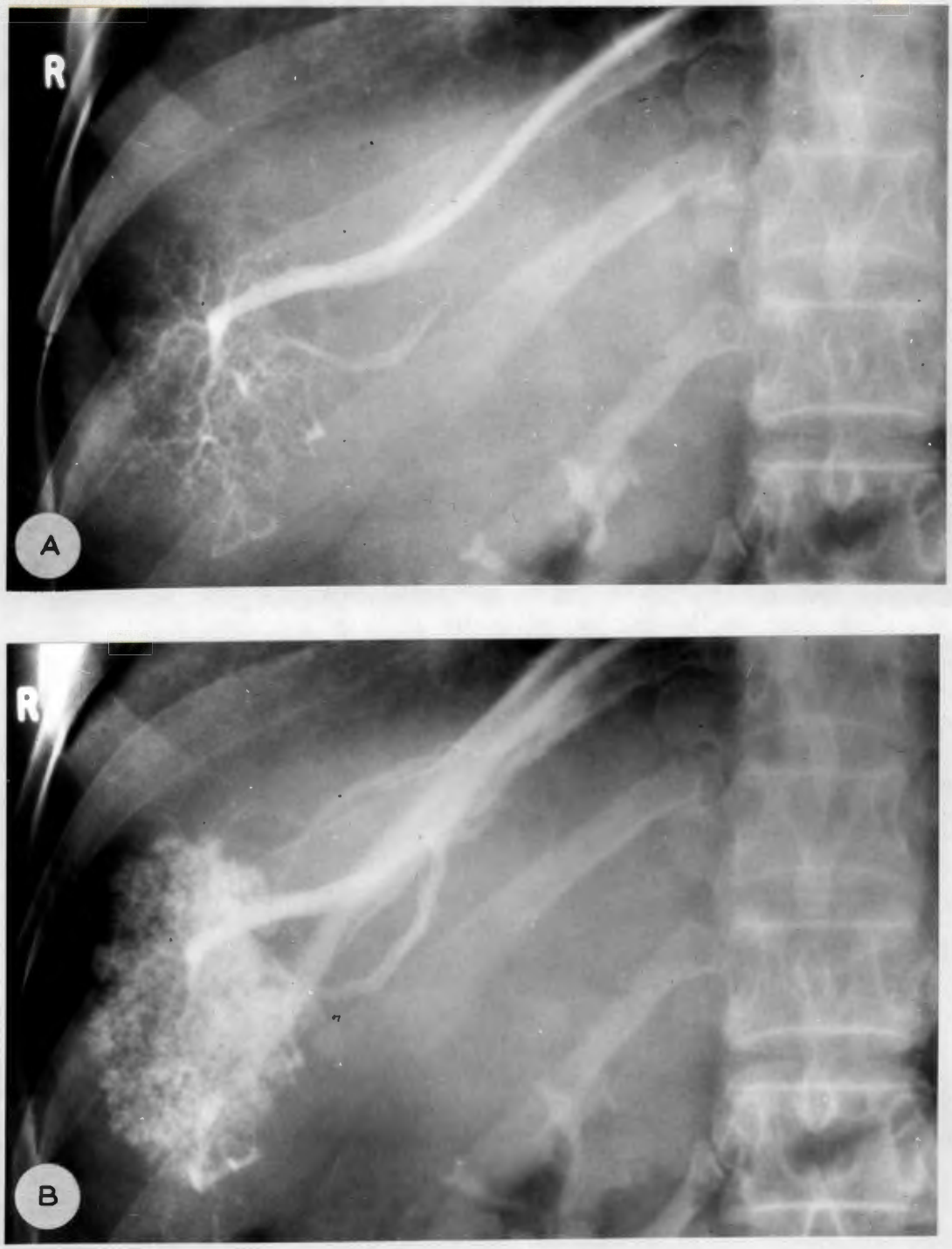

Fig: 5.7

Wedged hepatic venogram. Slow injection of contrast material shows a fine mesh of communicating vessels (A). In a later phase there is a mottled appearance due to filling of small lobules of parenchyma (B). Three hepatic veins are shown draining this area.

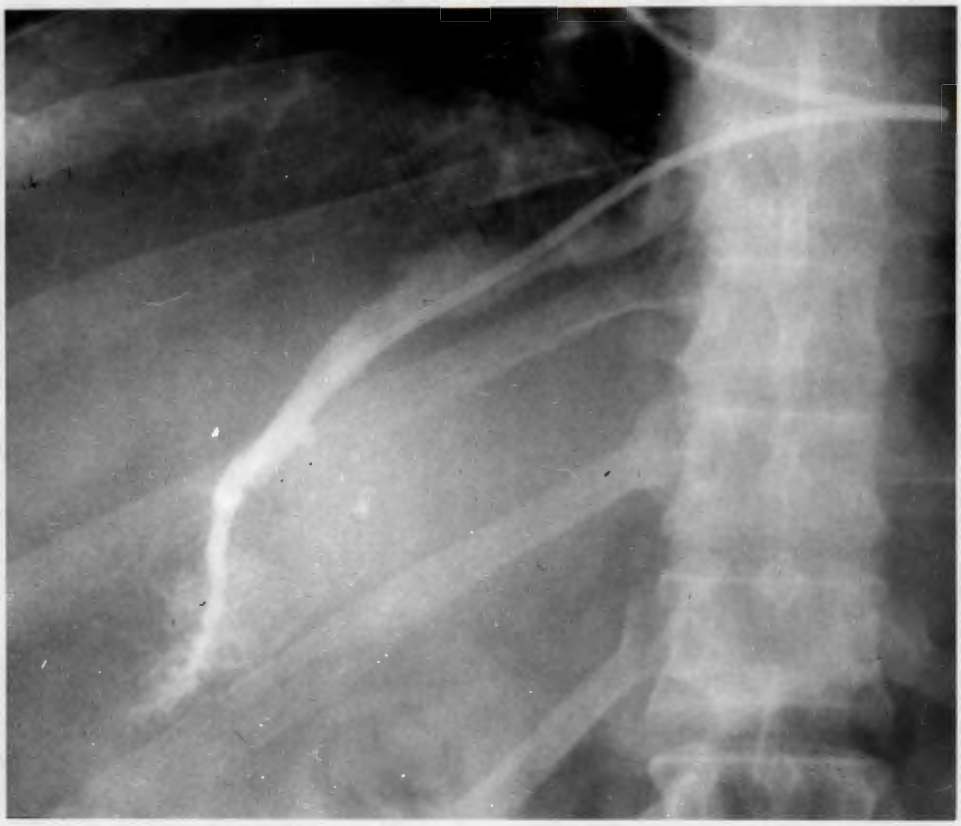

Fig: 5.8

Free hepatic venogram in a patient with cryptogenic cirrhosis. There is distortion of the vein and irregularity of the lumen. This appearance is seen with severe scarring and shrinkage of liver substance.

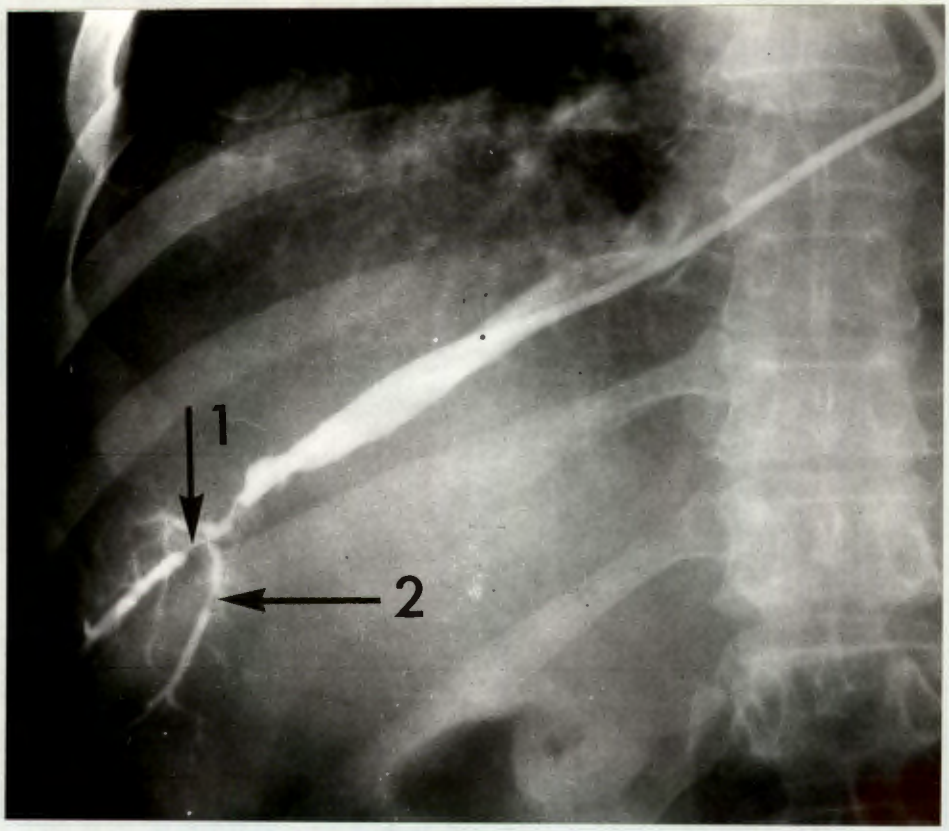

Fig: 5.9

Patient with alcoholic cirrhosis. An attempt was made to wedge the catheter but reflux is seen around the tip and the hepatic vein is opacified. Beyond the catheter tip there is a 1.5 cm. length of vein which has failed to fill normally (1). This could be an area of endophlebitis or a local thrombosis which has recanalized. A similar area is seen on a branch of this vein (2).

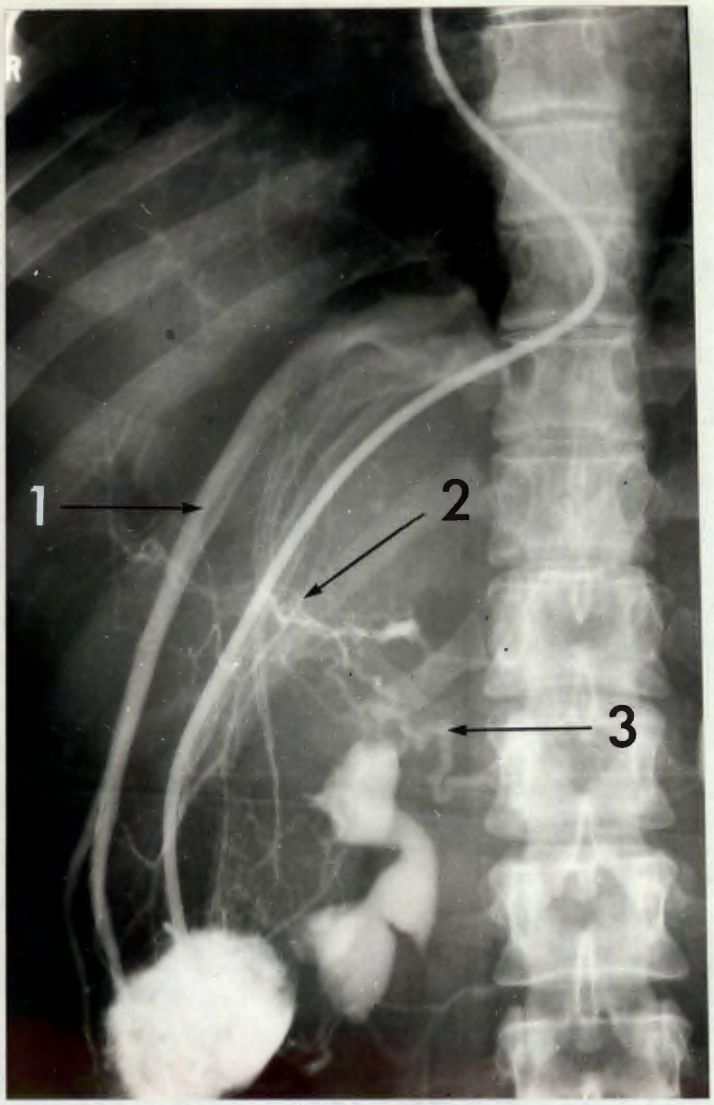

Fig: 5.10

Wedged hepatic venogram in a patient with a hepatic granulomata due to sarcoidosis. An area of parenchyma is opacified and drains into a large right hepatic vein (1). No definite filling of the portal system is seen. Two striking abnormalities are present. There is opacification of fine interlacing vessels which do not have the appearance of either hepatic or portal venous branches (2). In addition, lymph vessels are shown draining medially (3). The lymphatics seem to arise from the network of vessels (2) but their origin cannot be clearly seen.

varying from 3 x 3 cm to 10 x 10 cm. The strands of contrast medium which constituted the network were well defined and not at all like the granular sinusoidal pattern of the normal liver or the mottled appearance in cirrhosis. The catheter could not be advanced the usual distance along the hepatic vein and wedging occurred from 3 to 12 cm from the diaphragm. The features of a normal wedged venogram were absent (Fig. 5.2).

Catheterization of all hepatic veins was attempted but only in Case 2 could more than one be entered. In this patient, the characteristic network was demonstrated in a right hepatic venogram (Fig. 5.17) although the tip of the catheter was barely beyond the ostium. The catheter was not wedged and contrast material refluxed freely to outline the cava and part of the right atrium. It could not be induced to travel further from the vessel. Two hepatic veins were filled, but they were narrow and showed abnormal branches. An entirely different appearance was seen on the left side (Figs. 5.18 and 5.19). Here the tip of the catheter passed through a thrombus about 2 cm in length at the ostium of the hepatic vein, and became wedged. Contrast material outlined a patent and dilated hepatic venous tree proximal to the block. Tributaries of the thrombosed vein communicated with large adjacent branches and contrast material was seen to enter the inferior vena cava above the obstructed left hepatic vein. There were numerous, smaller, collateral vessels

following a tortuous course around the obstruction. There was also a major interlobar anastomosis between branches of the right and left hepatic veins.

The abnormal network was best seen in Case 1 (Figs. 5.11 and 5.12). It was formed by a profusion of tortuous vessels entering an irregular segment of hepatic vein which was opacified beyond the tip of the catheter. Proximal to the short segment of abnormal vein there seemed to be complete obstruction of the vessel. There were no normal hepatic veins running parallel to the catheter and none of the features of a normal wedged venogram was present (Fig. 5.2).

A similar appearance composed of even finer vessels was seen in Case 4 (Fig. 5.13). Again the catheter could not be advanced to the periphery and this was shown not to be due to a technical fault, by the failure to fill the vessel beyond the tip of the catheter and by the absence of reflux past the catheter. When the catheter was withdrawn into the free position (Fig. 5.14), contrast material was swept up the vessel, indicating brisk blood flow through an apparently obstructed vein. The free venogram also showed the network pattern, and in addition there was marked narrowing of the right hepatic vein. A venogram was carried out at autopsy by injection of the hepatic vein catheterized during life. The appearance was abnormal and showed the same pattern of fine vessels (Fig. 5.20). A normal liver was treated simiarly for comparison (Fig. 5.21).

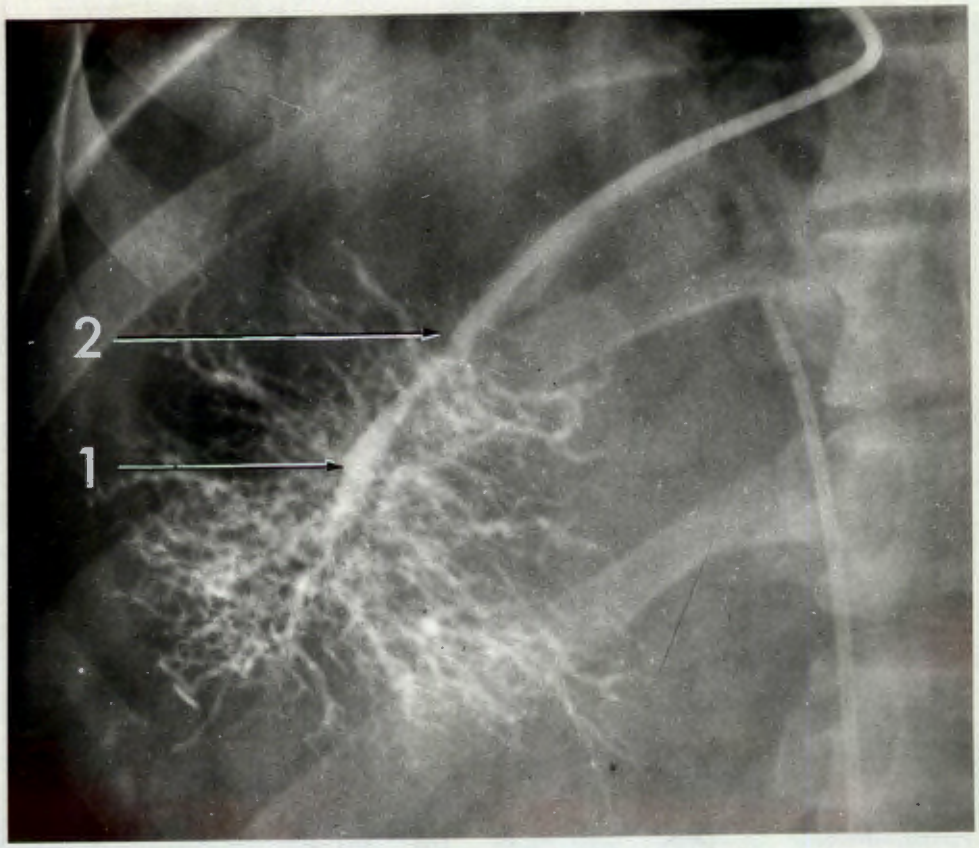

Fig: 5.11 CASE 1

Wedged hepatic venogram in the Budd-Chiari syndrome showing a pattern composed of tortuous vessels which communicate with a right hepatic vein of irregular calibre (1). The catheter tip (2) could not be advanced to the periphery. None of the features of a normal wedged venogram is present.

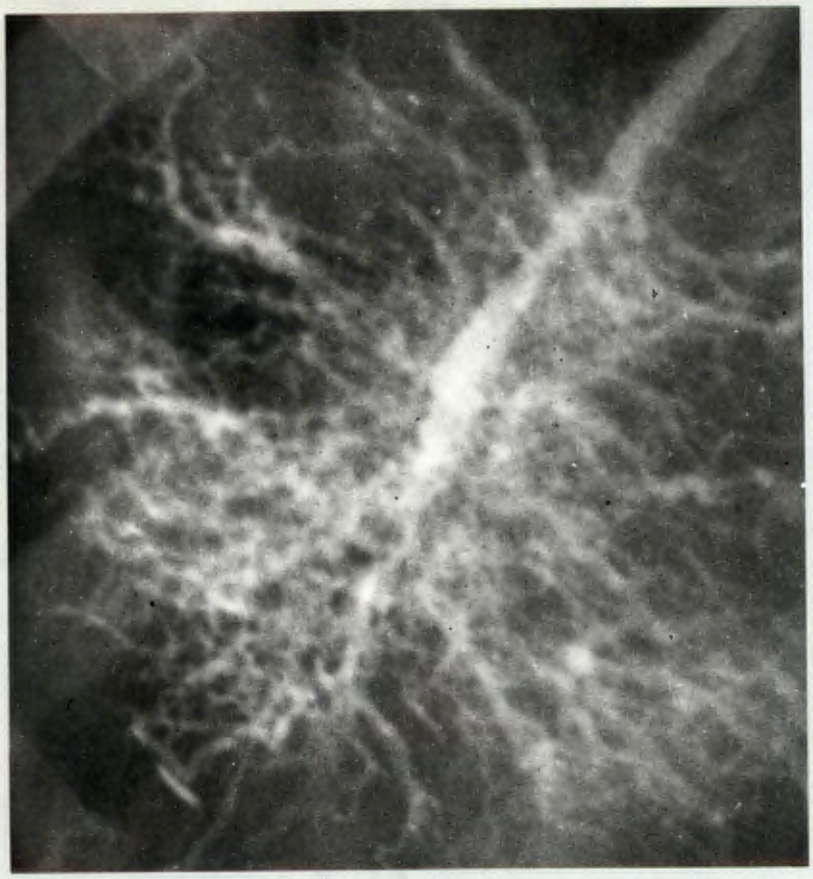

Fig: 5.12 CASE 1

Enlarged view of the vascular pattern from fig. 5.11 showing the irregular network. The lumen of the hepatic vein appears to be obstructed.

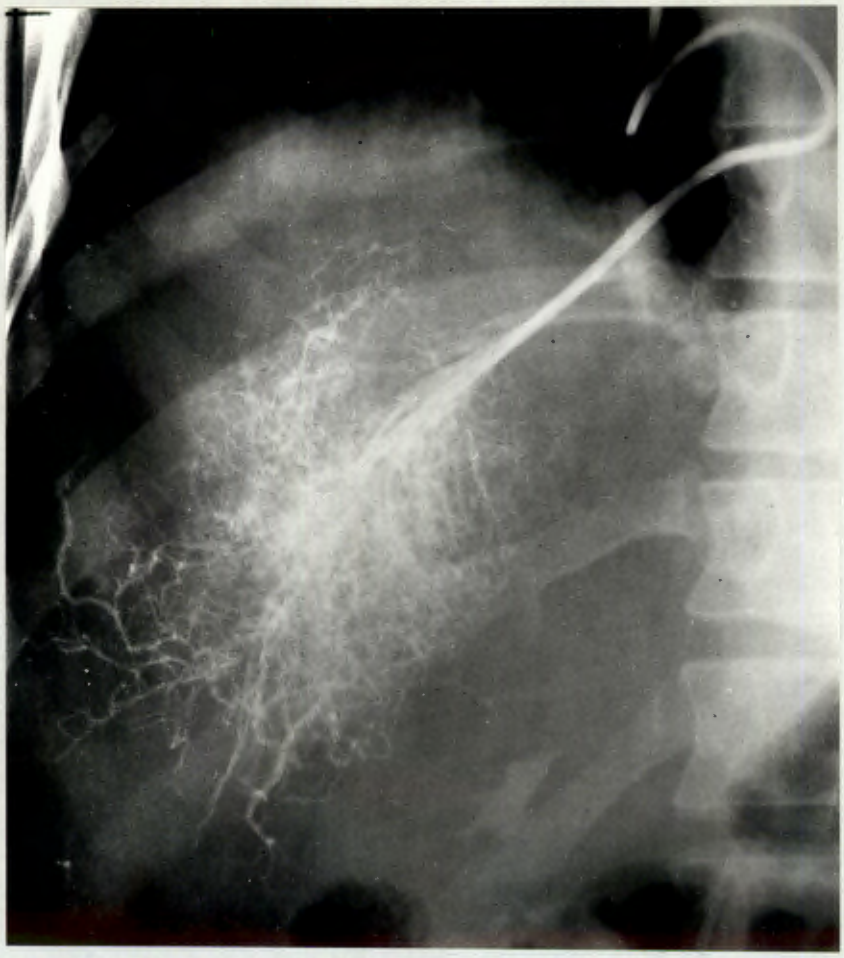

Fig: 5.13 CASE 4

Wedged hepatic venogram in the Budd-Chiari syndrome showing the same features as fig. 5.11 (Case 1). The vessels form a finer and more tortuous pattern.

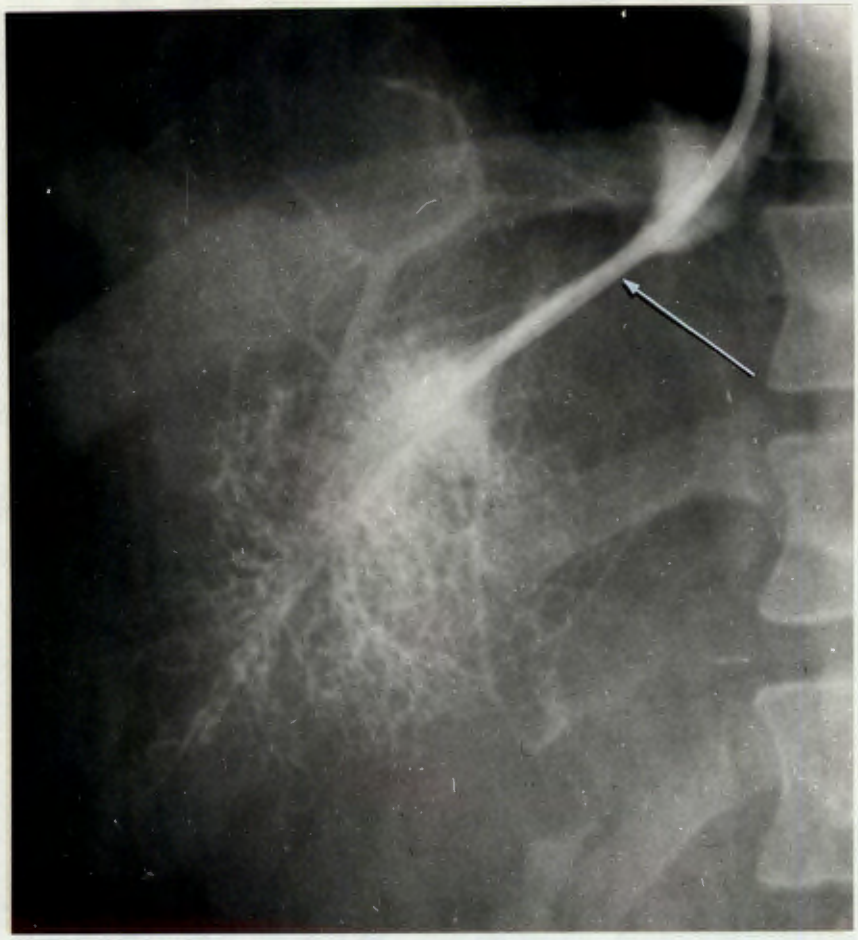

Fig: 5.14 CASE 4

Free hepatic venogram. Reflux of contrast material along the catheter indicates absence of wedging and shows a hepatic vein of reduced calibre (arrow). Filling of peripheral hepatic venous branches normally seen in free venograms is absent, but the network of fine vessels adjacent to the main vein is again shown.

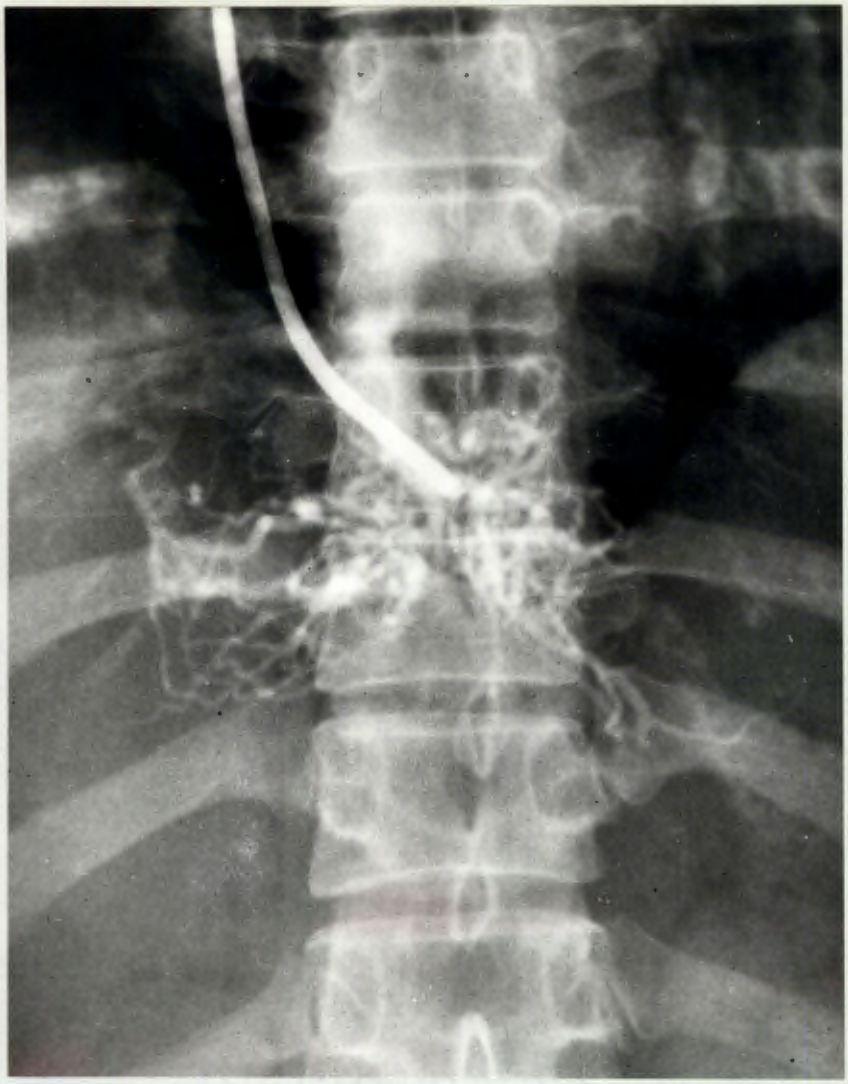

Fig: 5.15 CASE 3

Wedged hepatic venogram in the Budd-Chiari syndrome showing a catheter in a left hepatic vein. A neat pattern of collateral vessels is shown. Normal portal or hepatic venous radicles are not present.

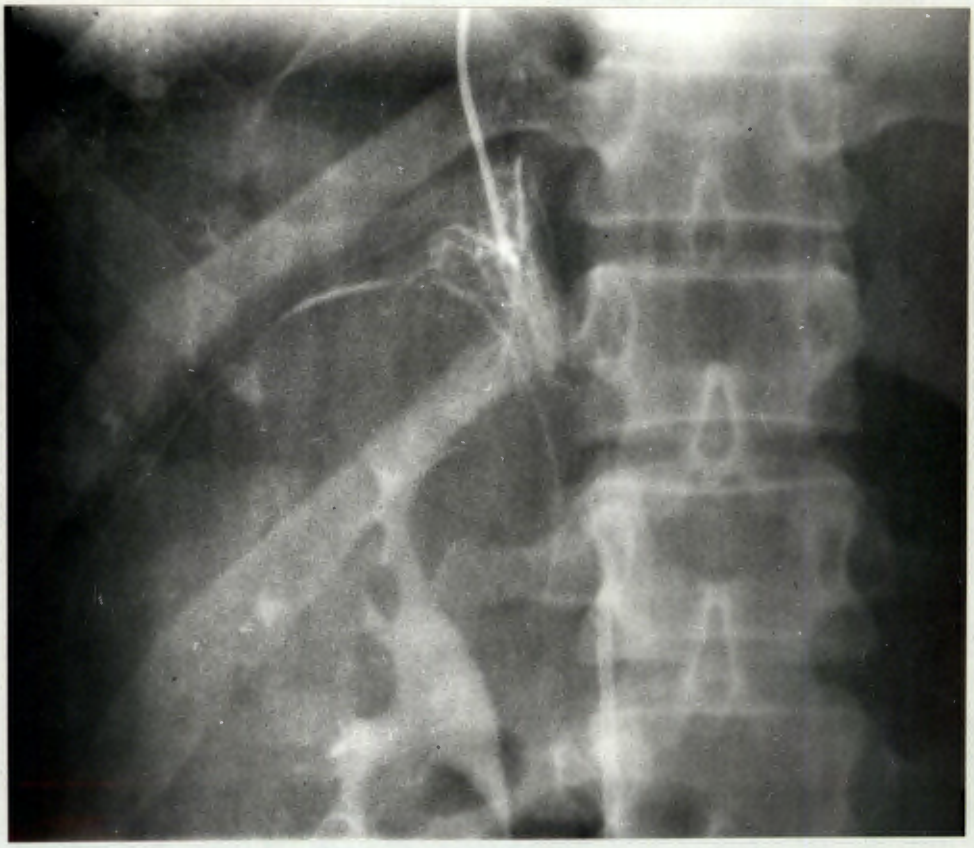

Fig: 5.16 CASE 5

In the Budd-Chiari syndrome a small left hepatic vein shows an abnormal pattern. There is a communication with an intercostal vessel.

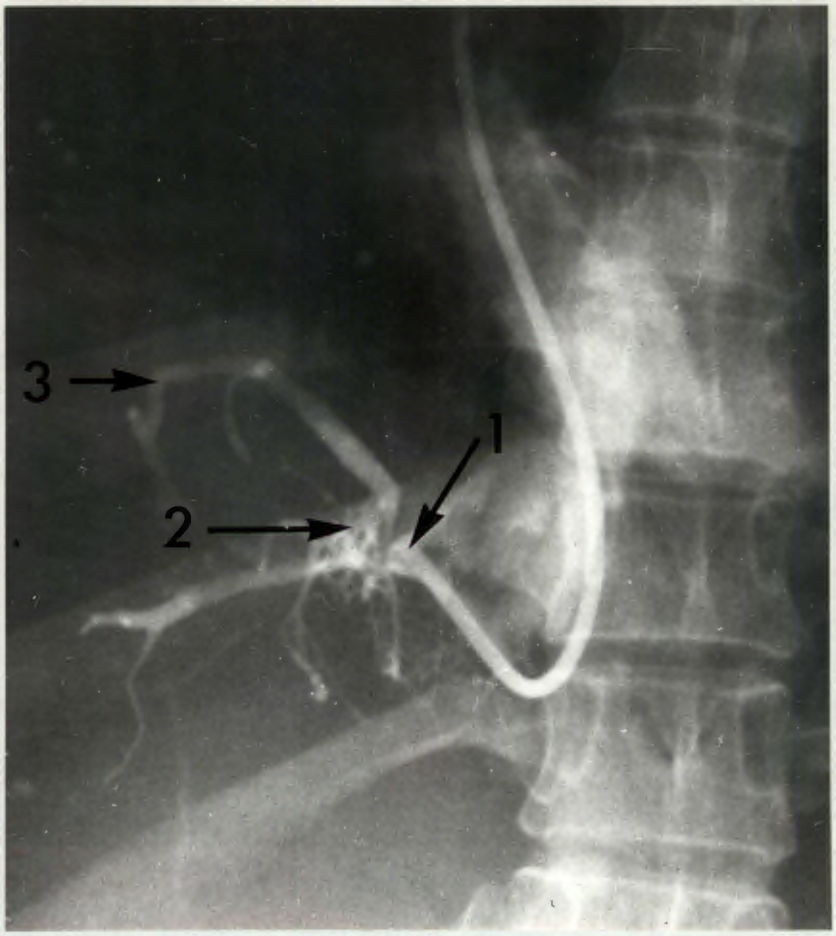

Fig: 5.17 CASE 2

The catheter is bent in the lumen of the inferior vena cava and the tip (1) is in the ostium of a right hepatic vein. Contrast material has entered the hepatic veins and is also refluxing freely to outline the cava and part of the right atrium. Abnormal vessels near the ostium (2) form a network appearance. Two hepatic veins fill, but they are narrow and show abnormal branches (3). This film should be read in conjunction with the hepatogram (fig. 5.32) which shows the proximal portion of the hepatic tree on the right.

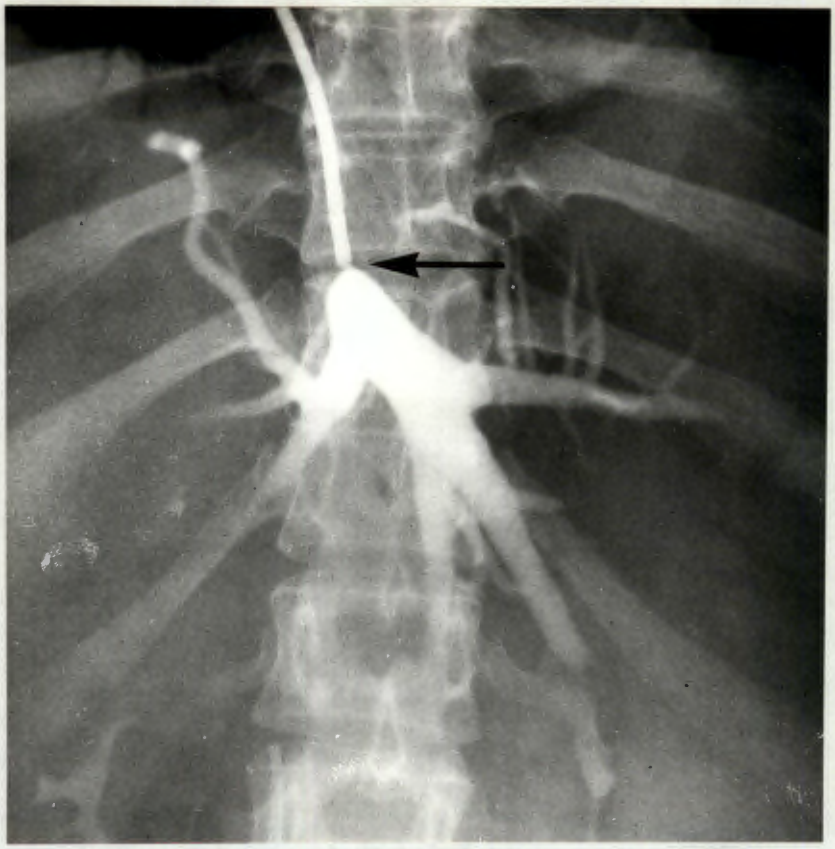

Fig: 5.18 CASE 2

The catheter has passed through a stenosed segment (1) at the ostium of a left hepatic vein and the proximal hepatic venous tree is patent. Collateral vessels are beginning to fill.

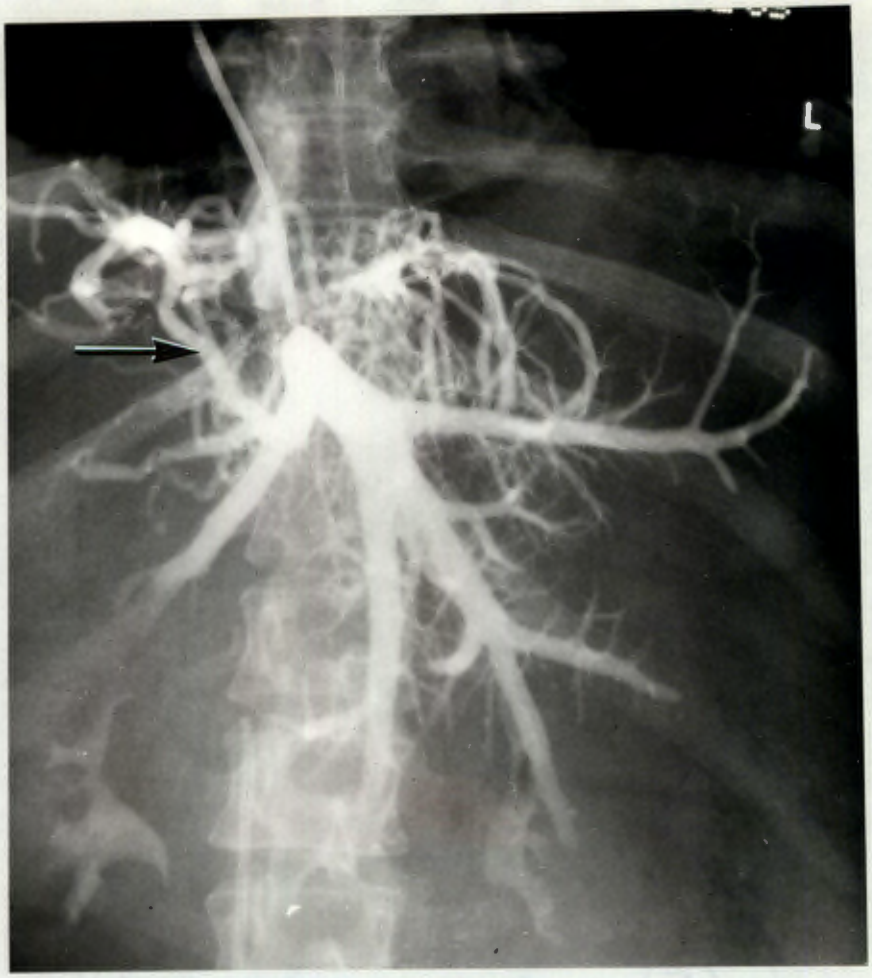

Fig: 5.19 CASE 2

Later film of the venogram in fig. 5.18. The hepatic veins are dilated. Numerous intralobar and interlobar collateral vessels are shown, some communicating with the inferior vena cava beyond the obstruction. There is a large vessel (arrow) which joins branches of the left and right hepatic veins.

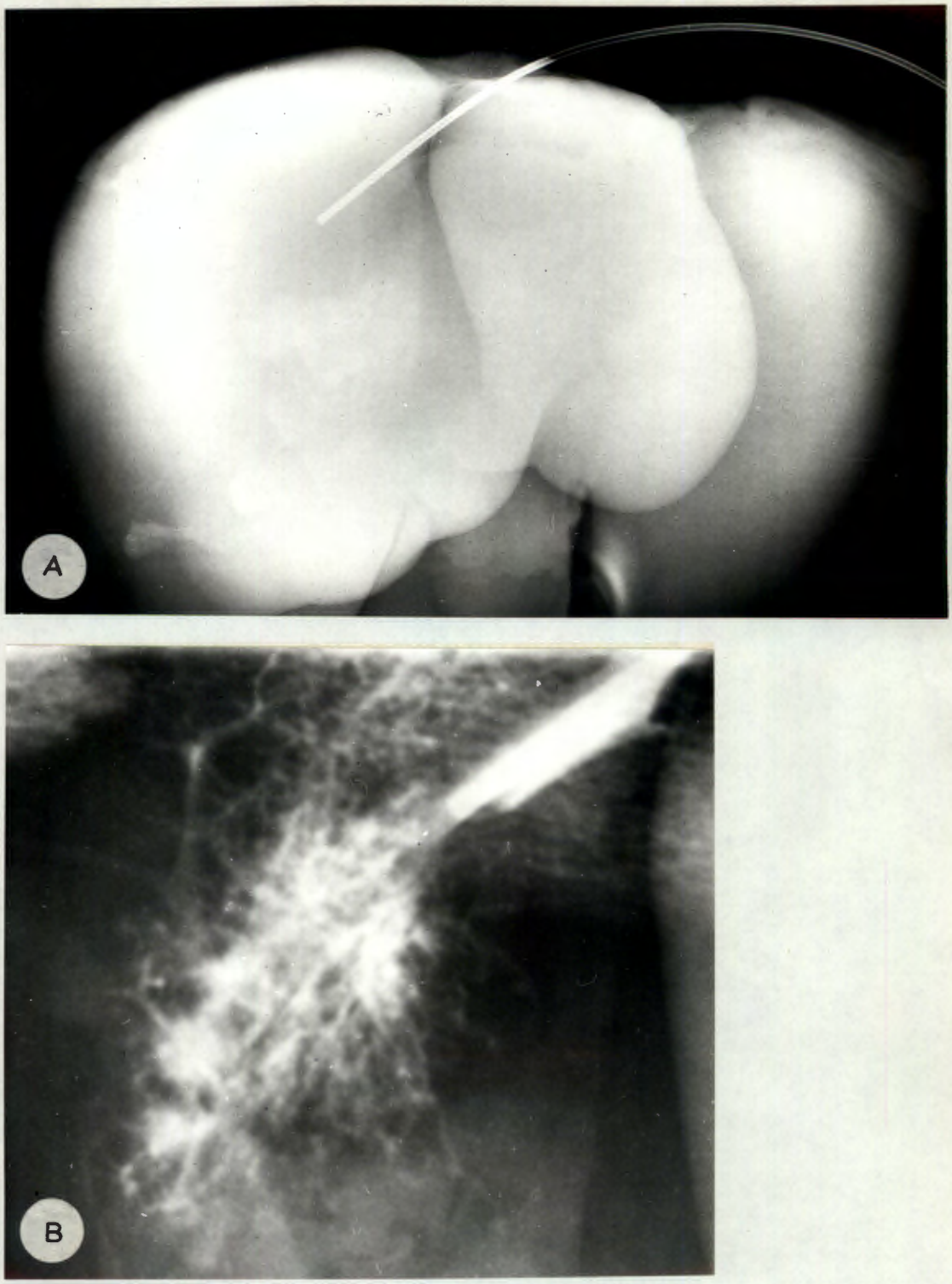

Fig: 5.20 A and B CASE 4

A post mortem venogram in the Budd-Chiari syndrome. The position of the catheter is indicated (A). The appearance is similar to that shown during life (fig. 5.13). The main vein is obstructed and numerous tortuous channels are demonstrated (B).

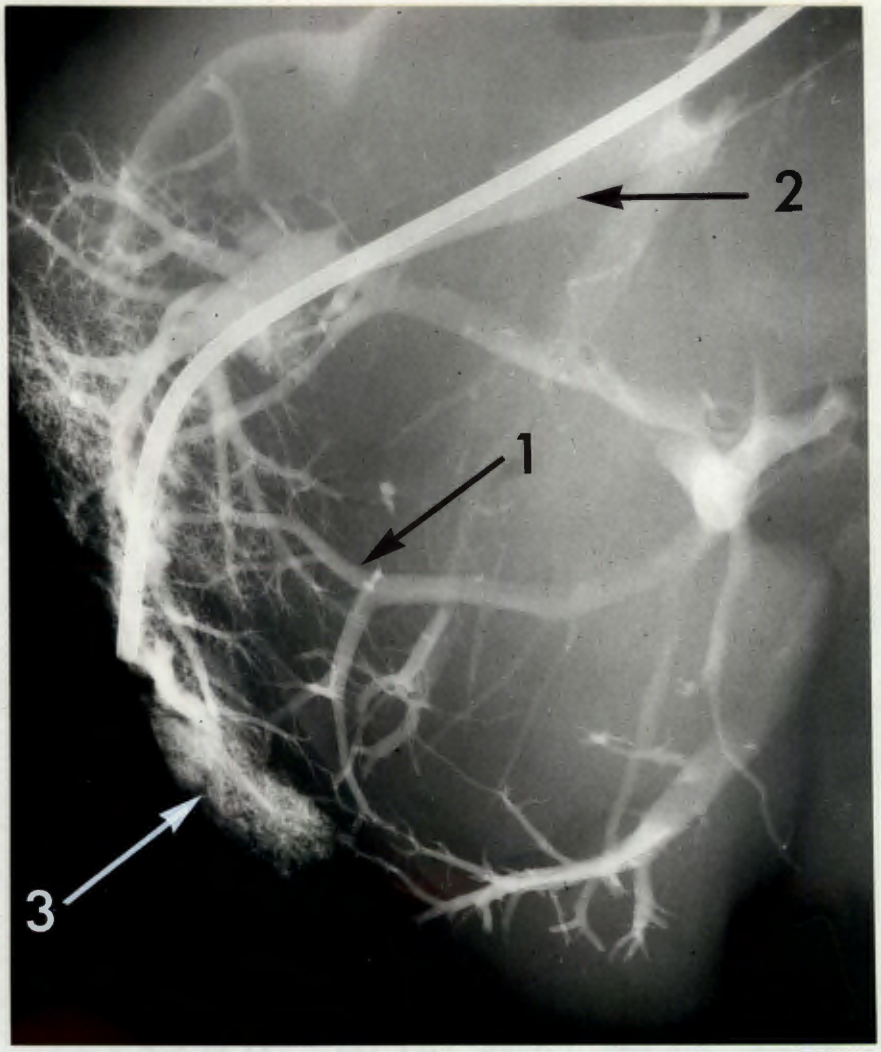

Fig: 5.21

A post mortem wedged hepatic venogram of a normal liver. The appearance is similar to fig. 5.2. The catheter is peripherally placed and there is opacification of portal (1) and hepatic (2) venous radicles. A stippled sinusoidal pattern is also shown (3).

In Case 3 (Fig. 5.15), the picture was slightly different. Instead of the irregular, spidery vessels of the previous films, there was a neat, interlacing pattern, forming a larger mesh in which each point of anastomosis between the vessels could be seen. Again the catheter could not be advanced peripherally and no normal hepatic or portal venous branches were seen. A similar but less distinctive venogram was present in Case 5 (Fig. 5.16). There seemed to be a communication between the hepatic veins and an intercostal vessel.

DISCUSSION

These studies show that the Budd-Chiari syndrome can be accurately diagnosed with the aid of hepatic venography and that thrombosis of the hepatic veins presents a characteristic radiographic appearance. Radiological procedures offer the only certain means of detecting the level at which the hepatic veins are blocked.

Hepatic venography was successfully performed in five patients and caval thrombosis was shown to involve the hepatic veins in a sixth (Fig. 8.9). There has been only one previous account of hepatic venography in the Budd-Chiari syndrome. Brink and Botha (1955) passed the tip of a catheter into the orifice of the left hepatic vein. Although the hepatic vessels are usually entered without difficulty it was found impossible in this case

to advance the catheter more than 1.5 cm. There was definite obstruction and the opening at the tip became occluded so that blood could not be withdrawn. Injection of contrast material outlined the obstruction and showed several small tributaries and a larger vessel which seemed to come from the diaphragmatic surface.

There have been several unsuccessful attempts to catheterize the hepatic veins in the Budd-Chiari syndrome, usually because of thrombus or tumour in the inferior vena cava (Levander and Ponten, 1959; Harland et al., 1960; Ginzler, 1963; Safouh and Shehata, 1965). On the other hand, in a number of cases with obstruction of the inferior vena cava above the liver, contrast material has outlined the hepatic veins by reflux during simple cavography. Hales and Scatliff (1966) advanced a catheter through the right atrium into a thrombosed cava. A single, partially thrombosed, hepatic vein and several diaphragmatic collateral vessels were opacified. Jonas and Lawrence (1954) described a venogram of the inferior vena cava which showed a conical block at the level of the 9th dorsal vertebra. Contrast material, injected from below, flowed retrogradely into a hepatic vein proximal to the obstruction. Distinct anastomoses between the hepatic veins in the right lobe carried blood back into the vena cava above the thrombosis. Similar results were obtained by Ohara et al. (1963),

Dupuy et al. (1964) and Schaffner et al. (1967) (see Chapter 8).

Kimura et al. (1963) have described several Japanese patients with membranous obliteration of the hepatic segment of the inferior vena cava. The haemodynamic and diagnostic problems are similar to those of hepatic vein thrombosis. They were unable to catheterise the hepatic veins, but in six patients they demonstrated the membrane directly above the ostium of the right hepatic vein by cavography through femoral and brachial catheters. A localised membrane in the hepatic segment of the cava has been demonstrated in 3 other patients by injection into the thoracic and abdominal portions of the inferior vena cava, through brachial and femoral vein catheters (Ohara et al., 1963; Eguchi et al., 1966; Schaffner et al., 1967).

In this study, a similar technique has been used for the first time in the Budd-Chiari syndrome. The cava has been opacified from below while the hepatic veins were entered via the right atrium.

There has been no previous reference to the unusual pattern of the hepatic venogram in the Budd-Chiari syndrome. The appearance is distinct from that in other forms of liver disease. In cirrhosis, there is a loss of the normal tapering and arborization of the hepatic and portal branches. The hepatic veins show the same distortion and angulation as the portal side, and

there is irregularity and narrowing especially of the small tributaries. These changes were present in the cirrhotic patients in this study and have been described previously (Tori, 1953; Celis et al., 1955; Ney, 1959; Nakamura et al., 1959; Reynolds et al., 1960; Britton et al., 1963; Delorme et al., 1963; Schlant et al., 1963; Rappaport et al., 1964; Shaldon and Sherlock, 1964; Britton, 1965; Nakamura et al., 1965). Partial thrombosis of hepatic veins is not uncommon in cirrhosis but is easily distinguished from the radiographic appearance in the Budd-Chiari syndrome (Fig. 5.9).

Space-occupying lesions such as hepatomas, neoplastic metastases, cysts and abscesses, show a characteristic displacement and deformity of the hepatic veins (Helander et al., 1958; Leevy and Gliedman, 1958; Servello, 1960). These filling defects are often best seen on wedged hepatic venography during the sinusoidal phase produced by retrograde flushing (Tori, 1964).

The appearance of the hepatic venogram in the Budd-Chiari syndrome is quite different. The interlacing vessels of fine calibre which communicate with narrow or occluded hepatic veins seem to be venous collaterals of abnormal configuration. This network of vessels does not resemble the normal or abnormal sinusoidal pattern, nor the fine arborization seen on splenic venograms or hepatic arteriograms. There is also no similarity to the appearance of the liver lymphatics which have been seen

radiologically after experimental ligation of the hepatic veins (Moreno et al., 1963). Radiological demonstration of lymphatics in cirrhosis, biliary obstruction and infective hepatitis is described in the next section on hepatography, but the pattern of lymphatics does not resemble that shown in the Budd-Chiari syndrome by hepatic venography. Moreover, lymphatics were filled following parenchymal injection of contrast material in Case 5, and they were distinct in detail and distribution from the typical network of the hepatic venogram.

The unique appearance of these veins suggests that they are an entirely new formation. Support for this theory has been obtained from recent studies of a corrosion cast in a single patient with the Budd-Chiari syndrome (Hales and Scatliff, 1966) which is discussed in the final section of this chapter.

Collateral vessels of greater size have also been demonstrated by hepatic venography. In Case 2 (Fig. 5.19) stenosis of the left hepatic vein caused a number of large vessels to follow an arching course from the hepatic vein branches to the cava above the block, and there were numerous smaller vessels of irregular distribution around the obstruction (Fig. 5.19).

The main hepatic veins in the Budd-Chiari syndrome have also shown distinct abnormalities on hepatic venograms. There was narrowing (Fig. 5.14), stenosis (Fig. 5.19), irregularity (Fig. 5.12) and obstruction (Fig. 5.15). Varying lengths of the large veins

were opacified but in all cases the advance of the catheter was held up. In one patient (Case 2) the obstruction was limited to short segments of the veins to both the left and the right lobes. This was shown by passage of the catheter through a narrow area of thrombus in the left hepatic vein and opacification of the patent vein proximal to this site (Fig. 5.19). The caval aspect of the obstruction had been earlier outlined by inferior vena cavography (Fig. 8.4A), and by superimposing the two films, the obstructed segment was found to be 2 cm in length. On the right side, in the same patient, the catheter could not be advanced beyond the ostia of the hepatic veins. The extent of the thrombi was determined by comparing the hepatic venogram, which showed the caval side of the occlusions, with the hepatogram, which clearly outlined the sudden termination of two hepatic veins at their ostia.

FUNCTIONAL HEPATOGRAPHY

Hepatography has been applied in this study of the Budd-Chiari syndrome for two reasons. Firstly, the most logical means of opacifying the obstructed hepatic veins is by observing the flow of contrast material away from a site of deposition in the liver substance. The extent of thrombosis and the presence, position and route of collateral vessels might be demonstrated.

Secondly, the standard experimental procedures to increase lymph flow are constriction of the inferior vena cava, and ligation of the major hepatic veins (Starling, 1894; Brauer et al., 1959). By analogy, the lymphatics of the liver may function as a compensatory outflow tract in the Budd-Chiari syndrome. Hepatic lymphatics have been shown by hepatography in cirrhosis (Moreno et al., 1963), and their radiological demonstration would be of great interest in hepatic vein thrombosis.

In the only previous report of hepatography, observations were restricted to patients with cirrhosis and heart failure (Moreno et al., 1963). Since hepatograms in other kinds of liver disease are not available, it has been necessary to make such studies for comparison with the results in the Budd-Chiari syndrome.

There were 33 control patients who were divided into normals, five varieties of cirrhosis, obstructive jaundice, infective hepatitis, sarcoidosis and chronic liver disease of unknown cause. 3 patients with the Budd-Chiari syndrome were examined and there was one case

of experimental hepatic vein occlusion (Table 5.2).

METHOD

A preliminary film of the right upper quadrant of the abdomen was taken with the patient supine. Using a sterile technique under local anaesthesia, a No. 18 spinal needle was introduced into the parenchyma of the liver to a depth of 3 - 4 cm in the right mid-axillary line. A negative pressure was applied to ensure that the needle was not in a hepatic or portal venous radicle. During manipulation of the needle, respiration was suspended, and quiet breathing was allowed with the needle in position. The needle was connected to a glass syringe containing 20 ml of 45 per cent sodium diatrizoate by means of polythylene tubing. During apnoea after normal expiration the contrast material was injected over 10 seconds and a series of antero-posterior films taken on a Schonander film changer at 0, 2, 4, 6, 10, 15, 20, 24, 26 and 30 seconds. Breaths were taken between the 10 and 15 second films.

The procedure was usually carried out at the same time as a liver biopsy for which the normal precautions were observed. The safety of this technique has been previously shown in animal and human studies (Moreno et al., 1962 a and 1962 b; Moreno et al., 1963).

RESULTS

CONTROL STUDY

After injection into the parenchyma of the normal liver, the contrast medium passed mainly into the major hepatic veins via small radicles draining the area of injection (Fig. 5.22). Streaming and rapid disappearance of the contrast agent from the hepatic vein at the end of injection indicated that flow was fast. This was clearly seen in serial exposures. Contrast medium often refluxed during injection into local intrahepatic portal branches (Fig. 5.23). Forward flow at the end of injection carried contrast material from the portal radicles into the capillaries and sinusoids where a fine stippled pattern was formed (Fig. 5.24).

Drainage of contrast medium from the hepatic vein was delayed in cardiac failure (Fig. 5.30) or if intrathoracic pressure was raised by the valsalva manoeuvre (Fig. 5.31). However, there was no detectable difference in the rate of hepatic outflow between the normals and the patients with cirrhosis.

In normal livers no lymphatic drainage of contrast material was seen. In the presence of liver disease, this technique frequently demonstrates efferent hepatic lymph channels. Lymphatics in the liver substance appeared as fine vessels which filled rapidly with contrast material, draining medially in tortuous fashion to the hilum of the liver and regional nodes or less commonly towards the diaphragm (Figs. 5.25 to 5.30). The rapid flow was in marked

TABLE 5.2

RADIOLOGICAL DEMONSTRATION OF LYMPHATICS

Condition	Number examined	Number with lymphatics
Normal	4	0
Cirrhosis		
Cryptogenic	7	6
Alcoholic	2	2
Chronic active hepatitis	3	3
Primary biliary	2	1
Secondary biliary	1	1
Obstructive jaundice		
Carcinoma pancreas	2	0
Carcinoma hepatic duct	1	1
Drug cholestasis	2	0
Infective hepatitis	6	1
Sarcoidosis	1	1
Chronic liver disease	1	1
Hepatic vein thrombosis	3	1
Acute hepatic vein occlusion	1	1

contrast to that ordinarily expected in lymphatics. The lymphatics varied in calibre and they did not contain valves. Several fine vessels or a few of larger diameter constituted the lymph flow. They arose from the interstitial site of injection, and in one case of chronic active hepatitis appeared to originate around biliary ducts which were incidentally filled (Fig. 5.28). Lymphatics were distinguished from hepatic and portal venous radicles by their direction of flow, tortuous course and irregular calibre. They remained opacified for at least 15 seconds after the contrast agent had left the portal and hepatic venous systems. The cisterna chyli and thoracic duct were opacified in 3 patients.

RESUME OF FINDINGS IN CONTROLS

Cirrhotic Patients: None of the patients with alcoholic or cryptogenic cirrhosis, which was inactive as assessed clinically and histologically, had abnormal hepatic veins, and there was no delay in hepatic venous drainage when compared with the normal. All but one of these nine cirrhotics showed definite lymphatic drainage of contrast material. Ascites was present in only one. Two or three large lymph vessels were seen which were often discrete in contrast to the multiple vessels seen in other disorders. In one of two patients with primary biliary cirrhosis small lymph vessels were present.

Fig: 5.22

Intraparenchymal deposition of contrast medium (hepatography) in a normal liver. Film at 4 seconds (A), shows the deposit of contrast medium (1) refluxing into portal venous radicles (2) and draining into a normal hepatic vein (3). At 6 seconds (B), the normal configuration of the main right hepatic vein is seen and contrast material is beginning to fill another hepatic vein (4). Contrast material has passed forward from the portal branches to opacify a triangular segment of the liver parenchyma (5). At 10 seconds (C), the venous drainage is fading and at 15 seconds (D), only the remainder of the deposit is visible. No lymphatics are present.

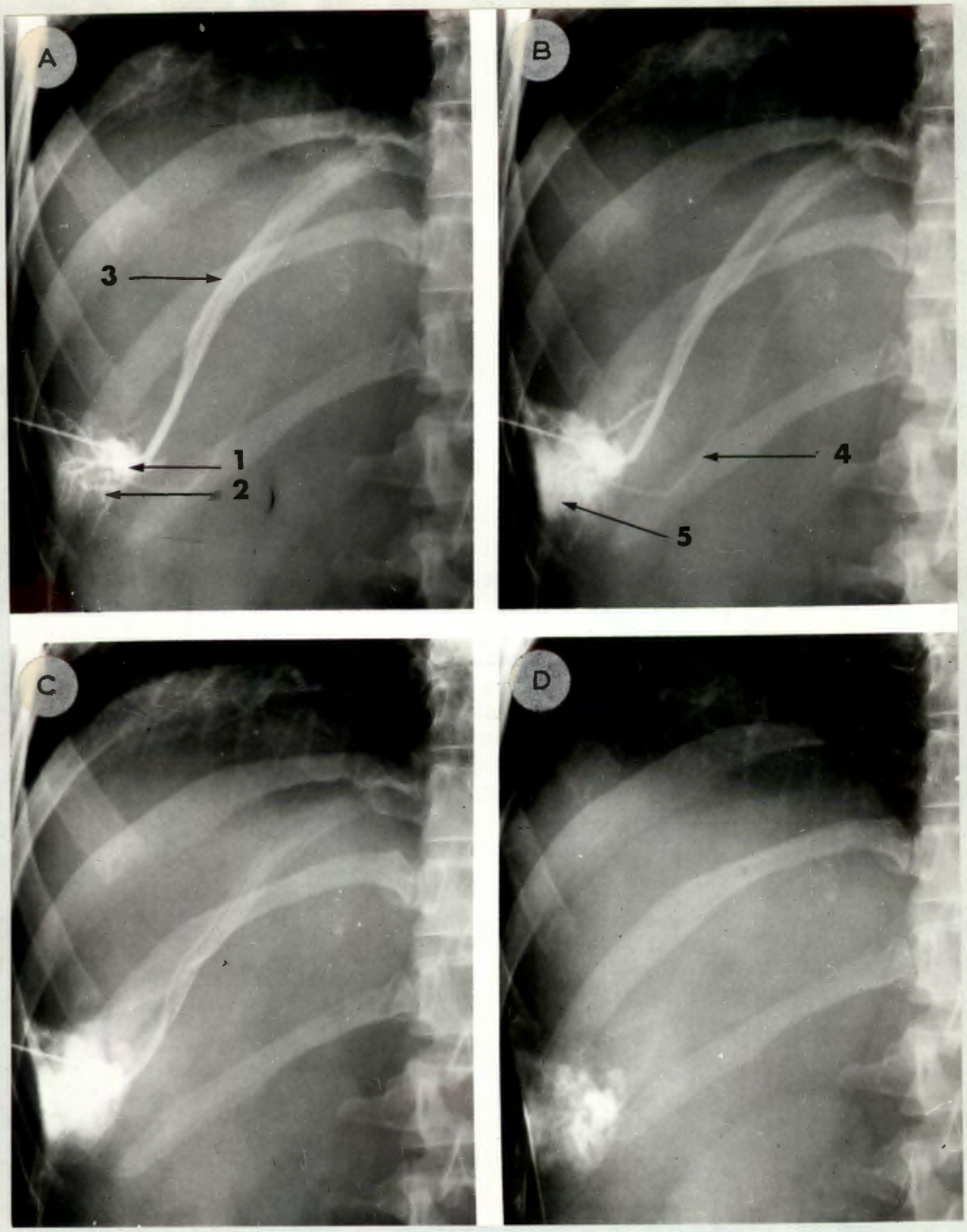
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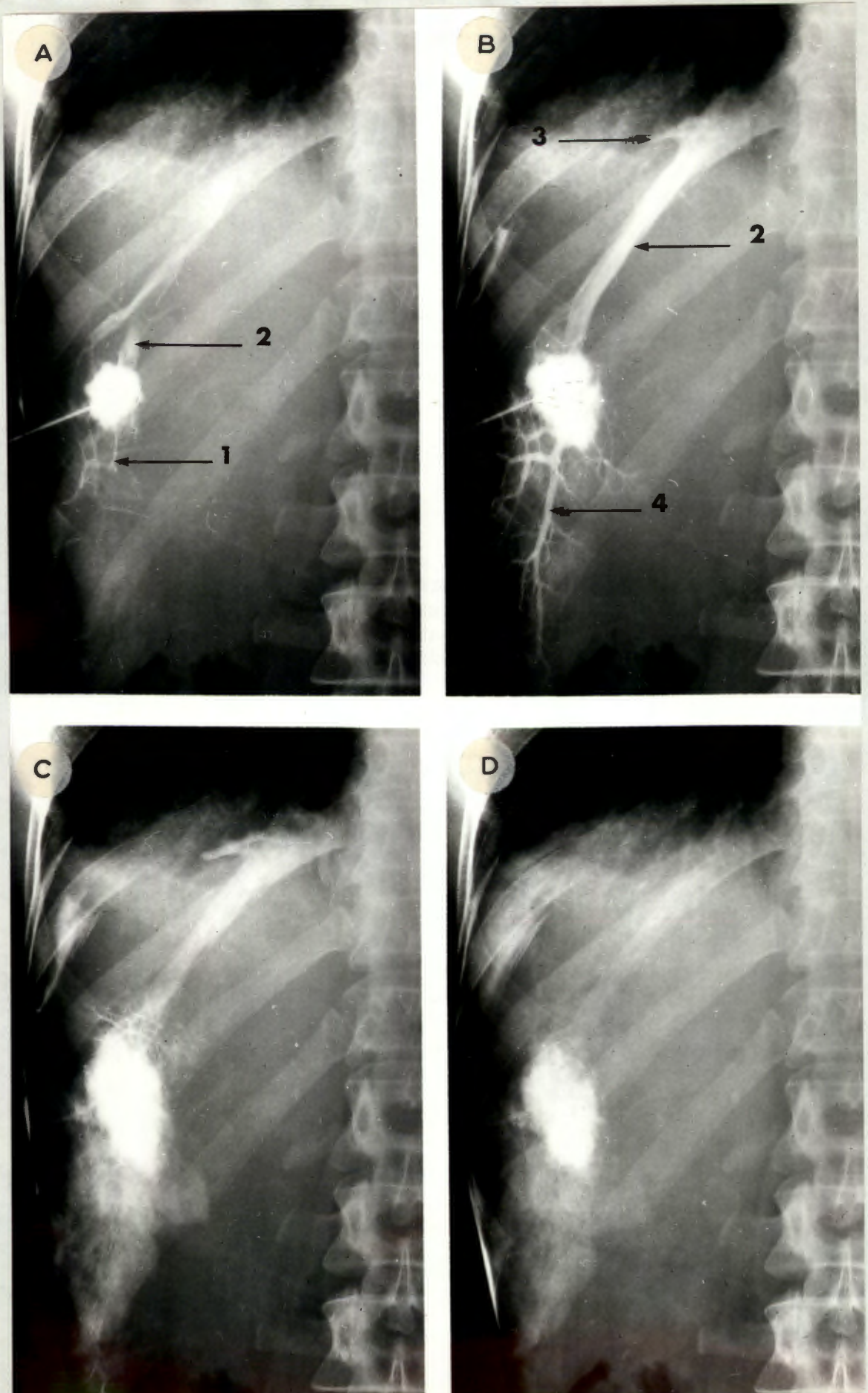
Fig: 5.23

Hepatography in a patient with infectious hepatitis. The films are entirely normal. The same features as in fig. 5.22 are demonstrated. At 2 seconds (A), portal reflex (1) and hepatic venous filling (2) have commenced and, at 6 seconds (B), are at their maximum. Several small branches converge to make up the main trunk of the hepatic vein which delivers the contrast material into the inferior vena cava. The large flow in the inferior vena cava dilutes the contrast material and the cava itself is not opacified. At the termination of the hepatic vein (3), there is slight reflux into an adjoining tributary.

The contrast material passes into the portal radicles against the normal flow (4) and produces a denser and more distinct outline than in the hepatic vein.

At the completion of injection (C), the portal flow resumes its normal direction and a sinusoidal phase follows similar to that seen in portography. At 15 seconds (D), the portal and hepatic veins have emptied. No lymphatics are present.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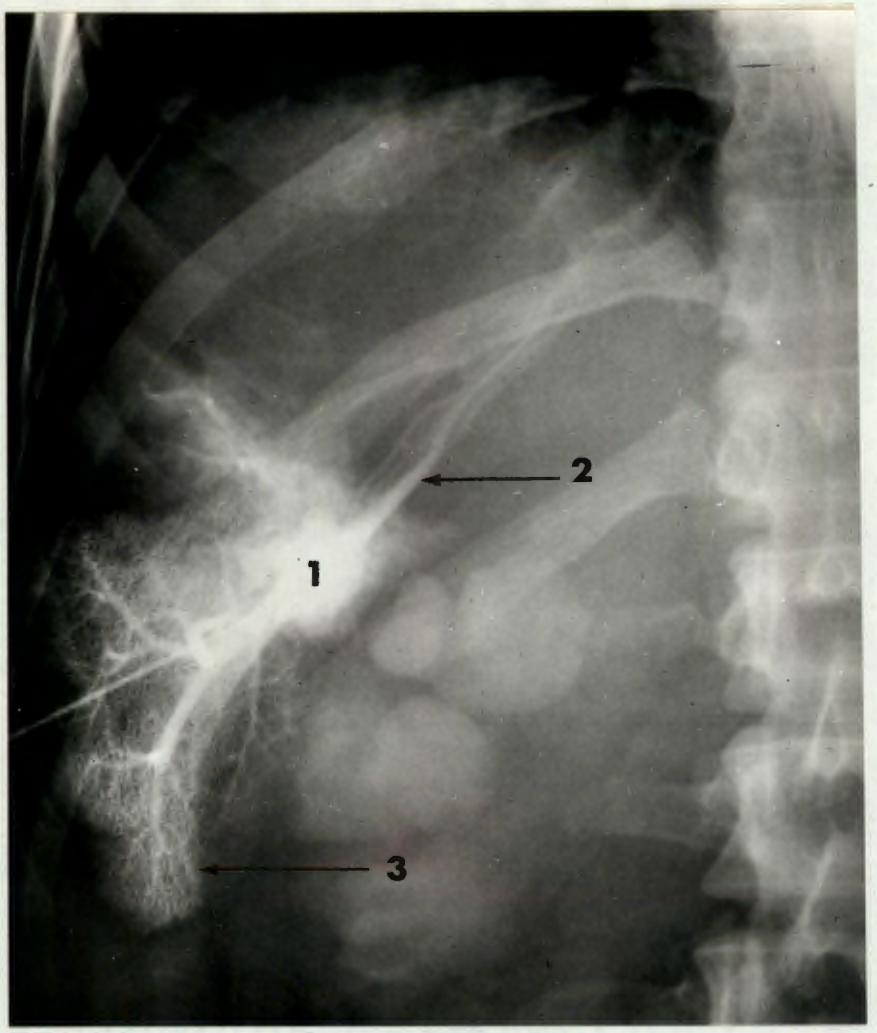

Fig: 5.24

Hepatography in a patient with serum hepatitis. The appearance is normal. Film at 10 seconds shows the deposit (1), and the hepatic veins (2) in which the contrast medium is now fading. The portal radicles are well opacified and a fine stippled pattern is formed by contrast medium in the portal capillaries (3). A later phase will show a uniform blush due to sinusoidal filling. Incidentally, a previous injection of contrast medium has opacified a right-sided hydronephrosis.

Fig: 5.25

Hepatography in a patient with alcoholic cirrhosis. Films at 2 and 4 seconds (A and B) show a deposit of contrast medium (1) refluxing into portal venous radicles (2) and beginning to drain normally into a hepatic vein. At 10 seconds (C), the hepatic vein (3) is well opacified and there is rapid filling of lymphatics towards the hilum (4). The cisterna chyli is outlined (5). Forward flow from portal vein forms a fine sinusoidal pattern. At 20 seconds (D), the hepatic and portal veins are empty but the lymphatic system is still well seen. The demonstration of lymphatics in these films is the only abnormal feature.

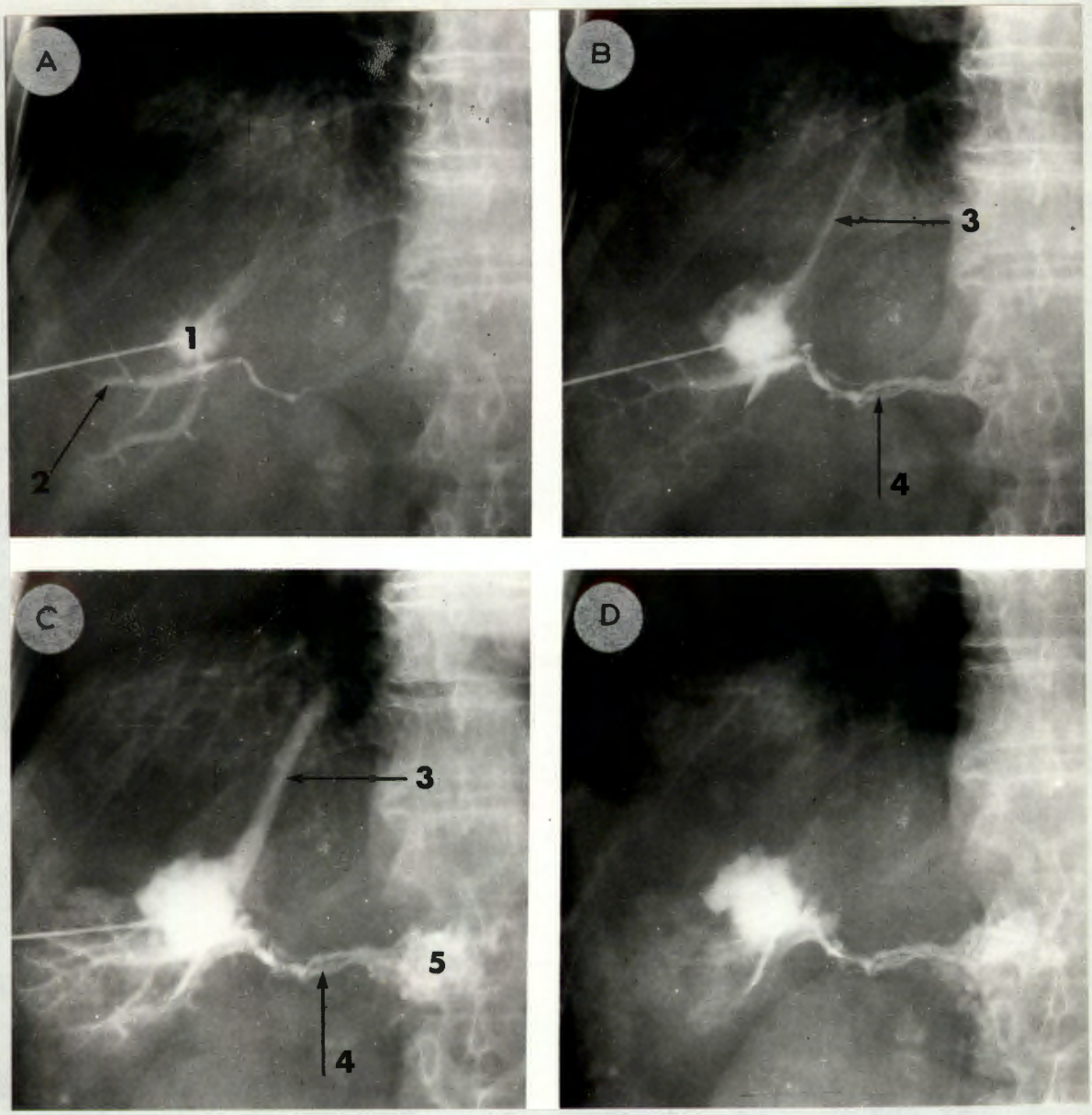
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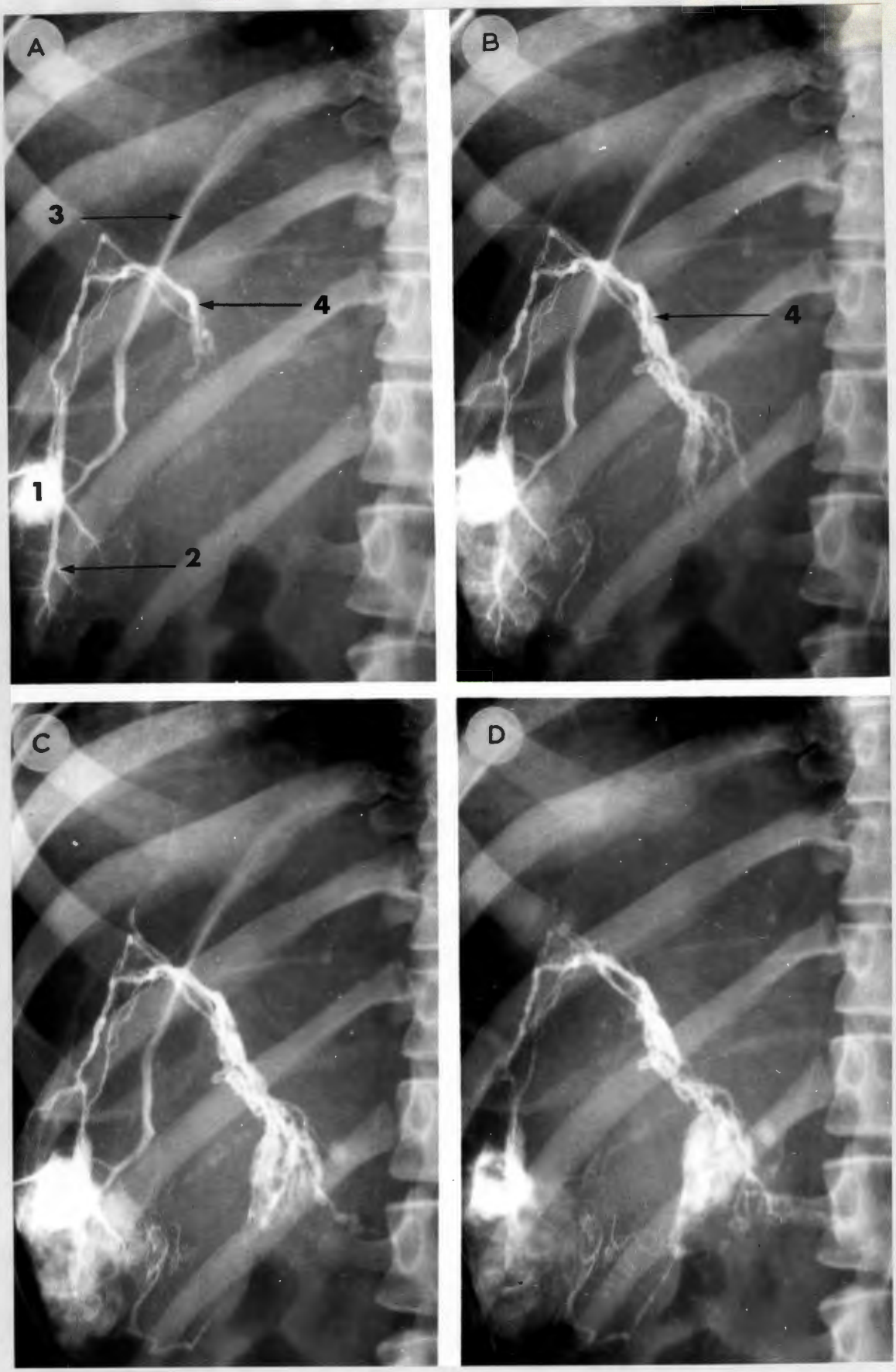
Fig: 5.26

Hepatography in a patient with chronic active hepatitis and cirrhosis. At 4 and 6 seconds (A and B), the contrast material passes from the site of injection (1) into portal venous radicles (2). A large hepatic vein (3) and a leash of lymphatics (4) fill simultaneously. By 10 seconds (C), the hepatic vein is less well seen and at 24 seconds (D) has emptied. Several lymphatics follow an arching course and fill lymph nodes at the hilum of the liver. Other lymph vessels pass inferiorly.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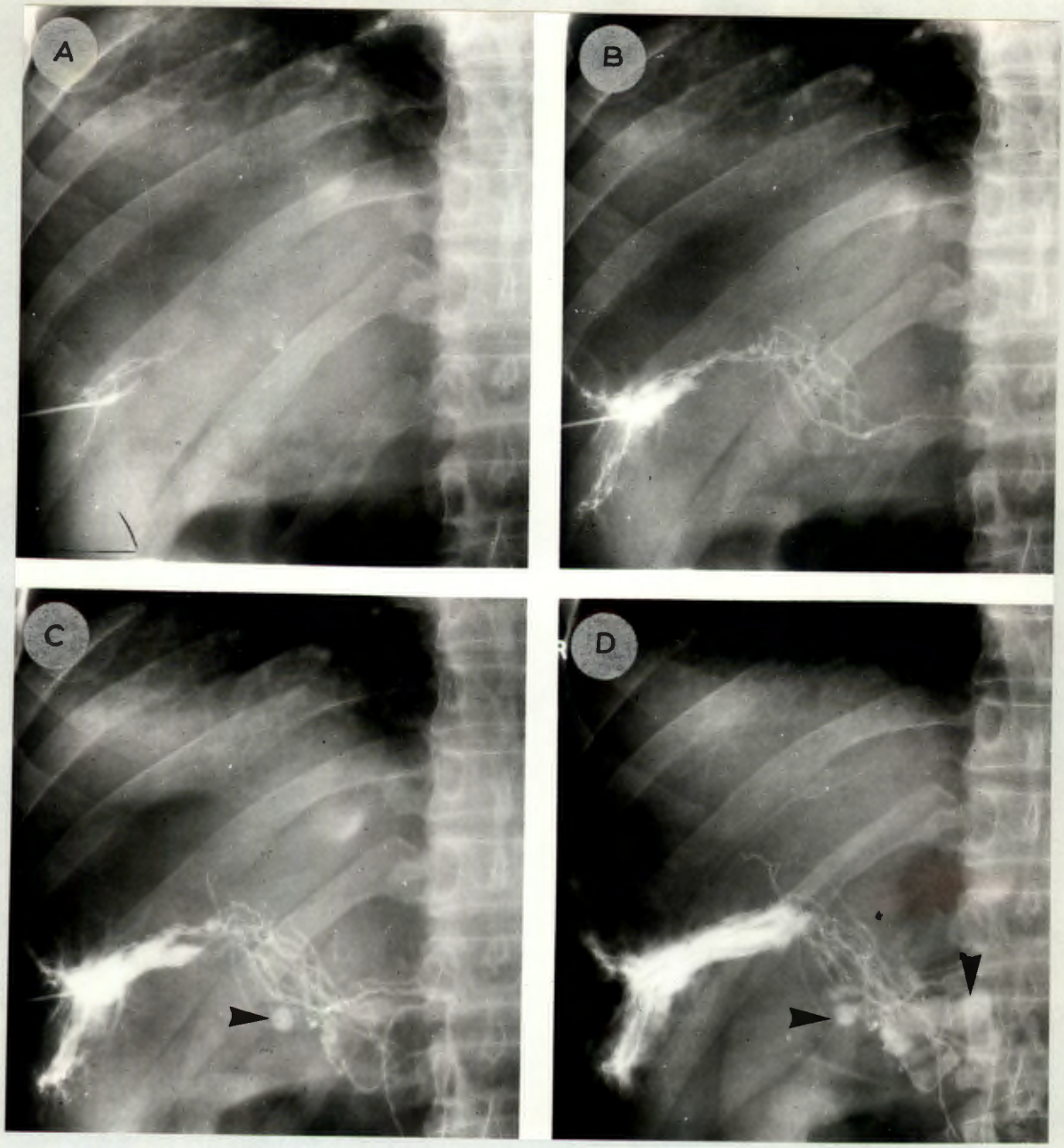


Fig: 5.27

The appearance after intraparenchymal injection was normal in all respects in five of six cases of infectious hepatitis (see fig. 5.23). In the sixth patient (illustrated), there was profuse lymphatic filling and visualization of lymph nodes. Films at 2, 4, 10 and 20 seconds (A, B, C and D) show the progression of the lymph flow and the opacification of lymph nodes (arrows). No contrast material was seen to drain by any other route.

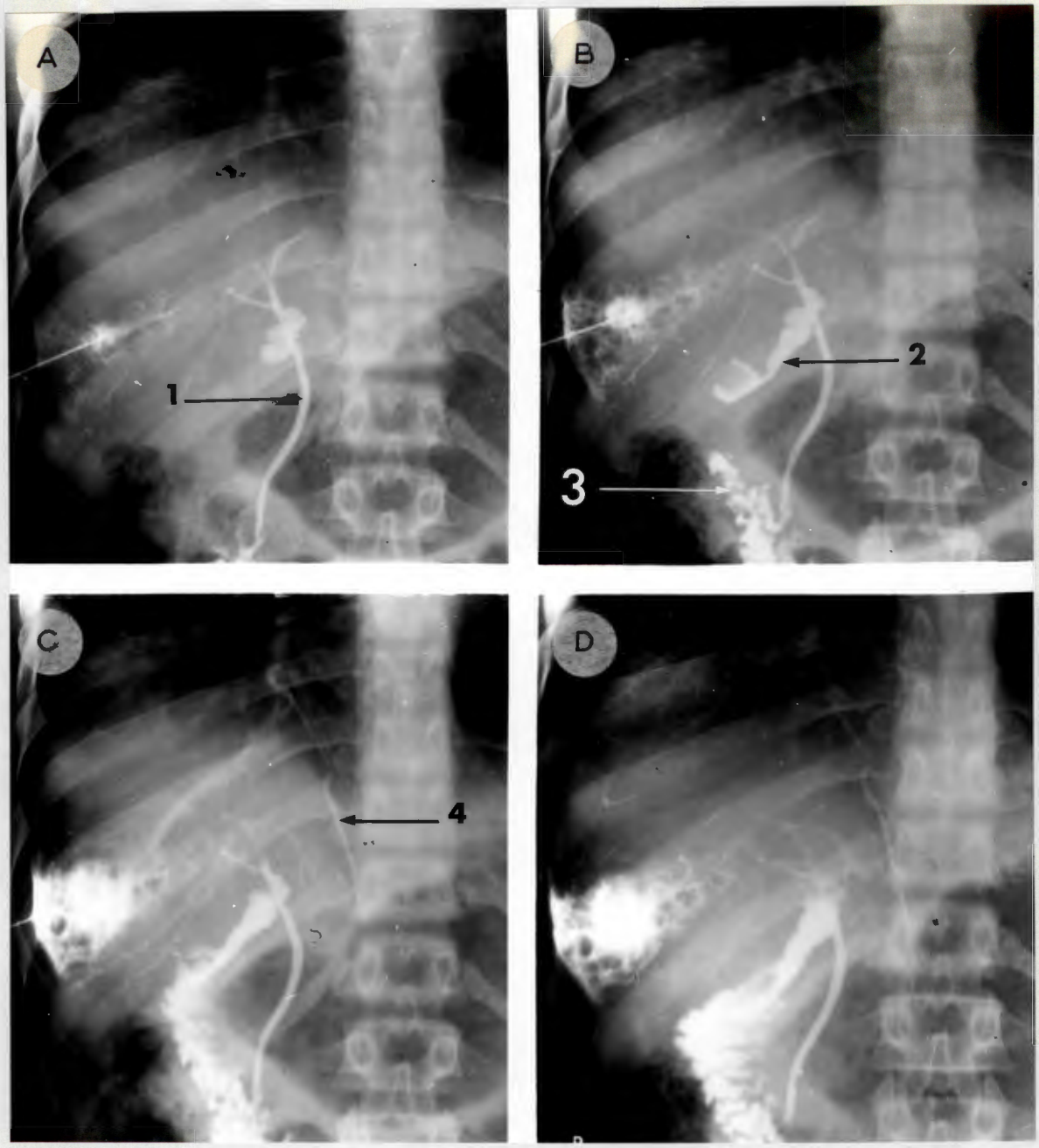
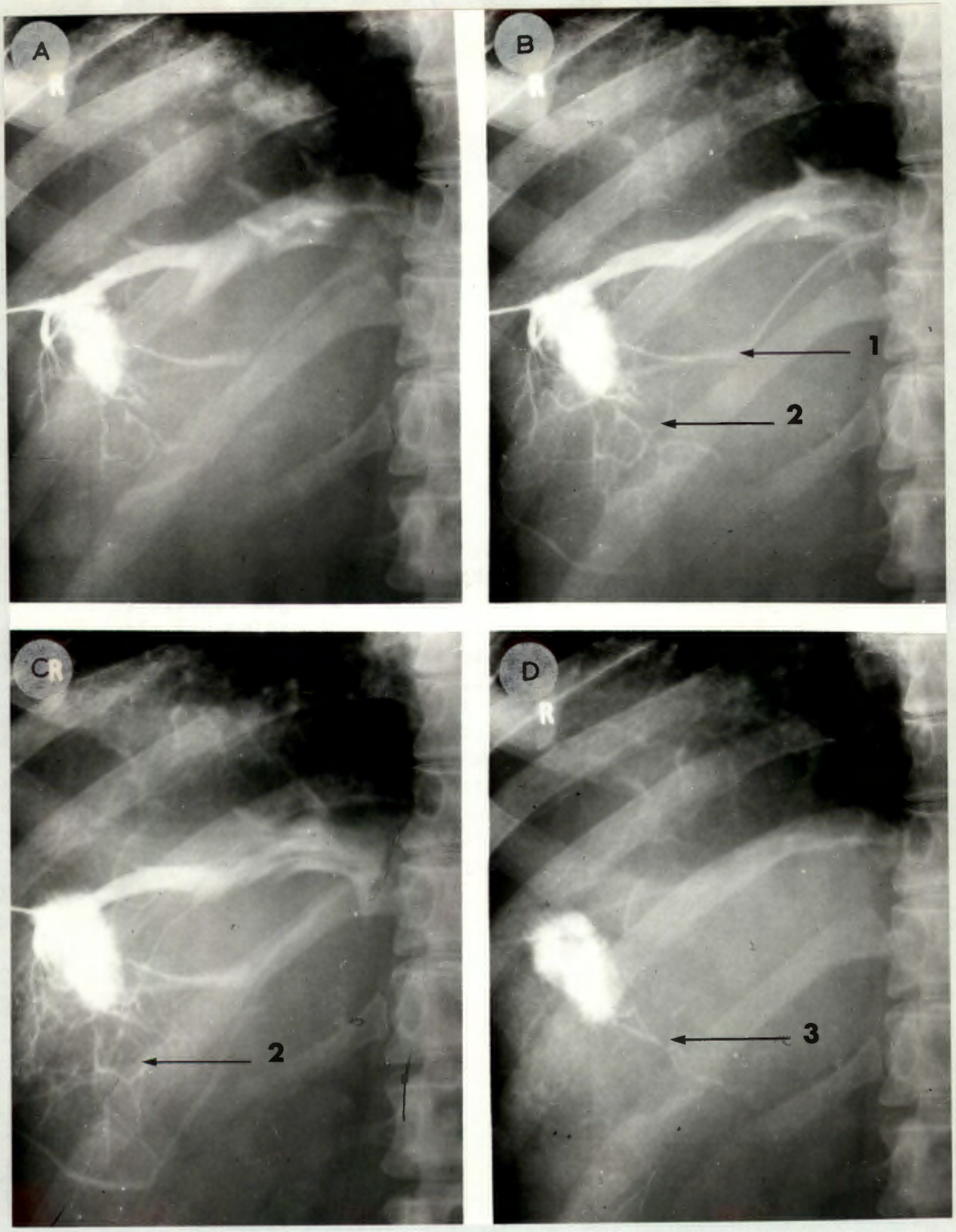


Fig. 5.28

Hepatography in a patient with chronic active hepatitis and cirrhosis. Nearly all of the contrast material has entered the biliary tree and has opacified the common bile duct (1), gall bladder (2) and the duodenum (3). However, there is filling of a single lymphatic which follows an unusual course from the eighth rib towards the spine at D 11 (4). The bile ducts were not opacified in any other patients.

Fig: 5.29

Hepatography in a patient who had undergone a portocaval anastomosis for portal hypertension caused by hepatic granulomata due to sarcoidosis. A right hepatic vein is well shown in A and B. Contrast medium has also drained via other hepatic veins (1). No definite portal reflux is present. An unusual network of delicate vessels (2) is seen at 6 and 10 seconds (B and C), which is distinct from the hepatic and portal systems. At 20 seconds (D), lymphatics are present draining towards the hilum (3). Their apparent communication with the network of vessels suggests the latter may be lymphatics. This is further supported by both splenic venography and wedged hepatic venography which showed lymphatics and lymph nodes.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In three patients with clinical, biochemical and histological evidence of chronic active hepatitis with cirrhosis there was extensive lymphatic drainage and several large vessels were demonstrated (Fig. 5.26).

Obstructive Jaundice: Four patients with drug cholestasis or a pancreatic neoplasm showed no lymphatic drainage of contrast material. A few small lymphatics were seen after intraparenchymal injection in a case of carcinoma of the hepatic duct. In none of these patients was there any abnormality of the hepatic veins.

Infective Hepatitis: The appearance after intraparenchymal injection was normal in all respects in five of six cases of infective hepatitis. In one patient with underlying ulcerative colitis there was profuse lymphatic filling and visualisation of lymph nodes (Fig. 5.27). No contrast material was seen to drain by any other route. The clinical and histological data in this case were diagnostic of acute infective hepatitis and there was no evidence of the chronic liver lesions complicating colitis. Full resolution occurred.

Sarcoidosis: The hepatic veins were normal in a patient who had undergone a portocaval anastomosis for portal hypertension caused by sarcoid granulomata in the liver. But there were inter-communicating lymphatics forming a fine, lace-like pattern distinct from the hepatic and portal systems (Fig. 5.29). In this same case, lymphatics and lymph nodes were demonstrated after

both splenic venography and wedged hepatic venography (Fig. 5.10).

BUDD-CHIARI SYNDROME

Two cases of the Budd-Chiari syndrome showed obstruction and prolonged filling of the hepatic veins. Density proximal to the block was increased and an extensive collateral circulation was clearly outlined.

In Case 2 (Fig. 5.32), there was opacification of several hepatic veins of reduced calibre. These were tributaries of the two large right hepatic veins which were occluded near their entrance to the inferior vena cava. There was loss of the smooth-walled tapered appearance of the hepatic veins. Streaming of the contrast medium was absent, indicating a slow rate of flow. Serial films showed numerous tortuous vessels bypassing the obstructions, and communication with each other. Despite the collateral channels, there was delay in emptying of the hepatic veins. There was no reflux into portal veins and no lymphatics were seen.

In Case 3 (Fig. 5.33), most of the contrast material entered the hepatic venous system but no normal veins were present. In contrast to Case 2, in whom the main veins were narrowed and obstructed, the vessels, demonstrated, were all collaterals. A mass of tortuous veins of varying calibre, drained the parenchymal deposit into the inferior vena cava. The appearance was not unlike

that of cavernous transformation of the portal vein. A few smaller veins travelled downwards towards the hilum. Hepatic venous emptying was delayed. There was slight portal reflux but no lymphatics were seen.

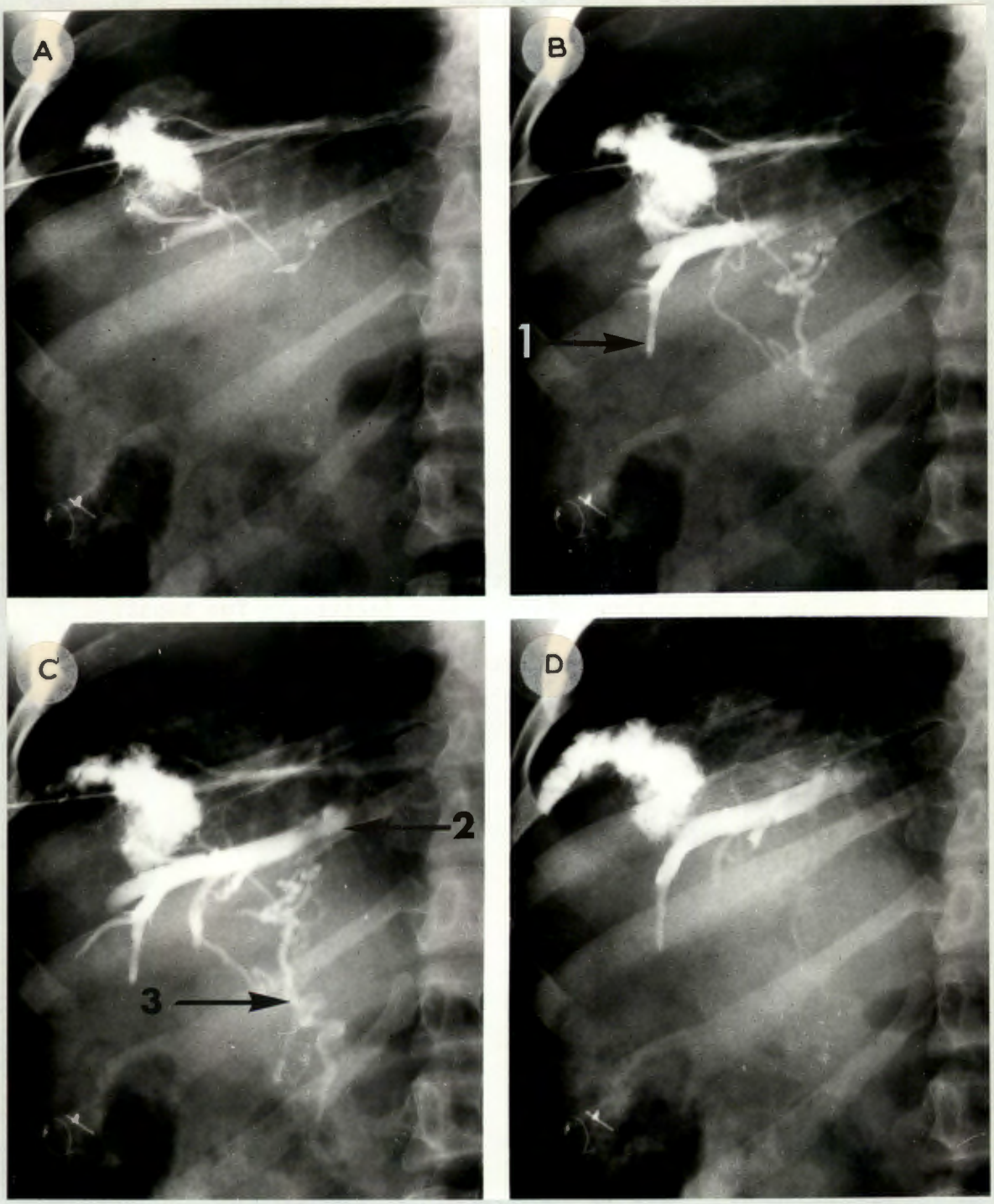
In Case 5 (Fig. 5.34), the contrast medium refluxed mainly into the portal system. The left branch of the portal vein was well shown. There were no normal hepatic veins, and dense collateral vessels were not present. In the later phase, after the contrast medium had passed forward from the portal branches into the sinusoids, narrow, straight veins were seen draining through the diaphragm, some towards the vena cava. Contrast medium was seen inferiorly in a few lymphatics of narrow calibre. They were recognised by their beaded appearance, persistent filling and direction of flow.

ACUTE HEPATIC VEIN OCCLUSION

In a patient with cirrhosis, contrast material was deposited in the parenchyma of the liver while a main right hepatic vein was acutely occluded with a balloon catheter which had been introduced to carry out hepatic venography to exclude a space-occupying lesion. There was extensive filling of lymph channels and lymph nodes (Fig. 5.35). The balloon and occluded hepatic vein were also outlined.

Fig: 5.30

Intraparenchymal deposition of contrast material in a cirrhotic subject with cardiac failure. Two hepatic veins are filled and there has been reflux into the hepatic venous tributaries (1). Film at 15 seconds (C) shows prolonged opacification of the hepatic veins (2) and tortuous lymphatics coursing down to the hilum of the liver (3). The hepatic veins are still filled at 30 seconds (D).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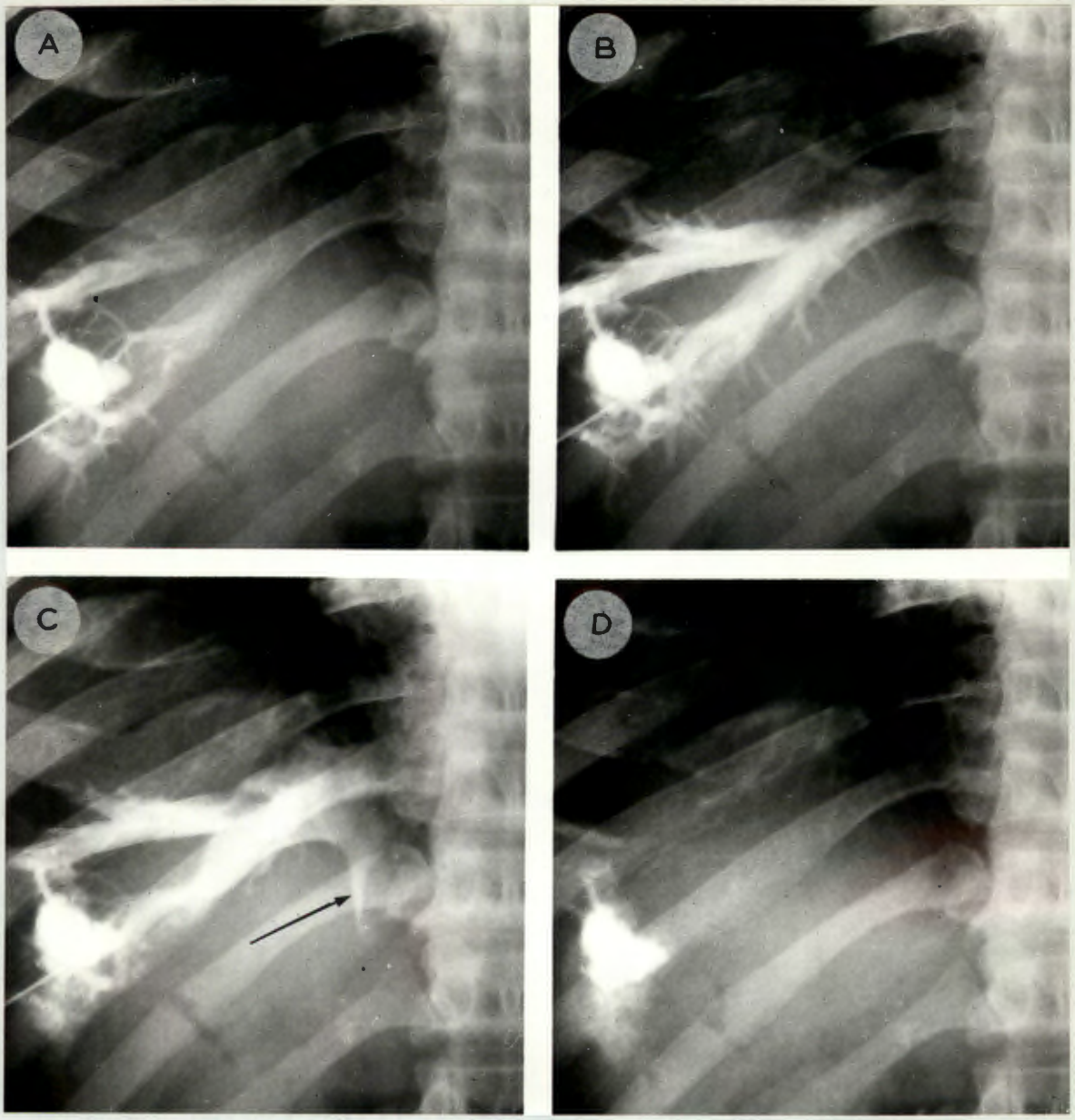

Fig: 5.31

Hepatography in a normal subject during the valsalva manoeuvre. Films at 4 and 6 seconds (A and B) show densely contrasted hepatic veins and tributaries. At 10 seconds (C), emptying of the hepatic veins is delayed and there has been reflux into the inferior vena cava (arrow). At 20 seconds (D), after a single breath, the vessels are no longer opacified. No lymphatics are present.

Fig: 5.32 CASE 2

Hepatography in a patient with the Budd-Chiari syndrome. Films at 4 and 6 seconds (A and B), show the deposit of contrast material (1) draining via small hepatic veins into two large veins which are occluded at their ostia (2). Delay in venous emptying produces unusually dense contrast which is still evident at 10 seconds (C). The main hepatic veins are reduced in calibre. There are numerous collateral vessels which by-pass the obstruction and anastomose with each other. This results in a maze of abnormal veins which is still present at 20 seconds (D). Portal reflux is not demonstrated and there are no lymphatics.

This film should be viewed in conjunction with the hepatic venogram (fig. 5.17) which shows the distal portion of these same veins on the caval side of the obstruction.

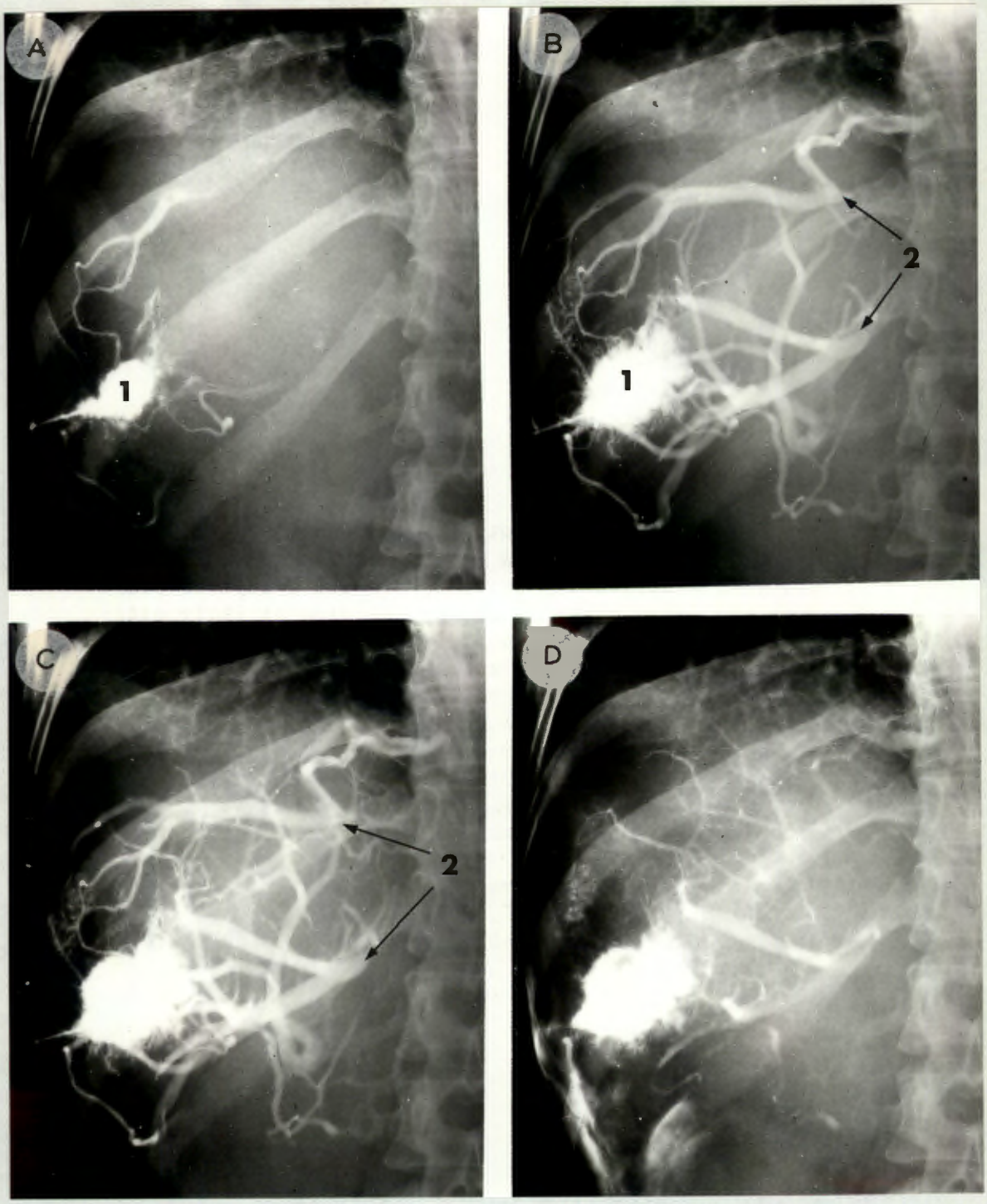
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Fig: 5.33 CASE 3

Hepatography in a patient with the Budd-Chiari syndrome. Films at 4, 6 and 10 seconds (A? B and C), show the deposit draining into a mass of tortuous hepatic vessels which take an irregular course to the inferior vena cava. None of these vessels seem to be normal hepatic veins. The appearance is similar to that of cavernous transformation of the portal vein and the vessels are probably all collateral to the obstruction. A hepatic vein is also seen inferiorly. There is notable delay in venous emptying evidenced by the films at 10 seconds (C) and 20 seconds (D). Slight portal reflux is present but no lymphatics are seen.

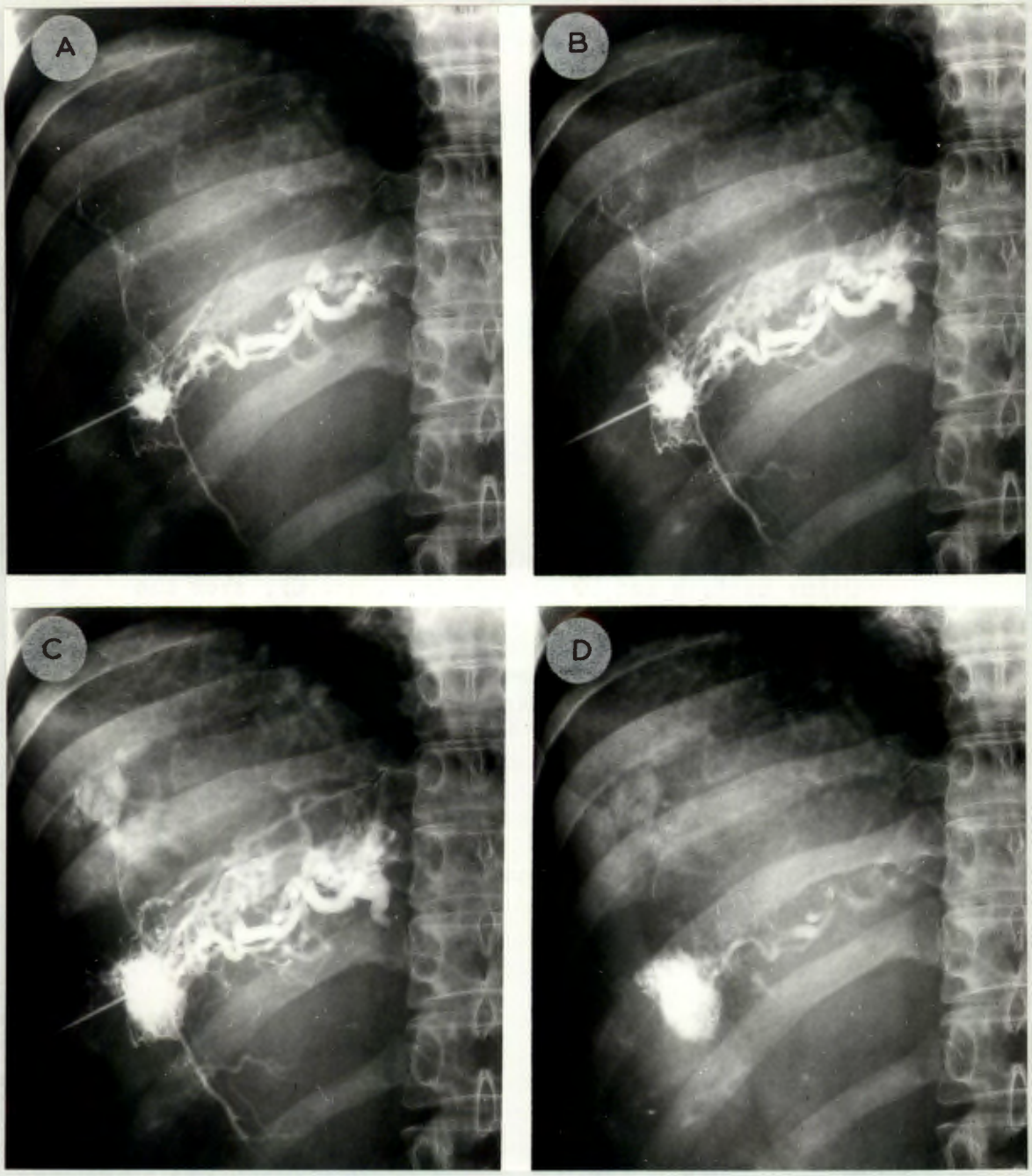
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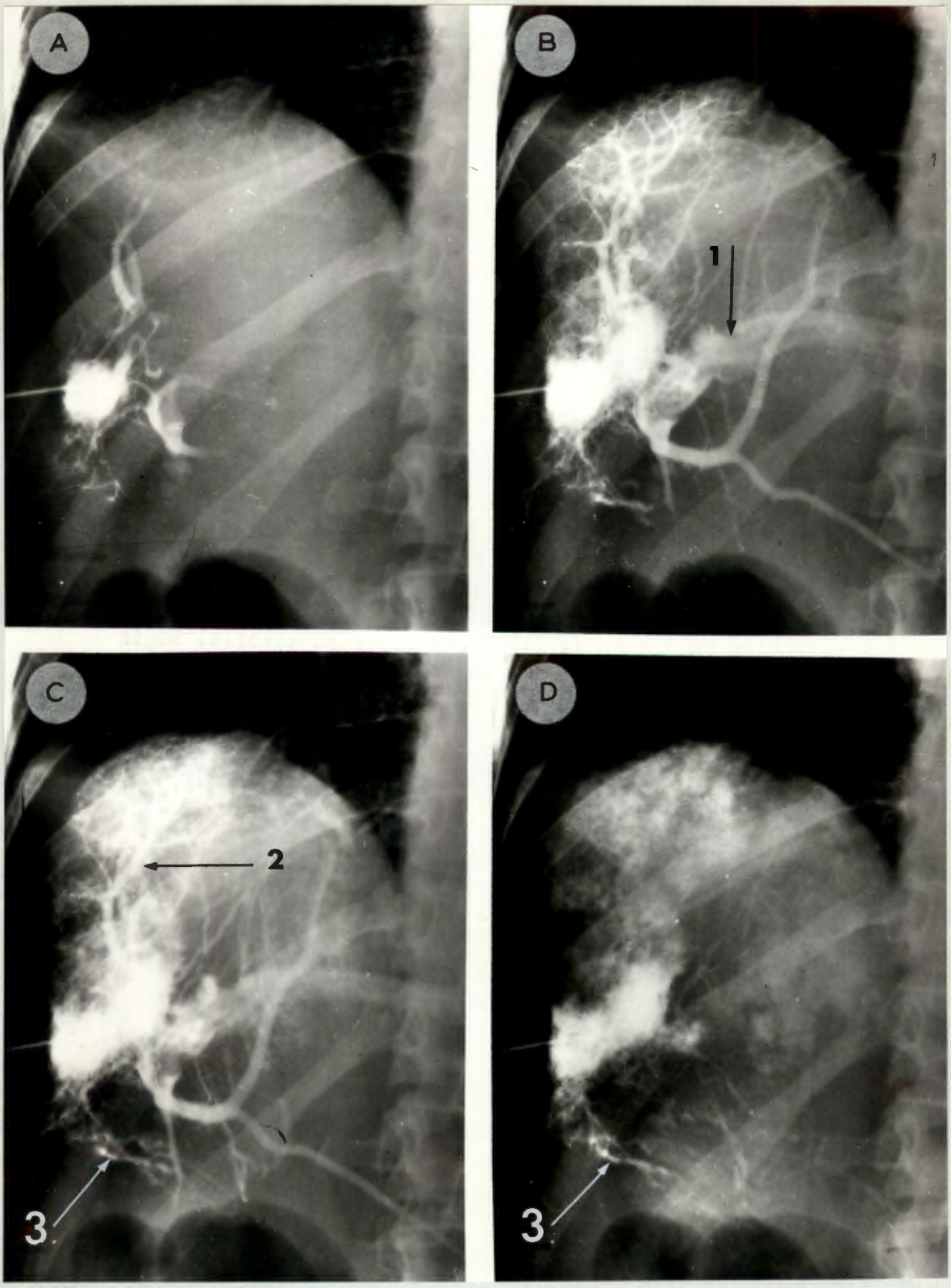
Fig: 5.34 CASE 5

Hepatography in a patient with the Budd-Chiari syndrome. Film at 4 seconds (A) shows contrast material beginning to reflux into portal radicles. At 6 and 10 seconds (B and C) a large area of the portal tree has filled including the left branch of the portal vein (1). Normal hepatic veins are not present. At 10 and 15 seconds (C and D), narrow, straight channels pass upwards towards the inferior vena cava, some through the diaphragm (2). These may be poorly opacified hepatic radicles. Inferiorly a few lymphatics pass towards the hilum (3). They are recognised by the direction of flow, slight irregularity and persistence after other vessels have emptied.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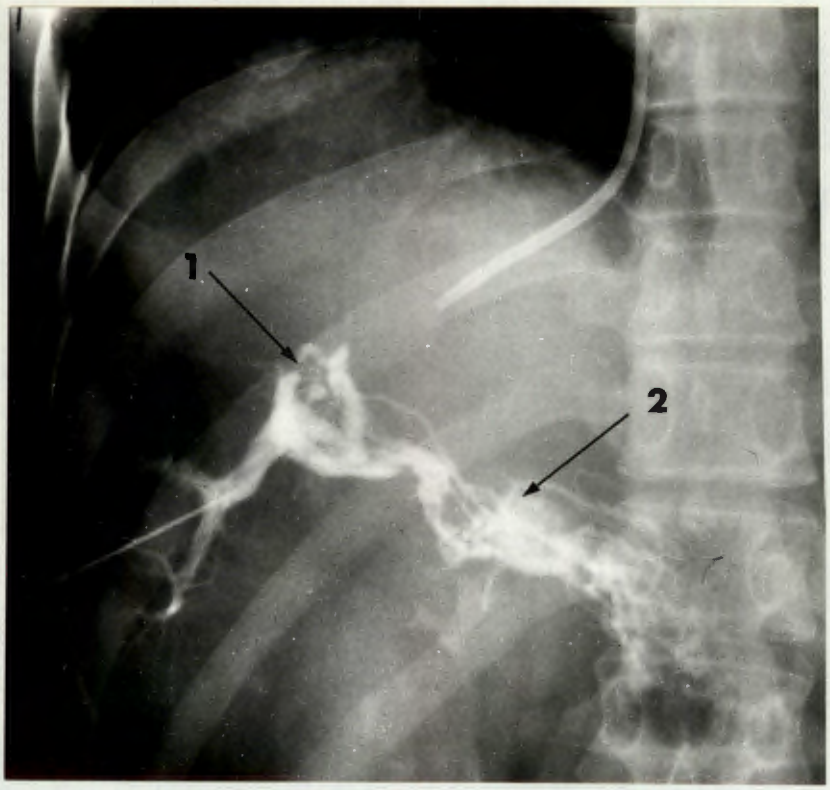


Fig: 5.35

Contrast material has been deposited in the parenchyma of the liver in a patient with haemochromatosis while a main right hepatic vein is acutely occluded with a balloon catheter which has been introduced to carry out hepatic venography to exclude a space occupying lesion (see fig. 5.3). Obstruction to the hepatic vein is shown (1). There is extensive filling of lymph channels and lymph nodes (2). There is no portal reflux.

DISCUSSION

This investigation has shown that intraparenchymal deposition of contrast material is a valuable means of examining hepatic venous outflow and of studying the lymphatics of the liver. The advantage of this technique is its ability to demonstrate haemodynamic events as well as morphological changes. In this respect it is superior to hepatic venography in which contrast medium is injected under pressure into the lumen of the vessel.

Hepatograms were carried out in three patients with the Budd-Chiari syndrome and they were abnormal in each case. The appearances were distinct from the hepatograms in 33 cases with other diseases of the liver (Table 5.2). The features were considered diagnostic in two patients (Cases 2 and 3). The important changes were delayed hepatic venous drainage, increased density of the contrast material, abnormalities of the hepatic veins and the presence of collateral vessels.

Hepatic veins and Collaterals

Each patient with the Budd-Chiari syndrome showed a different pattern. In Case 5 (Fig. 5.34), a few inconspicuous hepatic veins of narrow calibre were present and the bulk of the contrast material passed retrogradely into the portal system. In Case 2 (Fig. 5.32), the main right hepatic veins were opacified but they were abnormally narrow and completely obstructed at their entrance to the cava. In Case 3 (Fig. 5.33), a dense plexus of collateral vessels was

outlined but no normal hepatic veins were seen.

In Case 5, the predominant filling of the portal system could be explained either by a reversal of the portal flow or by a faulty injection directly into a portal radicle. The latter is unlikely in view of the substantial parenchymal deposit seen on the films and the failure to aspirate blood during insertion of the needle. Retrograde flow was probably limited to the right lobe because a large left hepatic vein was clearly seen. The evidence suggests that there was atrophy of the right lobe and great enlargement of the left. Clinically, the right lobe was impalpable while the enlarged left lobe was easily felt through an incisional hernia. The radiological point of origin of the left branch of the portal vein was significantly shifted to the right (Figs. 5.34 and 6.2), and a radioisotope scan showed activity limited to the left lobe (Fig. 6.10). The portal venogram adds further support to the absence of forward flow in the right branch of the portal vein. Whereas normal portal venograms show mainly the right branch opacified, in Case 5 (Fig. 6.2) there was no filling of the right portal tree, while the left was well seen.

The collateral vessels differed in Cases 2 and 3 because of the nature of the pathology. In Case 2, there were intralobar collateral vessels running a fairly straight course between hepatic veins which were patent as far as their ostia. The passage of blood

to adjacent veins allowed the short, obstructed segments to be circumvented. In Case 3, it is presumed that the hepatic veins were completely thrombosed and that the tortuous collaterals were either new vessels or that they represented hepatic veins which had recanalized.

Another abnormality of interest in Case 2, was the narrowing of the patent length of vein proximal to the obstruction. This was probably due to extrinsic compression by the engorged liver. Similar narrowing was seen on a hepatic venogram in Case 4 (Fig. 5.14), and at autopsy no evidence of thrombosis or fibrosis of the main vein was present.

Outflow Block

Despite the current theory that in cirrhosis portal hypertension is due to postsinusoidal obstruction, hepatography failed to show a delay in hepatic venous emptying compared with the normal. However, in heart failure, in hepatic venous thrombosis and during the Valsalva manoeuvre, there was prolonged opacification of the veins, and on this account, more densely contrasted film. In heart failure and during the Valsalva manoeuvre, the veins were of normal calibre and outline.

The role of the lymphatics in outflow obstruction

Recent observations in patients with cirrhosis have suggested the important role of increased lymph production in the pathogenesis of portal hypertension and ascites (Blomstrand et al., 1960; Dumont

and Mulholland, 1960). Dilated lymphatics have been shown at the hilum of the liver at autopsy in patients with cirrhosis, and at operations for portal hypertension (Bagenstoss and Cain, 1957). These findings have stimulated clinical interest in the lymphatic drainage in the liver. Knowledge of the mechanism of formation of liver lymph was not been substantially advanced since Starling (1894) described the unusual permeability of the hepatic sinusoids and recognised that small pressures sufficed to produce a great transudation of lymph. The causes of increased production of lymph by the liver are still obscure.

In animals, obstruction of hepatic outflow dilates the hilar lymphatics, increases the thoracic duct lymph flow (Starling, 1894) and causes a transudation of fluid at the liver surface (Brauer et al., 1959). Starling (1894) believed that the lymphatics served as a safety valve to prevent excessive pressure in the inferior vena cava and right atrium. In the light of this experimental evidence, it seemed likely that, in the Budd-Chiari syndrome, the lymphatics of the liver might function as a compensatory outflow tract. After injection of contrast material into the hepatic parenchyma, the presence of a few lymphatics in only one of three patients with extensive hepatic vein thrombosis was, therefore, unexpected. On the other hand, acute hepatic venous occlusion with a balloon catheter was immediately followed by flow through a rich network of lymph vessels and nodes (Fig. 5.35).

There is no doubt that hepatography is a satisfactory method of demonstrating the presence of augmented liver lymph flow. Although lymphatics were not shown in normal livers, they were almost invariably seen in hepatograms of patients with cirrhosis, and they were also opacified in several other disorders (Table 5.2). The failure to show increased lymph drainage in hepatic venous thrombosis might be explained by the widespread venous collateral circulation which was demonstrated by hepatic venography and hepatography. It is not clear what part the lymphatics play in compensating the hepatic outflow in longstanding hepatic venous obstruction. Gibson (1960) described dilated lymphatics in the hepatoduodenal ligament, portal tracts and capsule of the liver in patients with the Budd-Chiari syndrome, and a similar picture had been previously recorded (Jonas and Lawrence, 1954; Jorgensen, 1958). But Parker (1959) was not able to identify abnormal lymphatics in any of his eighteen cases, and long term hepatic vein occlusion in dogs does not appear to cause enlargement of the lymphatics (Widman et al., 1962).

While an acute rise in sinusoidal pressure is a potent cause of increasing hepatic lymph flow, it appears that longstanding outflow obstruction may be compensated in other ways. These findings may have wider application in chronic liver disease. For example, the increased lymph flow in cirrhosis has been conventionally ascribed to hydrostatic forces resulting from postsinusoidal

obstruction. However, it has been suggested that cirrhosis is primarily an inflammatory disorder and that the augmented lymph flow is on this basis (Moreno et al., 1963). This is supported by the lack of functional outflow obstruction shown by intra-parenchymal deposition of contrast medium in cirrhotic patients. Moreover, when there was biochemical and histological evidence of activity, lymphatic drainage was more prominent. Lymphatics have also been opacified following acute chemically indiced inflammation in dogs (Moreno et al., 1963). On the other hand, lymphatics were not present in five of the six hepatograms of patients with acute infective hepatitis in this study.

DISCUSSION OF THE COMPENSATORY VASCULAR MECHANISMS IN THE BUDD-CHIARI SYNDROME

In the Budd-Chiari syndrome, the hepatic congestion might be relieved by curtailing the blood supply to the liver or by diverting blood within the liver to bypass the obstruction (Table 5.3). The abnormal vessels seen on hepatography and hepatic venography represent some of the intrahepatic pathways by which obstruction to hepatic outflow is compensated. The extrahepatic mechanisms such as reduction of hepatic arterial and portal venous flow, reversal of portal flow and portal systemic anastomosis, are considered in Chapter 6.

Relatively little is known about the intrahepatic vascular changes which follow hepatic vein occlusion. This results in part

from the rarity of primary thrombosis of the hepatic veins in man and in part from the difficulty in inducing similar pathology in animals. Evidence obtained by several techniques, from different sources, is assembled here to give a better understanding of the alternative channels which develop (Table 5.3).

The backlog of blood might be shunted through intrahepatic collateral veins or drained via normal lymphatic pathways. While the lymphatics seem to play a relatively minor role as a compensatory outflow tract in hepatic vein thrombosis, there is a widespread proliferation of the intrahepatic venous system. Where the smallest veins are affected, blood may drain from one lobule to another via the sinusoids. Hales and Scatliff (1966) observed that in practically all parenchymal nodules in the Budd-Chiari syndrome, small vessels were so abundant as to produce an angiomatoid appearance. In veno-occlusive disease of the liver, thrombosed central veins are surrounded by new collateral channels (Bras and Hill, 1956). McClean et al. (1964) have shown similar changes in the experimental model of this disease in rats. However, in the Budd-Chiari syndrome, where the brunt of the damage falls on the medium-sized and large hepatic veins, these microscopical shunts can only have an insignificant role.

Widman et al. (1962) studied injection - corrosion vascular casts of the liver in dogs whose hepatic veins had been occluded by

TABLE 5.3

COMPENSATORY MECHANISMS IN THE BUDD-CHIARI SYNDROME

A. INTRA HEPATIC (Chapter 5)

1. Inter-lobular collaterals (Bras and Hall, 1956; Parker, 1959; McClean et al., 1964; Hales and Scatliff, 1966; Cases 1 to 4)
2. Intra-lobar collaterals (Widman et al., 1962; Hales and Scatliff, 1966; Cases 2 and 3)
3. Inter-lobar collaterals (Pietri, 1958; Burgeon and Guntz, 1959; Case 2)
4. Recanalized veins (Parker, 1959; Case 1)
5. Hepatic-systemic anastomoses (Brink and Botha, 1955; Case 5)
6. Portosystemic anastomoses (Chudacek, 1965; Hales and Scatliff, 1966)
7. Reversed portal flow -
   (a) Intrahepatic
   (b) Main portal vein

   (Maetani, 1966; Pollard and Nebesar, 1967; Case 5)
8. Increased lymph flow (Gibson, 1960; Case 5)

B. EXTRA HEPATIC (Chapter 6)

1. Reduced liver blood flow -
   (a) Portal venous
   (b) Hepatic arterial
2. Portosystemic shunts.

placing a wide-bore Teflon tube in the vena cava opposite the ostia. The majority of the animals failed to develop portal hypertension and ascites, and the vascular casts provided a convincing reason. Vessels beyond the obstructed segments had filled via collateral channels of several types. Intralobar collaterals developed as superficial and deep arcades connecting patent hepatic veins with the veins whose ostia were occluded, and interlobar collaterals developed between adjacent, normally separate, lobes through adhesions. There were also abnormal arcades of vessels, which passed dorsally and ventrally to the vena cava, joining the right and left lobes. The radiological counterpart of these collaterals, which were case in vinylite, was demonstrated by hepatic venography in Case 2. Contrast material outlined local anastomoses and also larger vessels following an arching course to connect with veins at a higher level.

In the section of hepatography, injection of contrast material into the hepatic parenchyma was also used to show these abnormal blood vessels. In Case 2, there appeared to be communication between fairly normal veins (Fig. 5.32), but in Case 3, the vessels followed a tortuous path and the pattern was quite unusual (Fig. 5.33). Some of these may have been re-canalized thrombi as described in sections of liver at autopsy (Parter, 1959). There was also resemblance to the cavernous transformation of the portal vein seen radiographically after portal thrombosis.

An injection-corrosion vascular cast has been prepared in one patient with thrombosis of the inferior vena cava and hepatic veins (Hales and Scatliff, 1960). The findings were of special interest in relation to the unusual network patterns seen on hepatic venography (Figs. 5.11 to 5.17). The vinylite casts showed numerous small vessels which pursued a winding "cross-country" course with no normal pattern of portal venous or hepatic venous arborization. To quote the authors; "these intrahepatic collaterals often exhibited rather abrupt variation in diameter from segment to segment, and separate limbs often communicated with each other. This resulted in an appearance of a loose plexiform mesh traversing the substance of the liver, unrelated to any normal vascular distribution. It was a pattern we have never seen in cirrhotic livers of the usual portal, postnecrotic or even congestive (cardiac) type." This description could be applied, without amendment, to the radiological appearances seen in several patients with the Budd-Chiari syndrome in this study. It seems highly probable that the vessels demonstrated by the corrosion cast technique are the same as those which constituted the unusual spider webs network on the hepatic venogram.

Burgeon and Guntz (1959) made a careful study of the anatomy of the liver and applied their findings to interpret some unusual radiographs in patients with partial thrombosis of the hepatic veins and inferior vena cava. Their main thesis was that separate

drainage of the several hepatic veins into the cava at different levels would allow reversal of flow in obstructed veins, followed by the development of interlobar collaterals and the exit of hepatic blood through lobes in which the veins remained patent. They drew special attention to the caudate lobe which drains via multiple, small veins into the infrahepatic segment of the cava and which is therefore seldom obstructed. If the main veins are occluded, the caudate lobe may become greatly enlarged and function as the principle route of egress.

Hess (1905) was the first to emphasize this marked compensatory hyperplasia of the caudate lobe in the Budd-Chiari syndrome. More than twenty-five examples have since been described. Parker (1959) and Gibson (1960) recently discussed this phenomenon, including a list of references to case reports. The best documented clinical study was reported by Caroli et al. (1958). The patient had polycythaemia vera. Peritoneoscopy showed a rather small liver which was a dark slate colour. Projecting from behind the inferior border of the liver was a rounded mass which looked like a large spleen. Colour photographs showed a striking picture. The purplish caudate lobe stuck out prominently below the small left and right lobes which were separated by a deep cleft. The authors referred to it as the, "trilobed liver caused by the development of a pseudo-tumour in the caudate lobe". They pointed out the danger of attempting

to excise the mass. Far from being abnormal, it was, in fact, the only part of the liver maintaining drainage of hepatic venous blood.

By the same mechanism, any segment of liver which retains a patent hepatic vein may become greatly enlarged. Parker (1959) described a patient in whom a single tributary to the upper part of the right lobe was spared, and this resulted in a localised mass, projecting from the liver surface.

To further illustrate these compensatory functions of the hepatic venous system, Burgeon and Guntz (1959) presented brief case records. They distinguished patients with purely intrahepatic thromboses from those with obstructions of the inferior vena cava. In two patients with a hydatic cyst pressing on the confluence of the hepatic veins they inadvertently injected the left lobe of the liver while attempting a splenic venogram. They demonstrated layers of anastomotic areas which united branches of the left lobe with the middle lobe.

In two other patients in whom there was a localized obstruction of the intrahepatic portion of the cava, cavography showed retrograde flow through the inferior right hepatic vein. An anastomosis with the principal right hepatic vein carried blood from the inferior vena cava through the liver and back into the cava above the block. A patient with similar interlobular

anastomosis was described by Jonas and Lawrence (1954).

Several other routes of collateral blood flow have been recorded but they are probably of less importance. Anastomoses between the capsular veins in the liver and veins in the diaphragm, hepatic ligaments and adhesions have long been recognised at autopsy (Thompson and Turnbull, 1912; Hutchison and Simpson, 1930; Thompson, 1947; Gibson, 1960). Injection studies showed that they arose mainly from bizarre intrahepatic vessels, but a few were derived from normal portal veins (Hales and Scatliff, 1966). Intrahepatic portal-systemic shunts have been demonstrated by portal venography (Chudacek, 1965), and vessels arising from peripheral portal branches have also been shown to leave the liver via the porta hepatis, falciform ligament and fossa overlying the vena cava (Hales and Scatliff, 1966).

There is, therefore, evidence not only of a widespread intrahepatic collateral blood flow in the Budd-Chiari syndrome, but also of portal-systemic and hepatic-systemic anastomoses which arise within the liver. The role of the pre-hepatic diversion of blood is discussed in Chapter 6.

CONCLUSIONS

The aims of the investigations and review in this chapter were -

1. To determine the value of contrast radiography of the hepatic veins in the diagnosis of the Budd-Chiari syndrome.
2. To demonstrate radiographically the presence of venous and lymphatic collateral vessels and to assess their significance as compensatory mechanisms in the Budd-Chiari syndrome.

The conclusions are as follows -

1. Hepatic venography and functional hepatography are essential for the accurate diagnosis of the Budd-Chiari syndrome. Thrombosis of the hepatic veins presents a characteristic radiographic appearance, and the position and extent of the hepatic vein occlusions can be precisely determined.
2. Abnormalities of the main hepatic veins, such as obstruction, narrowing, stenosis and irregularity, can be demonstrated radiographically.
3. The small vessels communicating with the main hepatic veins create an unusual network pattern which is distinct from the appearances in other forms of liver disease. This radiographic pattern represents a venous plexus of entirely new formation.
4. A widespread collateral circulation was evident. Interlobular, intralobular and interlobar vessels were shown to bypass the

obstruction. Collation of the data from this investigation, animal experiments and other human studies, reveals the importance of these diversionary channels within the liver in relieving the congestion caused by hepatic vein thrombosis. Blood is shunted through segments of liver maintaining a normal drainage; and these areas may enlarge while others atrophy.

5. Delayed drainage and increased density of contrast material in the hepatic veins, as shown by hepatography, is easily distinguished from the stasis in other causes of outflow obstruction (see also Chapter 9).

6. Hepatography is a satisfactory method for showing increased lymph flow in many varieties of liver disease but lymphatic drainage in the Budd-Chiari syndrome was not prominent as assessed radiographically.

CHAPTER 6

THE HEPATIC BLOOD SUPPLY IN THE BUDD-CHIARI SYNDROME

A better understanding of the vascular compensations in the Budd-Chiari syndrome might be obtained by measurement of total hepatic blood flow, determination of the hepatic arterial and portal venous components, and assessment of differences in regional liver blood flow. W th the exception of one estimate of total hepatic blood flow, reported in Chapter 7, none of these procedures has been attempted in patients with hepatic vein thrombosis.

There is no simple and accurate means of measuring blood flow through the liver. However, as an alternative approach to examination of the hepatic blood supply, radiographic and radio-isotope techniques may be of value. They are able to indicate the approximate rate and direction of flow, and they can also define anatomical changes in the hepatic vessels and in the liver parenchyma.

In this chapter, the diagnostic potential in the Budd-Chiari syndrome of portal venography, coeliac axis arteriography and isotope scanning has been assessed, and the observations on compensatory and collateral blood flow dealt with in Chapter 5 have been extended.

METHODS

Portal venography was performed by percutaneous splenic puncture (Turner et al., 1957). Selective coeliac axis arteriography was carried out via the femoral artery (Kreel and Williams, 1964). Hepatic scintiscans were recorded on a Picker Magnascanner. Scanning was commenced 20 minutes after an intravenous injection of 150 microcuries of colloidal radio-gold (Au-198). Scanning speed and channel width were 60 cm/minute and 310 - 410 keV respectively. Scans were recorded supine as coloured dots or by exposing radiographic film.

RESULTS

PORTAL VENOGRAMS (Figs. 6.1, 6.2 and 6.3).

In two patients (Cases 4 and 6), the contrast material was injected into the spleen. In Case 5, the portal system was opacified during the venous phase of coeliac axis arteriography. The portal vein was obstructed in Case 6, but in Case 4 it was patent, though poorly filled because of a blocked splenic vein. Both lesions were confirmed at autopsy. The splenic and portal veins were normal in Case 5.

There was no filling of the intrahepatic portal system in Case 6, and only the left branch of the portal vein was seen in Case 5. In Case 4, the portal tree was distorted; the main trunks were narrow and stretched, and the peripheral branches were absent.

The left lobe and part of the right lone were not opacified. In Cases 4 and 6, there were many collateral vessels arising mainly from the tributaries of the splenic vein. Dilatation and increased density of vessels were absent in all cases. Delay in venous drainage was not observed.

SELECTIVE ARTERIOGRAMS (Figs. 6.4 and 6.5)

Selective coeliac axis arteriography was performed in Cases 5 and 6. In both, the hepatic artery was small for the size of the liver, and branches were reduced in number and of fine calbire. The arteries supplying the spleen and stomach were increased in size. In Case 6, the vessels in the right lobe of the liver were stretched and displaced, producing the impression of multiple space occupying lesions in close proximity. The left lobe and the lower portion of the right lobe were relatively avascular and did not show this pattern. In Case 5, there was an area in the centre of the liver with splayed vessels presenting an appearance suggestive of a space occupying lesion. The liver remained opaque for more than 15 seconds. The venous phase, showing the portal vein, has been described in the previous paragraph.

SCINTILLATION SCANS (Figs. 6.7 through 6.11)

Scans were recorded in five patients (Cases 2 to 6) and they were all abnormal. In Cases 3 to 6 the striking feature was the

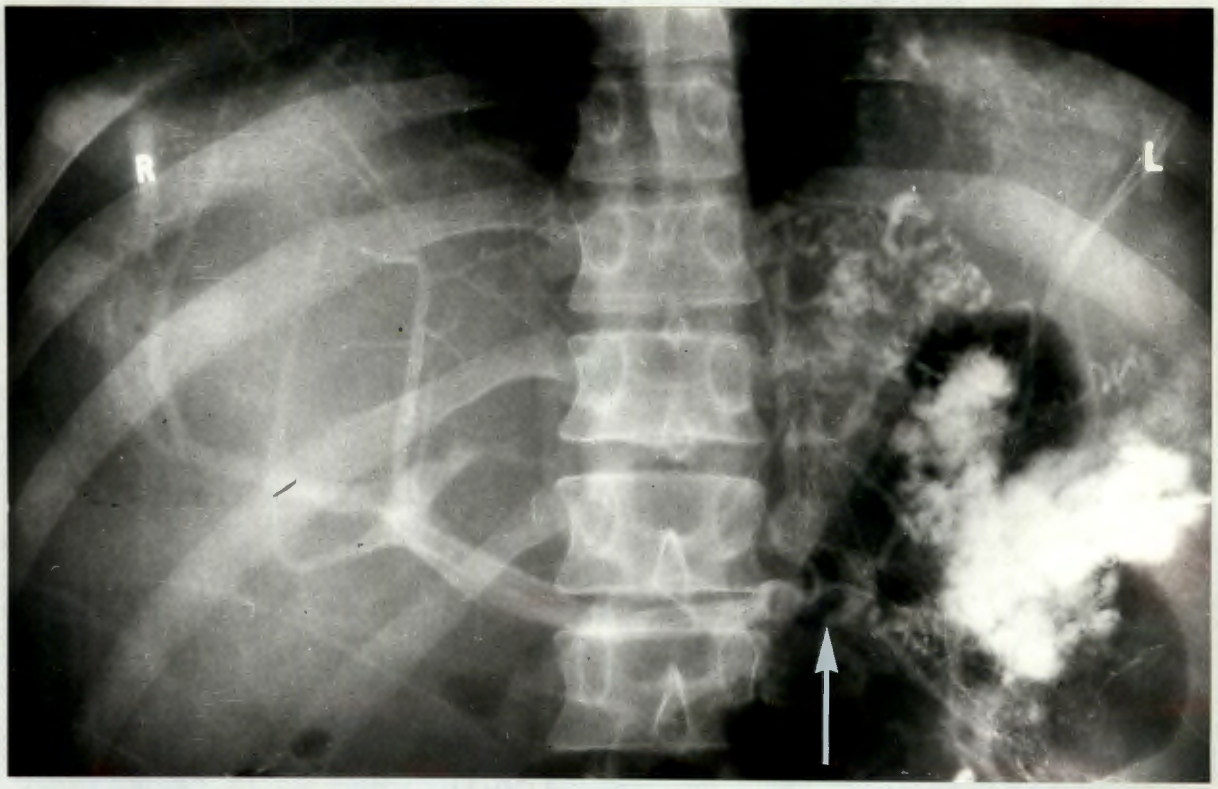


Fig: 6.1 CASE 4

The contrast material has been introduced into the spleen. Obstruction of the splenic vein is shown (arrow). Many collateral vessels are present mainly in the gastric area. The portal vein has filled via the collateral vessels and on this account it is not well opacified. The portal vein is not dilated. The intrahepatic portal branches appear narrow and stretched and their branching is sparse. Vessels in the left lobe and the lower part of the right lobe are not opacified.

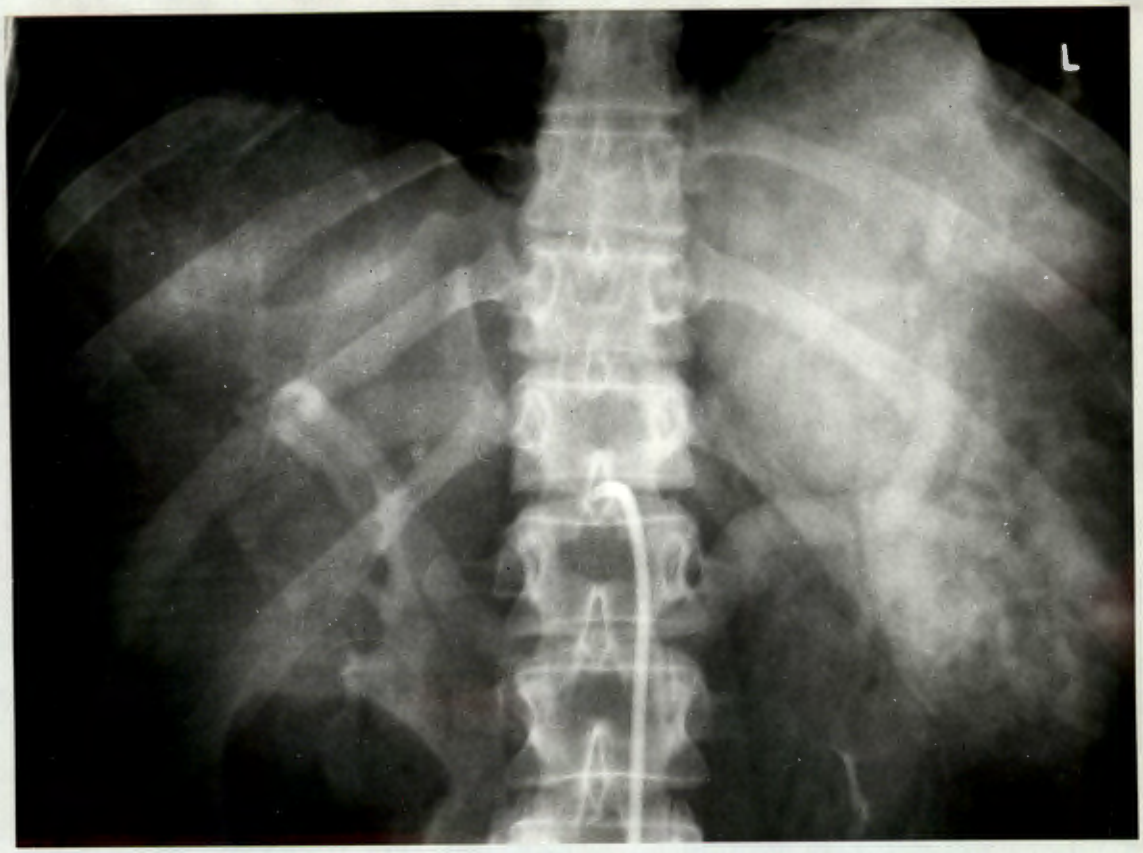


Fig: 6.2 CASE 5

The portal and splenic veins are normally outlined during the venous phase of a selective splenic artery injection. The left branch of the portal vein is opacified but there is no filling of the right main branch. No collateral vessels are demonstrated.

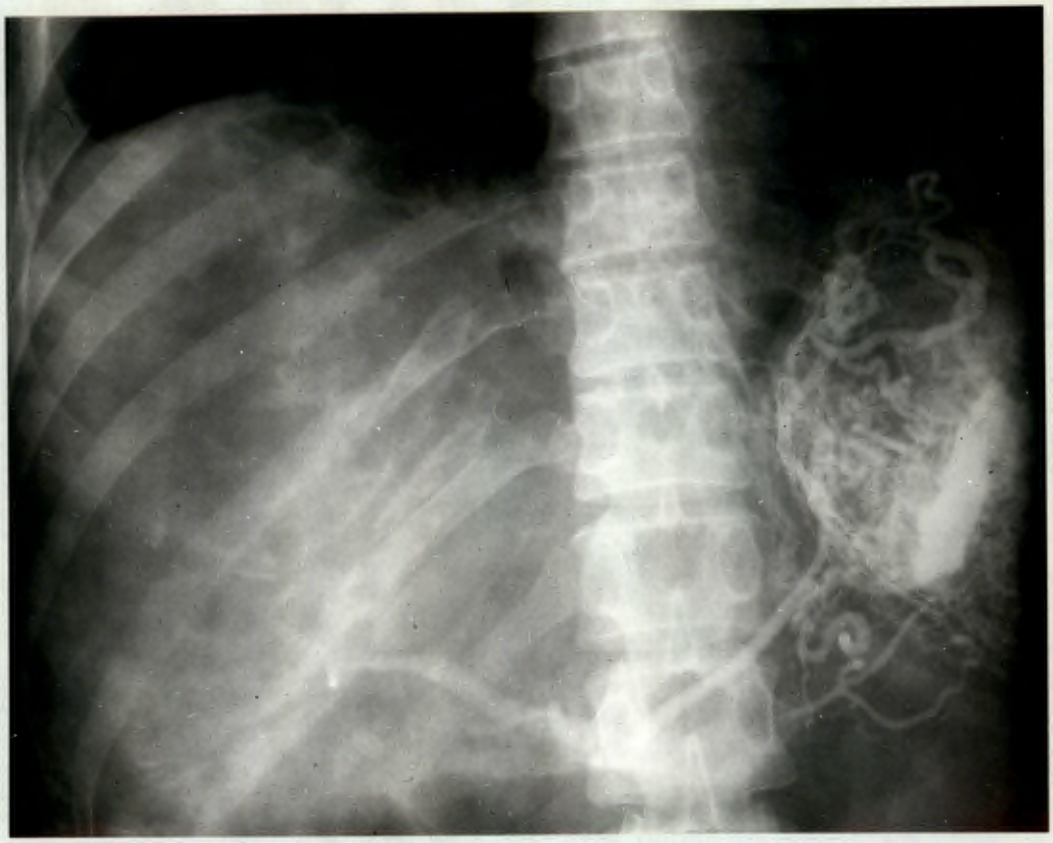


Fig: 6.3 CASE 6

Contrast material has been injected into the spleen. Two small splenic veins are draining into a narrow portal vein which is obstructed before entering the liver. No intrahepatic portal branches are filled. There are many collateral vessels arising from the splenic vein.

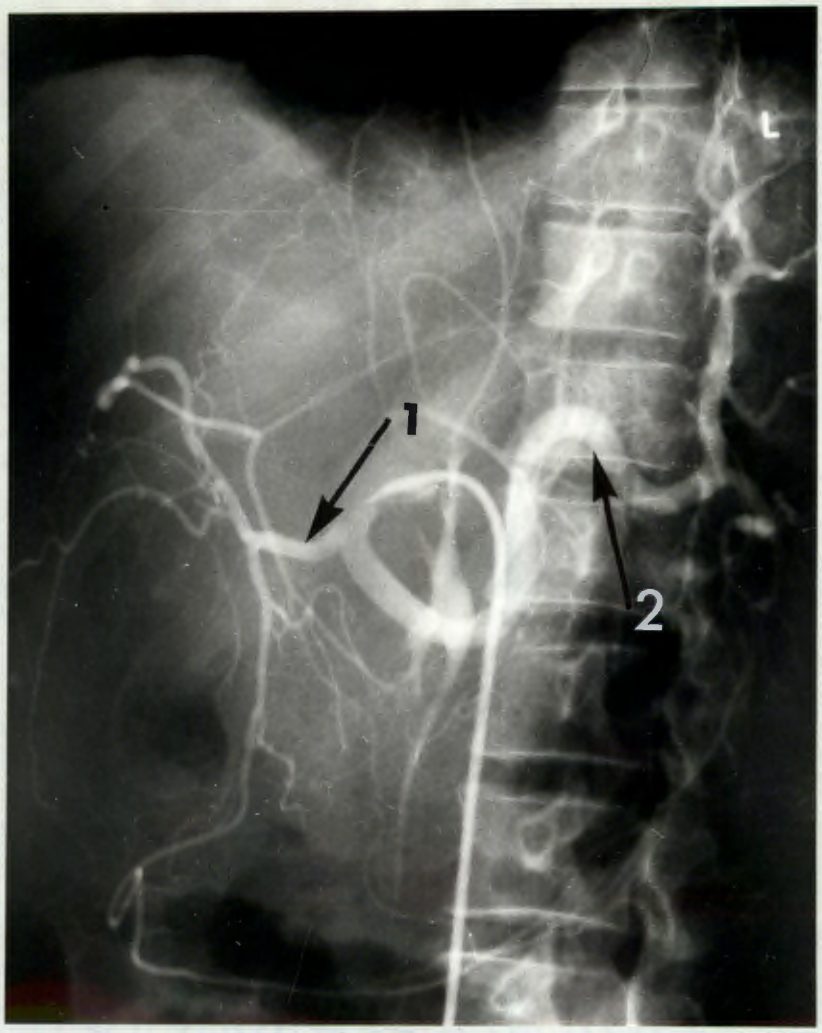


Fig: 6.4 CASE 5

The catheter is shown in the coeliac axis. The narrow calibre of the hepatic artery (1) is in contrast to the large splenic artery (2). Several vessels seem stretched and displaced. The arterial branches are sparse relative to the size of the liver.

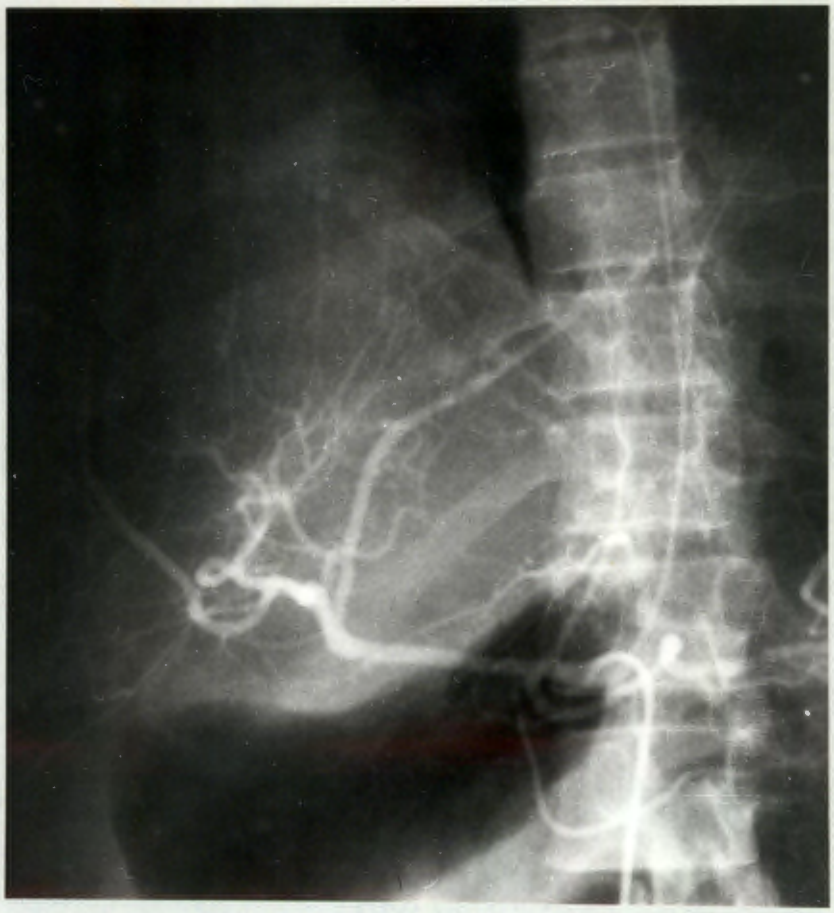


Fig: 6.5 CASE 6

Injection of contrast material shows a hepatic artery of narrow calibre. Many branches are displaced and give the impression of multiple space occupying lesions in close proximity. The regular branching of a normal hepatic arteriogram is entirely absent.

absence of radioactivity over the right lobe (Figs. 6.8 to 6.11). The greatest density was over the central zone of the liver, and the lateral aspect of the left lobe was never outlined. In fact, none of the hepatic margins was well delineated by the scans. The borders of the radioactive image faded off on all aspects unlike the clear definition of the liver seen in a normal scan. Within the area of uptake, the radioactivity was homogeneous. A normal hepatic scan is included for comparison (Fig. 6.6).

There was slight splenic uptake in Case 4 (Fig. 6.9). In Case 5 (Fig. 6.10), almost all the radioactivity was concentrated in a portion of the left lobe. There was no uptake in the right lobe or the spleen. The scan was repeated in this patient by injecting the radiogold directly into the hepatic artery and an identical result was obtained. Although the uptake was patchy in Case 2 (Fig. 6.7), both right and left lobes were fairly well outlined.

DISCUSSION

PORTAL VENOGRAMS

Portal venograms have been reported in twenty-two cases of the Budd-Chiari syndrome, including three patients in this series (Table 6.1). Unfortunately a detailed description has not been given in every case. The intrahepatic portal branches may be perfectly normal (Dupuy et al., 1964; Bonnette et al., 1965;

TABLE 6.1

PORTAL VENOGRAMS IN THE BUDD-CHIARI SYNDROME

Year	Author	Findings
*1955	Lebon et al.	Good contrast of normal portal tree, patent portal and splenic veins
*1956	Fitzgerald et al.	Operative mesenteric portography showed greatly distended portal vein and primary branches
1957	Ekstrom and Hagberg	Prolonged opacification of the liver
1957	Rosch et al.	Prolonged opacification of intra-hepatic portal tree; dilated and tortuous splenic portal veins
1958	Case records of the Massachusetts General Hospital	Right branch of portal vein displaced upwards and backwards; portal and splenic veins normal
1962	Demarty and Le Peltier	Absence of venous branching in right lobe; exceptional contrast in left lobe
*1962	Erlik et al.	Operative mesenteric portography normal
1962	Haeffner et al.	Intra-hepatic portal branches narrow, straight and well contrasted; portal vein narrow; profuse collateral flow
1963	Dykes et al.	Patent portal vein; collaterals present
1964	Dupuy et al.	Intra-hepatic portal tree normal except prolonged opacification; portal vein normal; collaterals present
1964	Leger et al.	Intra-hepatic portal tree partially filled on the right; no opacification of left lobe
1965	Bonnette et al.	Operative mesenteric photography showed many collaterals; portal vein normal
1965	Chudacek	Intra-hepatic portal branches stretched; prolonged opacification of splenic vein
1965	Chudacek	Normal intra-hepatic portal branches; entire portal system showed prolonged opacification, especially evident in left lobe
1965	Chudacek	Intra-hepatic portal branches normal except density increased; some flow into intercostal veins. Splenic vein dilated and tortuous
*1965	Ludwick et al.	Operative mesenteric portography showed normal portal vein; no filling of splenic vein; normal intra-hepatic portal tree on left; no filling of right lobe
✗1966	Case records of the Massachusetts General Hospital	Patent portal and splenic veins; reflux into superior mesenteric vein
1966	Hales and Scatliff	Intra-hepatic portal branches not seen; portal vein narrow; splenic vein dilated and tortuous; many collaterals present
1967	Schreiber and Gonzales	Narrow portal and splenic veins; collaterals present
Case 4	Present study	Blocked splenic vein; patent portal vein; intra-hepatic portal tree stretched and displaced; collaterals present
✗Case 5	Present study	Normal portal and splenic veins; right branch of portal vein not opacified, left normal
Case 6	Present study	Narrow and blocked portal vein. Intra-hepatic portal tree not seen. Collaterals present

* Operative portograms

✗ Venous phase of coeliac axis arteriogram

Chudacek, 1965), and one patient was described in whom post mortem injection of the portal vein showed a normal pattern (Catinat et al., 1960). But there is frequently reduction in calibre and paucity of branching which is indistinguishable from the changes in cirrhosis (Ruzicka, 1964; Chudacek, 1965). Four portal venograms have shown narrowing, straightening, stretching and displacement of branches (Case Records of the Massachusetts General Hospital, 1958; Haeffner et al., 1962; Chudacek, 1965; Case 4).

The most striking abnormalities of the portal venogram are the unusually dense contrast and the prolonged opacification of the intrahepatic portal vein branches (Ekstrom and Hagberg, 1957; Rosch et al., 1957; Denmarty and le Peltier, 1962; Haeffner, 1962; Dupuy et al., 1964; Ruzicka, 1964; Chudacek, 1965), although these features were not seen in the patients in this study. Liver enlargement on the portal venogram is prominent, but most authors have failed to comment on this aspect. Where illustrations are available, hepatomegaly has been invariable. Uneven filling of the portal tree, especially failure to visualize branches in one or other lobe, has been seen on five occasions (Demarty and le Peltier, 1962; Leger et al., 1964; Ruzicka, 1965; Ludwick et al., 1965; Case 5). A notable example was the patient of Demarty and le Peltier (1962) who showed no venous branches on the right, while the left lobe was densely contrasted

for two minutes after the injection.

Some of these abnormalities can be explained by the uneven congestion and perfusion of the liver which follow hepatic vein occlusion. Prolonged opacification and increased density of portal branches is not a surprising consequence of hepatic outflow obstruction.

The failure to outline segments of the portal tree may be due either to localized portal thrombosis or to areas of reversed flow. Ruzicka (1964) suggested that reduction of portal filling was due to stasis caused by regional hepatic vein thrombosis. However, this would seem to be faulty reasoning because hepatic vein obstruction would tend to produce dense and prolonged opacification (Demarty and le Peltier, 1962), and not absence of filling. Indeed, complete cessation of the circulation in an area of liver would lead to infarction, and this is a rare event. Moreover, of the eight cases of infarction reported, four have had extensive portal thrombosis (Parker, 1959).

There is no theoretical objection to the concept of reversed flow, provided that the portal vein is patent. By injecting contrast material through a hepatic vein catheter, the portal vein has been shown to act as the outflow tract after a side-to-side portcaval shunt in cirrhosis (Reynolds and Redeker, 1965). Simiarly, in dogs, complete experimental obstruction of hepatic

veins causes reflux into the portal vein of contrast material injected into the hepatic artery (Rousselot et al., 1964; Maetani, 1966). Parker (1959) has commented on the histological evidence for reversed flow. "In a lobule in which the hepatic artery was the afferent and the portal vein the efferent channel, it is unlikely that an adequate circulation would be maintained in the central zone, for the hepatic arterioles most probably open into the periportal sinusoids. Severe damage to, and probably destruction of, the centrilobular sinusoids would therefore be expected, and these changes are indeed often found.

Reversal of flow in the Budd-Chiari syndrome is not merely hypothesis. Pollard and Nebesar (1967) showed retrograde filling of the portal vein by selective hepatic arteriography in a case of hepatic vein thrombosis. Confirmation was obtained by injection of the splenic artery. The contrast material opacified the splenic vein but stopped short at the portal vein which was known to be patent. They concluded that when all the hepatic veins were obstructed, the major route of egress of hepatic arterial blood was via the hepatic sinusoids and back through the portal system. Flow then continued via gastric, oesophageal and mesenteric collaterals to the systemic system.

In Case 5, there was evidence to suggest an intrahepatic reversal of portal flow. Hepatography after intra-parenchymal

injection into the right lone showed the contrast material draining mainly into the left branch of the portal vein (Chaoter 5). A similar appearance was present on the portal venogram (Fig. 6.2) which showed all the contrast material from the main portal trunk passing into its left branch.

Portal venography has shown several abnormalities of the extra-hepatic portal system. The duration and density of the contrast material in the portal and splenic veins may be increased (Demarty and Peltier, 1962; Chudacek, 1965), and dilatation and tortuosity of the splenic vein has been described (Fitzgerald et al., 1956; Chudacek, 1965; Hales and Scatliff, 1966). On the other hand, there are three reports of a narrow portal vein which might have been due to partial thrombosis (Haeffner et al., 1962; Hales and Scatliff, 1966; Schreiber and Gonzales, 1967). Total obstruction by thrombus was present in the splenic vein in Case 4, and in the portal vein in Case 6. Both findings were confirmed at autopsy. Portal vein thrombosis is found at autopsy in 20 per cent of cases (Parker, 1959) so that its infrequency on splenoportography is surprising.

It has been consistently stressed that compensation in the Budd-Chiari syndrome is achieved by extrahepatic shunts through which portal venous blood bypasses the liver (Gee, 1871; Nishikawa, 1918; Hutchison and Simpson, 1930; Gibson, 1960). Portal and

splenic collateral vessels have been demonstrated in 10 portal venograms and they indicated no more than the presence of portal hypertension. The proportion of shunted flow is unknown and prograde filling of the portal vein argues against reversal of portal blood flow in these cases.

SELECTIVE ARTERIOGRAMS

Portosystemic shunts, both inside and outside the liver, and reversed portal flow, provide channels for the diversion of inflowing blood from the congested sinusoids. Reduction in the arterial blood flow to the liver may be a further compensation but the evidence is conflicting. On the ~~other~~ one hand, the hepatic artery has been shown to be small, radiographically (Figs. 6.4 and 6.5), and, on the other, corrosion cases have demonstrated enlargement of the hepatic arterial diameter and the injectable arterial bed (Hales and Scatliff, 1966). Animal experiments have also been inconclusive. Increased tension within the liver causes a reduction in hepatic blood flow in rats (Brauer, 1959). Hepatic vein ligation in dogs produces an early, profound fall in portal venous and hepatic arterial flow, but in the chronic phase both approach the control values (Maetani, 1966).

Selective coeliac axis arteriography has been reported in only three documented cases of the Budd-Chiari syndrome apart from the two recorded here (Pollard and Nebesar, 1967).

Opacification of the hepatic and splenic arterial trees serves several useful purposes. In the late venous phase, the splenic and portal veins may demonstrate reversal of blood flow and collateral vessels, changes in haemodynamics which have already been discussed in relation to portal venography. Hepatomegaly is easily seen, and congestion of the liver produces an intense and prolonged hepatogram phase (Pollard and Nebesar, 1966; Case 5). Depayed passage of contrast material through the liver has also been a feature of portal venography and hepatography (Chapter 5), and it is a valuable pointer to the diagnosis of hepatic outflow obstruction.

The special value of hepatic angiography is the displacement of vessels which draws attention to underlying space occupying lesions. Pollard and Nebesar (1967) reported a 52-year old woman in whom a coeliac axis injection showed stretching and semi-lunar displacement of intrahepatic arteries. In the late arterial phase, the liver had a "swiss-cheese" appearance with many radiolucent areas. Autopsy revealed adenocarcinoma of the pancreas, metastatic to the liver.

However, arteriograms in the Budd-Chiari syndrome need to be interpreted with caution. In four of the five cases, arteries to large areas of liver failed to fill, although no other evidence of a space occupying lesion was evinced. In Case 6 (Fig. 6.5), there

Fig: 6.6

Scintillation scan of a normal liver showing a well demarcated edge. Equal uptake of radioactivity by all lobes produces a homogenous appearance. The costal margin is faintly outlined in red.

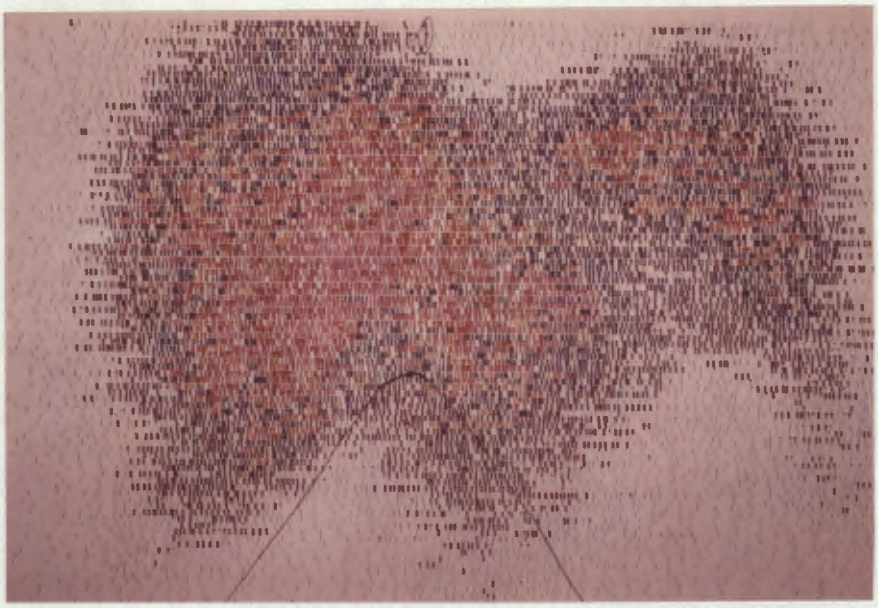
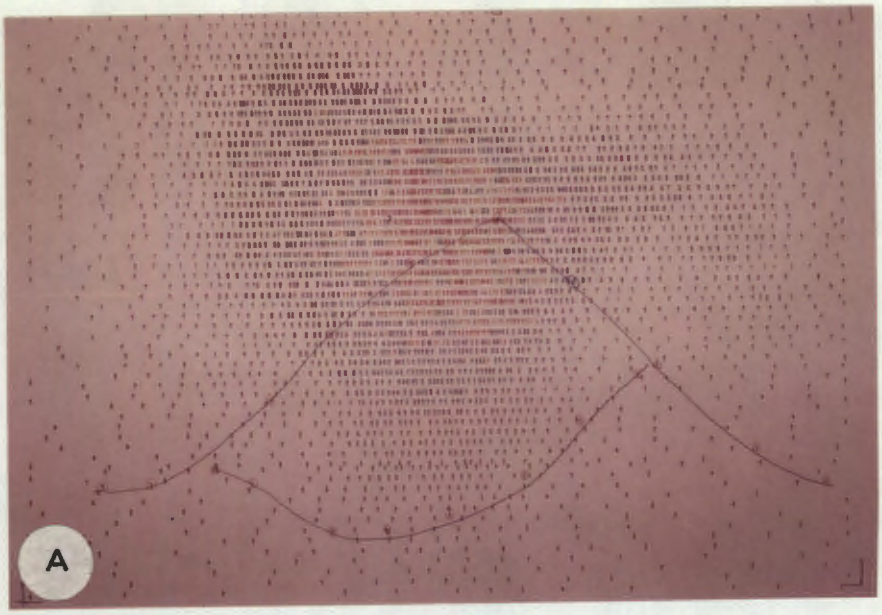


Fig: 6.7 **CASE 2**

Liver scan in the Budd-Chiari syndrome. Both the right and the left lobes are moderately well outlined. The radioactivity is patchily distributed. There is notable enlargement of the left lobe of the liver. No splenic uptake is present.



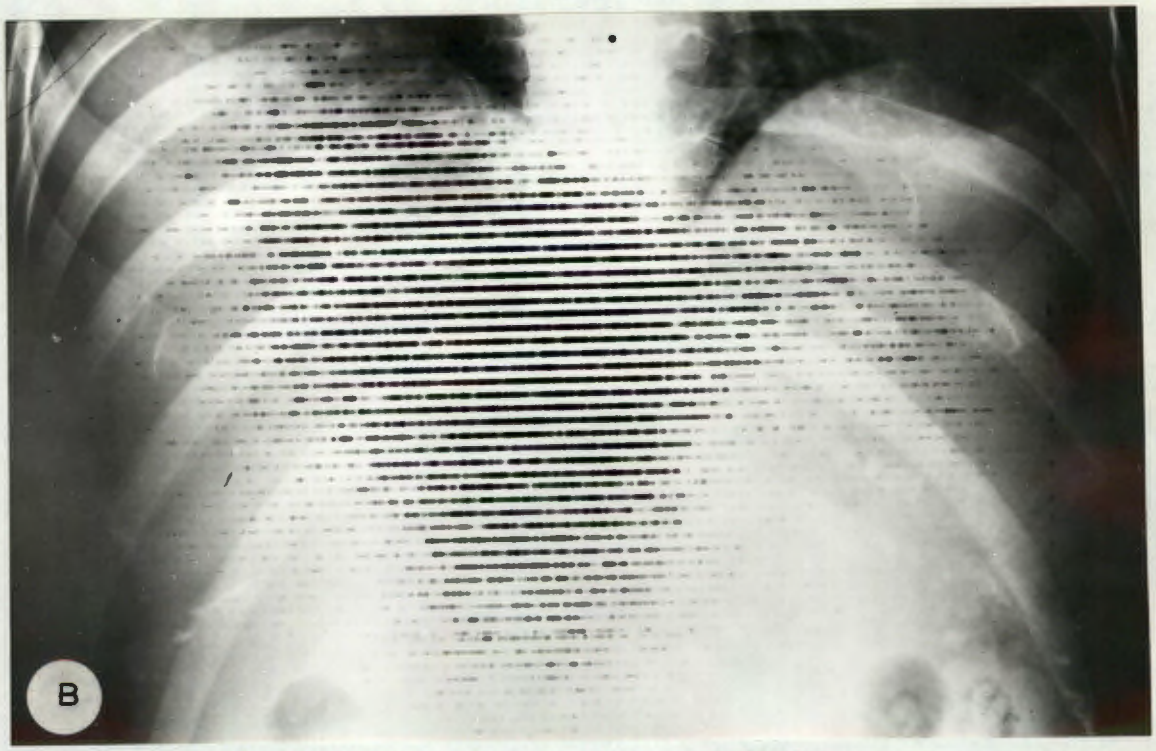


Fig: 6.8 **CASE 3**

Liver scan in the Budd-Chiari syndrome. The radioactivity is densest over the central area of the liver. None of the hepatic borders is outlined. There is scanty uptake by the right lobe. A colour (A) and a monochrome scan (B), are shown. They were simultaneously recorded.

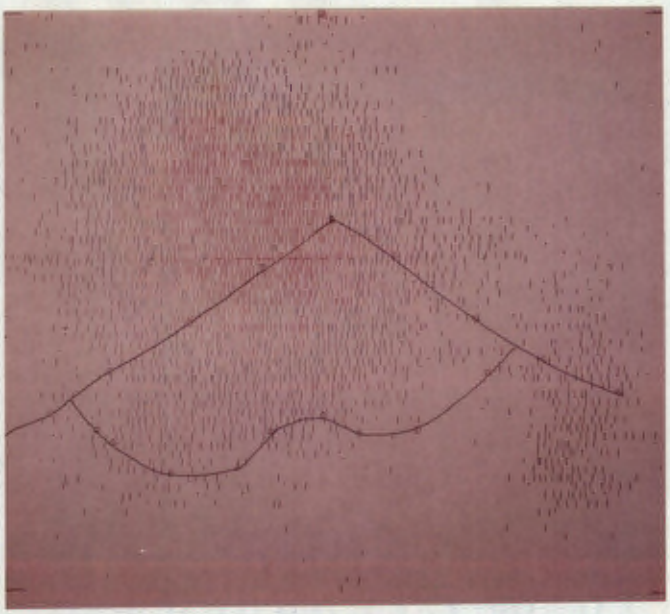


Fig: 6.9 CASE 4

Liver scan in the Budd-Chiari syndrome. Radioactivity is again limited to the central area of the liver. There is slight splenic uptake. The rib margins and the liver edge are drawn in black.

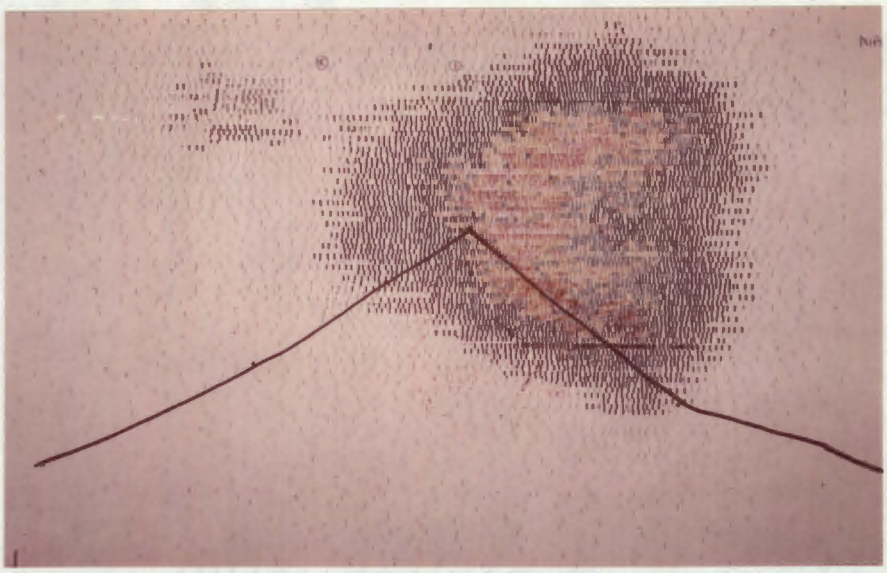


Fig: 6.10 **CASE 5**

Liver scan in the Budd-Chiari syndrome. Radioactivity has been taken up by a part of the left lobe of the liver. The rib margins are drawn in black.

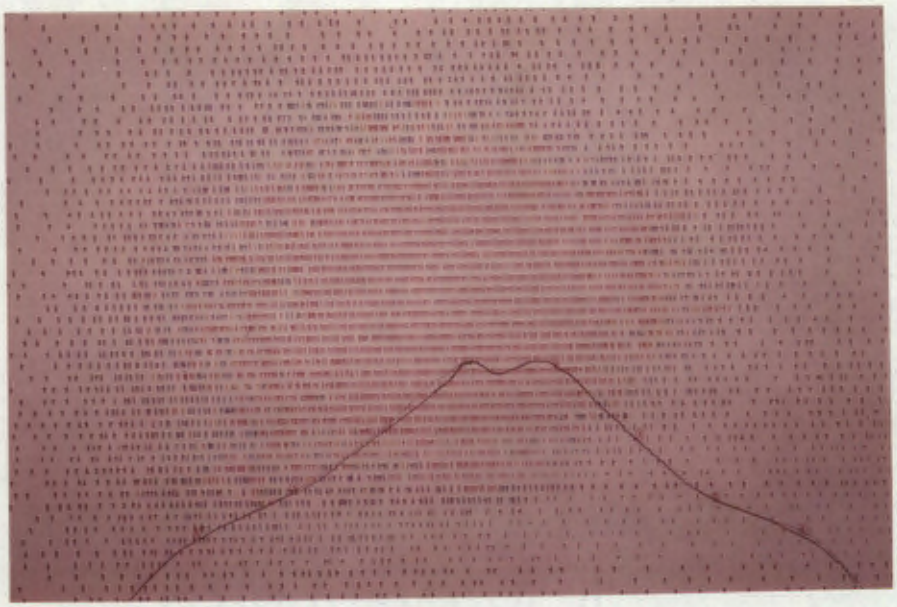


Fig: 6.11 **CASE 6**

Liver scan in the Budd-Chiari syndrome. Radioactivity is again limited to the central area, and none of the margins of the liver is outlined. There is no splenic uptake.

was displacement of many branches, giving the impression of multiple space occupying lesions in close proximity. At autopsy there were no tumours present so that distortion of the vascular pattern in the Budd-Chiari syndrome may be related to areas of lobular congestion rather than to neoplastic lesions.

SCINTILLATION SCANS

The main value of scintillation scans in liver disease is to demonstrate the presence and position of space occupying lesions. Although the five scans in this study were distinctly abnormal, the features of space occupying lesions were absent, and autopsy in two cases showed only the pathological changes of hepatic vein occlusion. The abnormalities in the Budd-Chiari syndrome were more severe than, and differed from, the mottled scan of cirrhosis. Except in Case 2 (Fig. 6.7) the radioactivity over the right lobe was absent. Most of the radioisotope was over the central portion of the liver, presumably in the middle and caudate lobes. These features have not been noted in the few previously reported scans in the Budd-Chiari syndrome. Some were recorded as normal (Nicollof et al., 1964; Case Records of the Massachusetts General Hospital, 1965), and others showed uneven radioactivity over the liver (Clinico-pathological Conference, 1965; Ludwick et al., 1965).

Uptake of colloidal gold (Au-198) by the liver depends on an intact blood supply and normal function of the Kupffer cells. In

hepatic vein thrombosis it is likely that the vascular aberration is responsible for the peculiar pattern of the scan. Some of the features already describedm such as reversed portal flow intrahepatic portal systemic shunts and blank areas on hepatic arteriography would account for lack of blood supply to large areas of the lover. Experimentally, ligation of the left hepatic vein caused an immediate fall in the uptake of colloidal gold in the occluded lobe to 30 per cent of that in the open lobe (Maetani, 1966). Finally, the marked abnormality of bromsulphthalein retention in the Budd-Chiari syndrome, when other modalities of liver function are only moderateby impaired, also points to a vascular rather than a hepatocellular basis to these changes.

The prominence of the radioactivity over the middle of the liver probably relates to the remarkable compensatory hyperplasia which may occur in the caudate lobe, and the important role which this central portion of the liver plays in maintaining the outflow of blood (Chapter 5).

CONCLUSIONS

The aims of the investigations and review in this chapter were -

1. To assess the value of coeliac axis arteriography, portal venography and isotope scintiscans in the diagnosis of the Budd-Chiari syndrome.

2. To obtain an understanding of compensatory vascular changes in the Budd-Chiari syndrome, using these techniques.

The conclusions are as follows -

1. Portal venography, coeliac axis arteriography and isotope scanning are valuable ancillary methods in the diagnosis of the Budd-Chiari syndrome.
2. Hepatic vein occlusion may cause increased density of contrast material and prolonged opacification of vessels in the liver on portal venography and hepatic arteriography.
3. The portal venogram shows changes similar to those in cirrhosis, and both the portal venogram and the hepatic arteriogram may reveal avascular areas of liver infrequently seen in other disorders.
4. Reversal of blood flow in the portal vein acts as a compensatory mechanism in some cases.
5. Prolonged opacification and thrombosis of the portal vein have been demonstrated by portal venography.
6. Isotope scans show the radioactivity concentrated over the central zone of the liver. This probably relates to the compensatory hyperplasia of the caudate lobe and the reduced blood flow to other lobes.
7. Neoplasms and other space occupying lesions, underlying

hepatic vein occlusion, can be outlined by selective arteriography and scintiscans. However, both methods may show filling defects, caused by lobular congestion or regional changes in blood flow which are the consequence of hepatic vein thrombosis.

CHAPTER 7

HEPATIC HAEMODYNAMICS IN THE BUDD-CHIARI SYNDROME

Portal hypertension is a frequent complication of hepatic vein thrombosis. Oesophageal varices are seen in cases of longstanding (Cases 1 and 6) and haematemesis may be the presenting feature (Parker, 1959) or the immediate cause of death (Catinat et al., 1960; Hernandez de la Portilla and Rojas Natera, 1961; Gagne and Bertrand, 1963). Measurement of portal pressure in the Budd-Chiari syndrome has been made indirectly by intrasplenic pressure (Demarty and Peltier, 1962; Haeffner et al., 1962; Soscia and Bonano, 1963; Dupuy et al., 1964; Leger et al., 1964; Schreiber and Gonzeles, 1967) or directly at laparotomy by portal manometry (Fitzgerald et al., 1956; Parkinson and Miller, 1961; Tapie et al., 1961; Erlik et al., 1962; Ludwick et al., 1965; Fonkalsrud et al., 1966; Hales and Scatliff, 1966).

Hepatic congestion and portal hypertension gave rise to ascites in 93 per cent of 164 cases of the Budd-Chiari syndrome (Parker, 1959). In fact, abdominal swelling is the most frequent presenting symptom, and gross ascites dominates the clinical picture throughout the illness in most patients. The effect of ascites itself on the hepatic circulation has not been investigated. Quite apart from the Budd-Chiari syndrome there is very little information on the effects of ascites in chronic liver disease in

general. Ascites is known to raise intra-abdominal pressure in cirrhosis (Reynolds et al., 1957) and this may adversely affect hepatic haemodynamics. Resolution of ascites after bed rest and diuretics is accompanied by a fall in intra-abdominal (Atkinson, 1959), intrasplenic (Atkinson, 1959; Shaldon, 1961), and wedged hepatic vein pressures (Reynolds et al., 1958). These changes are largely a consequence of improved liver cell function during convalescence, rather than a result of treating the ascites. On the other hand, removal of peritoneal fluid by by paracentesis is followed by an immediate fall in intra-abdominal tension (Krook, 1956) and this, too, may alter portal pressure and hepatic blood flow.

Although hepatic vein thrombosis might be thought to preclude measurement of hepatic vein pressures, the successful passage of a catheter in five cases has allowed this to be achieved. The results of intrasplenic and hepatic vein pressures are recorded in this chapter.

To study the effects of a reduction in intra-abdominal pressure, an attempt was made to measure hepatic blood flow and hepatic vein pressures, before and after abdominal paracentesis, in the Budd-Chiari syndrome. Since data in hepatic cirrhosis are not available, such studies were made in ten patients with cirrhosis for comparison.

In four cases of the Budd-Chiari syndrome, it proved impossible

carry out measurements both before and after paracentesis because of technical difficulties or the poor general condition of the patients.

METHODS

Hepatic vein catheterization was carried out via a right brachial vein (Paton et al., 1953). Pressures were recorded in the right atrium (RA), inferior vena cava (IVC) and in the hepatic vein in the free (FHV) and wedged (WHV) positions. The WHV pressure is the pressure recorded when the cather is advanced until it occludes a hepatic venule. This measures the pressure attained when flow in the obstructed area reaches equilibrium and is believed to approximate to the sinusoidal pressure. Intraperitoneal (IP) pressure was recorded through a No. 15 g. needle. Intrasplenic (IS) pressure was measured by direct puncture (Turner et al., 1957). Pressures were measured with a Schonander strain-gauge transducer and recorded by a multi-channel direct writing instrument (Minograf 81). The zero reference level was 5 cm posterior to the sternal angle with the patient supine.

Total estimated hepatic blood flow (EHBF) was determined by a modification of the method of Caesar et al. (1961), which is based on the indirect Fick principle using a constant intravenous infusion of indocyanine green. Each result is expressed as the

mean of at least three blood flows calculated from serial arterial-hepatic venous dye differences.

The post sinusoidal resistance is a measure of resistance to outflow from the liver and is calculated from the formula:-

$$\frac{\text{WHV Pressure - FHV Pressure (mm Hg)}}{\text{EHBF (litres per min)}} \times 80 \text{ dynes/second cm}^5$$

Cardiac output was determined by an indicator dilution technique using (Cr-51) red blood cells. The labelled cells were injected via a catheter introduced percutaneously into the inferior vena cava, and samples were withdrawn from a catheter in the femoral artery using a Watson Marlow pump. The curves obtained were analysed by the method of Hamilton et al. (1932). Blood volume was measured with (Cr-51) red blood cells or (I-131) serum albumin by the methods of Veall and Vetter (1958).

RESULTS

BUDD-CHIARI SYNDROME: Portal Hypertension (Table 7.1)

Clinical evidence of portal hypertension was not conclusive in every case. Ascites was a feature common to all, oesophageal varices were seen in Cases 1 and 6 (Fig. 2.6) and collateral vessels were demonstrated on portal venograms in Cases 4 (Fig. 6.1) and 6 (Fig. 6.3). Splenomegaly was present in Cases 1, 3 and 4 but polycythaemia vera may have been the cause in two of these. Portal hypertension was confirmed in four patients, by an abnormally

high wedged hepatic vein pressure in Cases 1 and 2 (43 and 35 mm Hg) and by intrasplenic pressure in Cases 4 and 6 (36 and 25 mm Hg). In the presence of tense ascites, these measurements of portal pressure were related to intra-peritoneal and inferior vena caval pressures. Raised intrasplenic pressure in Case 4 was associated with splenic vein thrombosis. Case 4 was the only patient in whom both intrasplenic and wedged hepatic vein pressures were measured, and there was a difference of 19 mm Hg.

BUDD-CHIARI SYNDROME: Pressure Studies (Table 7.1)

The catheter was introduced into a heptaic vein in five of six patients with hepatic vein thrombosis. The catheter could not be advanced to the periphery and wedging occurred from 3 to 12 cm from the diaphragm. In four patients (Cases 1 to 4), wedging was confirmed by the absence of reflux of injected contrast material past the tip of the catheter. Superimposition of the arterial pulse on the hepatic vein trace was further evidence of wedging and was present in Cases 1, 2 and 4. By this token, the wedging in Case 3 was doubtful.

Wedged and free hepatic vein pressures were recorded in Cases 1 and 4. Free pressure could not be obtained in Cases 2 and 3 because the catheter was wedged close to the ostia of the hepatic veins. Wedging was not achieved in Case 5 and only a free pressure was taken. In Case 3, the catheter entered a left hepatic vein

TABLE 7.1

BUDD-CHIARI SYNDROME: PRESSURE STUDIES

Case	Pressure mm. Hg					
	Wedged hepatic vein	Free hepatic vein	Inferior vena cava	Intra-Peritoneal	Intra-splenic	Right atrium
1	43	23	28	20	-	1
2	35	-	17	20	-	2
3	10	-	(a) 4* (b) 16	-	-	2
4	17	12	11	-	36	0
5	-	13	11	-	-	3
6	-	-	(a) 3♦ (b) 15	-	25	2

*(a) above, (b) below, constriction

♦(a) above, (b) below, thrombus

TABLE 7.2

Clinical Features of Patients studied and Heart Rate, Systemic Arterial Blood Pressure, Cardiac Output and Blood Volume, before and after paracentesis.

Case no.	Weight Kg.	Surface area M^2	Diagnosis	Heart rate Beats/min.		Mean blood pressure mm. Hg.		Cardiac output l/min./M^2		Blood volume ml.	
				C	Ch	C	Ch	C	Ch	C	Ch
1	72	1.90	Budd-Chiari	100	102	105	102	4.6	6.4	7330	7130
2	58	1.59	Budd-Chiari	80	90	100	85			4350	4420
A	69	1.87	Cryptogenic cirrhosis	104	108	100	70	5.0	4.4	6370	6500
B	67	1.79	Cryptogenic cirrhosis	64	64	90	82	3.7	4.0	6520	6270
C	77	1.88	Cryptogenic cirrhosis	80	88	105	90	4.9		5490	
D	80	1.85	Cryptogenic cirrhosis	104	102	82	77	3.1	3.4	3720	3650
E	54	1.61	Obstructive jaundice	116	107	90	87	2.9	3.2	4730	4560
F	69	1.85	Cryptogenic cirrhosis	80	84	100	105	3.7		4480	
G	63	1.88	Haemochromatosis	86	100	100	77				
H	71	1.92	Alcoholic cirrhosis	100	104	110	110	6.0	5.5	5470	5830
J	56	1.63	Primary biliary cirrhosis	88	90	90	85				
K	78	1.95	Alcoholic cirrhosis	90	90	95	95				

TABLE 7.3

Estimated Hepatic Blood Flow and Pressure Measurements before and after Paracentesis*

Case No.	EHBF (ml/min) C	EHBF (ml/min) Ch	PRESSURES (mm. Hg.) WHV C	WHV Ch	FHV C	FHV Ch	IVC C	IVC Ch	RA C	RA Ch	IP C	IP Ch
1	550	830	43	37	23	18	28	25	1	1	20	13
2			35	27			17	9	2	1	20	17
A	2,080	2,090	27		13	11	15	11	3	3	13	10
B	690	1,020	23	23	4	4	7	7	1	1	6	6
C	1,430	1,210									15	11
D			39	32	12	10	18	14	2	2	17	13
E			20	17	11		14	10	1		11	9
F			23	19	13	7	11	6	4	3	1	
G			26	21	2	2	3	1	1	1	5	3
H			35	31	13	15	11	11	10	8	6	5
J			35	27	17	8	14	10	6	6	14	9
K			35	24	17	6	13	6	3	1	13	3

EHBF, estimated hepatic blood flow
WHV, wedged hepatic vein
FHV, free hepatic vein
IVC, inferior vena cava
RA, right atrium
IP, intra-peritoneal
C, control; Ch, after paracentesis
*2 litres

which arose almost directly from the right atrium.

The inferior vena caval pressure was raised in all cases and was attributed in part to increased tension due to ascites. The intra-peritoneal pressure was measured in two patients (Cases 1 and 2) and was notably elevated. In Case 3 there was a gradient of 12 mm Hg across a constriction of the intrahepatic portion of the cava, and in Case 6 there was increased caval pressure below the thrombosis (see Chapter 8). Right atrial pressures varied from 0 to 3 mm Hg and they were always lower than the pressures in the inferior vena cava.

EFFECT OF PARACENTESIS (Tables 7.2 and 7.3)

Pressures (Table 7.3)

Pressures were measured before and after paracentesis in 2 patients with the Budd-Chiari syndrome (Case 1, Fig. 7.1; Case 2, Fig. 7.2) and in 8 patients with cirrhosis. As the results were essentially the same in the cirrhotics as in the Budd-Chiari syndrome, they have been analysed together.

There was a significant fall in WHV pressure in the 10 patients following removal of 2 litres of ascitic fluid ($t = 7.80$, p less than 0.001). The pressure was reduced by 3 - 11 mm Hg in 9 patients but in Case B there was no change in any of the pressures measured. The fall in WHV pressure was significantly greater than the fall in IP pressure ($t = 3.21$, p less than 0.02). The fall in

WHV pressure also exceeded the fall in IVC pressure ($t = 3.33$, $p < 0.01$) but there was not a significant difference between the changes in WHV and FHV pressures.

The greatest reduction in pressure tended to occur when the pressures were high but there was not a statistically significant correlation between the initial IP pressure and the fall in pressure during paracentesis. For example, IP pressure was highest in the two cases of the Budd-Chiari syndrome, but the fall in pressure during paracentesis was greater in Case D.

Hepatic Blood Flow (Table 7.3)

Total EHBF was measured in 4 patients (Cases 1, A, B and C) before and after removing two litres of ascitic fluid. Hepatic blood flow rose by 51 per cent in the one patient with the Budd-Chiari syndrome in whom it was measured (Fig. 7.1). In the cirrhotics with ascites, there was a varied response. Flow increased by 32 per cent in Case B, was unchanged in Case A, and fell by 15 per cent in Case C.

Postsinusoidal resistance was calculated in one case of the Budd-Chiari syndrome (Case 1) and one case of cirrhosis with ascites (Case B). There was a fall in resistance from 2910 to 1830 and from 2200 to 1490 dynes/seconds cm 5 in the respective patients. The two results were insufficient to show statistical significance.

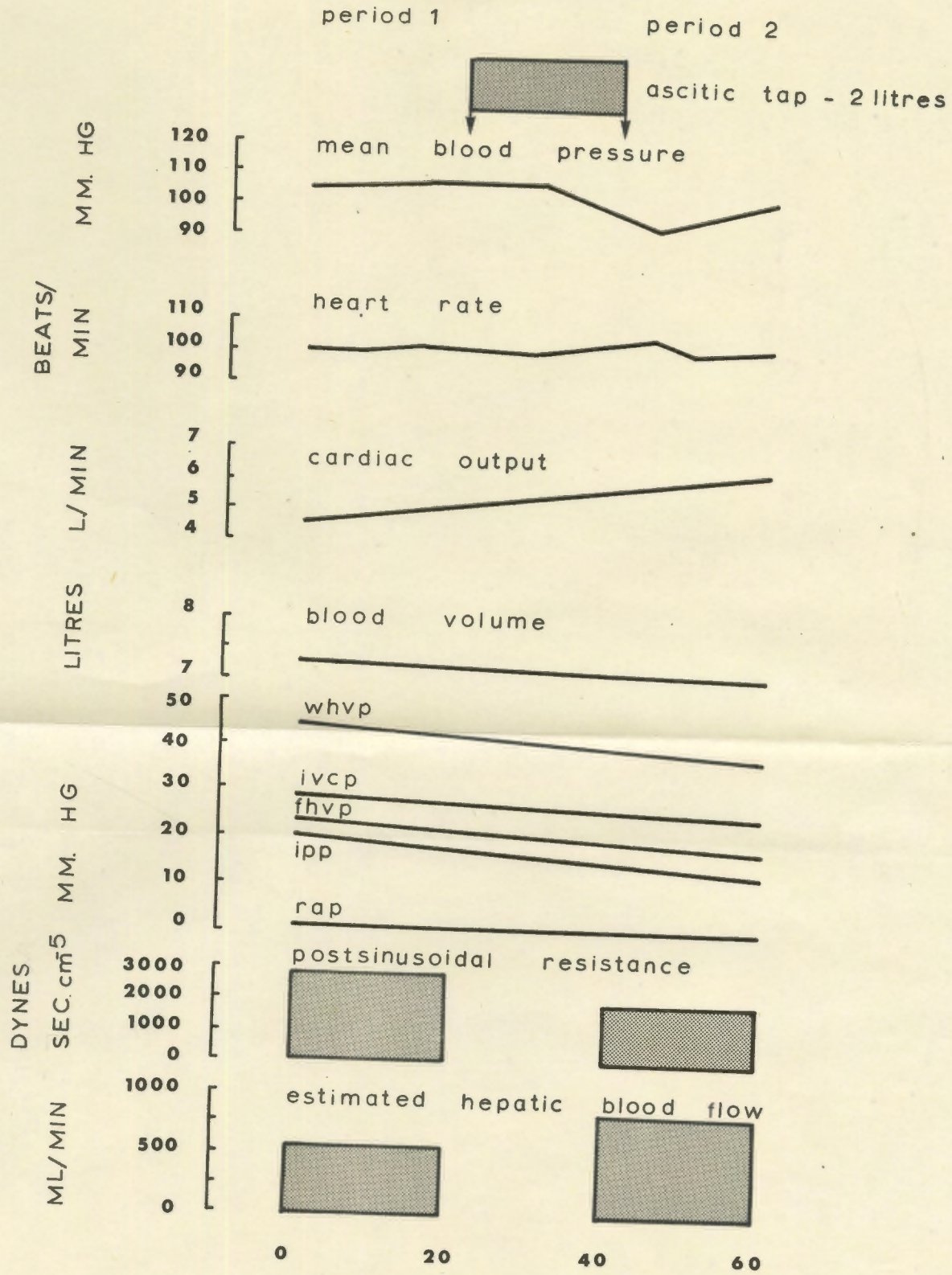


FIGURE 7·1

Haemodynamic studies before and after paracentesis in case 1.

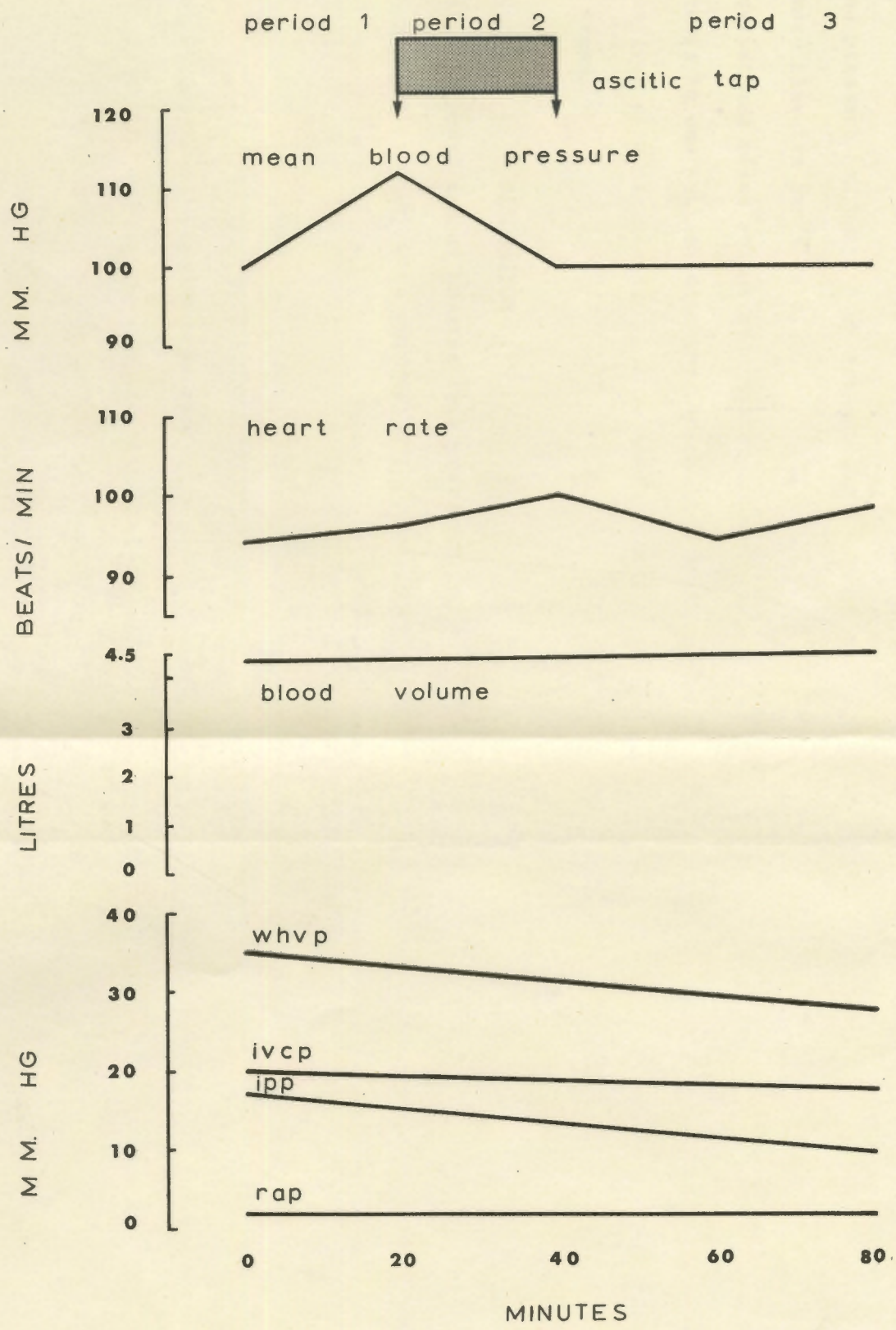


FIGURE 7.2

Haemodynamic studies before and after paracentesis in case 2.

Systemic Circulation (Table 7.2)

The heart rate and systemic blood pressure were recorded at regular intervals during the study. Values before and after paracentesis are included in Table 7.2 Several patients showed a fall in blood pressure but only in Case G was the heart rate increased by more than ten per minute.

Cardiac output and blood volume were measured before and after paracentesis in one patient with the Budd-Chiari syndrome (Case 1) and in five with cirrhosis. The results did not show a significant trend.

DISCUSSION

The ability to record wedged hepatic vein pressures in 4 cases of the Budd-Chiari syndrome is evidence of blood flow through veins which, radiologically, were shown to be obstructed. There are three mechanisms by which blood might reach the distal segment of a thrombosed vessel. Firstly, the thrombosis might be incomplete. An unusual example was Case 2, in whom the partially obstructed vein was occluded by the catheter when it became wedged (Fig. 5.18). This "WHV pressure" was in fact the pressure in the hepatic venous system proximal to the block which, by analogy, must have approximated to sinusoidal and portal pressure. Expressed as "effective" WHV pressure, that is the difference between actual WHV and IVC pressure, the result was 18 mm Hg.

Secondly, the collateral vessels which were shown radiologically (Figs. 5.13 and 5.15) might carry a sufficient volume flow to transmit the pressure from a proximal segment of vein to the catheter. In Case 4, there was a marked difference between the "effective" WHV pressure of 6 mm Hg and the IS pressure of 25 mm Hg. Splenic vein thrombosis was insufficient to account for the disparity. Therefore, the collateral vessels are presumed to have been too narrow to convey accurately the venous pressure proximal to the thrombosis. The pressure of 10 mm Hg, recorded in Case 3, was probably low for the same reason.

Thirdly, hepatic veins can recanalise (Parker, 1959), and extensive recanalization, shown microscopically in Case 1, might have accounted for the recording of a high wedged pressure. Whatever its source, the blood flow through the hepatic vein was sufficiently brisk to allow samples to be withdrawn for the measurement of EHBF.

The doubtful validity of WHV pressures when the hepatic veins are thrombosed, in no way detracts from the value of pressure measurement in the hepatic veins, inferior vena cava and right atrium in distinguishing the Budd-Chiari syndrome from other forms of suprahepatic obstruction (Chapter 9). In the Budd-Chiari syndrome, the RA pressure may be increased by a few mm Hg due to the elevated diaphragm, but there is always a rising gradient from

the atrium to the inferior vena cava. This is accentuated when there is gross ascites. On the other hand, in heart failure and constrictive pericarditis, the pressure gradient falls as the cather is advanced into the inferior vena cava and hepatic veins. This is not altered by the presence of ascites, as is well exemplified by a patient with constrictive pericarditis studied during the same period. She had been erroneously treated for resistant ascites due to chronic liver disease for 10 years. The pressures were:- RA : 16 mm Hg; IVC : 14 mm HG; and IP : 8 mm Hg. After paracentesis the pressures were:- RA : 13 mm Hg; IVC : 12 mm Hg.; and IP : 5 mm Hg.

Measurements of venous pressure in the legs has been suggested as an aid to the diagnosis of the Budd-Chiari syndrome (Jonas and Lawrence, 1954; Soscia and Bonano, 1963) but the results are misleading because thrombosis of the vena cava is not always combined with hepatic vein occlusion. In fact, the raised venous pressure in the legs is usually a reflection of increased caval pressure due to the ascites and therefore a high pressure does not mean caval thrombosis. In any event, neither caval thrombosis nor ascites is specific for the Budd-Chiari syndrome (see Chapter 8).

The presence of ascites also has a notable effect on pressure in the peritoneal cavity and hepatic veins. When IP pressure was reduced by tapping tense ascites, there was a substantial fall in WHV pressure. The patients with the Budd-Chiari syndrome showed

the same response as the cases of cirrhosis. The mechanism is uncertain. The absence of significant changes in cardiac output and plasma volume suggests that this is a local pressure effect rather than a systemic circulatory response. However, direct transmission of intra-abdominal pressure might be expected to affect equally pressures in the inferior vena cava and hepatic veins, and there was a significant difference between the changes in WHV, IVC and IP pressures after ascitic tap. Unequal ahcnages in pressure have also been recorded by Krook (1956) and by Knauer and Lowe (1967) in patients with cirrhosis.

These results might be explained by a direct effect of intra-abdominal pressure on the liver, causing alterations in hepatic resistance to portal flow. Compression of the liver has been shown to increase portal pressure in both animals (Brauer, 1963) and man (olerud, 1961). Conversely, protection of the liver in rats prevent elevation of portal pressure when intra-abdominal pressure is raised (Olerud, 1953). In this study, the substantial fall in post-sinudoidal resistance after paracentesis in one case of the Budd-Chiari syndrome and one of cirrhosis, supports this hypothesis. It may be relevant to the unequal changes in pressure, that an outflow block is the cardinal feature of both cirrhosis and hepatic vein thrombosis. When a tight cuff is bound around the abdomen in cirrhosis, the results are the reverse

of the changes after paracentesis, but there is little alteration in portal pressure after similar manoeuvres, if the liver is normal or if there is a portocaval shunt (Clain et al., in preparation).

The hepatic blood flow studies were not conclusive. After paracentesis, there was a substantial rise in EHBF in one case of the Budd-Chiari syndrome, but the results in cirrhosis were equivocal. Animal experiments support the idea that a rise in intra-abdominal pressure reduces hepatic blood flow. Olerud (1953) showed that gas distension of small bowel in rabbits produced a fall in portal blood flow which ceased when intra-abdominal pressure reached 30 cm of water. In rats, direct pressure over the liver reduced hepatic blood flow and the reverse occurred on relieving the pressure (Brauer, 1963). Application of a tight abdominal corset at a pressure of 50 mm Hg produced a fairly consistent fall in EHBF in human cirrhosis (Bradley et al., 1952).

In the present study, systemic circulatory changes did not play an important role in the splanchnic adjustments which followed changes in intra-abdominal pressure. Despite the evidence that a diminished plasma volume partly accounts for the effect of paracentesis on portal pressure (Shaldon, 1961), there was no significant change in blood or plasma volume for the period of this study. RA pressure, too, was usually unchanged, but in four patients it

fell with IP pressure. The increase of RA pressure with tense ascites is not a factor in producing a high cardiac output. Sherlock (1951) observed a stable cardiac output when RA pressure fell after paracentesis. Kowalski et al. (1953) found no difference between the cardiac output in cirrhotics, with or without ascites, and they showed that after abdominal paracentesis the resting cardiac output was essentially unchanged.

Similar observations were made in the present study. Reducing intra-abdominal pressure did not have a consistent effect on cardiac output. Serial measurements of cardiac output over long periods after paracentesis have also failed to show significant changes (Clain et al., in preparation). Rather different results were recently reported by Knauer and Lowe (1967) who recorded increments in cardiac output in ten subjects after withdrawing from 250 ml to 1,000 ml of ascitic fluid. They suggested that the change in cardiac output followed an augmented venous return which resulted from relief of functional constriction of the inferior vena cava by the increased intra-abdominal pressure. However, paracentesis in excess of 1 litre abolished this effect and in some patients the cardiac output fell below control values. In this study, cardiac output was measured after withdrawing 2 litres of fluid and this may explain the discrepancy between the results.

There is insufficient evidence to draw firm conclusions about

splanchnic circulatory adjustments after paracentesis, but the results of this investigation suggest that the presence of ascites may have a deleterious effect in the Budd-Chiari syndrome and in cirrhosis. Tense ascites caused a marked increase in venous pressures and augmented the gradient between the portal system in the abdomen and oesophageal collateral veins in the chest. Enlargement of portosystemic shunts and variceal bleeding might be a direct consequence. The congested liver in the Budd-Chiari syndrome is known to compress the inferior vena cava (see Chapter 8). Transmission of intra-abdominal pressure to the liver might aggravate this effect and add a further element of suprahepatic obstruction. Direct pressure of the ascitic fluid has also been suggested as a cause of caval obstruction (Bergstrand et al., 1964; Knauer and Lowe, 1967). Whatever the mechanism, in Case 3 there was sufficient compression to produce a gradient across the caval constriction (Fig. 8).

If the increase of EHBF in the patient with the Budd-Chiari syndrome is a valid reflection of the response to paracentesis in this condition, then intra-abdominal pressure must have a substantial effect on hepatic resistance. The fall in post-sinusoidal resistance supports this idea. Further measurements of blood flow in the Budd-Chiari syndrome would be of great interest.

CONCLUSIONS

The aims of the investigations and review in this chapter were:-

1. To establish whether hepatic vein pressures can be measured in the Budd-Chiari syndrome, and to study their value in the diagnosis.
2. To assess the effects of paracentesis on hepatic haemodynamics in the Budd-Chiari syndrome.
3. To consider whether pressure measurements in the inferior vena cava or femoral veins are an aid to diagnosis, as has been suggested.

The conclusions are as follows:-

1. The hepatic veins were successfully catheterized in 5 patients.
2. Pressure measurements in the hepatic veins, inferior vena cava and right atrium, easily distinguish the Budd-Chiari syndrome from other forms of suprahepatic obstruction (Chapter 9).
3. Pressure measurements in the legs are misleading because of the tension exerted by the ascites on the inferior vena cava. When intra-peritoneal pressure was reduced by tapping tense ascites, there was a substantial fall in wedged hepatic vein pressures both in the Budd-Chiari syndrome and in cirrhosis. This appeared to be due to local pressure as cardiac output and blood volume did not change significantly. Alterations

in post-sinusoidal resistance after paracentesis suggested a direct effect on the liver.

4. Hepatic blood flow studies, after paracentesis, were equivocal although animal experiments suggest that a rise in intra-abdominal pressure reduces hepatic blood flow.

CHAPTER 8

THE INFERIOR VENA CAVA IN THE BUDD-CHIARI SYNDROME

Inferior vena cavography was performed in all cases prior to hepatic vein catheterization. Percutaneous catheterization of the femoral vein provided a suitable route for injection of contrast material (Seldinger, 1953).

RESULTS

In five patients (Cases 1 to 5), the hepatic segment of the vena cava showed side-to-side narrowing (Figs. 8.3 to 8.7). Antero-posterior compression was also present in Case 5 (Fig. 8.7, B). At autopsy in Cases 1 and 4, the narrowing of the inferior vena cava was confirmed and found to be due to extrinsic pressure by the liver.

The deformity of the cava had a characteristic shape. There was a gradual tapering in diameter within the liver substance until the narrowest point was reached just below the diaphragm. On entering the thorax the inferior vena cava broadened to its normal size.

No hepatic vein branches were seen on cavography in the Budd-Chiari syndrome. In Case 2 (Fig. 8.4, A), the ostia of a left and a right hepatic vein were outlined. Both were subsequently catheterized (Chapter 5, Figs. 5.17 to 5.19). The ostium of the

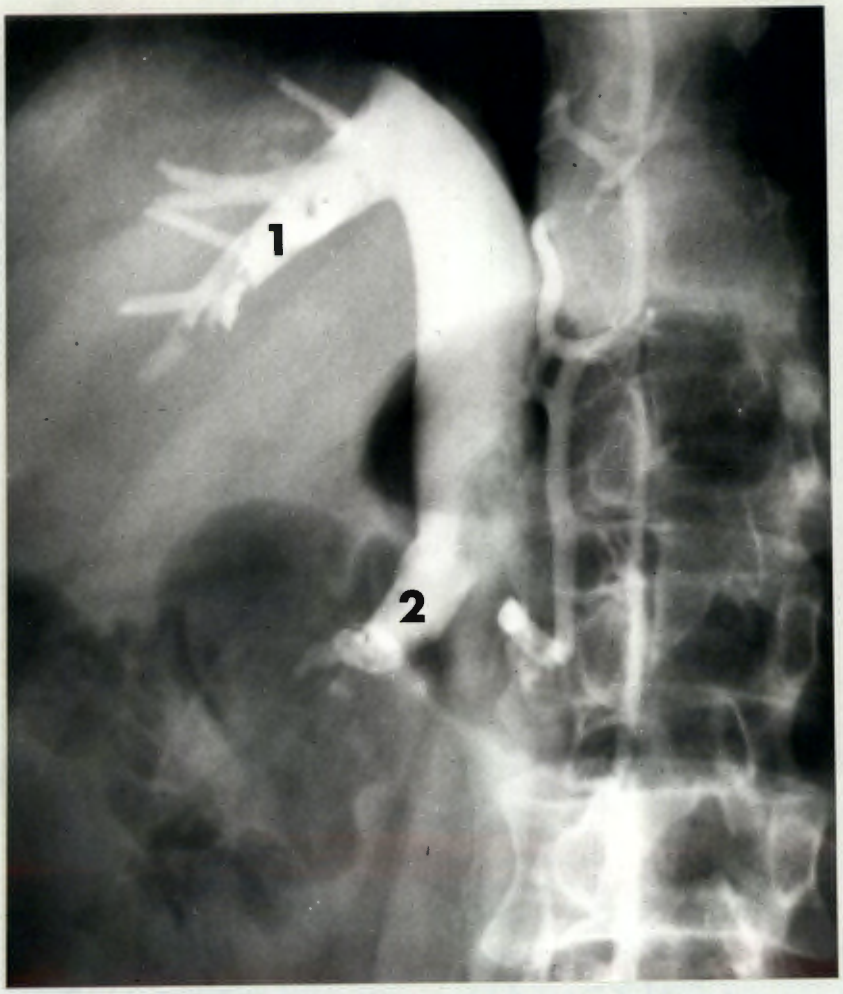


Fig: 8.1

Inferior vena cavogram in a normal subject during the Valsalva manoeuvre. There is opacification of the distal half of the inferior vena cava and the increased pressure has filled the right hepatic veins (1), renal veins (2) and perithecal vessels. The normal diameter of the cava and the hepatic veins is demonstrated. There is no narrowing of the cava as it passes through the liver.

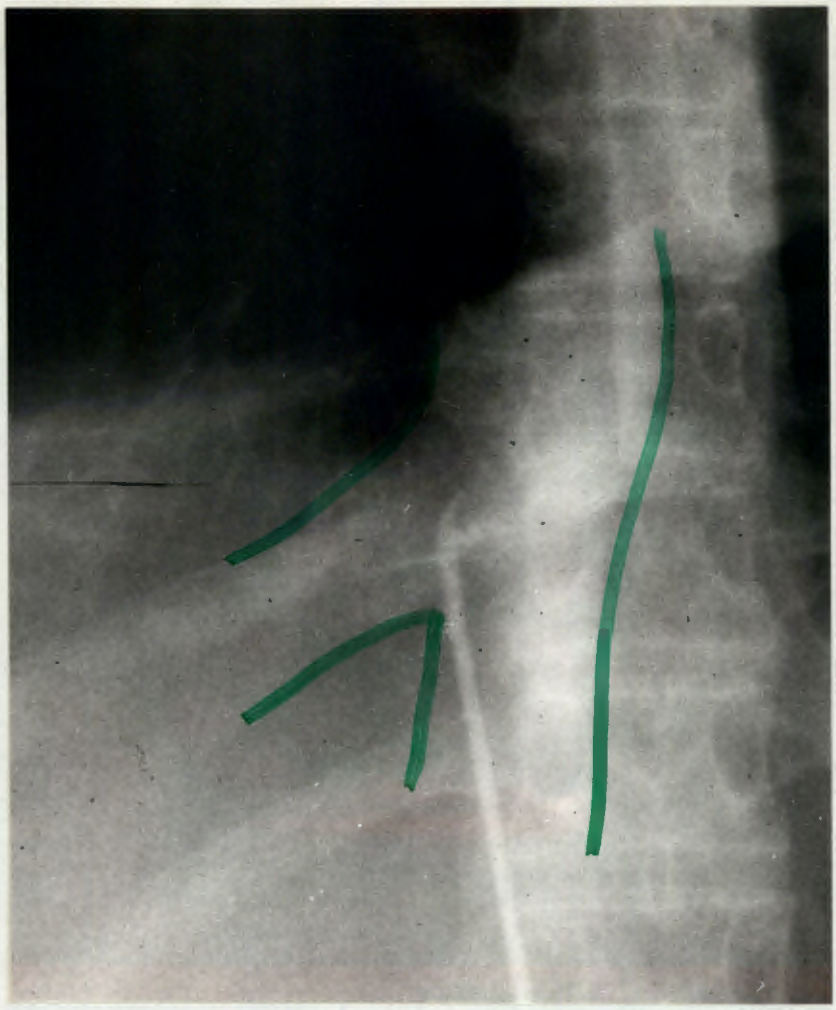


Fig: 8.2

Inferior vena cavogram in a patient with constrictive pericarditis. The large diameter of the cava and the main right hepatic vein is shown. There is no narrowing of the cava as it passes through the liver.

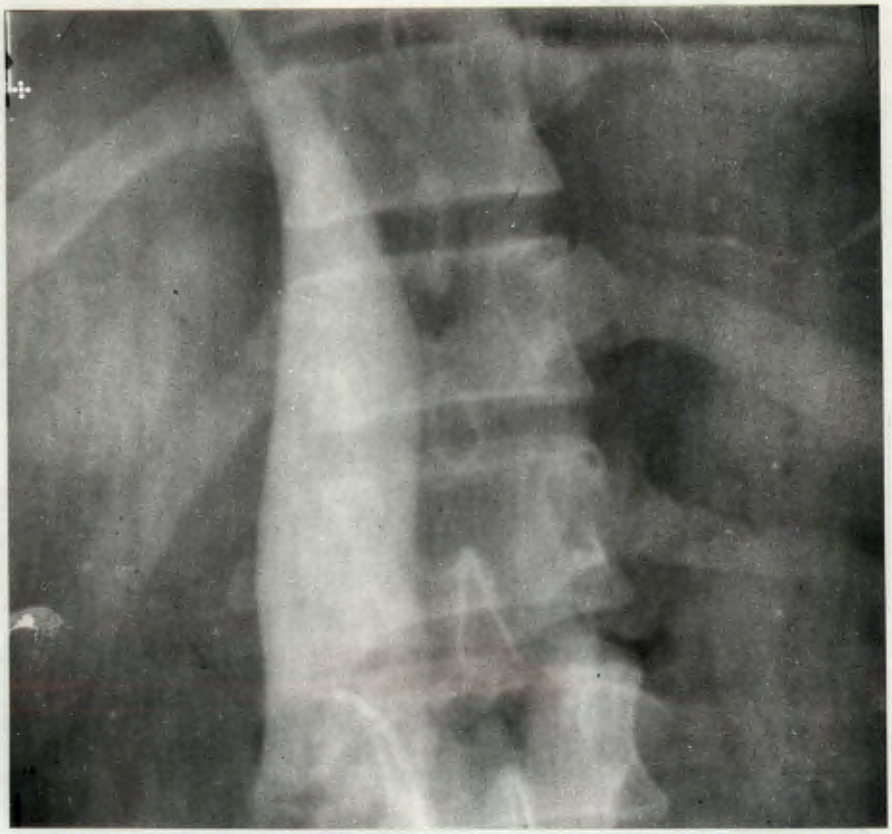


Fig: 8.3 CASE 1

Inferior vena cavogram in a patient with the Budd-Chiari syndrome. There is conical narrowing of the cava as it passes through the liver.

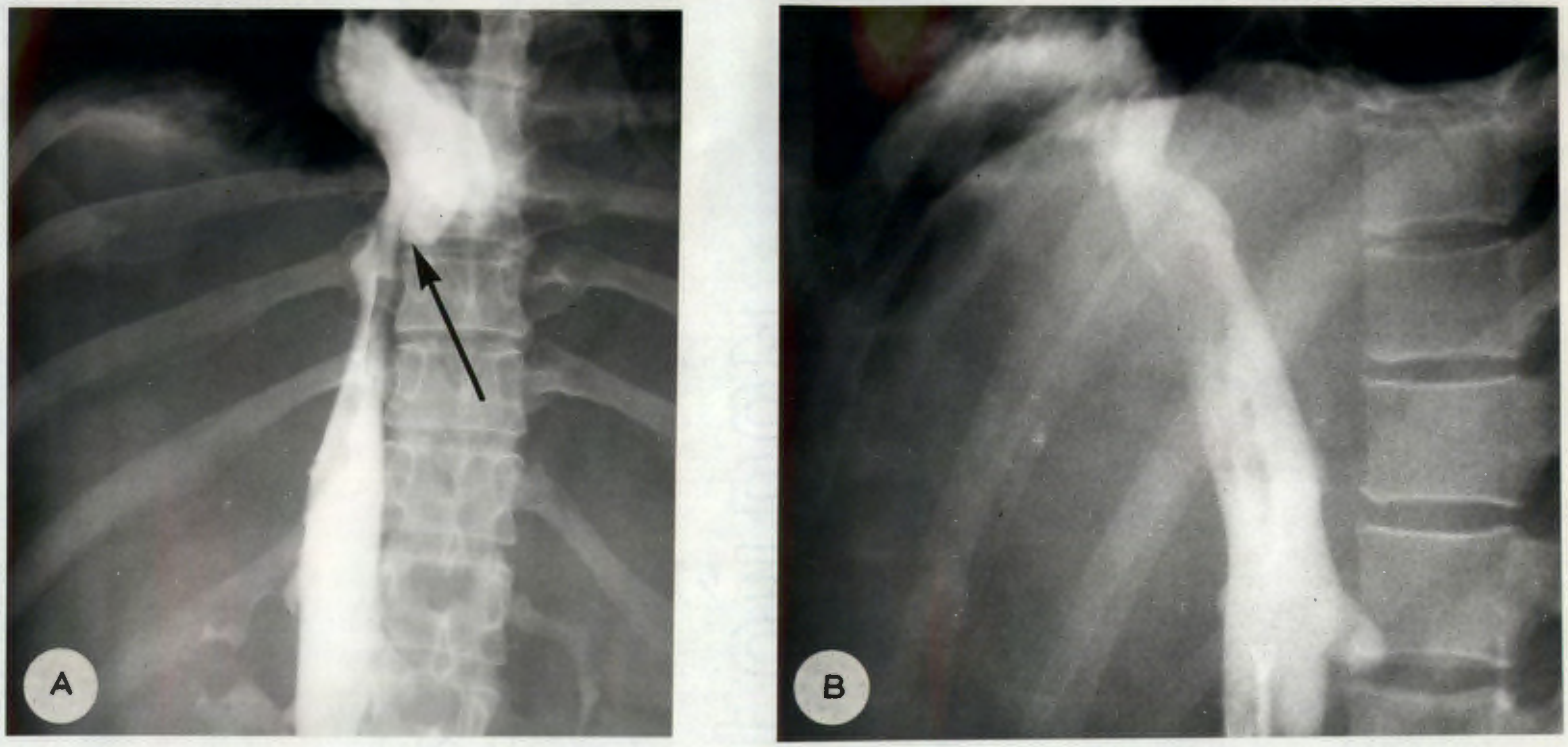


Fig: 8.4 CASE 2

Inferior vena cavogram in a patient with the Budd-Chiari syndrome, showing antero-posterior (A) and lateral (B) views. There is side-to-side narrowing of the upper end of the cava with internal streaking which suggests the presence of thrombus formation. The origin of a left hepatic vein is clearly outlined (arrow). Reference to hepatic venogram (fig. 5.19) in this case will demonstrate that at this point there is a stenosis of the vein through which the catheter was passed. In the lateral view, there is posterior compression of the cava.

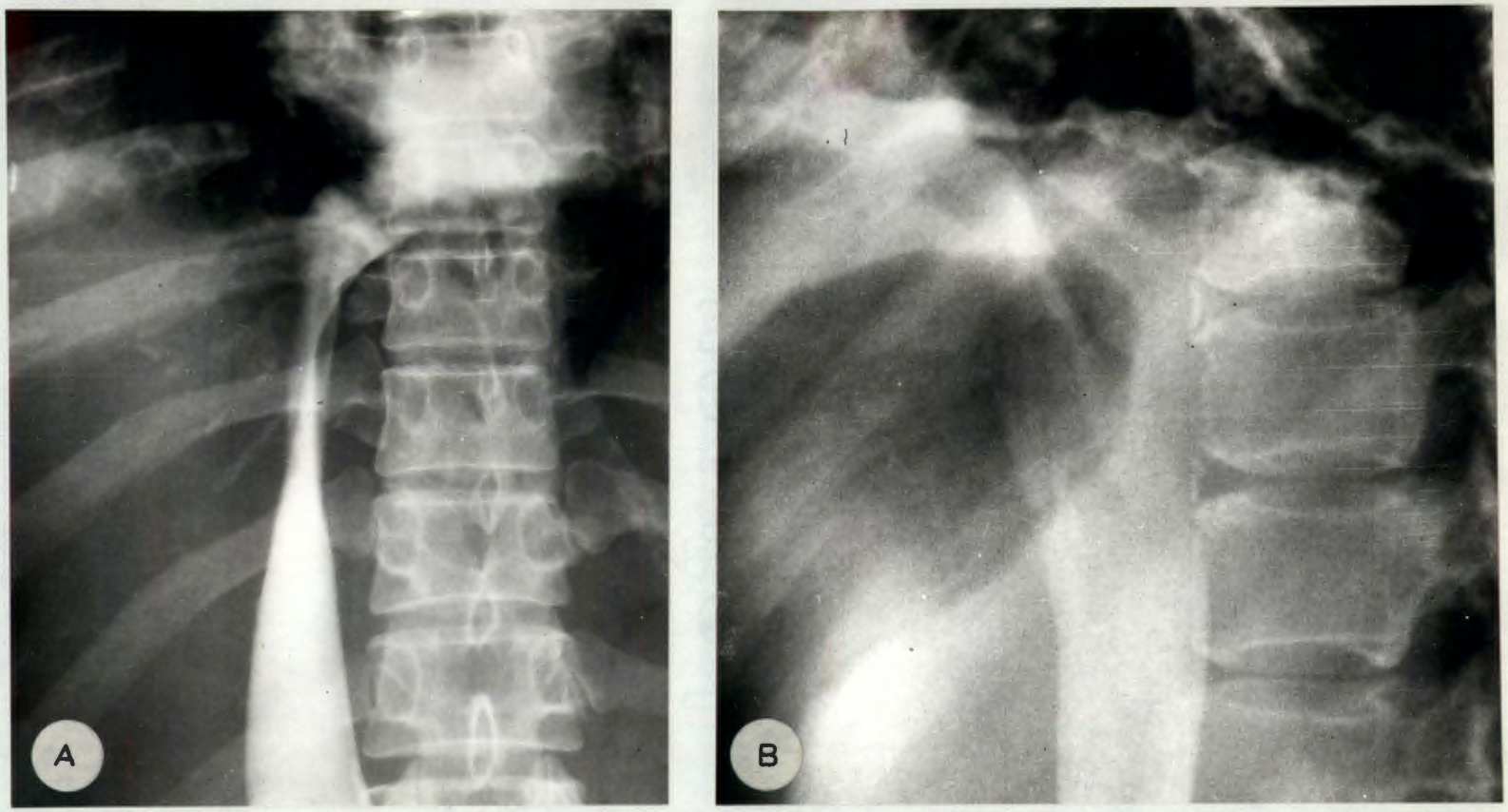


Fig: 8.5 CASE 3

Inferior vena cavogram showing antero-posterior (A) and lateral (B) views. There is marked side-to-side narrowing of the hepatic portion of the cava. No filling defects are seen. The hepatic veins have not been opacified.

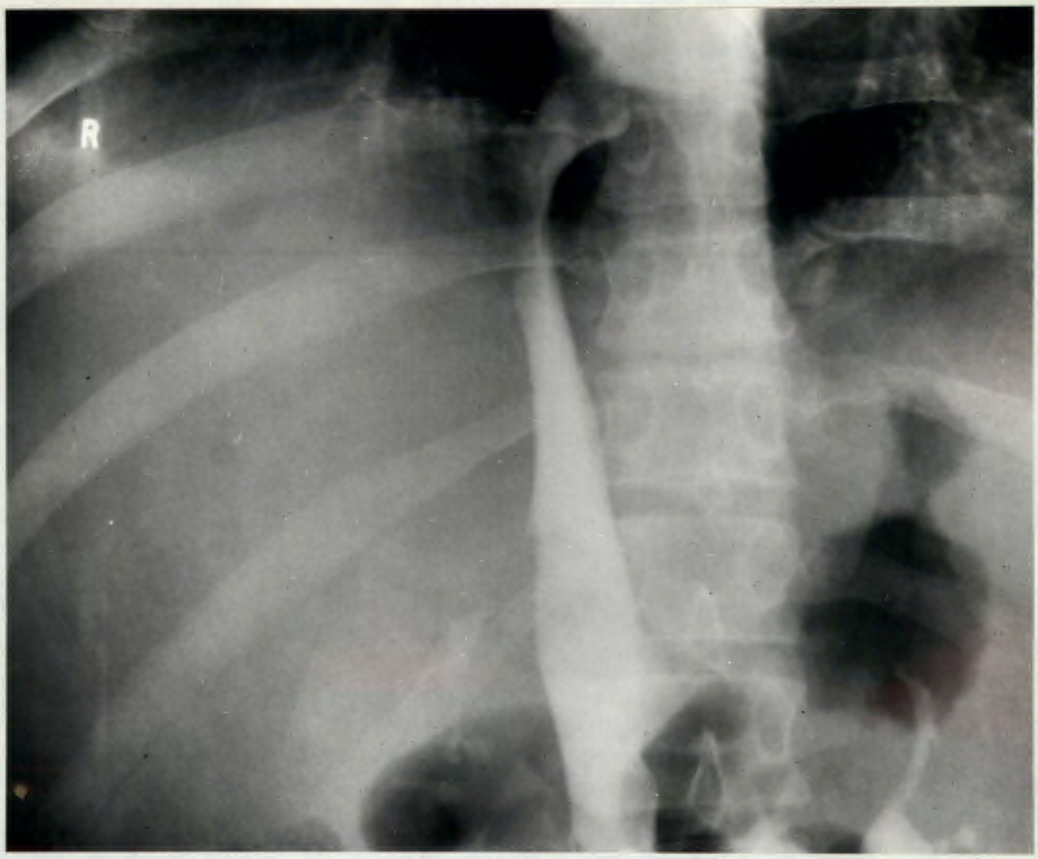


Fig: 8.6 CASE 4

Inferior vena cavogram in a patient with the Budd-Chiari syndrome. The appearance is almost identical to that in Case 3 (fig. 8.5). There is extrinsic compression producing side-to-side narrowing of the inferior vena cava.

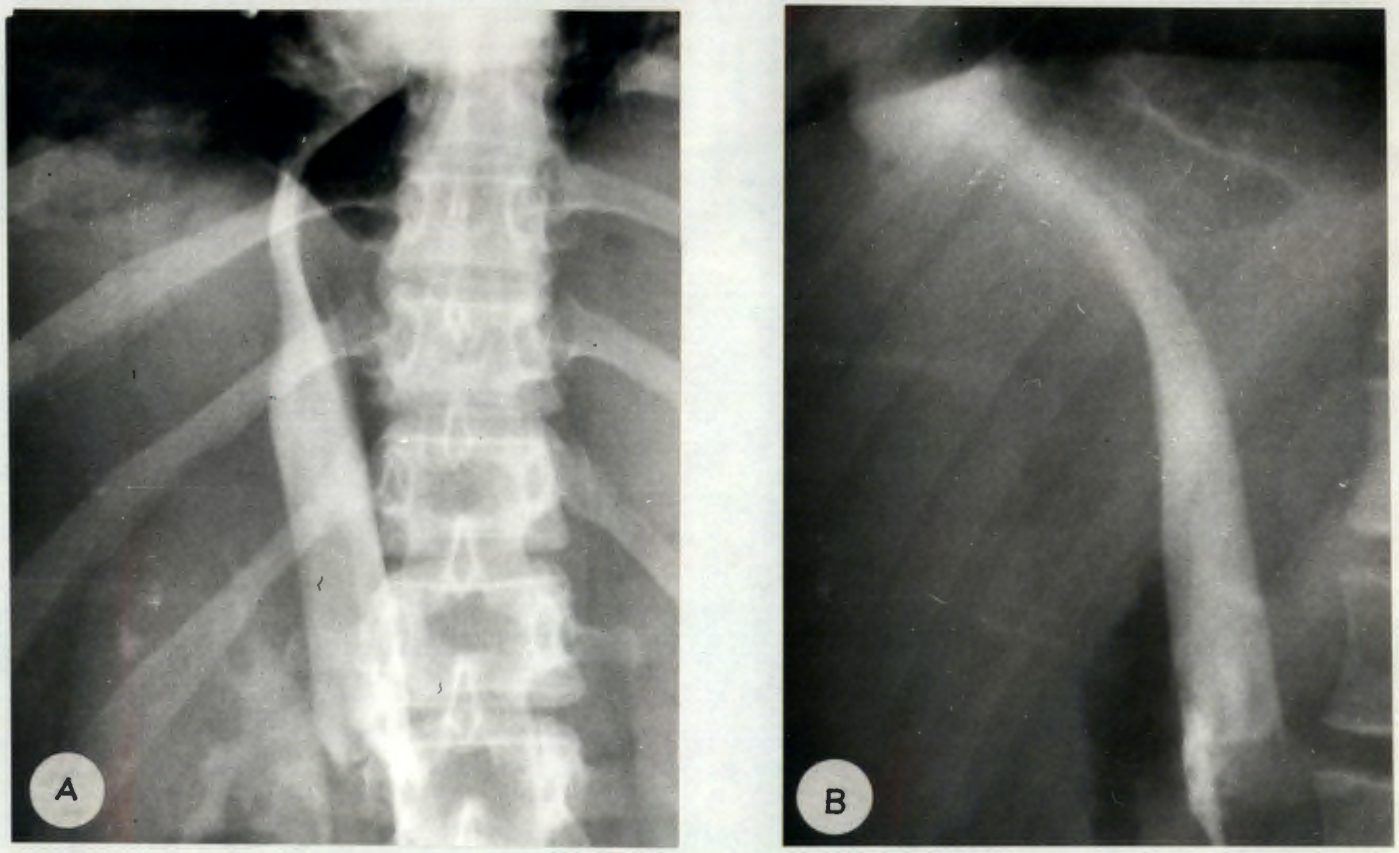


Fig: 8.7 CASE 5

Inferior vena cavogram in a case of the Budd-Chiari syndrome. There is concentric narrowing of the hepatic segment of the cava which is demonstrated on the antero-posterior (A) and lateral (B) views. No hepatic veins are shown.

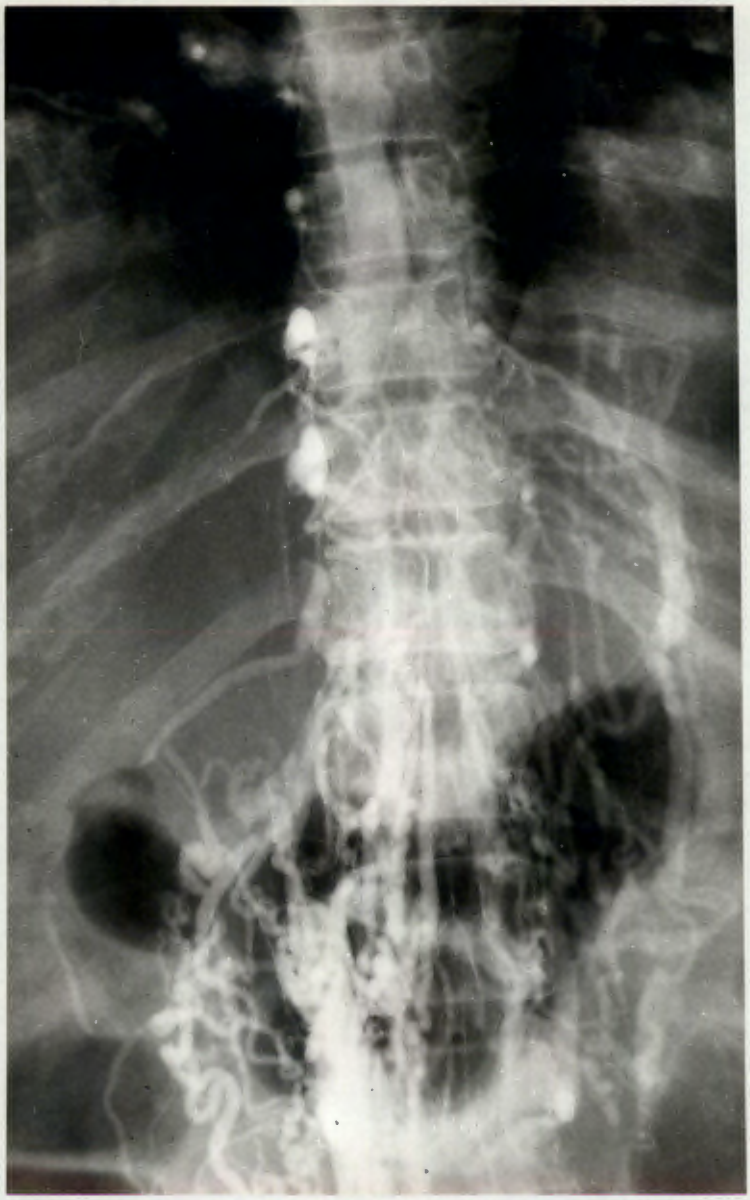


Fig: 8.8 CASE 6

Inferior vena cavogram in the Budd-Chiari syndrome showing complete obstruction of the cava below the renal veins. Large numbers of tortuous collateral vessels are shown.

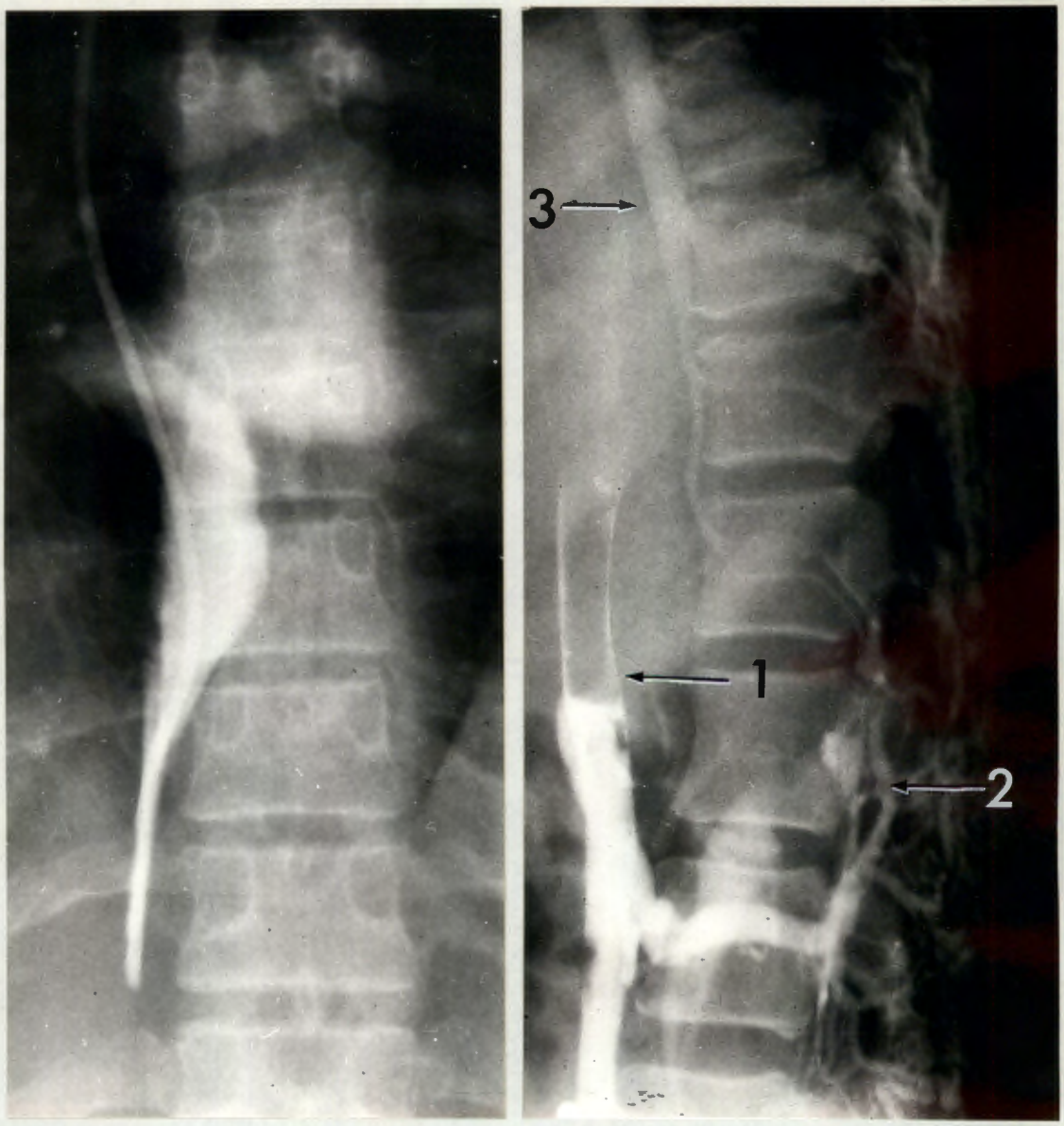


Fig: 8.9 CASE 6

Cavogram from the same patient as Fig. 8.8 showing thrombosis of the inferior vena cava. A, the catheter has been introduced via the right atrium and narrowing and occlusion of the hepatic segment of the vena cava are shown. B (lateral view), catheter shows obstruction (1) and collateral flow through peri-thecal (2) and azygos veins (3).

right hepatic vein appeared as a dimple of contrast material, but the left hepatic vein was sharply cut off. A catheter was passed through the thrombus, and by superimposing the hepatic and caval venograms, the obstruction was shown to be about 2 cm in length.

Evidence of thrombus in the inferior vena cava was present in two patients. In Case 2, there were irregular filling defects in the lumen on both antero-posterior and lateral views (Figs. 8.4,A and B). Complete obstruction of the inferior vena cava was demonstrated in Case 6 (Figs. 8.8 and 8.9, A and B). Innumerable collateral vessels, following a tortuous course, were outlined in the antero-posterior films. On the lateral view, the route of the contrast material was clearly demonstrated from the obstructed cava through perithecal vessels to the azygos veins. The upper extent of the thrombus was established by cavography through a catheter introduced via the right atrium. Narrowing and occlusion of the hepatic segment of the cava were shown.

DISCUSSION

Radiological visualization of the hepatic veins is essential for the diagnosis of the Budd-Chiari syndrome. Inferior vena cavography has been suggested as an alternative (Jonas and Lawrence, 1954; Soscia and Bonanna, 1963) but it is misleading because thrombosis of the vena cava is not always combined with hepatic

vein occlusion. In fact, there is obstruction to the vena cava in only 30 per cent of cases (Parker, 1959) and the hepatic veins and the inferior vena cava may be separately involved in the same patient (Kelsey and Comfort, 1947; Thompson, 1947; Parker, 1959; Gibson, 1960; Case 6). Jonas and Lawrence (1954), in advocating the diagnostic value of cavography, suggested that the presence or absence of caval occlusion in the Budd-Chiari syndrome produced two distinct clinical entities, each with a difference course and prognosis. These contentions are not borne out by the reported cases of the Budd-Chiari syndrome. Furthermore, inferior vena caval obstruction occurs in a wide variety of conditions quite unrelated to hepatic vein thrombosis.

Hepatic vein catheterization may be difficult and hazardous if the inferior vena cava is thrombosed. On this account the cava was examined first in all the patients in this study. In Case 6, knowledge of the obstruction ensured a cautious introduction of the catheter via the right atrium. Contrast material was injected under fluoroscopic control as the catheter was advanced. The extent of the thrombus was safely established in this way.

Simultaneous opacification of the inferior vena cava from above and below has been previously described. Dupuy et al. (1964) reported a patient with an adrenal tumour in whom the neoplastic tissue invaded the cava and spread up to the right atrium. They outlined the mass by what they termed "deuxieme

cavographie". Schaffner et al. (1966) demonstrated a stricture of the hepatic segment of the inferior vena cava by catheterization through a femoral and an antecubital vein. Some contrast material passed through the stenotic area, but neither catheter could traverse the obstruction.

Sometimes the distal extent of the thrombus precludes entry of the catheter into the inferior vena cava from above (Schreiber and Gonzales, 1967). Membranous obliteration of the inferior vena cava has been recorded in several Japanese patients. Kimura (1964) and Eguchi et al. (1966) have described their diagnostic methods which include caval venography using two catheters, one placed above and the other below the obstructed segment. The membrane was always situated slightly below the diaphragmatic hiatus and immediately above the ostium of the right hepatic vein.

Inferior vena cavography has been carried out in a number of patients with the Budd-Chiari syndrome (Bronte-stewart and Goetz, 1952; Jonas and Lawrence, 1954; Fitzgerald et al., 1956; Caroli et al., 1958; Levander and Ponten, 1959; Haeffner et al., 1962; Case Records of the Massachusetts General Hospital, 1963; Ohara et al., 1963; Dupuy et al., 1964; Nicoloff et al., 1964; Saito, 1964; Ludwick et al., 1965; Ecker et al., 1966; Hoffbauer, 1966; Hales and Scatliff, 1966). Apart from establishing the

patency of the cava or the extent of its involvement, cavography occasionally provides additional information. Caval flow has been examined after a shunt procedure (Erlik et al., 1962) and localised obstruction of the cava has caused reversal of flow in, and opacification of the hepatic veins (see Chapter 5).

Side-to-side narrowing which was seen on cavography in Cases 1 to 5 has been observed previously in the Budd-Chiari syndrome (Fitzgerald et al., 1956). In normal cavograms the hepatic and intrahepatic segments have the same diameter (Fuchs, 1961). Constriction of the hepatic segment of the cava has been reported in cirrhosis (Petersen et al., 1961; Bergstrand et al., 1964; Nordenstrom and Norhagen, 1967), and may contribute to portal hypertension (Winkler et al., 1960). Fitzgerald et al. have ascribed the narrowing to recanalization of thrombus, but there is no evidence to support this opinion. Extrinsic compression by the engorged liver seems the more likely explanation and the findings at autopsy in Cases 1 and 4 confirmed this view.

CONCLUSIONS

The aims of the investigations and review in this chapter were to consider the usefulness of inferior vena cavography in the Budd-Chiari syndrome.

The conclusions are:-

1. That cavography through the femoral route in combination with radiography via the right atrium, can ascertain the nature and precise extent of the lesion in the Budd-Chiari syndrome.
2. Contrast material may demonstrate the hepatic veins by reflux if there is an obstruction of the suprahepatic portion of the cava.
3. The engorged liver regularly produces compression of the cava which may contribute to the hepatic outflow obstruction.

CHAPTER 9

DIAGNOSIS OF THE BUDD-CHIARI SYNDROME

The main features of hepatic vein obstruction are pain, ascites and hepatomegaly (Chapters 1 and 2). Clinical evaluation and laboratory tests reflect moderate hepatocellular dysfunction, but usually give no clue to its cause (Chapter 3). Hepatic histology is essential for diagnosis. Needle biopsies are satisfactory for showing the centrizonal changes of hepatic vein occlusion. The appearance is not specific and may result from any obstruction to hepatic outflow. Occlusion of the inferior vena cava above the liver produces a clinical picture similar to the Budd-Chiari syndrome. Heart failure and constrictive pericarditis are important causes of hepatic congestion and must be distinguished by clinical examination, fluoroscopy and electrocardiography. Pressure studies and radiography easily separate these conditions.

RESUME OF DIFFERENTIAL DIAGNOSIS (Table 9.2)

Clinical Features (Chapters 1 and 2)

Abdominal pain accompanying liver enlargement and ascites should bring the Budd-Chiari syndrome to mind. Polycythaemia associated with these clinical findings should also draw attention to the diagnosis (Chapter 4). Jaundice, haematemesis, vomiting

and diarrhoea may be features of hepatic vein thrombosis (Parker, 1959).

When hepatic congestion is due to heart failure, there are frequently symptoms of cardiac decompensation such as cough and dyspnoea, or a history of rheumatic fever or pulmonary disease. But patients with cardiomyopathy or constrictive pericarditis are often free from cardiac symptoms and they may present with ascites, abdominal pain and hepatomegaly. Signs of mitral or tricuspid valve disease, abnormal heart sounds and evidence of chronic lung disease point to a cardiac cause. A notable increase of the jugular venous pressure is a valuable sign, but the diagnosis may be further confused because tense ascites can elevate the jugular venous pressure, displace the cardiac apex and alter the electocardiograph (Case 6).

Hepato-jugular reflux and distended abdominal wall veins are reputed to be of value in the differential diagnosis but are often misleading. Pressure over the abdomen may elevate the jugular venous pressure even when the hepatic veins are occluded (Case 2), but reflux is not present when the cava is blocked (Case 6). Collateral veins which radiate from the umbilicus may occur with any cause of portal hypertension. Veins running upwards over the abdomen do not always signify inferior vena caval thrombosis because tense ascites (Chapter 7) and extrinsic compression of the cava (Chapter 8) may produce a difference of pressures between the

veins in the upper and lower extremities (Cases 1 and 4). By the same token, oedema of the lower limbs in the Budd-Chiari syndrome does not indicate caval obstruction (Cases 1, 2, 4 and 5). Abdominal wall veins are not prominent in heart failure because there is no portal-systemic or cavo-caval pressure gradient.

Splenomegaly and oesophageal varices, caused by portal hypetension, are frequently present in supra-hepatic caval obstruction, the Budd-Chiari syndrome and cirrhosis, but they are rarely found in heart failure or constrictive pericarditis. Heavy proteinuria draws attention to caval obstruction complicating hepatic vein thrombosis, although heart failure and constrictive pericarditis may be the cause.

Heart failure, constrictive pericarditis and cirrhosis of the liver can usually be separated from the Budd-Chiari syndrome by the history and physical examination. But pure hepatic vein thrombosis, thrombosis of the cava accompanying hepatic vein thrombosis, and isolated inferior vena caval occlusion above the hepatic veins cannot often be distinguished on clinical grounds. Although the hepatic haemodynamics are similar, it is important that the lesions be accurately defined, because the cause, prognosis and treatment are different.

Liver Function Tests (Chapter 3)

In the Budd-Chiari syndrome there is a moderate disturbance of

liver function which is not of diagnostic value. Bromsulphthalein retention is usual in any cause of hepatic congestion and is, indeed, the most sensitive method of detecting hepatic involvement in patients with heart failure (Felder et al., 1950). Results parallel both clinical severity and the extent of the hepatic cell necrosis (Sherlock, 1951). On the other hand, the serum alkaline phosphatase is generally normal in heart failure (Sherlock, 1951) while it is almost invariably raised in hepatic vein thrombosis (Chapter 3). Increased values are also found in hepatic involvement by amyloid, abscess, leukaemia sarcoidosis or tuberculosis.

Hepatic Venography and Hepatography (Chapter 5)

Radiological visualization of the hepatic veins is essential for the diagnosis of the Budd-Chiari syndrome. Hepatic venography shows obstruction, narrowing, stenosis and irregularity of the main hepatic veins. The catheter cannot be advanced to the periphery of the liver. The small vessels communicating with the main hepatic veins create an unusual network pattern and the appearance is quite distinct from that in other forms of liver disease. In cirrhosis, there is loss of the normal tapering and arborization of the hepatic venous branches. In heart failure, hepatic venography is normal apart from slight venous dilatation.

The injection of contrast material into the hepatic parenchyma

TABLE 9.1

BUDD-CHIARI SYNDROME: RADIOLOGICAL FEATURES

Investigation	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Barium swallow	varices	normal	normal	normal	normal	varices
Portal venogram	-	-	-	blocked splenic vein	normal*	blocked portal vein
Hepatic venogram	network pattern	narrow segment on left; network pattern on right	network pattern	network pattern	main veins blocked; fine vessels on left	no vein entered
Inferior vena cavogram	extrinsic compression	extrinsic compression; plaques of thrombus	extrinsic compression	extrinsic compression	extrinsic compression	thrombus from renal to hepatic veins
Coeliac axis arteriogram	-	-	-	-	displaced hepatic vessels	displaced hepatic vessels
Hepatogram	-	occlusion of hepatic vein ostia; no lymphatics	narrow, tortuous hepatic veins; no lymphatics	-	No filling of hepatic veins; lymphatics present	-
Liver scan	-	patchy uptake by right and left lobes	uptake mainly over central zone of liver	uptake mainly over central zone of liver	no uptake by right lobe	uptake mainly over central zone of liver

*venous phase of coeliac axis arteriogram

is an excellent means of establishing the presence and site of hepatic vein thrombosis. The normal and collateral vessels are well outlined as the contrast material leaves the liver. Increased density of the contrast material and delayed venous drainage also occur in other causes of hepatic outflow obstruction, but in heart failure and, presumably in suprahepatic obstruction of the cava, the hepatic veins are normal.

Pressure Studies (Chapter 7)

Pressure measurements on withdrawal of the catheter from the wedged position in the hepatic vein to the right atrium easily distinguish heart failure and constrictive pericarditis from hepatic vein thrombosis. Patients with a cardiac cause of hepatic congestion have an elevated right atrial pressure which is transmitted through the inferior vena cava to the liver so that there are almost identical pressures in the right atrium in the cava and in the free and wedged hepatic vein positions (Winkler et al., 1960; Benhamou et al., 1962 A; Chapter 7). In the Budd-Chiari syndrome, although tense ascites may elevate the right atrial pressure, there is always a marked gradient between the hepatic veins and the right atrium (Chapter 7).

Intrapleural pressure is not of differential value, although portal hypertension in cardiac disease is seldom as marked as in cirrhosis or hepatic vein thrombosis (Benhamou et al., 1962 b).

Inferior Vena Cavography (Chapter 8)

Contrast radiography is the surest method of diagnosing thrombosis or membranous obstruction of the inferior vena cava (Kimura, 1963; Chapter 8). Contrast material may reflux into the hepatic veins if there is an isolated obstruction of the suprahepatic segment of the inferior vena cava (Jonas and Lawrence, 1954). In combination with radiography via the right atrium, the nature and precise extent of the lesion can also be ascertained (Kimura et al., 1963; Schaffner et al., 1966; Chapter 8).

Other Procedures (Chapter 6)

Selective coeliac axis arteriography may show retrograde flow in the portal vein which is pathognomonic of hepatic vein occlusion. Displacement of small arterial branches is caused by congested liver lobules and can be mistaken for neoplastic space occupying lesions. On portal venograms the vascular pattern may be distorted in a similar fashion to the cirrhotic liver but the striking feature is the dense contrast and delayed emptying of the portal tree. Failure to visualise segments of the portal tree is probably due to regional retrograde flow, but it cannot be distinguished on portal venograms from branch thrombosis which may complicate cirrhosis or neoplasms. Portosystemic collateral vessels may be present in any cause of portal hypertension, except heart failure.

Scintillation scans generally show the radioactivity restricted to the central zone of the liver near the midline (Chapter 6). Although not diagnostic, this appearance of the scan should draw attention to the Budd-Chiari syndrome. Space occupying lesions such as cysts and neoplasms, which are the underlying cause, may also be demonstrated.

Hepatic congestion can be recognised on peritoneoscopy by the deeply coloured hyperaemic looking liver. In cases of the Budd-Chiari syndrome an extensive collateral circulation has been noted and an enormous congestive hyperplasis of the caudate lobe has been described, lifting the liver, the lesser omentum and its vessels (Caroli et al., 1958; Burger et al., 1961; Caroli, 1961; Dupuy et al., 1964; Strotmeyer, 1964; Clauvel, 1967).

SURGICAL EXPLORATION

The role of surgery is controversial. Exploratory operations rarely contribute information which cannot be obtained more easily. Indeed, in four patients in this study who underwent laparotomy prior to referral, the surgeon failed to reach a conclusion, whereas examination of a liver biopsy suggested the diagnosis. Moreover, as in other forms of liver cell disease, there is a high post-operative mortality. Parker (1959) quoted 4 deaths in 5 cases operated, and Thompson (1947) stated that of 9 patients surgically explored, 8 died, the majority within three days. Out of 30

TABLE 9.2

DIFFERENTIAL DIAGNOSIS OF THE BUDD-CHIARI SYNDROME

Test	Budd-Chiari Syndrome	Suprahepatic caval obstruction	Heart failure	Cirrhosis
Tender hepatomegaly	very frequent	very frequent	very frequent	not present
Ascites	almost invariable	almost invariable	occasionally	often
Ascitic fluid protein	usually + 2 Gm/100 ml.	usually + 2 Gm/100 ml.	variable	usually - 2 Gm/100 ml.
Splenomegaly	frequent	frequent	rare	frequent
Abdominal wall veins	portosystemic/ cavo-caval	portosystemic/ cavo-caval	absent	porto-systemic
Oesophageal varices	occasional	occasional	very rare	frequent
Liver function	moderate impairment	moderate impairment	often normal	moderate/severe impairment
BSP retention	high	high	high	variable
Alkaline phosphatase	raised	raised	usually normal	usually normal
Right atrial pressure	normal/slight elevation	normal/slight elevation	elevated	normal/slight elevation
Free hepatic vein pressure	above right atrial	above right atrial	same as right atrial	above right atrial
Wedged hepatic vein pressure	above right atrial	above right atrial	same as right atrial	high
Intrasplenic pressure	raised	raised	slightly raised	raised
Hepatic venography	obstructed veins, network pattern	normal	normal	reduction and distortion of branches
Hepatography	obstructed veins, delayed drainage, intrahepatic collaterals	delayed drainage	delayed drainage	lymphatics filled, normal drainage
Portal venogram	delayed drainage, "bare areas"	delayed drainage	?	reduction and distortion of branches
Coeliac axis arteriography	Retrograde flow, vessel displacement	?	normal	tortuosity and bunching of arteries
Scintillation scan	uptake mainly over central zone of liver	?	normal	patchy
Inferior vena cavogram	narrow intrahepatic segment/occlusion	occlusion	normal	narrow intrahepatic segment

laparotomies in the last decade there has been a 42 per cent mortality during the first four weeks after the operation (personal assessment).

On the other hand, surgery might be contemplated as a definitive procedure in selected cases after careful evaluation of liver function and delineation of the site of obstruction. The value of surgery will be discussed in the next chapter.

CONCLUSION

The Budd-Chiari syndrome can be accurately diagnosed during life. In the last decade, it has been suspected in 39 out of 80 patients in whom adequate clinical details were recorded (personal assessment). Clinical awareness of this rare disease will allow the application of the special techniques which have been discussed. Needle biopsy of the liver draws attention to hepatic congestion. Functional hepatography is simply performed and will be diagnostic in most instances. Hepatic venography will resolve any doubt and, in addition, should be carried out to determine the extent of the thrombosis. Selective arteriography and scintillation scans are mainly of use in detecting underlying space occupying lesions, but they may also show features which draw attention to thrombosis of the hepatic veins.

CHAPTER 10

TREATMENT OF THE BUDD-CHIARI SYNDROME

Treatment of the Budd-Chiari syndrome has seldom been successful. The high incidence of autopsies testifies to the poor prognosis. An underlying cause is identified in only one third of patients (Parker, 1959) and is usually an inoperable tumour. Polycythaemia vera, however, must be treated.

Treatment of Polychthaemia

Venesection and intravenous (P-32) were successful in reducing the haemocrit in my three patients and, in two, normal levels have been maintained for 30 months after initial treatment (Chapter 4). Case 2 still requires intensive diuretic therapy for fluid retention but, in Case 3, the liver has shrunk in size, ascites has resolved and diuretics have been discontinued. The only other patients with polycythaemia to approach this length of survival are one of the cases reported by Burger et al. (1961), and a patient described by Tapie (1961) who was alive 27 months after hepatic artery ligation (Chapter 3).

Although eminently treatable, patients with polycythaemia and the Budd-Chiari syndrome also have a high mortality. Of the sixteen cases recorded since 1956, only four were alive at the time of reporting (Caroli et al., 1958; Parkinson and Miller, 1961; Burger et al., 1962; Tapie et al., 1961), and the mean

survival of those who died was 2.5 months (personal assessment). Nevertheless, the best outlook is in those patients in whom the underlying cause can be corrected. In my two surviving cases with polycythaemia, a policy of vigorous treatment with initial heparinization and venesections, and subsequent meticulous control of the polycythaemia, seems to have paid dividends.

Diuretic Therapy

Therapy in the Budd-Chiari syndrome remains largely symptomatic. In the past, fluid retention has been refractory to diuretics, and paracenteses have been necessary to relieve tense ascites. However, five of my patients responded to a diuretic regimen consisting of salt restriction, lasix or ethacrynic acid and potassium supplements.

There are few previous accounts of successful treatment with diuretics in the Budd-Chiari syndrome (Cole, 1960; Frank and Peckholz, 1960; Parkinson and Miller, 1961; Beaird and Scofield, 1962). Parkinson and Miller (1961) reported a patient, treated for polycythaemia, who required paracenteses every two weeks. Fluid retention gradually diminished on diuretics and was ultimately controlled by hydroflumethiazide, 200 mg daily, and Mersalyl, 2 ml twice weekly. The case described by Cole (1960) also had polycythaemia and underwent five venesections. Mersalyl injections cleared the peripheral oedema but paracenteses were required every six days. Prednisone and chlorothiazide

were also unsuccessful but a brisk diuresis followed the addition of spironolactone. Urinary sodium excretion rose to 118 mEqu per day, and serum sodium and potassium fell. During this phase, the patient suddenly went into coma from which he never recovered.

Four of my patients with the Budd-Chiari syndrome were closely observed during treatment with diuretics. They received a diet containing 22 mEqu of sodium, approximately 80 mEqu of potassium and 70 gm protein. The patients were weighed daily and the urinary volume, sodium, potassium and chloride were estimated 24-hourly. Serum sodium, potassium, chloride, bicarbonate and blood urea levels were usually measured twice and often thrice weekly. The results are shown in detail for each case in Tables 10.1 to 10.4.

A diuresis was achieved in 3 out of 4 cases (Cases 2, 3, and 5). In Case 6, there was persistent oliguria. She was on the verge of hepatic coma and small doses of lasix and chlorothiazide caused increased drowsiness and tremor, although urinary sodium excretion was seldom more than a few mEqu per day. Death occurred as a result of hepatic coma without a diuresis being effected.

Lasix alone produced a diuresis in Cases 2 and 5, but the latter required spironolactone to curtail the enormous urinary potassium loss. In Case 3, lasix proved ineffective and a diuresis was obtained with 125 mg of ethacrynic acid, daily.

It is often difficult to separate the complications that seem to follow diuretic therapy from those that might develop spontaneously in patients with severe liver disease. For example, in Cases 3 and 6 (Tables 10.2 and 10.4) hyponatraemia and hypochloraemia were present before the onset of treatment and persisted during the administration of diuretics. On the other hand, alkalosis developed in Case 3 during treatment with large doses of ethacrynic acid which caused urinary chloride losses up to 190 mEqu per day. Azotaemia occurred on only one patient (Case 6) as a terminal event.

However, serum electrolytes are a poor indication of urinary losses and total body stores of electrolytes. When large doses of potent diuretics are being administered, the daily output of urinary electrolytes is a valuable guide to treatment. The 3 patients in whom a diuresis was successfully achieved had a peak daily potassium loss of from 133 to 200 mEqu. Supplements of up to 180 mEqu per day of potassium were given as tablets containing 9 mEqu of potassium and 4 mEqu of chloride. As the oral dose of potassium was increased, the urinary loss frequently rose. This was clearly shown in Case 5 (Tables 10.3 a and b). Measured faecal losses were insignificant. An attempt was made to counteract chloride loss and alkalosis by the administration of betaine and glycine hydrochloride, as the use of ammonium chloride is unwise in liver disease. However, gastric side effects limited

TABLE 10.1

CASE 2

TREATMENT OF FLUID RETENTION

Day	Diuretic	24-hour urine volume ml.	Na mEqu.	Cl mEqu.	K mEqu.	Daily Potassium Supplement mEqu.	per litre plasma Na mEqu.	K mEqu.	Cl. mEqu.	CO 2 mEqu.	Urea mg.
1	0	1,320	2	24	16	0	130	3.9	88	28	200
2	0	320	1	1	8	0					
3	L 40	660	1	1	2	0					
4	L 40	770	3	2	12	0					
5	L 40	1,680	3	5	19	0	127	3.4	88	25	470
6	L 40	780	3	8	12	0					
7	L 40	1,100	1	4	11	0					
8	L 40	630	4	10	11	0					
9	L 40	985	6	13	19	0					
10	L 80	1,615	18	44	35	0					
11	L 120	2,100	63	124	66	0	130	3.6	83	29	
12	L 160	1,600	40	95	54	0					
13	L 120	1,460	30	60	41	0					
14	L 120	1,345	25	50	39	0					
15	L 120	1,050	5	50	37	0	120	2.9	81	28	
16	L 120	1,240	15	42	61	0					
17	L 120	1,220	12	42	96	144	130	4.8	84	32	340
18	L 120	1,530	39	75	115	144					
19	L 120	1,150	7	52	88	144					
20	L 120	1,710	50	109	134	144					
21	L 120	1,335	40	72	119	144					
22	L 120	1,400	47		122	144	130	4.6	91	26	
23	L 120	1,200	25		130	144					
24	L 120	1,220	18		142	144					
25	L 120	1,350	35		142	144					
26	L 120	1,290	20		149	144	137	4.8	90	35	
27	L 120	1,220	39		95						
28	L 120	1,270	37		74						
29	L 120	1,060	23		55		140	4.8	85	36	
30	L 120	905	17		42						
31	L 120	1,060	18		46	(100)					
32	L 120	1,220	21		40	(100)					
33	L 120	1,300	20		48	(100)	130	4.4	90	25	380
34	L 120	1,210	10		44	(100)					
35	L 120	1,460	27		50	(100)	130	3.8	90		380
36	L 120	1,430	42		47	(100)					
		RE-ADMITTED AFTER 3.5 MONTHS									
1	L 80	1,680	10	54	65	72	133	4.2	87	31	
2	L 80	1,380	9	48	62	72	130	3.7	89	23	
3	L 80	2,080	25	83	73	72					
4	L 80	1,610	14	76	42	72					
5	L 80	1,660	17	76	56	72					
6	L 80	1,760	9	74	60	72					
7	L 80	1,800	50	65	65	72	123	3.9	88	28	380
8	L 80	1,000	10	35	74	72					
9	L 80	1,410	11	51	73	72					

Abbreviations (Tables 10.1 - 10.4)

Diuretics: L, lasix; A, spironolactone; EA, ethacrynic acid;
C, chlorothiazide; numbers, daily dose in milligrams.

Potassium supplement: an effervescent preparation containing 4 mEqu. of chloride for every 9 mEqu. of potassium.

Figures in parenthesis refer to mEqu. of chloride supplement as glycine or betaine hydrochloride.

TABLE 10.2

CASE 3

TREATMENT OF FLUID RETENTION

Day	Diuretic	24-hour urine volume ml.	Na mEqu.	Cl mEqu.	K mEqu.	Daily Potassium Supplement mEqu.	per litre plasma Na mEqu.	K mEqu.	Cl mEqu.	CO_2 mEqu.	Urea mg.
1	0	780	8	3	72	0					
2	0	590	1	2	24	0					
3	0	910	1	4	29	0					
4	0	1,350	1	5	31	0					
5	0	1,200	1	5	24	0					
6	0	1,200	1	5	20	0					
7	0	900	1	5	17	0	120	4.0	79	20	300
8	0	435	1	3	12	0	120	4.0	79	20	
9	L 40	1,050	1	6	13	0					
10	L 40	1,930	1	8	18	0					
11	L 80	2,090	2	29	36	0					
12	L 80	2,600	2	26	57	0	117	4.2	79	29	320
13	L 80	1,280	2	19	36	0					
14	L 80	850	1	8	22	0	120	3.4	76	26	260
15	L 80	1,530	1	9	20	0					
16	L 120	1,750	5	37	39	0					
17	L 160	1,420	19	19	14	0	120	3.1	83	26	280
18	L 160	1,120	12	50	23	0					
19	EA 12.5	670	1	4	23	0					
20	EA 25	810	1	5	28	0					
21	EA 25	880	1	14	45	0	120	3.8	78	31	300
22		590	1	4	35	0					
23		770	1	4	31	0					
24	EA 25	1,100	2	16	56	0					
25	EA 25	1,260	2	49	48	0	120	3.7	87	32	300
26	EA 25	950	1	10	41	0					
27	EA 25	1,260	1	12	38	0					
28	EA 25	930	1	5	27	0	117	2.9	80	27	220
29	EA 50	1,180	14	80	68	144					
30	EA 50	1,130	7	127	112	144	127	3.8	80	33	
31	EA 100	1,350	18	151	112	144					
32	EA 125	1,600	40	157	98	144	123	4.1	82	32	
33	EA 125	2,120	102	157	74	144					
34	EA 125	1,570	36	166	106	144					
35	EA 125	1,680	44	165	98	144					
36	EA 125	1,710	47	145	85	144	127	3.2	80	32	
37	EA 125	1,900	61	181	95	144					
38	EA 125	1,690	32	188	111	144 (100)					
39	EA 125	1,880	43	192	102	144 (100)	127	2.8	72	38	490
40	EA 125	880	1	117	133	144 (100)	127	3.4	74	36	450
41	EA 125	1,900	45	129	68	144 (100)					
42	EA 125	1,920	60	111	58	144 (100)	123	3.7	79	36	

TABLE 10.3 a CASE 5

TREATMENT OF FLUID RETENTION (FIRST ADMISSION)

Drug	Diuretic	24-hour urine				Daily Potassium Supplement	per litre plasma				
		Volume ml.	Na mEqu.	Cl mEqu.	K mEqu.	mEqu.	Na mEqu.	K mEqu.	Cl mEqu.	CO_2 mEqu.	Urea mg.
1	0	450	1	2	40	0					
2	L 40	520	1	2	41	0	137	3.2	99	32	220
3	L 80	450	1	2	10	0					
4	L 120	1,450	37	105	62	0	133	3.4	94	32	
5	L 120	2,000	84	178	74	0	134	3.9	88	28	220
6	L 120	1,600	40	86	54	0					
7	L 120	1,460	26	54	48	0					
8	L 120	1,670	57	75	48	0					
9	L 120	1,380	40	52	57	0					
10	L 120	1,470	31	44	62	0	137	3.0	85	39	300
11	L 120	940	25	41	56	0	133	2.5	84	39	
12	L 120	1,330	12	24	101	0					
13	L 120	1,350	8	20	163	144	127	2.6	80	39	
14	L 120	1,170	3	28	131	144					
15	L 120	1,445	11	40	160	144					
16	L 120	1,330	13	58	172	144					
17	L 120	1,770	53	116	195	144	140	3.8	90	34	
18	L 120	1,182	17	69	149	144					
19	L 120	1,020	16	59	103	144	140	3.2	93	33	
20	L 120	1,850	55	109	150	144					
21	L 120	1,605	10	47	177	144					
22	L 120	1,300	12	28	157	144					
23	L 120	1,180	11	39	113	144	140	3.1	93	34	
24	L 120	1,670	32	99	192	144					
25	L 120	1,460	11		158	144					
26	L 120	1,400	19		170	144	137	3.6	100	30	300
27	L 120	1,910	74		183	144					

TABLE 10.3 b CASE 5

TREATMENT OF FLUID RETENTION (READMITTED AFTER 4 MONTHS)

Day	Diuretic	24-hour urine Volume	Na mEqu.	Cl mEqu.	K mEqu.	Daily Potassium Supplement mEqu.	per litre plasma Na mEqu.	K mEqu.	Cl mEqu.	CO 2 mEqu.	Urea mg.
1	L 120	1,770	74	103.	117	180	137	2.6	84	39	320
2	0	1,200	2	19	148	180	148	2.6	86	36	370
3	L 120	1,770	62	119	174	180					
4	L 120	1,600	54	110	168	180	137	2.6	83	39	
5	0	1,050	1	8	200	180					
6	0	1,660	1	7	125	180					
7	0	900	2	5	158	180	130	3.1	91	36	
8	0	620	1	5	186	180	140	3.3	96	35	
9	L 40 A 200	1,060	28	91	148	180	140	3.7	91	33	
10	L 40 A 200	700	20	22	140	180					
11	L 80 A 200	1,600	85	189	173	180	130	4.2	97	30	
12	L 80 A 200	1,260	49	139	194	180					
13	L 80 A 200	1,640	53	138	198	180					
14	L 80 A 200	1,210	23	103	166	180					
15	L 80 A 200	1,400	42	116	165	180	127	3.8	94	32	340
16	L 80 A 200	1,970	7	56	96	180	133	4.0	96	28	320
17	L 80 A 200	1,200	10	58	73	180					
18	L 80 A 200	1,250	38	63	50	180	133	3.7	91	32	400
19	L 80 A 200	1,640	64	118	72	180	137	3.4	80	37	340
20	L 80 A 200	1,410	52	65	56	180					
21	L 80 A 200	1,670	51	63	53	180	127	3.5	86	32	380
22	L 80 A 200	1,490	52	54	72	180					
23	L 80 A 200	1,150	27	30	66	180					
24	L 80 A 200	-	-	-	-	180					
25	L 80 A 200	1,300	14	50	35	180	137	3.8	83	35	400
26	L 80 A 200	1,030	6	40	45	180					
27	L 80 A 200	1,400	19	22	66	180					
28	L 80 A 200	1,525	28	40	86	180					
29	L 80 A 200	2,000	37	52	94	180					
30	L 80 A 200	1,100	6	13	76	180					
31	L 80 A 200	1,400	11	25	64	180					
32	L 80 A 200	1,300	9	14	75	180					
33	L 80 A 200	1,200	10	11	76	180					
34	L 80 A 200	1,200	20	7	45	180					
35	L 80 A 200	1,800	18	22	75	180					
36	L 80 A 200	1,500	8	15	44	180					
37	L 80 A 200	1,400	8	36	67	180	133	3.3	89	27	320

TABLE 10.4

CASE 6

TREATMENT OF FLUID RETENTION

Day	Diuretic	24-hour urine Volume ml.	Na mEqu.	Cl mEqu.	K mEqu.	Daily Potassium Supplement mEqu.	per litre plasma Na mEqu.	K mEqu.	Cl mEqu.	CO_2 mEqu.	Urea mg.
1		980	0.8	6	39	0	123	4	83	30	360
2		1,480	0.6	12	33	0					
3		710	0.5	5	27	0					
4	L 40	1,270+	2.7	10	20	0	124	4.6	86	30	300
5		75	2.5	3	1	0					
6		1,470				0	120	4.4	77	22	630
7		350+	1.7	4	9	0					
8		430+	2.9	2	16	0	133	3.2	88	28	690
9		48+	0.1	0.2	2	108					
10		530+	1.2	2	39	108	137	3.2	82	34	460
11		270+	0.8+	1	20+	108	137	3.2	82	34	460
12		380	1.0	1	38	108	130	3.2	89	34	450
13		250	0.5	3	35	108	127	3.8	86	30	380
14		970	40.0	8	135	108					
15		260	0.6	2	32	108	140	3.0	87	30	500
16		-	-	-	-	108					
17		240	0.6	1	31	108	127	3.7	89	30	500
18		230	0.4	1	34	108					
19		145	0.2	1	28	108	120	4.6	88	25	480
20		280	0.4	2	52	108					
21		300	0.4	3	47	108	127	4.6	93	25	420
22	L 20	310	0.3	2	42	108					
23	L 20	380	0.3	5	55	108					
24	L 20	430	0.3	3	72	108					
25	L 40	350	0.3	4	56	0	124	5.3	90	27	550
26	L 40	480	0.4	17	82	0	124	5.2	90	26	500
27	L 40	600	0.5	3	8	0					
28	L 40	360	0.4	1	26	0					
29	L 40	250	0.3	1	15	0					
30	L 40	550	0.4	2	26	0					
31	L 40	480	0.8	3	11	0					
32	L 40	210	0.2	3	9	0					
33	L 40	360	0.2	1	11	96					
34	L 40	300	0.3	2	17	96	124	3.1	88	25	460
35	L 40	590	0.5	1	34	96					
36	C 1,000	220	0.2	1	16	96					
37	C 1,000	220	0.7	3	17	96					
38	C 1,000	-	-	-	-	96					
39	C 1,000	700	0.8	1	68	96					
40	C 2,000	290	0.1	3	32	96					
41	C 2,000	650	0.5	1	63	96	124	4.5	84	26	500
42	C 2,000	-	-	-	-	96	120	4.0	85	21	
43	C 2,000	540	0.4	3	58	96					
44	L 80	390	0.4	4	45	96	120	5.8	75	17	800
45	C 80	850	0.1	59	98	108					
46	L 120	750	2.6	66	71	108	130	5.2	75	19	
47	L 120	1,600	4.0	109	112	108					
48	L 120	630	1.1	19	28	144	127	3.0	82	22	660
49	L 120	240				144					
50	L 120	nil					124	5.4	85	16	1,230
51	-	250	0.5	3	17						
52	Died										

the dose which could be tolerated.

Treatment of fluid retention in the Budd-Chiari syndrome raises the same problems as the management of refractory ascites in cirrhosis (Sherlock et al., 1966). Hypokalaemia, hypochloraemia, metabolic alkalosis and azotaemia are frequent side effects of the powerful drugs which are needed to produce a diuresis. Patients with borderline hepatic functions are easily precipitated into coma by these metabolic derangements. Careful manipulation of drug dosage and electrolyte supplements is essential. Cole's (1960) patient, mentioned above, almost certainly lapsed into coma as a result of diuretic therapy, and the same is probably true of Case 6 in this study. It is concluded that fluid retention can usually be dispelled in the Budd-Chiari syndrome if salt is rigidly restricted and large doses of diuretics and electrolyte supplements are administered. For the same degree of liver dysfunction, the doses of diuretics required in the Budd-Chiari syndrome are much greater than in cirrhosis, and the side effects are correspondingly increased. Control of ascites increases the patient's comfort, but does not necessarily improve the prognosis.

Surgical Treatment

Surgical treatment in hepatic vein thrombosis holds out the only real hope of cure, and it is the only effective means of relieving established portal hypertension. In practise, the results of surgery have been disappointing. The hepatic veins are

TABLE 10.5

SURGICAL TREATMENT OF THE BUDD-CHIARI SYNDROME

Procedure	Authors	Fate	Post-operative survival (months)
Splenorenal shunt	Blakemore, 1948	alive	18
Splenorenal shunt	Fitzgerald et al., 1956	died	12
Portocaval shunt (end to side)	Lebon, 1955	died	0
Portocaval shunt (end to side)	Case records, 1958	Died	2
Portocaval shunt (end to side)	Wantz and Payne, 1961	died	0
Portocaval shunt (side to side)	Erlik et al., 1962	alive	6
Portocaval shunt (side to side)	Dukes et al., 1963	died	0
Portocaval shunt (side to side)	Leger et al., 1964	alice	36
Portocaval shunt (side to side)	Ludwick et al., 1965	died	1
Portocaval shunt (side to side)	Hoffbauer, 1966	died	0
Mesenteric-caval shunt	Cox et al., 1966	died	0
Splenic vein - pulmonary artery shunt	Fonkalsrud et al., 1966	alive	9
Splenic vein - pulmonary artery shunt	Leger et al., 1966	alive	9
Mesenteric - right atrial Dacron shunt	Hales and Scatliff, 1966	died	0
Cavo - right atrial Dacron shunt	Ohara et al., 1963	alive	10
Thrombectomy and cavo -caval prosthetic shunt	Case records, 1965	died	0
Cavo - caval Nylon shunt	Eguchi et al., 1966	alive	7
Thoracic transposition of the spleen	Schreiber and Gonzales, 1967	alive	48
Ligation of hepatic and splenic arteries	Norris, 1956	died	12
Ligation of hepatic artery	Tapie et al., 1961	alive	27
Ligation of hepatic artery	Safouh and Shehata, 1965	died	0
Haematoma evacuated	Ekstrom and Hagberg, 1957	alive	4
Probing of hepatic veins	Nicollof et al., 1964	alive	?
*Transcardiac membranotomy	Kimura et al., 1963	died	0
*Transcardiac membranotomy	Kimura et al., 1963	alive	?
*Transcardiac membranotomy	Kimura et al., 1963	alive	?
*Transcardiac membranotomy	Kimura et al., 1963	alive	?
*Transcardiac membranotomy	Kimura et al., 1963	dead	0
*Transcardiac membranotomy	Watkins and Fortin, 1964	alive	?
*Transcardiac membranotomy	Lam et al., 1965	alive	?
*Transcardiac membranotomy	Lam et al., 1965	alive	?
*Transcardiac membranotomy	Schaffner et al., 1966	alive	5
*Caval endovenectomy	Manabe, 1964	alive	2

*Cases of suprahepatic caval obstruction, not Budd-Chiari Syndrome.

relatively inaccessible so that most operations have aimed at decompressing the portal system. Removal of the outflow obstruction would be ideal but this has been described in only two patients, both with an intrahepatic haematoma. Evacuation of the blood in one case (Ekstrom and Hagberg, 1957) and probing of the hepatic veins in the other (Nicoloff et al., 1964) resulted in post-operative improvement and apparent recovery.

In obstruction of the suprahepatic portion of the cava, operative treatment has been highly successful. The clinical features are often indistinguishable from hepatic vein thrombosis and several patients have, in fact, been incorrectly reported as cases of the Budd-Chiari syndrome (Schaffner et al., 1966). Most of the patients have had a membranous obstruction of the cava just below the diaphragm. The simplest surgical manoeuvre has been to split manually the fibrous membrane after gaining access to the cava from the right atrium (Kimura et al., 1963; Lam et al., 1965; Schaffner et al., 1967). In one case (Watkins and Fortin, 1964), the membrane was excised after opening the inferior vena cava, and the deficiency in the vessel wall was grafted with a pericardial patch. Schaffner et al. (1967) have described the use of a mitral guillotine knife and valve dilator to increase the final size of the orifice.

This experience with operations for removing membranous obliteration of the inferior vena cava might be extended to cases of occlusion of the hepatic vein ostia. Resection of localised thrombi has never been reported, but with advances in vascular surgery, definitive operations might be contemplated in selected patients after careful evaluation of liver function and delineation of the site of the obstruction. For example, in Case 2 in this study, hepatic venography and hepatography precisely determined the nature and site of the lesion, and operative removal of the localized thrombi was considered. This was avoided by the improvement that followed vigorous treatment of her polycythaemia. In many cases, the underlying cause is a malignant tumour of the liver, adrenal gland or inferior vena cava, and a direct surgical approach would clearly be impossible.

Surgery for the Budd-Chiari syndrome has been mainly directed at reducing the portal pressure and the hepatic congestion by diverting blood from the liver. This has been achieved by hepatic artery ligation and by a variety of portosystemic shunts. There have been reports of splenorenal, end-to-side and side-to-side portocaval, mesenteric-caval, splenic vein-pulmonary arterial and mesenteric-right atrial shunts. These bypass procedures have reduced hepatic blood flow, decompressed the portal system and, with the exception of side-to-side portocaval shunts, have also provided a route of egress for reversed portal blood flow. The

end-to-side portocaval shunts have been universally fatal. Out of a total of 14 portosystemic shunts, 6 patients survived more than two months (Table 10.5). Although clinical progress was evident in several cases (Erlik et al., 1962; Leger et al., 1964; Fonkalsrud et al., 1966; Leger et al., 1966), liver function improved in only one (Fitzgerald et al., 1956) (Chapter 3).

Inferior vena caval obstruction complicating hepatic vein thrombosis precludes the use of this vessel for portosystemic shunting, but the right atrium and the pulmonrary artery have been used on three occasions. A mesenteric-right atrial bypass using a Dacron prosthesis was unsuccessful in a patient with the Budd-Chiari syndrome of longstanding who had persistent variceal bleeding. Operative measurements of portal pressure showed that the shunt was patent but the patient never regained full consciousness post-operatively (Hales and Scatliff, 1966). In two other patients, surgical decompression of the portal venous system was accomplished by splenectomy and placement of a Teflon graft between the splenic vein and the divided pulmonary artery to the left lower lobe, since the standard methods of portosystemic shunting were not possible (Fonkalsrud et al., 1966; Leger et al., 1966). Both patients showed marked clinical improvement during the nine months following operation.

In two cases of membranous obstruction of the inferior vena cava, there was secondary caval and hepatic vein thrombosis which

prevented simple membranotomy (Ohara et al., 1963; Eguchi et al., 1966). One of the main hepatic veins remained patent in each case so that hepatic decompression was possible by constructing a bypass from the cava to the right atrium or back into the cava above the obstruction. In both patients a prosthesis was successfully inserted, and clinical improvement ensued. The patency of the graft was confirmed by venography after seven months in one case (Eguchi et al., 1966) and liver biopsy showed resolution of congestion after four months in the other (Ohara et al., 1963).

Also faced with the problem of caval occlusion complicating the Budd-Chiari syndrome, Schreiber and Gonzales (1967) elected to treat the portal hypertension by transplanting the spleen into the thoracic cavity. They based their decision on the experimental work of Turcotte et al. (1961), who showed that splenic transposition after caval constriction and portal vein occlusion caused reversal of flow in the splenic vein and the production of multiple collateral vessels in the chest. The patient of Schreiber and Gonzales (1967) improved after this procedure and required no paracentesis for four years. Splenic venography after three months demonstrated collateral vessels in the thoracic cavity but the intrasplenic pressure was unchanged from the pre-operative level of 32 cm of saline.

Hepatic artery ligation has also been used to reduce hepatic congestion (Norris, 1956; Tapie et al., 1961; Safouh and Shehata, 1965) and two out of three cases survived the operation.

CONCLUSION

It is not possible to draw valid comparisons between the various operative procedures. Definite improvement followed surgery in a few cases but the data are insufficient to conclude that operative intervention holds out a better hope of survival. Surgery should certainly be considered in patients with satisfactory liver function who have bled from varices, but one hesitates to recommend operations in all cases when there is such a high operative mortality.

When the inferior vena cava is occluded, caval bypass procedures seem to be of value if at least one hepatic vein is patent below the obstruction. With advances in vascular surgery, a direct approach to the hepatic veins might be contemplated in selected cases after precise determination of the site of the obstruction by hepatography, inferior vena cavography and hepatic venography.

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