CHAPTER 9
The Hepatic Artery, Portal Venous System and Portal Hypertension: the Hepatic Veins and Liver in Circulatory Failure

Andrew K. Burroughs
Royal Free Sheila Sherlock Liver Centre, Royal Free Hospital and University College, London, UK

Learning points
• The hepatic artery forms a capillary plexus around the bile ducts. Thrombosis or ischaemia of the hepatic artery leads to bile duct injury, such as due to surgical injury, or after liver transplantation.
• Hepatic arterial flow increases in cirrhosis and is modulated together with portal venous inflow. Hepatic arterial flow is the main blood supply to liver tumours.
• Portal vein thrombosis is frequently associated with pro-thrombotic conditions; in cirrhosis it is also associated with the severity of the liver disease.
• Portal hypertension develops due to increasing hepatic fibrosis, together with increased splanchnic venous flow. There is a component of reversible intrahepatic resistance. A collateral circulation develops, including varices in the oesophagus and stomach, which can bleed.
• Increased portal pressure and its surrogate the hepatic venous pressure gradient, are associated with the development of complications and mortality in cirrhosis, independently from the severity of liver dysfunction.
• Primary prevention of bleeding from varices or portal hypertensive gastropathy is best undertaken with non-selective beta-blockers, with banding ligation of varices as an alternative. Secondary prevention is best undertaken with combined ligation and non-selective-beta blockers.
• Acute variceal bleeding is best treated with combined vasoactive drugs and endotherapy, together with antibiotics. Failure can be managed with transjugular intrahepatic portosystemic shunt (TIPS), variceal injection of adhesive glue and temporarily with balloon or stent tamponade.
• Hepatic venous outflow obstruction is mainly due to thrombosis of the hepatic veins, frequently associated with thrombophilic conditions. Constrictive pericarditis should always be excluded. Anticoagulation and venoplasty often cure the condition, TIPS is used for failures. Liver transplantation may be needed.
• Hypoxic hepatitis results from severe hypotension, such as shock, and is also seen with heart failure. Treatment is of the primary cause.

The hepatic artery
The hepatic artery is a branch of the coeliac axis. It runs along the upper border of the pancreas to the first part of the duodenum where it turns upwards between the layers of the lesser omentum, lying in front of the portal vein and medial to the common bile duct. Reaching the porta hepatis it divides into right and left branches. Its branches include the right gastric artery and the gastroduodenal artery. Aberrant branches are common. Surgical anatomy has been defined in donor livers [1]. The common hepatic artery usually rises from the coeliac axis to form the gastroduodenal and proper hepatic artery which divides into right and left branches. A replaced or accessory right hepatic artery may originate from the superior mesenteric artery. A replaced or accessory left hepatic artery may arise from the left gastric artery. Rarely, the entire common hepatic artery
The Hepatic Artery, Portal Venous System and Portal Hypertension

of blood and oxygen they supply to the liver according to demand [6].

**Hepatic arteriography**

Hepatic arteriography can be used for the diagnosis of space-occupying lesions of the liver, but cross-sectional imaging has greatly reduced this indication. Lesions include cysts, abscesses and benign and malignant tumours (Chapter 35), as well as vascular lesions such as aneurysms (Fig. 9.2) or arteriovenous fistulae. Embolization via a catheter is used for treating tumours and hepatic trauma, and in the management of

![Fig. 9.1. The hepatic artery (HA) forms a peribiliary plexus supplying the bile duct (BD). PV, portal vein.](a)

![Fig. 9.2. Hepatic artery aneurysm in a patient with subacute bacterial endocarditis. CT scans of the upper abdomen: (a) before and (b) after contrast enhancement. The aneurysm shows as a filling defect (arrow) which highlights following contrast injection.](b)
The size of the infarct depends on the extent of the collateral arterial circulation. It rarely exceeds 8 cm in diameter and has a pale centre with a surrounding congested haemorrhagic band. Liver cells in the infarcted area are jumbled together in irregular collections of eosinophilic, granular cytoplasm without glycogen or nuclei. Subcapsular areas escape because they have an alternative arterial blood supply.

Hepatic infarction can develop without arterial occlusion in shock, cardiac failure, diabetic ketosis, toxoaemia of pregnancy [9], after liver transplant or systemic lupus erythematosus [10]. If sought by scanning, small hepatic infarcts are frequent after percutaneous liver biopsy.

Aetiology

Occlusion of the hepatic artery is very rare. Hitherto it was regarded as a fatal condition. However, hepatic angiography has allowed earlier diagnosis and the prognosis has improved. Some of the causes are polyarteritis nodosa, giant cell arteritis and embolism in patients with acute bacterial endocarditis. A branch of the artery may be tied during cholecystectomy but recovery is usual. Trauma to the right hepatic or cystic artery may complicate laparoscopic cholecystectomy [11]. Hepatic arterial dissection may follow abdominal trauma or hepatic arterial catheterization. Gangrenous hepatic arterial aneurysms or arteriovenous fistulae (Figs 9.3, 9.4).

Hepatic arterial catheterization is used to introduce cytotoxic drugs or radioactive beads into hepatocellular neoplasms and for pump perfusion in patients with metastases, particularly from colorectal cancer (Chapter 35).

Spiral CT is of great value in diagnosing hepatic arterial thrombosis after liver transplant [7] and variations in intrahepatic anatomy before liver resection [8].

Hepatic artery occlusion

The effects depend on the site and extent of available collateral circulation. If the division is distal to the origins of the gastric and gastroduodenal arteries the patient may die. Survivors develop a collateral circulation. Slow thrombosis is better than sudden block. Simultaneous occlusion of the portal vein is nearly always fatal.
cholecystitis can complicate hepatic artery embolization [12].

Clinical features
The condition is rarely diagnosed ante-mortem. The patient exhibits the features of the cause, such as bacterial endocarditis or polyarteritis nodosa, or has undergone a difficult upper abdominal operation. Sudden pain in the right upper abdomen is followed by collapse and hypotension. Right upper quadrant tenderness develops and the liver edge is tender. Jaundice deepens rapidly. There is usually fever and leucocytosis and liver function tests show hepatocellular damage. The prothrombin time rises precipitously and haemorrhages develop. With major occlusions the patient passes into coma and is dead within 10 days.

Hepatic arteriography. This is essential. The obstruction to the hepatic artery may be shown. Intrahepatic arterial collaterals develop in the portal zones and subcapsular areas. Extrahepatic collaterals form in the suspensory ligaments and with adjacent structures.

Scanning. The infarcts are round, oval or wedge-shaped and are centrally located. Early lesions are hypoechoic on ultrasound. CT shows infarcts as low attenuation, peripheral wedged-shaped lesions. Occluded arterial vessels may be identified. Later lesions are confluent with distinct margins. MRI shows a lesion of low signal intensity on T1-weighted images and with high signal intensity on T2-weighted images [10]. Bile lakes follow large infarcts and these may contain gas.

Treatment. The causative lesion must be treated. Antibiotics and antifungals may prevent secondary infection in the anoxic liver. The general management is that of acute hepatocellular failure. Trauma to the artery is treated by percutaneous arterial embolization.

Hepatic arterial lesions following liver transplantation
The term ischaemic cholangitis is used to describe bile duct damage due to ischaemia [13]. It follows post-transplant-associated thrombosis or stenosis of the hepatic artery or occlusion of peribiliary arteries [14] and is associated with a poor quality donor liver such as one from a non-heart-beating donor. Later, thrombosis or stenosis of the hepatic artery or occlusion of peribiliary arterials leads to segmental hepatic infarction with abscesses and biloma [14]. The picture may be asymptomatic or present as relapsing bacteraemia.

Early diagnosis is made by duplex ultrasound. Spiral CT is highly accurate [7].

Re-transplantation is the only management for lesions of the hepatic artery following transplant. Ischaemic cholangitis manifesting as segmental strictures and cholangiectases with resultant impaired bile flow can also follow hepatic arterial chemotherapy and systemic vasculitis.

Aneurysms of the hepatic artery
These are rare but make up about one-fifth of all visceral aneurysms. The aneurysm may complicate bacterial endocarditis, polyarteritis nodosa or arteriosclerosis. Trauma is becoming increasingly important, including motor vehicle accidents and iatrogenic causes such as biliary tract surgery, liver biopsy and interventional radiological procedures. Pseudoaneurysms may complicate chronic pancreatitis with pseudocyst formation. Bile leaks are significantly associated with pseudoaneurysm [15]. It may be congenital. The aneurysm may be extra- or intrahepatic and may vary in size from a pin point to a grapefruit: it may be congenital.

Clinical presentation. The classical triad of jaundice [16], abdominal pain and haemobilia is present in only about one-third. Abdominal pain is frequent and may last as long as 5 months before the aneurysm ruptures. Between 60 and 80% of patients present for the first time with rupture into the peritoneum, biliary tree or gastrointestinal tract with resultant haemoperitoneum, haemobilia or haematemesis.

Diagnosis. The diagnosis is suggested by sonography and confirmed by hepatic arteriography and a CT scan after enhancement (Fig. 9.2) [17]. Pulsed Doppler ultrasound may show turbulent flow in the aneurysm [18].

Treatment. Intrahepatic aneurysms are treated by angiographic embolization (Figs 9.3, 9.4). Aneurysms of the common hepatic artery may also be treated surgically by proximal and distal ligation.

Hepatic arteriovenous shunts
These are usually secondary to blunt trauma, liver biopsy or neoplasms, usually primary liver cancer. Multiple shunts may be part of hereditary haemorrhagic telangiectasia, when they can be so extensive that congestive heart failure follows.

Large shunts cause a bruit in the right upper quadrant. The diagnosis is confirmed by hepatic angiography. Embolization with particles and/or placement of occluding devices is the usual treatment.
Chapter 9

Fig. 9.5. The anatomy of the portal venous system. The portal vein is posterior to the pancreas.

The portal venous system

The portal system includes all veins that carry blood from the abdominal part of the alimentary tract, the spleen, pancreas and gallbladder. The portal vein enters the liver at the porta hepatis in two main branches, one to each lobe; it is without valves in its larger channels (Fig. 9.5) [19].

The portal vein is formed by the union of the superior mesenteric vein and the splenic vein just posterior to the head of the pancreas at about the level of the second lumbar vertebra. It extends slightly to the right of the midline for a distance of 5.5–8 cm to the porta hepatis. The portal vein has a segmental intrahepatic distribution, accompanying the hepatic artery.

The superior mesenteric vein is formed by tributaries from the small intestine, colon and head of the pancreas, and irregularly from the stomach via the right gastroepiploic vein.

The splenic veins (5–15 channels) originate at the splenic hilum and join near the tail of the pancreas with the short gastric vessels to form the main splenic vein. This proceeds in a transverse direction in the body and head of the pancreas, lying below and in front of the artery. It receives numerous tributaries from the head of the pancreas, and the left gastroepiploic vein enters it near the spleen. The inferior mesenteric vein, bringing blood from the left part of the colon and rectum, usually enters its medial third. Occasionally, however, it enters the junction of the superior mesenteric and splenic veins.

Portal blood flow in man is about 1000–1200 mL/min. The fasting arteriportal oxygen difference is only 1.9 volumes per cent (range 0.4–3.3 volumes per cent) and the portal vein contributes 40 mL/min or 72% of the total oxygen supply to the liver. During digestion, the arteriportal venous oxygen difference increases due to increased intestinal utilization.

Stream-lines in the portal vein: there is no consistent pattern of hepatic distribution of portal inflow. Sometimes splenic blood goes to the left and sometimes to the right. Crossing-over of the bloodstream can occur in the portal vein. Flow is probably stream-lined rather than turbulent.

Portal pressure is about 7 mmHg (Fig. 9.6).

Collateral circulation

When the portal circulation is obstructed, whether it be within or outside the liver, a remarkable collateral circulation develops to carry portal blood into the systemic veins (Figs 9.7, 9.8).

Intrahepatic obstruction (cirrhosis)

Normally 100% of the portal venous blood flow can be recovered from the hepatic veins, whereas in cirrhosis only 13% is obtained [20]. The remainder enters collateral channels which form four main groups.

Group I: where protective epithelium adjoins absorptive epithelium:

(a) At the cardia of the stomach, where the left gastric vein, posterior gastric [21] and short gastric veins of the portal system anastomose with the intercostal, diaphragmo-oesophageal and azygos minor veins of the caval system. Deviation of blood into these channels leads to varicosities in the submucous layer of the lower end of the oesophagus and fundus of the stomach.

(b) At the anus, the superior haemorrhoidal vein of the portal system anastomoses with the middle and inferior haemorrhoidal veins of the caval system. Deviation of blood into these channels may lead to rectal varices.

Group II: in the falciform ligament through the paraumbilical veins, relics of the umbilical circulation of the fetus (Fig. 9.9).

Group III: where the abdominal organs are in contact with retroperitoneal tissues or adherent to the abdominal wall. These collaterals run from the liver to
Fig. 9.6. The flow and pressure in the hepatic artery, portal vein and hepatic vein.

Flow and Pressure:
- **Hepatic vein**: Flow 1600 ml, Pressure 4 mmHg
- **Portal vein**: Flow 1200 ml, Pressure 7 mmHg
- **Hepatic artery**: Flow 400 ml, Pressure 100 mmHg

Fig. 9.7. The sites of the portal-systemic collateral circulation in cirrhosis of the liver.

Sites of Collateral Circulation:
- **Veins of Sappey**
- **Diaphragm**
- **Oesophageal varices**
- **Stomach**
- **Coronary vein**
- **Liver**
- **Para-umbilical vein**
- **Abdominal wall**
- **Inferior mesenteric vein**
- **Omentum**
- **Abdominal wall**
- **Renal vein**
- **Spleen**
- **Veins of Retzius**
- **Spermatic vein**
- **Epigastric vein**
- **Subcutaneous abdominal vein**
- **Superior haemorrhoidal vein**
- **Inferior haemorrhoidal vein**
- **Rectum**
- **Vein of Retzius**
diaphragm and in the splenorenal ligament and omentum. They include lumbar veins and veins developing in scars of previous operations or in small or large bowel stomas.

**Group IV:** portal venous blood is carried to the left renal vein. This may be through blood entering directly from the splenic vein or via diaphragmatic, pancreatic, left adrenal or gastric veins.

Blood from gastro-oesophageal and other collaterals ultimately reaches the superior vena cava via the azygos or hemiazygos systems. A small volume enters the inferior vena cava. An intrahepatic shunt may run from the right branch of the portal vein to the inferior vena cava [22]. Collaterals to the pulmonary veins have also been described.

**Extrahepatic obstruction**

With extrahepatic portal venous obstruction, additional collaterals form, attempting to bypass the block and return blood towards the liver. These enter the portal vein in the porta hepatis beyond the block. They include the veins at the hilum, venae comitantes of the portal vein and hepatic arteries, veins in the suspensory ligaments of the liver and diaphragmatic and omental veins. Lumbar collaterals may be very large.
**Effects**

When the liver is cut off from portal blood by the development of the collateral circulation, it depends more on blood from the hepatic artery. It shrinks and shows impaired capacity to regenerate. This might be due to lack of hepatotrophic factors, including insulin and glucagon, which are of pancreatic origin.

Collaterals usually imply portal hypertension, although occasionally if the collateral circulation is very extensive portal pressure may fall. Conversely, portal hypertension of short duration can exist without a demonstrable collateral circulation.

A large portal–systemic shunt may lead to hepatic encephalopathy, septicaemias due to intestinal organisms, and other circulatory and metabolic effects.

**Pathology of portal hypertension**

Collateral venous circulation is disappointingly insignificant at autopsy. The oesophageal varices collapse.

The spleen is enlarged with a thickened capsule. The surface oozes dark blood (fibrocongestive splenomegaly). Malpighian bodies are inconspicuous. Histologically, sinusoids are dilated and lined by thickened epithelium (Fig. 9.10). Histiocytes proliferate with occasional erythropagocytosis. Periarterial haemorrhages may progress to siderotic, fibrotic nodules.

The splenic artery and portal vein are enlarged and tortuous and may be aneurysmal. The portal and splenic vein may show endothelial haemorrhages, mural thrombi and intimal plaques and may calcify (see Fig. 9.7). Such veins are usually unsuitable for portal surgery.

In 50% of patients with cirrhosis small, deeply placed splenic arterial aneurysms are seen [23]. **Hepatic changes** depend on the cause of the portal hypertension.

The height of the portal venous pressure correlates poorly with the apparent degree of cirrhosis and in particular of fibrosis. There is a much better correlation with the degree of nodularity.

**Varices**

**Oesophageal**

The major blood supply to oesophageal varices is the left gastric vein. The posterior branch usually drains into the azygos system, whereas the anterior branch communicates with varices just below the oesophageal junction and forms a bundle of thin parallel veins that run in the junction area and continue in large tortuous veins in the lower oesophagus. There are four layers of veins in the oesophagus (Fig. 9.11) [24]. **Intraepithelial veins** may correlate with the red spots seen on endoscopy and which predict variceal rupture. The superficial venous plexus drains into larger, deep intrinsic veins. **Perforating veins** connect the deeper veins with the fourth layer which is the adventitial plexus. Typical large varices arise from the main trunks of the deep intrinsic veins and these communicate with gastric varices.

The connection between portal and systemic circulation at the gastro-oesophageal junction is extremely complex [25]. Its adaptation to the cephalad and increased flow of portal hypertension is ill-understood. A palisade zone is seen between the gastric zone and the perforating zone (Fig. 9.12). In the palisade zone, flow is bidirectional and this area acts as a water shed between the portal and azygos systems. Turbulent flow in perforating veins between the varices and the perioesophageal veins at the lower end of the stomach may explain why rupture is frequent in this region [26]. Recurrence
mucosal changes due to abnormalities in the microcirculation [30].

Portal hypertensive gastropathy. This is almost always associated with cirrhosis and is seen in the fundus and body of the stomach. Histology shows vascular ectasia in the mucosa. The risk of bleeding is increased, for instance from non-steroidal anti-inflammatory drugs (NSAIDs). These gastric changes may be increased after sclerotherapy. They are relieved only by reducing the portal pressure [31].

Gastric antral vascular ectasia. This is marked by increased arteriovenous communications between the muscularis mucosa and dilated precapillaries and veins [32]. Gastric mucosal perfusion is increased. This must be distinguished from portal hypertensive gastropathy. It is not directly related to portal hypertension, but is influenced by liver dysfunction [33].

Congestive jejunopathy and colonopathy. Similar changes are seen in the duodenum and jejunum. Histology shows an increase in size and number of vessels in jejunal villi [34]. The mucosa is oedematous, erythematous and friable [35]. Congestive colonopathy is shown by dilated mucosal capillaries with thickened basement membranes but with no evidence of mucosal inflammation [30].

Others

Portal–systemic collaterals form in relation to bowel–abdominal wall adhesions secondary to previous surgery or pelvic inflammatory disease. Varices also form at mucocutaneous junctions, for instance, at the site of an ileostomy or colostomy.

Haemodynamics of portal hypertension

This has been considerably clarified by the development of animal models such as the rat with a ligated portal vein or bile duct or with carbon tetrachloride-induced cirrhosis. Portal hypertension is related both to vascular resistance and to portal blood flow (Fig. 9.13). The fundamental haemodynamic abnormality is an increased resistance to portal flow. This is mechanical due to the disturbed architecture and nodularity of cirrhosis or due to an obstructed portal vein and also due to dynamic changes related to dysfunction of the endothelium and reduced bioavailability of nitric oxide (NO) [36]. Other intrahepatic factors such as collagen deposition in the space of Disse [37] leading to loss of fenestrae (capillarization of the sinusoids), hepatocyte swelling [38,39] and the resistance offered by portal–systemic collaterals contribute.
The Hepatic Artery, Portal Venous System and Portal Hypertension

Fig. 9.13. Forward flow theory of portal hypertension.

Cardiac output increases

Splanchnic vasodilatation

Collaterals

Portal flow increased

Fig. 9.14. Regulation of sinusoidal blood flow. Endothelial and stellate cells are potential sources of endothelin (ET) which is contractile on stellate cells. Nitric oxide (NO) relaxes stellate cells. NO synthase is the precursor of NO and is produced by endothelial and stellate cells.

There is also a dynamic increase in intrahepatic vascular resistance [36].

Stellate (Ito) cells have contractile properties that can be modulated by vasoactive substances [40]. These include NO which is vasodilatory [41] (Chapter 7) and endothelin which is a vasoconstrictor [42]. These may modulate intrahepatic resistance and blood flow, especially at a sinusoidal level (Fig. 9.14) [43].

Collaterals develop when the pressure gradient between the portal vein and hepatic vein rises above a certain threshold, a process which involves angiogenic factors [44]. At the same time portal flow increases in the splanchnic bed due to splanchnic vasodilatation and increased cardiac output. It is uncertain whether the hyperdynamic circulation is the cause or the consequence of the portal hypertension or both. It is related to the severity of liver failure. Cardiac output increases further and there is generalized systemic vasodilatation (Fig. 9.15). Arterial blood pressure is normal or low (Chapter 7).

Splanchnic vasodilatation is probably the most important factor in maintaining the hyperdynamic circulation. Azygous blood flow is increased. Gastric mucosal blood flow rises. The increased portal flow raises the oesophageal variceal transmural pressure. The increased flow refers to total portal flow (hepatic and collaterals). The actual portal flow reaching the liver is reduced. The factors maintaining the hyperdynamic splanchnic circulation are multiple. There seems to be an interplay of vasodilators and vasoconstrictors. These might be formed by the hepatocyte, fail to be inactivated by it or be of gut origin and pass through intrahepatic or extrahepatic venous shunts.

Endotoxins and cytokines, largely formed in the gut, are important triggers [45]. NO and endothelin-1 are synthesized by vascular endothelium in response to endotoxin. Prostacyclin is produced by portal vein endothelium and is a potent vasodilator [46]. It may play a major role in the circulatory changes of portal hypertension due to chronic liver disease.

Glucagon is vasodilatory after pharmacological doses but is not vasoactive at physiological doses. It is not a primary factor in the maintenance of the hyperkinetic circulation in established liver disease [47].

Fig. 9.15. The pathophysiology of portal hypertension in cirrhosis.
Clinical features of portal hypertension

Table 9.1. Investigation of a patient with suspected portal hypertension

<table>
<thead>
<tr>
<th>History</th>
<th>Relevant to cirrhosis or chronic hepatitis (Chapter 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gastrointestinal bleeding: number, dates, amounts, symptoms, treatment</td>
</tr>
<tr>
<td></td>
<td>Results of previous endoscopies</td>
</tr>
<tr>
<td></td>
<td>Patient history: alcoholism, blood transfusion, hepatitis B, hepatitis C, intra-abdominal, neonatal or other sepsis, oral contraceptives, myeloproliferative disorder</td>
</tr>
<tr>
<td>Examination</td>
<td>Signs of hepatocellular failure</td>
</tr>
<tr>
<td></td>
<td>Abdominal wall veins: site</td>
</tr>
<tr>
<td></td>
<td>direction of blood flow</td>
</tr>
<tr>
<td></td>
<td>Splenomegaly</td>
</tr>
<tr>
<td></td>
<td>Liver size and consistency</td>
</tr>
<tr>
<td>Ascites</td>
<td>Oedema of legs</td>
</tr>
<tr>
<td>Rectal examination</td>
<td>Endoscopy of oesophagus, stomach and duodenum</td>
</tr>
<tr>
<td>Additional investigations</td>
<td>Liver biopsy</td>
</tr>
<tr>
<td></td>
<td>Hepatic vein catheterization</td>
</tr>
<tr>
<td></td>
<td>Splanchnic arteriography</td>
</tr>
<tr>
<td></td>
<td>Hepatic ultrasound, CT scan or MRI</td>
</tr>
</tbody>
</table>

Abdominal wall veins

In intrahepatic portal hypertension, some blood from the left branch of the portal vein may be deviated via paraumbilical veins to the umbilicus, whence it reaches veins of the caval system (Fig. 9.16). In extrahepatic portal obstruction, dilated veins may appear in the left flank.

**Distribution and direction.** Prominent collateral veins radiating from the umbilicus are termed caput Medusae. This is rare and usually only one or two veins, frequently epigastric, are seen (Figs 9.16, 9.17). The blood flow is away from the umbilicus, whereas in inferior vena caval obstruction the collateral venous channels carry blood upwards to reach the superior vena caval system (Fig. 9.16). Tense ascites may lead to functional obstruction of the inferior vena cava and cause difficulty in interpretation.

**Murmurs.** A venous hum may be heard, usually in the region of the xiphoid process or umbilicus. A thrill, detectable by light pressure, may be felt at the site of maximum intensity and is due to blood rushing through a large umbilical or paraumbilical channel to veins in the abdominal wall. A venous hum may also be heard over other large collaterals such as the inferior mesenteric vein. An arterial systolic murmur usually indicates primary liver cancer or alcoholic hepatitis.

The association of dilated abdominal wall veins and a loud venous murmur at the umbilicus is termed the Cruveilhier–Baumgarten syndrome [48,49]. This may be due to congenital patency of the umbilical vein, but more usually to a well-compensated cirrhosis [48–50].

The paraxiphoid umbilical hum and caput Medusae indicate portal obstruction beyond the origin of the umbilical veins from the left branch of the portal vein.

Ascites
This is rarely due to portal hypertension alone, although a particularly high pressure may be a major factor. The portal hypertension raises the capillary filtration pressure, and determines fluid localization to the peritoneal cavity. Ascites in cirrhosis always indicates liver cell failure in addition to portal hypertension.

Rectum
Anorectal varices are visualized by sigmoidoscopy and may bleed. They are found in 44% of patients with cirrhosis, increasing in those who have bled from oesophageal varices [51]. They must be distinguished from simple haemorrhoids which are prolapsed vascular cushions and which do not communicate with the portal system.

X-ray of the abdomen and chest
This is useful to delineate liver and spleen. Rarely, a calcified portal vein may be shown (Fig. 9.18) [52]. Branching, linear gas shadows in the portal vein radicles, especially near the periphery of the liver and due to gas-forming organisms, may rarely be seen in adults with intestinal infarction or infants with enterocolitis. Portal gas may be associated with disseminated intravascular coagulation. CT and ultrasound may detect portal gas more often, for instance in supplicative cholangitis when the prognosis is not so grave [53].

Tomography of the azygos vein may show enlargement (Fig. 9.19) as the collateral flow enters the azygos system. A widened left paravertebral shadow may be due to lateral displacement of the pleural reflection between the aorta and vertebral column by a dilated hemiazygos vein. Massively dilated paraoesophageal collaterals may be seen on the chest radiograph as a retrocardiac posterior mediastinal mass.

Diagnosis of varices
Barium studies have largely been replaced by endoscopy. Oesophageal varices show as filling defects in the regular contour of the oesophagus (Fig. 9.20). They are most often in the lower third, but may spread upwards so that the entire oesophagus is involved. Widening and finally gross dilatation are helpful signs.

Gastric varices pass through the cardia, line the fundus in a worm-like fashion and may be difficult to distinguish from mucosal folds. Occasionally gastric varices show as a lobulated mass in the gastric fundus simulating a carcinoma. Portal venography is useful in differentiation.
Endoscopy is the best screening test to detect varices. The size of the varix should be graded (Figs 9.21, 9.22) [54]. Varices are small (≤5 mm diameter) or large (>5 mm diameter) when assessed with full insufflation.

The larger the varix the more likely it is to bleed. Varices usually appear white and opaque (Fig. 9.23). Red colour correlates with blood flow through dilated subepithelial and communicating veins. Dilated subepithelial veins may appear as raised cherry-red spots (Fig. 9.24) and red wheal markings (longitudinal dilated veins resembling whip marks). They lie on top of large subepithelial vessels. The haemocystic spot is approximately 4 mm in diameter (Fig. 9.25). It represents blood coming from the deeper extrinsic veins of the oesophagus straight out towards the lumen through a communicating vein into the more superficial submucosal veins. Red colour is usually associated with larger varices. All these signs are associated with a higher risk of variceal bleeding. Intraobserver error may depend on...
Fig. 9.21. Endoscopic classification of oesophageal varices (adapted from [54]).

Fig. 9.22. The form (F) of the oesophageal varices (from [54]).

Fig. 9.23. Variceal colour through the endoscope (from [54]).

Fig. 9.24. Endoscopic view of cherry-red spots on oesophageal varices (arrows).

Fig. 9.25. Haemocystic spots on oesophageal varices (from [54]).

Fig. 9.26. Portal gastropathy. A mosaic of red and yellow is seen together with petechial haemorrhages.

the skill and experience of the endoscopist. Intraobserver agreement is only good for size and presence of red signs [55].

Portal hypertensive gastropathy is seen largely in the fundus and antrum, but can extend throughout the stomach (Fig. 9.26). It is shown as a mosaic-like pattern with small polygonal areas, surrounded by a whitish-yellow depressed border [56]. Red point lesions and cherry-red spots predict a high risk of bleeding. Black-brown spots are due to intramucosal haemorrhage. Sclerotherapy may increase the gastropathy [57]. Capsule endoscopy is an accurate diagnostic tool to
detect oesophageal varices and portal hypertensive gastro- 
dropyth, but not as good as endoscopy [58]. Its use should be confined to patients in whom endoscopy is con- 
traindicated. If neither type of endoscopy is possible the 
presence of oesophageal varices can be predicted using 
platelet count / spleen diameter ratio [59] with a 
positive likelihood ratio of 2.77 and negative likelihood 
ratio of 0.13.

Variceal (azygos) blood flow can be assessed during 
diagnostic endoscopy by a Doppler ultrasound probe 
passed down the biopsy channel of the standard gas- 

troscopy.

Portal hypertensive colopathy is seen in about half the 
patients with portal hypertension, usually in those with 
gastropathy. Colonoscopy may be needed to diagnose 
lower gastrointestinal bleeding in patients with cirrhosis 
[60].

**Imaging the portal venous system**

**Ultrasound**

Longitudinal scans at the subcostal margins and trans- 
verse scans at the epigastrium are essential (Fig. 9.27). 
The portal and superior mesenteric veins can always be 
seen. The normal splenic vein may be more difficult. 

A large portal vein suggests portal hypertension, but this is not diagnostic. If collaterals are seen, this con- 


![Fig. 9.27. Transverse ultrasound shows a patent portal vein (P); the arrow indicates the inferior vena cava.](image)

**Doppler ultrasound**

Doppler ultrasound demonstrates the anatomy of the portal veins and hepatic artery (Table 9.2). Satisfactory 
results depend on technical expertise. Small cirrhotic 
livers are difficult to see as are those of the obese. Colour- 
coded Doppler improves visualization (Fig. 9.28). Portal 
venous obstruction is demonstrated by Doppler ultra- 
sound as accurately as by angiography provided the Doppler is technically optimal.

Doppler ultrasound shows spontaneous hepatofugal 
flow in portal, splenic and superior mesenteric veins in 
8.3% of patients with cirrhosis [61]. Its presence corre- 
lates with severity of cirrhosis and with encephalopathy. Variceal bleeding is more likely if the flow is hepatopetal.

Abnormalities of the intrahepatic portal veins can be shown. These are important if surgery is con- 

![Fig. 9.28. Colour Doppler ultrasound of the porta hepatis shows the hepatic artery in red and portal vein in blue.](image)

Table 9.2. Clinical uses of Doppler ultrasound

<table>
<thead>
<tr>
<th>Portal vein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patency</td>
</tr>
<tr>
<td>Hepatofugal flow</td>
</tr>
<tr>
<td>Anatomical abnormalities</td>
</tr>
<tr>
<td>Portal-systemic shunt patency</td>
</tr>
<tr>
<td>Acute flow changes</td>
</tr>
<tr>
<td>Hepatic artery</td>
</tr>
<tr>
<td>Patency (post-transplant)</td>
</tr>
<tr>
<td>Anatomical abnormalities</td>
</tr>
<tr>
<td>Hepatic veins</td>
</tr>
<tr>
<td>Screening Budd–Chiari syndrome</td>
</tr>
</tbody>
</table>

![Table 9.2](image)
lar intrahepatic portosystemic shunts (TIPS). Intrahepatic portal–systemic shunts may be visualized [62].

Colour Doppler screening is useful for patients suspected of the Budd–Chiari syndrome.

The hepatic artery is more difficult than the hepatic veins to locate because of its small size and direction. Nevertheless, duplex Doppler is the primary screening procedure to show a patent hepatic artery after liver transplantation.

Duplex Doppler has been used to measure portal blood flow. The average velocity of blood flowing in the portal vein is multiplied by the cross-sectional area of the vessel (Fig. 9.29). There are observer errors in measurement. The method is most useful in measuring rapid, large, acute changes in flow rather than monitoring chronic changes in portal haemodynamics.

Portal blood flow velocity correlates with the presence and size of oesophageal varices. In cirrhosis, the portal vein velocity tends to fall and when less than 16 cm/s portal hypertension is likely.

Computed Tomography

After contrast, portal vein patency can be established and retroperitoneal, perivisceral and paraoesophageal varices may be visualized (Fig. 9.30). Oesophageal varices may be shown as intraluminal protrusions enhancing after contrast. The umbilical vein can be seen. Gastric varices show as rounded structures, indistinguishable from the gastric wall.

CT arteriopography is done by rapid CT scanning during selective injection of contrast into the superior mesenteric vein via a catheter [63]. It is particularly useful in showing focal lesions, the collateral circulation and arteriovenous shunts [64], but is rarely used due to the improvement of dynamic scanning with CT or MR following intravenous contrast.

Magnetic resonance angiography

Magnetic resonance angiography gives excellent depiction of blood vessels as regions of absent signal (Figs 9.31–9.33). Portal patency, morphology and flow of velocity may be demonstrated. Magnetic resonance angiography is more reliable than Doppler [65].

Venography

If the portal vein is patent by scanning, confirmation by venography is not necessary even when portal surgery or hepatic transplantation is being considered.

Patency of the portal vein is important, particularly in the diagnosis of splenomegaly in childhood and in excluding invasion by a hepatocellular carcinoma in a patient with cirrhosis.

Anatomy of the portal venous system must be known before such operations as portal–systemic shunt, or transjugular intrahepatic stent shunt, hepatic resection or hepatic transplantation. The patency of a surgical shunt may be confirmed.

The demonstration of a large portal collateral circulation is essential for the diagnosis of chronic hepatic encephalopathy (Figs 9.8, 9.30).

A filling defect in the portal vein or in the liver due to a space-occupying lesion may be demonstrated. Intrasplenic pulp pressure is an index of portal hypertension [66], but has been replaced by direct intrahepatic puncture of the portal vein.

Venographic appearances

When the portal circulation is normal, the splenic and portal veins are filled but no other vessels are outlined. A filling defect may be seen at the junction of the splenic and superior mesenteric veins due to mixing with non-opacified blood. The size and direction of the splenic and portal veins are very variable. The intrahepatic
branches of the portal vein show a gradual branching and reduction in calibre. Later the liver becomes opaque due to sinusoidal filling. The hepatic veins may rarely be seen in later films.

In cirrhosis, the venogram varies widely. It may be completely normal or may show filling of large numbers of collateral vessels with gross distortion of the intrahepatic pattern (‘tree in winter’ appearance) (Fig. 9.34).

In extrahepatic portal or splenic vein obstruction, large numbers of vessels run from the spleen and splenic
vein to the diaphragm, thoracic cage and abdominal wall. Intrahepatic branches are not usually seen, although, if the portal vein block is localized, paraportal vessels may short circuit the lesion (Fig. 9.32) and produce a delayed but definite filling of the vein beyond.

**Visceral angiography**

Safety has increased with the use of smaller (French 5) arterial catheters. New contrast materials are less toxic to kidneys and other tissues and hypersensitivity reactions are rare. However, diagnostic angiography is rarely needed except to demonstrate shunting and when evaluating patients with hepatocellular carcinoma for targeted radioactive bead therapy, and for hepatic arterial problems after liver transplantation.

The coeliac axis is catheterized via the femoral artery and contrast is injected. The material that flows into the splenic artery returns through the splenic and portal veins and produces a splenic and portal venogram. Similarly, a bolus of contrast introduced into the superior mesenteric artery returns through the superior mesenteric and portal veins, which can be seen in radiographs exposed at the appropriate intervals (Figs 9.35, 9.36).

Visceral angiography demonstrates the hepatic arterial system, so allowing space-filling lesions in the liver to be identified. A tumour circulation may diagnose hepatocellular cancer or another tumour.

Knowledge of splenic and hepatic arterial anatomy is useful if surgery is contemplated. Haemangiomas, other space-occupying lesions and aneurysms may be identified.

The portal vein may not opacify if flow in it is hepato-fugal or if there is ‘steal’ by the spleen or by large collateral channels. A superior mesenteric angiogram will confirm that the portal vein is in fact patent.

**Digital subtraction angiography**

The contrast is given by selective arterial injection with immediate subtraction of images. The portal system is very well visualized free of other confusing images (Fig. 9.37). Spatial resolution is poorer than with conventional film-based angiography. The technique is particularly valuable for the parenchymal phase of hepatic angiography and for the diagnosis of vascular lesions such as haemangiomas or arteriovenous malformations.

**Splenic venography**

Contrast material, injected into the pulp of the spleen, flows into the portal venous system with sufficient
Carbon dioxide occluded venography

Injection of carbon dioxide into a catheter in the wedged hepatic venous position allows an excellent venogram of the hepatic venous and portal venous tree (Fig. 9.38) [68].

Portal pressure measurement

A balloon catheter is introduced into the femoral vein or internal jugular vein and, under fluoroscopic control, into the hepatic vein (Fig. 9.39). Measurements are taken in the wedged hepatic venous pressure (WHVP) and free hepatic venous pressure (FHVP) positions by inflating and deflating the balloon in the tip of the catheter [67,69]. The hepatic venous pressure gradient (HVPG) is the difference between WHVP and FHVP. This is the portal (sinusoidal) venous pressure. When the cause of portal hypertension is mainly sinusoidal (alcohol, viral hepatitis) the WHVP is the same as the portal pressure, but this relationship does not hold when there is a large presinusoidal component [70]. The normal HVPG is 5–6 mmHg and values of 10 mmHg or more represent clinically significant portal hypertension when complications of cirrhosis (decompensation) can occur [71]. Measurements can be performed at the same time as transjugular liver biopsy [72].
HVPG is related to survival [73] and also to prognosis in patients with bleeding oesophageal varices [74]. The procedure may be used to monitor therapy, for instance the effect of beta-blockers such as propranolol, with optimal target reduction of HVPG by 20% from baseline or to less than 12 mmHg, which results in a reduced risk of bleeding [75].

Experimental portal venous occlusion and hypertension

Survival following acute occlusion depends on the development of an adequate collateral circulation. In the rabbit, cat or dog this does not develop and death supervenes rapidly. In the monkey or man, the collateral circulation is adequate and survival is usual.

Acute occlusion of one branch of the portal vein is not fatal. The liver cells of the ischaemic lobe atrophy, but bile ducts, Kupffer cells and connective tissues survive. The unaffected lobe hypertrophies.

Experimental portal hypertension can be produced by occluding the portal vein, injecting silica into the portal vein, infecting mice with schistosomiasis, by any experimental type of cirrhosis or by biliary obstruction. An extensive collateral circulation develops, the spleen enlarges but ascites does not form.

Classification of portal hypertension

Portal hypertension usually follows obstruction to the portal blood flow anywhere along its course. Portal hypertension has been classified into two types: (1) presinusoidal (extrahepatic or intrahepatic); and (2) a larger group of hepatic causes (intrahepatic ‘sinusoidal’ and postsinusoidal) (Fig. 9.40, Table 9.3). This distinction is a practical one. The presinusoidal forms, which include obstruction to the sinusoids by Kupffer and other cellular proliferations, are associated with relatively normal hepatocellular function. Consequently, if patients with this type suffer a haemorrhage from varices, liver failure is rarely a consequence. In contrast, patients with the hepatic type may develop liver failure after bleeding.

Extrahepatic portal venous obstruction

This causes extrahepatic presinusoidal portal hypertension. The obstruction may be at any point in the course of the portal vein, usually due to thrombosis. The venae comitantes enlarge in an attempt to deliver portal blood to the liver, so assuming a leash-like cavernous appearance. The portal vein, represented by a fibrous strand, is recognized with difficulty in the multitude of small vessels. This cavernous change follows any block in the main vein (see Fig. 9.32). Confluent thrombosis may extend to the splenic and/or superior mesenteric vein [82].

Aetiology

Infections

Umbilical infection with or without catheterization of the umbilical vein may be responsible in neonates [83].
Chapter 9

Portal vein occlusion is particularly common in India, accounting for 20–30% of all variceal bleeding. Neonatal dehydration and infections may be responsible. Ulcerative colitis and Crohn’s disease can be complicated by portal or hepatic vein thrombosis. Portal vein obstruction may be secondary to biliary infections due, for instance, to gallstones or primary sclerosing cholangitis.

**Postoperative**

The portal and splenic veins commonly thrombose after splenectomy, especially when, preoperatively, the patient had a normal platelet count. The thrombosis spreads from the splenic vein into the main portal vein. It is especially likely in patients with myeloid metaplasia. A similar sequence follows occluded surgical porto-systemic shunts.

---

**Table 9.3. Classification of portal hypertension**

<table>
<thead>
<tr>
<th>Presinusoidal</th>
<th>Extrahepatic</th>
<th>Blocked portal vein</th>
<th>Increased splenic flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrahepatic</td>
<td>Portal zone infiltrates</td>
<td>Toxic</td>
<td></td>
</tr>
<tr>
<td>Hepatic</td>
<td>Cirrhosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrahepatic (sinusoidal)</td>
<td>Other nodules</td>
<td>Blocked hepatic vein</td>
<td></td>
</tr>
</tbody>
</table>

The infection spreads along the umbilical vein to the left portal vein and hence to the main portal vein. Acute appendicitis and peritonitis are causative in older children.

**Fig. 9.40.** Causes of portal hypertension. (a) Pre- and posthepatic. (b) Intrahepatic (NB an overlap exists; wedge hepatic vein pressure may be high in patients with ‘presinusoidal’ causes, especially as the disease progresses, indicating sinusoidal and/or collateral involvement. Some ‘postsinusoidal’ conditions may also have a sinusoidal component).
The portal vein may thrombose as a complication of major, difficult hepatobiliary surgery, for instance repair of a stricture or removal of a choledochal cyst.

**Trauma**

Portal vein injury may rarely follow vehicle accidents or stabbing. Laceration of the portal vein is 50% fatal and ligation may be the only method to control the bleeding.

**Hypercoagulable state**

This is a frequent cause of portal vein thrombosis in adults and less often in children [84]. It is commonly due to a myeloproliferative disorder which may be latent, or the presence of G20210A prothrombin gene mutation, and/or one or more heterozygous or homozygous deficiency states for protein C, S, antithrombin III or other prothrombotic tendencies [85]. At autopsy, thrombotic lesions are found in macroscopic and microscopic portal veins of patients dying with portal hypertension and myelomegaly [86]. Ascites and oesophageal varices are associated.

**Invasion and compression**

The classic example is hepatocellular carcinoma. Carcinoma of the pancreas, usually of the body, and of other adjacent organs may lead to portal vein thrombosis. Chronic pancreatitis is frequently associated with splenic vein obstruction, but involvement of the portal vein is rare (5.6%) [82,87].

**Congenital**

Congenital obstruction can be produced anywhere along the line of the right and left vitelline veins from which the portal vein develops. The portal vein may be absent with visceral venous return passing to systemic veins, particularly the inferior vena cava [88]. Hilar venous collaterals are absent.

Congenital abnormalities of the portal vein are usually associated with congenital defects elsewhere [88,89].

**Cirrhosis**

Portal vein thrombosis is not infrequent as a complication of cirrhosis [90]. Invasion by a hepatocellular carcinoma is a frequent cause. Postsplenectomy thrombocytosis is another aetiologic factor. Mural thrombi found at autopsy are probably terminal. It is easy to over-diagnose thrombosis by finding a non-filled portal vein on imaging. This usually represents ‘steal’ into massive collaterals or into a large spleen [90].

**Miscellaneous**

Portal vein thrombosis has very rarely been associated with pregnancy and with oral contraceptives, especially in older women and with long usage [91] and with thrombophlebitis migrans and other general disease of veins.

In retroperitoneal fibrosis, the portal venous system may be encased by dense fibrous tissue.

Portal vein occlusion with recanalization is a common manifestation of Behçet’s disease [92].

**Unknown**

In about half of patients the aetiology remains obscure. Some of these patients have associated autoimmune disorders such as hypothyroidism, diabetes, pernicious anaemia, dermatomyositis or rheumatoid arthritis [82]. In some instances, the obstruction may have followed undiagnosed intra-abdominal infections such as appendicitis or diverticulitis.

**Clinical features**

The patient may present with features of the underlying disease, for instance polycythaemia rubra vera [86] or primary liver cancer. Children may have growth retardation [93].

Bleeding from oesophagogastric varices is the most common presentation. In those of neonatal origin, the first haemorrhage is at about the age of 4 years (Fig. 9.41). The frequency increases between 10 and 15 years and decreases after puberty. However, some patients with portal venous thrombosis never bleed and in others haemorrhage may be delayed for as long as 12 years. If blood replacement is adequate, recovery usually ensues in a matter of days. Apart from frank bleeds, intermittent minor blood loss is probably common. This is diagnosed only if the patient is having repeated checks for faecal blood or iron deficiency anaemia.

Especially in children, haemorrhage may be initiated by a minor, intercurrent infection. The mechanism is unclear. Aspirin or a similar drug may be the precipitating factor. Excessive exertion or swallowing a large bolus does not seem to initiate bleeding.

The spleen is always enlarged and symptomless splenomegaly may be a presentation, particularly in children. Periumbilical veins are not seen but there may be dilated abdominal wall veins in the left flank.

The liver is normal in size and consistency. Stigmata of hepatocellular disease, such as jaundice or vascular spiders, are absent. With acute portal venous thrombosis, ascites is early and transient, subsiding as the collateral circulation develops. Ascites is usually related to an additional factor that has depressed hepatocellular
function, such as a haemorrhage or a surgical exploration. It may be seen in the elderly where it is related to the deterioration of liver function with ageing [94]. Hepatic encephalopathy is not uncommon in adults, usually following an additional insult such as haemorrhage, infection or anaesthetic. Chronic encephalopathy may be seen in elderly patients with a particularly large portal-systemic circulation. Rarely, compression of the common bile duct can occur, termed ‘portal biliopathy’ [95], which may cause jaundice.

**Imaging**

Ultrasound shows echogenic thrombus within the portal vein and colour Doppler shows slow flow velocity in the cavernous collaterals and no portal venous signal [96,97].

CT shows the thrombus as a non-enhancing filling defect within the lumen of the portal vein and dilatation of many small veins at the hilum (Fig. 9.42).

MRI shows an area of abnormal signal within the lumen of the portal vein which appears isointense on a T1-weighted image with a more intense signal on a T2-weighted image.

Angiography in the portal venous phase shows a filling defect or non-opacification of the portal vein. However, the portal vein may not be visualized if blood is diverted away from it into extensive collaterals.

**Haematology**

Haemoglobin is normal unless there has been blood loss. Leucopenia and thrombocytopenia are related to...
the enlarged spleen. Circulating platelets and leukocytes, although in short supply, are adequate and function well.

Hypersplenism is not an indication for splenectomy. Blood coagulation is normal.

**Serum biochemistry**

All the usual tests of ‘liver function’ are normal. Elevation of serum globulin may be related to intestinal antigens, bypassing the liver through collaterals. Mild pancreatic hypofunction is related to interruption of the venous drainage of the pancreas [98].

**Prognosis**

This depends on the underlying disease [82]. The outlook is much better than for cirrhosis as liver function is normal. The prognosis is surprisingly good in the child and, with careful management of recurrent bleeding, survival to adult life is expected. The number of bleeds seems to reduce as time passes. Women may bleed in pregnancy but this is unusual; their babies are normal.

**Treatment**

Any cause must be identified and treated. This may be more important than the portal hypertension. For instance, hepatocellular carcinoma, invading the portal vein, precludes aggressive therapy for bleeding oesophageal varices. If the variceal bleeding is related to polycythemia rubra vera, reduction of the platelet count must precede any surgical therapy; anticoagulants may be needed [82].

Prophylactic treatment of varices is not indicated. They may never rupture and as time passes collaterals open up.

With acute portal vein thrombosis, anticoagulant therapy will result in recanalization in one-third of patients [99]. If diagnosed early, anticoagulants may prevent spreading thrombosis and intestinal infarction or severe bleeding. Presence of ascites and splenic vein thrombosis should lead to alternative therapies [99].

Children should survive haemorrhage with proper management, including transfusion. Care must be taken to give compatible blood and to preserve peripheral veins. Aspirin ingestion should be avoided. Upper respiratory any other infections should be treated seriously as they seem to precipitate haemorrhage.

Endoscopic therapy is valuable as an emergency procedure; balloon tamponade may be needed.

Major or recurrent bleeds may be treated by repeated sclerotherapy, particularly in children, or ligation. Unfortunately this does not treat gastric fundal varices and the congestive gastropathy remains.

Definitive surgery to reduce portal pressure maybe impossible as there are no suitable veins for a shunt. Even apparently normal-looking veins seen on venography turn out to be in poor condition, presumably related to extension of the original thrombotic process. In children, veins are very small and difficult to anastomose.

Results for all forms of surgery are unsatisfactory. Splenectomy is the least successful.

A shunt (portacaval, mesocaval or splenocaval) is the most satisfactory treatment. In children a mesenterico-portal shunt, anastomosing to a patent left portal vein branch, not only prevents bleeding, but improves growth [100].

When the patient is exsanguinating, despite massive blood transfusion, an oesophageal transection may have to be performed. Here again gastric varices are not treated. Postoperative complications are common.

TIPS may be possible providing the superior mesenteric vein is patent [101].

**Splenic vein obstruction**

Isolated splenic vein obstruction causes sinistral (left-sided) portal hypertension. It may be due to any of the factors causing portal vein obstruction (Fig. 9.43).
Pancreatic disease such as carcinoma (18%), pancreatitis (65%), pseudocyst and pancreatectomy are particularly important [87].

If the obstruction is distal to the entry of the left gastric vein, a collateral circulation bypasses the obstructed splenic vein through short gastric veins into the gastric fundus and lower oesophagus, so reaching the left gastric vein and portal vein. This leads to very prominent varices in the fundus of the stomach but few in the lower oesophagus.

The selective venous phase of an angiogram, an enhanced CT scan or MRI are diagnostic. Splenectomy, by blocking arterial inflow, is usually curative but unnecessary if the patient has not bled from varices [102].

### Hepatic arterioportal venous fistulae

Portal hypertension results from increased portal venous flow. Increase in intrahepatic resistance due to a rise in portal flow may also be important. Portal zones show thickening of small portal radicles with accompanying mild fibrosis and lymphocyte infiltration. The increased intrahepatic resistance may persist after obliteration of the fistula.

These fistulae are usually congenital, traumatic (including after liver biopsy) or related to adjacent malignant neoplasm [103]. Inferior mesenteric arteriovenous fistulae may be associated with acute ischaemic colitis.

With large fistulae, a loud arterial bruit is heard in the right upper abdomen. Pain may be pronounced. Others present with portal hypertension.

Ultrasound and enhanced CT show an enlarged hepatic artery and a dilated intrahepatic portal vein. The diagnosis is confirmed by arteriography.

Selective non-invasive embolization of fistulae has replaced surgery.

### Portohepatic venous shunts

These are probably congenital and represent persistence of the omphalomesenteric venous system. They may be between the main portal and hepatic veins or between the right or left portal vein and hepatic veins [104]. They are diagnosed by ultrasound, enhanced CT scan, MRI and colour Doppler imaging and confirmed by arteriography.

### Presinusoidal intrahepatic and sinusoidal portal hypertension (Fig. 9.44)

#### Portal tract lesions

In *schistosomiasis*, the portal hypertension results from the ova causing a reaction in the minute portal venous radicles.

In *congenital hepatic fibrosis*, the portal hypertension is probably due to a deficiency of terminal branches of the portal vein in the fibrotic portal zones.

Portal hypertension has been reported with *myeloproliferative diseases* including myelosclerosis, myeloid leukaemia and Hodgkin’s disease [105]. The mechanism is complex. In part it is related to infiltration of the portal zones with haemopoietic tissue, but thrombotic lesions in major and minor portal vein radicles and nodular regenerative hyperplasia contribute [86].

In *systemic mastocytosis*, portal hypertension is related to increased intrahepatic resistance secondary to mast cell infiltration. Increased splenic flow, perhaps with splenic arteriovenous shunting and with histamine release, may contribute.

In *primary biliary cirrhosis*, portal hypertension may be a presenting feature long before the development of the nodular regeneration characteristic of cirrhosis (Chapter 15). The mechanism is uncertain, although portal zone lesions and narrowing of the sinusoids because of cellular infiltration have been incriminated. The portal hypertension of *sarcoidosis* may be similar. Massive fibrosis is usually associated.

### Toxic causes

The injurious substance is mainly taken up by hepatic stellate cells in Disse’s space; these are fibrogenic. Minute portal vein radicles are obstructed and intrahepatic portal hypertension results.
Inorganic arsenic has caused portal hypertension in patients being treated for psoriasis.
Liver disease in vineyard sprayers in Portugal may be related to exposure to copper. Angiosarcoma may be a complication.
Exposure to the vapour of the polymer of vinyl chloride leads to sclerosis of portal venules with portal hypertension and angiosarcoma.
Reversible portal hypertension may follow vitamin A intoxication—vitamin A being stored in hepatic stellate cells. Prolonged use of cytotoxic drugs, such as methotrexate, 6-mercaptopurine and azathioprine, can lead to perisinusoidal fibrosis and portal hypertension.

**Hepatoporal sclerosis**

This is marked by splenomegaly, hypersplenism and portal hypertension without occlusion of portal and splenic veins and with no obvious pathology in the liver [106]. It has also been termed non-cirrhotic portal fibrosis, non-cirrhotic portal hypertension and idiopathic portal hypertension. Banti’s syndrome, an obsolete term, probably fell into this group. Injury to intrahepatic portal venous radicles and sinusoidal endothelial cells is the common denominator.

An increase in intrahepatic resistance indicates an obstruction to hepatic blood flow. Increased lymph flow may help to reduce the high portal pressure [107].

The aetiology may be infectious, toxic or, in many instances, unknown (Fig. 9.45). In childhood, intrahepatic thrombosis of small portal veins could be the primary disorder.

In Japan, it affects largely middle-aged women. A very similar condition in India, called non-cirrhotic portal fibrosis, largely affects young males [108]. It has been related to arsenic taken in drinking water and in unorthodox medicines. In both countries, it is probably due to the effects of multiple intestinal infections on the liver. It is therefore decreasing with improved hygiene.

Somewhat similar patients have been reported from the USA [109] and the UK [110].

Liver biopsy shows sclerosis and sometimes obliteration of the intrahepatic venous bed but the changes, and especially the fibrosis, may be minimal. Large portal veins near the hilum may be thickened and narrow, but this is usually seen only at autopsy. Some of the changes seem to be secondary to partial thrombosis of small portal venous channels with recanalization. Perisinusoidal fibrosis is usually present but may be seen only by electron microscopy.

Portal venography shows small portal vein radicles to be narrowed and sparse. The peripheral branches may be irregular with acute-angle division. Some of the large intrahepatic portal branches may be non-opacified with an increase of very fine vasculature around the large intrahepatic portal branches. Hepatic venography confirms the vascular abnormalities and vein-to-vein anastomoses are frequent.

**Tropical splenomegaly syndrome**

This is marked by residence in a malarial area, splenomegaly, hepatic sinusoidal lymphocytosis and Kupffer cell hyperplasia, raised serum IgM and malarial antibody titres and response to prolonged antimalarial chemotherapy. Portal hypertension is not marked and variceal bleeding is rare [108].

---

**Fig. 9.45.** Factors concerned in so-called idiopathic ‘primary’ portal hypertension.
therefore believed to be at all levels from portal zones through the sinusoids to the hepatic venous outflow (Fig. 9.48).

The hepatic artery provides the liver with a small volume of blood at a high pressure. The portal vein delivers a large volume at a low pressure (see Fig. 9.6). The two systems are equilibrated in sinusoids. Normally, the hepatic artery probably plays little part in maintaining portal venous pressure. In cirrhosis, more direct arterioportal shunting has been suspected. Hypertrophy of the hepatic artery and relative increase in flow help to maintain sinusoidal perfusion.

Intrahepatic sinusoidal portal hypertension

*Cirrhosis*

All forms of cirrhosis lead to portal hypertension and the primary event is obstruction to portal blood flow [20]. Portal venous blood is diverted into collateral channels and some bypasses the liver cells and is shunted directly into the hepatic venous radicles in the fibrous septa. These portohepatic anastomoses develop from pre-existing sinusoids enclosed in the septa (Fig. 9.46) [111]. The hepatic vein is displaced further and further outwards until it lies in a fibrous septum linked with the portal venous radicle by the original sinusoid. The regenerating nodules become divorced from their portal blood supply and are nourished by the hepatic artery. Even larger portohepatic venous anastomoses are found in the cirrhotic liver. About one-third of the total blood flow perfusing the cirrhotic liver may bypass sinusoids, and hence functioning liver tissue, through these channels [112].

The obstruction to portal flow is partially due to nodules which compress hepatic venous radicles (Fig. 9.47) [113]. This would lead to a postsinusoidal portal hypertension. However, in cirrhosis, the wedged hepatic venous (sinusoidal) and main portal pressures are virtually identical and the stasis must extend to the portal inflow vessels. Sinusoids probably provide the greatest resistance to flow. Changes in the space of Disse, particularly collagenization, result in sinusoidal narrowing and this may be particularly important in the alcoholic. Hepatocyte swelling in the alcoholic may also reduce sinusoidal flow [38]. Obstruction is therefore believed to be at all levels from portal zones through the sinusoids to the hepatic venous outflow (Fig. 9.48).

The hepatic artery provides the liver with a small volume of blood at a high pressure. The portal vein delivers a large volume at a low pressure (see Fig. 9.6). The two systems are equilibrated in sinusoids. Normally, the hepatic artery probably plays little part in maintaining portal venous pressure. In cirrhosis, more direct arterioportal shunting has been suspected. Hypertrophy of the hepatic artery and relative increase in flow help to maintain sinusoidal perfusion.
Non-cirrhotic nodules
See Chapter 34.

Bleeding oesophageal varices

Predicting rupture

The first appearance and subsequent growth of gastro-oesophageal varices following diagnosis of cirrhosis is approximately 7% per year [114,115].

The precipitating event is not known, but may be an inflammatory response or infection [116], on a background of raised intravariceal pressure. The first variceal haemorrhage occurs within the first year after diagnosis of varices in approximately 12%, depending on the size of varices, red signs on varices and the degree of liver dysfunction, which are the best predictors of bleeding (Fig. 9.49) [54]. Patients with moderate to severe liver dysfunction, irrespective of the size of varices and presence of red signs, should receive prophylaxis.

Intravariceal pressure is less important than size and appearance of varices, although a portal pressure above 10 mmHg appears necessary for varices to form and 12 mmHg for them to subsequently bleed [117]. Patients with alcoholic cirrhosis may be at most risk [118]. Doppler sonography may predict likelihood of bleeding, based on velocity and diameter of the portal vein, spleen size and the presence of collaterals [119].

Child’s grade is used to assess hepatocellular function in cirrhosis (Table 9.4). Every patient should be assigned a grade. It is the most important predictor of the likelihood of bleeding. It correlates with variceal size and with the presence of endoscopic red signs and with the response to emergency treatment.

Prevention of first bleeding [120]

Liver function must be improved, for instance, by abstaining from alcohol. Aspirin and NSAIDs should be avoided. No protection comes from avoiding certain foods such as spices or from taking long-term H₂-blockers.

Propranolol or nadalol are non-selective beta-blockers which reduce portal pressure by splanchnic vasoconstriction and, to a lesser extent, by reducing cardiac output. Hepatic arterial blood flow falls [121,122]. The drug is given in a dose which reduces the resting pulse

Non-cirrhotic nodules
See Chapter 34.

Bleeding oesophageal varices

Predicting rupture

The first appearance and subsequent growth of gastro-oesophageal varices following diagnosis of cirrhosis is approximately 7% per year [114,115].

The precipitating event is not known, but may be an inflammatory response or infection [116], on a background of raised intravariceal pressure. The first variceal haemorrhage occurs within the first year after diagnosis of varices in approximately 12%, depending on the size of varices, red signs on varices and the degree of liver dysfunction, which are the best predictors of bleeding (Fig. 9.49) [54]. Patients with moderate to severe liver dysfunction, irrespective of the size of varices and presence of red signs, should receive prophylaxis.

Intravariceal pressure is less important than size and appearance of varices, although a portal pressure above 10 mmHg appears necessary for varices to form and 12 mmHg for them to subsequently bleed [117]. Patients with alcoholic cirrhosis may be at most risk [118]. Doppler sonography may predict likelihood of bleeding, based on velocity and diameter of the portal vein, spleen size and the presence of collaterals [119].

Child’s grade is used to assess hepatocellular function in cirrhosis (Table 9.4). Every patient should be assigned a grade. It is the most important predictor of the likelihood of bleeding. It correlates with variceal size and with the presence of endoscopic red signs and with the response to emergency treatment.

Prevention of first bleeding [120]

Liver function must be improved, for instance, by abstaining from alcohol. Aspirin and NSAIDs should be avoided. No protection comes from avoiding certain foods such as spices or from taking long-term H₂-blockers.

Propranolol or nadalol are non-selective beta-blockers which reduce portal pressure by splanchnic vasoconstriction and, to a lesser extent, by reducing cardiac output. Hepatic arterial blood flow falls [121,122]. The drug is given in a dose which reduces the resting pulse

Non-cirrhotic nodules
See Chapter 34.

Bleeding oesophageal varices

Predicting rupture

The first appearance and subsequent growth of gastro-oesophageal varices following diagnosis of cirrhosis is approximately 7% per year [114,115].

The precipitating event is not known, but may be an inflammatory response or infection [116], on a background of raised intravariceal pressure. The first variceal haemorrhage occurs within the first year after diagnosis of varices in approximately 12%, depending on the size of varices, red signs on varices and the degree of liver dysfunction, which are the best predictors of bleeding (Fig. 9.49) [54]. Patients with moderate to severe liver dysfunction, irrespective of the size of varices and presence of red signs, should receive prophylaxis.

Intravariceal pressure is less important than size and appearance of varices, although a portal pressure above 10 mmHg appears necessary for varices to form and 12 mmHg for them to subsequently bleed [117]. Patients with alcoholic cirrhosis may be at most risk [118]. Doppler sonography may predict likelihood of bleeding, based on velocity and diameter of the portal vein, spleen size and the presence of collaterals [119].

Child’s grade is used to assess hepatocellular function in cirrhosis (Table 9.4). Every patient should be assigned a grade. It is the most important predictor of the likelihood of bleeding. It correlates with variceal size and with the presence of endoscopic red signs and with the response to emergency treatment.

Prevention of first bleeding [120]

Liver function must be improved, for instance, by abstaining from alcohol. Aspirin and NSAIDs should be avoided. No protection comes from avoiding certain foods such as spices or from taking long-term H₂-blockers.

Propranolol or nadalol are non-selective beta-blockers which reduce portal pressure by splanchnic vasoconstriction and, to a lesser extent, by reducing cardiac output. Hepatic arterial blood flow falls [121,122]. The drug is given in a dose which reduces the resting pulse
rate to that best tolerated by the patient, but not below 55/min. There is marked individual variation in the lowering of the portal pressure. Even with large doses, 60–70% of patients do not respond in optimal fashion, especially those with advanced cirrhosis [123]. The optimal HVPG reduction is to or below 12 mmHg and/or a 20% fall from baseline. However, the low risk of first bleeding with therapy makes HVPG measurement not very applicable outside of research protocols.

Propranolol should not be given to patients with obstructive airways disease. No fatal effects have been reported. If resuscitation is difficult intravenous glucagon can be given. Propranolol causes some mental depression, sometimes impotence and fatigue. Nadolol has similar effects.

Randomized trials of non-selective beta blockers against placebo or no treatment showed a significant reduction in bleeding, but survival was not statistically different [124] (Fig. 9.50). Sclerotherapy is potentially harmful [121]; banding ligation is safer. A meta-analysis of randomized trials of non-selective beta-blockers versus ligation, showed no survival difference, but less bleeding with ligation [125]. However, to avoid one bleeding episode in the ligation group, one needs to treat five to six patients and perform about 33 sessions of endoscopy [126], so that it is not cost effective. Ligation should be used when there are contraindications or intolerance to non-selective beta-blockers. One study has compared carvedilol versus banding ligation [127], resulting in less bleeding with carvedilol. However, the dose used was smaller than in other studies in which side effects of carvedilol precluding continuation occurred, and the efficacy of banding was one of the least effective rates reported [128]. Studies versus non-selective beta-blockers are needed. Combination therapy with ligation or other drugs is not recommended.

Isosorbide mononitrate may worsen fluid retention, particularly in patients over 50 years old [129].

### Diagnosis of bleeding

The clinical features are those of gastrointestinal bleeding with the added picture of portal hypertension.

Bleeding is most often a sudden haematemesis, but may be a slow ooze with melaena, and sometimes presents with iron deficiency anaemia usually due to portal hypertensive gastropathy or colopathy. The intestines may be full of blood before the haemorrhage is recognized and the bleeding episode is liable to continue for days.

Bleeding varices in cirrhosis have injurious effects on the liver cells. These may be due to anaemia diminishing hepatic oxygen supply, or to increased metabolic demands resulting from the protein catabolism following haemorrhage or to secondary stimulation and release of cytokines. The fall in blood pressure diminishes hepatic arterial flow, on which the regenerating liver nodules depend, and ischaemic hepatitis may ensue as well as renal injury. The increased nitrogen absorption from the intestines often leads to hepatic coma (Chapter 8). Deteriorating liver cell function may precipitate jaundice or ascites, and renal impairment.

Non-variceal bleeding from duodenal ulcers, gastric erosions and the Mallory–Weiss syndrome is frequent.

Endoscopy should always be performed following resuscitation and within 12 h to confirm the source of the bleeding [130] (Fig. 9.51). Bleeding varices may be diag-

---

**Table 9.4.** Child’s classification of hepatocellular function in cirrhosis

<table>
<thead>
<tr>
<th>Group designation</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum bilirubin* (mg/dL)</td>
<td>Below 2.0</td>
<td>2.0–3.0</td>
<td>Over 3.0</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>Over 3.5</td>
<td>3.0–3.5</td>
<td>Under 3.0</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Easily controlled</td>
<td>Poorly controlled</td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>None</td>
<td>Minimal</td>
<td>Advanced coma</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Excellent</td>
<td>Good</td>
<td>Poor: ‘wasting’</td>
</tr>
</tbody>
</table>

*1 mg = 17 μmol/L.

---

**Fig. 9.50.** Meta-analysis of six trials of prophylactic propranolol (beta-blocker) therapy. Data on dying cannot be relied upon because of significant heterogeneity (Heterog.) in groups. There is, however, a significant reduction in those bleeding [124].

---
The importance of hepatocellular function is emphasized by the relatively good prognosis for bleeding in patients where hepatocellular function is relatively well preserved, as in schistosomiasis, the non-cirrhotic portal hypertension of India and Japan, and portal vein thrombosis.

Management of acute variceal bleeding [74,130] (Fig. 9.51)

Child’s grade is recorded (Table 9.4). Bleeding is likely to continue and observations must be close. If possible, the patient should be managed by an experienced intensive care team. Haemodynamic monitoring (central venous pressure) and peripheral drip are instigated. The patient is transfused to a 0.3 haematocrit or haemoglobin to less than or equal to 8 g/L. Over-transfusion

Admission with haematemesis and/or melaena
Vaso-active drug and antibiotics
Diagnostic endoscopy
Actively bleeding oesophageal varices (spurting or oozing)
Sclerotherapy/band ligation
Success
Failure
Drug stopped
Drug continued
(4-5 days)
(continued)

Technical failure
Balloon tamponade
(4-5 days)
gastric and/or oesophageal balloon without traction (24 h maximum)

Failure
Balloon tamponade
Success
(continued)
(4-5 days)

2nd therapeutic endoscopy

Problem bleeders TIPS
(grade B and C patients, if TIPS unavailable, injection of glue, or transection)

Shunt surgery or TIPS (grade A patients)

Transplantation decision

Fig. 9.51. Common practice for the management of oesophageal varices actively bleeding at diagnosis. Acute therapeutic endoscopy should only be performed by an experienced endoscopist [130].

Assessment

Prognosis
Sixty-five per cent of varices in patients with cirrhosis will not rupture within 2 years of diagnosis [54].

The prognosis is determined by the severity of the hepatocellular disease, with death within 6 weeks between 0 and 10% for Child A cirrhosis and 20 and 40% for Child C cirrhosis. Survival has improved over the past decades [132]. The 1-year survival in good-risk (Child grade A and B) patients is about 85% and in bad-risk (Child grade C) patients about 30% (Table 9.5). Survival scores [74] can be based on a combination of variables reflecting severity of liver disease and bleeding and the presence of active bleeding [133], encephalopathy, prothrombin time and the number of units transfused in the previous 72 h. Abstention from alcohol considerably improves the prognosis. Patients with continuing chronic hepatitis do poorly. Patients with primary biliary cirrhosis tolerate the haemorrhage reasonably well [134], particularly if not very jaundiced.

Table 9.5. Deaths from upper gastrointestinal bleeding in cirrhosis

<table>
<thead>
<tr>
<th>Sources of bleeding</th>
<th>Number of patients</th>
<th>Deaths within 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sources</td>
<td>465</td>
<td>92 (20%)</td>
</tr>
<tr>
<td>Variceal</td>
<td>336</td>
<td>70 (21%)</td>
</tr>
<tr>
<td>Non-variceal</td>
<td>114</td>
<td>17 (15%)</td>
</tr>
<tr>
<td>Undefined</td>
<td>15</td>
<td>5 (33%)</td>
</tr>
</tbody>
</table>

Table 9.5. Deaths from upper gastrointestinal bleeding in cirrhosis

nosed endoscopically when an ooze of blood is seen from an area within 5 cm of the gastroesophageal junction or as a venous spurt (active bleeding). Alternatively a platelet ‘plug’ (a white raised spot) may indicated a varix that has bled [131]; if no other lesion is seen in the upper gastrointestinal tract, varices are considered to be the source of bleeding.

Prognosis

Sixty-five per cent of varices in patients with cirrhosis will not rupture within 2 years of diagnosis [54].

The prognosis is determined by the severity of the hepatocellular disease, with death within 6 weeks between 0 and 10% for Child A cirrhosis and 20 and 40% for Child C cirrhosis. Survival has improved over the past decades [132]. The 1-year survival in good-risk (Child grade A and B) patients is about 85% and in bad-risk (Child grade C) patients about 30% (Table 9.5). Survival scores [74] can be based on a combination of variables reflecting severity of liver disease and bleeding and the presence of active bleeding [133], encephalopathy, prothrombin time and the number of units transfused in the previous 72 h. Abstention from alcohol considerably improves the prognosis. Patients with continuing chronic hepatitis do poorly. Patients with primary biliary cirrhosis tolerate the haemorrhage reasonably well [134], particularly if not very jaundiced.
is avoided. Systolic blood pressure is maintained at equal or greater than 90 mmHg. Saline infusions are avoided.

Fresh frozen plasma and platelet transfusions may be necessary to prevent further worsening of coagulation by dilution of transfused blood. Vitamin K₁ intravenously is routine. Acid secretion is suppressed although there is little controlled evidence of benefit; H₂ receptor antagonists have less risk of inducing *Clostridium difficile* infections than proton pump inhibitors. However, stress-induced mucosal ulcers are frequent.

Liver function is monitored and electrolyte balance and renal function maintained.

Prophylactic antibiotics, currently third-generation cephalosporins, are given immediately as they prevent infection [135], reduce bleeding and improve survival [136,137]. Pneumonia is prevented by special care during endoscopy, and endotracheal intubation is warranted if the patient has encephalopathy.

Hepatic encephalopathy is prevented by lactulose and phosphate enemas.

Sedatives should be avoided, and, if essential low-dose zopliclone should be used. Oral chlormethiazole or chlordiazepoxide may be required to treat or prevent delirium tremens in alcoholics.

If ascites is very tense, intra-abdominal pressure may be reduced by a cautious paracentesis and intravenous albumin replacement and the use of spironolactone.

Management requires the availability of many therapeutic options and these may need to be combined in the individual patient (Fig. 9.51). They include vasoactive drugs, endoscopic sclerotherapy and variceal banding, the Sengstaken tube, or other tamponade devices, TIPS and very rarely emergency surgery.

**Vasoactive drugs**

Vasoactive drugs lower portal venous pressure and should be started even before diagnostic and therapeutic endoscopy [130,138]. Treatment can be given even before the patient is admitted to hospital and certainly in the emergency room. Early treatment facilitates the ease with which endoscopic therapy can be done as active bleeding has been reduced.

*Vasopressin and terlipressin* lower portal venous pressure by constriction of the splanchic arterioles, so causing an increase in resistance to the inflow of blood to the gut (Fig. 9.52). They control variceal bleeding by lowering the portal venous pressure. Terlipressin has replaced vasopressin in countries where it is available.

Vasopressin and terlipressin can cause coronary vasocostriction and an electrocardiogram should be taken before they are given. Abdominal colicky discomfort and evacuation of the bowels together with facial pallor are usual during the infusion. Myocardial intestinal ischaemia and rarely infarction are other possible complications.

Terlipressin is given in a dose of 2 mg intravenously every 6 h for 48 h. It may be continued for a further 3 days at 1 mg every 4–6 h. It is the only vasoactive drug for which there is evidence for improved survival.

*Somatostatin* reduces the portal pressure by increasing splanchnic arterial resistance. It also inhibits a number of vasodilatory peptides, including glucagon. It has less side effects than vasopressin or terlipressin [139], but does not substantially reduce blood transfusion requirement [140]. An intravenous bolus of 250 μg or 500 μg is given followed by an infusion of 6 mg/24 h for 120 h [130,138].

*Octreotide* and *vapreotide* are synthetic analogues of somatostatin. They have a much longer half-life (1–2 h). Trials have given conflicting results and data are far less robust than for terlipressin and somatostatin in acute variceal bleeding [140].

**Sengstaken–Blakemore tube (Figs 9.53, 9.54) and self-expanding oesophageal stent**

The use of oesophageal tamponade has decreased markedly with the use of vasoactive drugs, oesophageal sclerotherapy and TIPS. The four-lumen tube has an oesophageal and a gastric balloon, an aspirating channel for the stomach and a fourth lumen for continuous aspiration above the oesophageal balloon. Ideally, endotracheal intubation should be performed first, but this may not be possible. If so two, but preferably three, assistants
The Hepatic Artery, Portal Venous System and Portal Hypertension

Fig. 9.53. Sengstaken–Blakemore oesophageal compression tube modified by Pitcher. Note the fourth oesophageal tube which aspirates the oesophagus above the oesophageal balloon.

Fig. 9.54. The Sengstaken–Blakemore tube in position.

Gastric balloon
Gastric tube (aspirated)
Clamped
Oesophageal balloon
Presssure bulb
Manometer
To oesophageal balloon
Oesophageal tube (aspirated)
Oesophageal aspiration holes
Oesophageal balloon
Gastric balloon
Gastric aspiration holes
Stomach
Oesophagus

The tube is easier to insert if it has been allowed to stiffen in the icebox of a refrigerator. The stomach is emptied. A new, tested and lubricated tube is passed through the mouth into the stomach. The gastric balloon is inflated with 250 mL of air and doubly clamped. The gastric tube is aspirated continuously. The whole tube is pulled back until resistance is encountered and the oesophageal tube is then inflated to a pressure of 40 mmHg, greater than that expected in the portal vein. The tube should be taped securely to the side of the face to provide adequate traction. Too little traction means that the gastric balloon falls back into the stomach. Too much causes discomfort with retching, and also potentiates gastro-oesophageal ulceration. The initial position of the tube is checked by X-ray (Fig. 9.54). The head of the bed is raised.

The oesophageal tube has continuous low-pressure suction and occasional aspiration. Tube traction and oesophageal balloon pressure are checked hourly. After 12 h, traction is released and the oesophageal balloon deflated, leaving the gastric balloon inflated. If bleeding recurs, the traction is reapplied and the oesophageal balloon reinflated until emergency therapeutic endoscopy or TIPS can be performed. A further procedure should always follow tamponade as rebleeding reoccurs in over 50% after withdrawal. If bleeding is not controlled the tube has slipped or the source of bleeding is fundal varices or another lesion.

Complications include obstruction to upper airways. If the gastric balloon bursts or deflates, the oesophageal balloon may migrate into the oropharynx causing asphyxia. The oesophageal balloon must be deflated, and if necessary the tube cut through immediately with scissors.

Ulceration of the lower oesophagus complicates prolonged or repeated use. Aspiration of secretions into the lung is prevented by continuous suction above the oesophageal balloon. Oesophageal rupture can occur, usually when the gastric balloon is wrongly inflated in the oesophagus.
The Sengstaken tube is the most certain method for continued control of oesophageal bleeding over hours. Complications are frequent and are in part related to the experience of the operating team. It is unpleasant for the patient. It is useful when transferring patients from one centre to another, when haemorrhage is torrential and when variceal ligation or injection, TIPS or surgery are not immediately available. The oesophageal tube should not be kept inflated for more than 24 h.

A new self-expanding, covered oesophageal stent device, which can be subsequently removed endoscopically, also results in tamponade, but allows the patient to eat and drink. It can also be used to treat oesophageal tears caused by the Sengstaken tube [141]. It requires expertise to place the tube, but this can also be done solely under radiological screening [141,142].

Endoscopic banding ligation and injection of varices

The combination of immediate use of a vasoactive agent and endoscopic banding ligation or injection is the therapeutic gold standard for the acute treatment of bleeding varices in the oesophagus and for subcardial gastric varices. In over 85% of patients the haemorrhage will be controlled with one or two sessions of endoscopic therapy [74].

Both banding ligation and injection of oesophageal varices are effective in treating bleeding from oesophageal or subcardial gastric varices. Banding ligation is slightly more effective compared to injection sclerotherapy with 5% ethanolamine or 1% sodium tetradecylsulphate, particularly when there is no active bleeding (Fig. 9.55), but survival following either procedure is the same [143]. The endoscopist must use the procedure that he/she is most used to, and judge the risk of lung aspiration if using ligation, as a further endoscopic intubation is required in order to fit the banding device.

If the patient rebleeds, a second emergency ligation or injection may be given. If more sessions are necessary, the salvage rate is poor and alternative therapy, such as injection of glue or TIPS [144] should be considered (Fig. 9.51) [74].

Patients who are likely to fail one session of therapeutic endoscopy are Child C patients with more severe bleeding at presentation. These patients often have higher (≥200 mmHg) HVPG [145]. In this group earlier switch to alternative therapies if available (or their use as first-line therapy) can be considered [74], such as injection of cyanoacrylate glue, oesophageal stenting or TIPS [146]. Double-channel endoscopies are preferred as continued suction is possible to obtain clearer views at the same time as applying bands to varices or injecting them. An assessment must be made regarding protection of the airway. If in doubt, endotracheal intubation rather than sedation must be used. Injection is made just above the gastro-oesophageal junction, and rarely more than 2 mL per varix is needed. More than 4 mL per varix should be avoided. Ligation requires loading of the ligation device at the tip of the endoscope and then ligation is started at the gastro-oesophageal junction and confined to the lower 3–5 cm of the oesophagus. The varices are strangulated by the application of small elastic O rings (Fig. 9.56) pulling a trip wire threaded through the operating channel of the endoscope. At least one band is applied to each varix in a spiral fashion. There is no current evidence that more bands per varix are more effective. Both injection and ligation can result in transient dysphagia, retrosternal chest pain and sometimes fever. Aspiration pneumonia must be avoided. Oesophageal ulcers are almost a universal consequence of therapy and sometimes cause recurrent bleeding. Sucralfate can speed up healing and prevent bleeding. Injection of cyanoacrylate glue is particularly indicated for bleeding gastric varices in the fundus [147] as it is more effective than ligation or sclerotherapy. Bleeding from fundal varices is often severe and has a higher mortality than from bleeding oesophageal varices. TIPS is also a first-line therapy [144,146].
Emergency transjugular intrahepatic stent shunt

TIPS is a radiological procedure, which in the emergency situation is best performed under general anaesthetic, but can be done under simple sedation and local anaesthesia. The internal jugular vein is punctured and the hepatic vein (usually middle right) is cannulated. Using ultrasound localization a needle puncture of the portal vein is made, and a track, which is then ballooned, is fashioned between the hepatic and portal veins. Then a self-expanding metal stent, covered in its central area by PTFE, is placed through the track. Care must be taken not to encroach on the inferior vena cava and nor to place the stent too far into the portal vein, as either can render future liver transplantation difficult (Figs 9.57, 9.58). The use of PTFE stents [148] has greatly reduced the rate of occlusion compared to bare metal stents [149], due to reduced pseudointimal hyperplasia as well as thrombosis [150,151].

An adequate portocaval gradient pressure reduction must be achieved by using the correct diameter stent (10–12 mm), usually to 12 mmHg. More than one stent may be required.

Control of bleeding

TIPS controls bleeding resulting from portal hypertension, whether it be oesophageal, gastric, intestinal, colonic or stomal. It is of particular value as salvage therapy in acute variceal bleeding which cannot be controlled by endoscopy and vasoactive drugs [74,144,152]. Embolization of collaterals performed during TIPS may also be necessary, particularly for bleeding from ectopic varices [153]. This is a difficult technique and a skilled interventional radiologist must be part of the team. The technical failure rate is about 5–10% and control of bleeding achieved in over 90% (Table 9.6).

Complications

Procedural mortality is less than 1%. Complications include haemorrhage, due to liver capsule puncture, or intrahepatic and which may result in intra-abdominal or bleeding into the biliary tract. TIPS can be placed in patients with thrombosis confined to the main portal vein [101].
Table 9.6. Complications of non-covered and covered TIPS in a randomized trial

<table>
<thead>
<tr>
<th>Complication</th>
<th>Non-covered (%)</th>
<th>Covered (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical failure</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Shunt thrombosis</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Shunt stenosis</td>
<td>32</td>
<td>5</td>
</tr>
<tr>
<td>Severe hepatic encephalopathy</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Shunt dysfunction</td>
<td>44</td>
<td>15</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>46</td>
<td>30</td>
</tr>
</tbody>
</table>

Infections are prevented by a careful aseptic technique and early removal of central venous lines.

Intravascular haemolysis may be related to damage to erythrocytes by the steel mesh of the stent [154], which is much less frequent with covered stents. Hyperbilirubinaemia developing postshunt has a poor prognosis [155]. Hypersplenism and, in particular, thrombocytopenia is unaffected [154,156].

Follow-up of shunt patency is essential. This may be done by routine portography or Doppler sonography [157]. Shunt occlusion is treated by revision of the shunt under local anaesthesia. The shunt may be dilated by percutaneous catheterization or a further stent may be inserted [158]. Selected patients with stenosed TIPS, can be treated with distal splenorenal shunt if they have Child’s A and B cirrhosis [159].

Emergency surgery

This is hardly ever required, but may be needed if TIPS is not available and other measures have failed. An emergency end-to-side portacaval shunt is effective in stopping bleeding [160]. Mortality is high in grade C patients, and the postsurgical encephalopathy rate is also high. If a shunt must be avoided or if there is portal vein occlusion, emergency oesophageal transection may be done using a staple gun technique [161,162]. Varices recur, enlarge and frequently rebleed [162].

Prevention of rebleeding

Following variceal bleeding, rebleeding occurs without prevention within 1 year in up to 70% of patients, more frequently if Child C grade. All patients should receive preventative therapy before discharge from hospital and replacement of depleted iron stores.

The most effective therapy is a combination of repeated endoscopic band ligation (which is more effective than repeated sclerotherapy) with non-selective beta-blockers [163]. Varices are rebanded at 2 to 3-week intervals allowing ulcers to heal in these intervals, until the varices are rendered too small to band or are eradicated. Follow-up endoscopies should be scheduled as varices can regrow. Non-selective beta-blockers are given in maximal doses as tolerated by the patient providing the pulse rate is above 55/min; they are also effective in prevention of bleeding from portal hypertensive gastropathy [164].

Portal-systemic shunt procedures (Fig. 9.59)

The aim is to reduce portal venous pressure, maintain total hepatic and, particularly, portal blood flow and, above all, not have a high incidence of hepatic encephalopathy. There is no currently available procedure that fulfils all these criteria. Hepatic reserve determines survival. Hepatocellular function deteriorates after shunting. Surgically fashioned shunts are rarely performed if TIPS can be placed.

Portacaval

In 1877, Eck [165] first performed a portacaval shunt in dogs and this remains the most effective way of reducing portal hypertension in man.

The portal vein is joined to the inferior vena cava either end-to-side, with ligation of the portal vein, or side-to-side, maintaining its continuity. The portal blood pressure falls, hepatic venous pressure falls and hepatic arterial flow increases.

Portacaval shunts are rarely performed because of the high incidence of postshunt encephalopathy. Liver function deteriorates due to reduction of portal perfusion. Subsequent hepatic transplantation can be made more difficult. It is still used, after the bleeding episode has been controlled, in patients with good liver reserve, who do not have optimal access to tertiary care including TIPS. It is useful in some patients who have had proven variceal bleeding and a patent portal vein, with early primary biliary cirrhosis, congenital hepatic fibrosis with good hepatocellular function and those with portal vein obstruction at the hilum of the liver. Patients with cirrhosis should preferably be aged less than 50 years. After the age of 40, survival is reduced and encephalopathy is twice as common.

The patient should not have a history of hepatic encephalopathy, and should be Child’s grade A or B.

Mesocaval

This shunt is made between the superior mesenteric vein and the inferior vena cava using a Dacron graft (Fig. 9.60) [166]. It is technically easy. Shunt occlusion is usual with time and is followed by rebleeding [166]. It does not interfere with subsequent hepatic transplantation.
Selective ‘distal’ splenorenal (Fig. 9.61)

Veins feeding the oesophagogastric collaterals are divided while allowing drainage of portal blood through short gastric–splenic veins through a splenorenal shunt to the inferior vena cava. Portal perfusion is maintained, but only for between 1 and 2 years [167,168].

The mortality and encephalopathy results are similar to those reported for non-selective shunts. Better results are reported in non-alcoholic patients and where gastric varices are the main problem. The operation does not interfere with a subsequent liver transplant.

Selective splenorenal shunt is technically difficult and fewer and fewer surgeons are able or willing to perform it.

General results of portal–systemic shunts

The mortality rate in good-risk patients is about 5%. For poor-risk patients the mortality is 50%.
Bleeding from gastro-oesophageal varices is prevented or greatly reduced. Variceal size decreases and varices may disappear within 6 months to 1 year.

Blood pressure and hepatic blood flow fall so that hepatic function deteriorates. Postoperative jaundice is related to this and to haemolysis. Ankle oedema is due to a fall in portal venous pressure while serum albumin level remains low. Increased cardiac output with failure may contribute. Shunt patency is confirmed by ultrasound, CT, MRI, Doppler or angiography.

Hepatic encephalopathy may be transient. Chronic changes develop in 20–40% and personality deterioration in about one-third (Chapter 8). The incidence increases with the size of the shunt. Encephalopathy is more common in older patients.

Myelopathy with paraplegia and parkinsonian cerebellar syndrome are rare (Chapter 8).

**TIPS (transjugular intrahepatic portosystemic shunt)**

As for surgical shunts, TIPS should not be used as first-line therapy for prevention of rebleeding as survival is not increased [169]. Health-care costs may not be less than with surgical shunts [170]. It is more effective than endoscopic therapy in terms of rebleeding, but there is no difference in survival and there is more encephalopathy [168].

**TIPS encephalopathy**

This is a side-to-side portal–systemic shunt and is followed by encephalopathy in about the same percentage (25–30%) as that following surgically performed portacaval shunts [171]. Encephalopathy is related to the age of the patient, Child’s grade and shunt size [172]. It declines after the first 3 months perhaps due to cerebral adaptation [173] and is reduced if the shunt occludes. It can be treated by placing a smaller stent within the intrahepatic shunt. Resistant encephalopathy may be an indication for liver transplant.

**Circulatory changes**

The hyperdynamic circulation of cirrhosis persists [174] and systemic vasodilatation is initially increased. Cardiac output and systemic blood volume increase. Patients with underlying cardiac problems may be precipitated into heart failure. In alcoholic cirrhotic patients, a preclinical cardiomyopathy may be unmasked [175]. Pulmonary hypertension may develop [176].

**Other indications**

TIPS effectively controls ascites in Child’s grade B patients, and survival can be improved (Chapter 10), as well as nutritional status. Hepatic hydrothorax may be resolved completely. Budd–Chiari syndrome can be effectively treated (see below).

Renal function may improve in some patients with the hepatorenal syndrome (Chapter 10).

**Hepatic transplantation**

Patients with cirrhosis and bleeding varices die because their hepatocytes fail, not from blood loss per se. The end-point is death or a liver transplant. Previous endoscopic therapy or portal–systemic shunts do not affect post-transplant survival [177]. Liver transplant must be considered for variceal bleeding occurring with end-stage liver disease [178], or if there have been at least two episodes of bleeding from varices despite optimal therapy.

Previous surgical shunts make the transplant technically more difficult, particularly if there has been dissection at the hepatic hilum. Splenorenal and mesocaval shunts and TIPS are not contraindications, but migrated or misplaced TIPS can cause complications [179].

Most of the haemodynamic and humoral changes of cirrhosis are reversed by liver transplant [180].

**Pharmacological control of the portal circulation and reduction of HVPG**

Portal hypertension is part of a hyperdynamic state with increased cardiac output and reduced peripheral resistance. There are profound changes in autonomic nervous system activity. The various hormonal factors probably involved make pharmacological control possible.

Theoretically, portal blood pressure (and flow) could be reduced by lowering cardiac output, by reducing inflow through splanchnic vascular obstruction, by splanchnic venodilatation, by reducing intrahepatic vascular resistance or, of course, by surgical portacaval shunting (Fig. 9.62). It is preferable to reduce pressure by lowering resistance rather than decreasing flow as hepatic blood flow and function will be maintained. New therapies ideally should not worsen systemic haemodynamics, but act specifically on the liver microcirculation without reducing portal inflow. Statin agents fulfil this function, and induce further reduction of HVPG added to non-selective beta-blockers. Monitoring of HVPG reduction and adjustment of therapy to achieve a HVPG less than 12 mmHg or a 20% reduction from baseline is recommended by some [181], but not by others [182]. However, a HVPG guided therapy, although achieving target reductions in more patients, does not result in less rebleeding than in non-monitored patients treated with combined ligation and drug therapy [183].

There is evidence that non-selective beta-blockers may have important therapeutic effects at lesser reduc-
The portal pressure can be reduced by arterial hypotension, splanchnic vasoconstriction, portal venodilatation or reduction in intrahepatic resistance.

Fig. 9.62. The portal pressure can be reduced by arterial hypotension, splanchnic vasoconstriction, portal venodilatation or reduction in intrahepatic resistance.

Reductions of HVPG [184], even if rebleeding is not effectively prevented [185]. Bacterial translocation may be reduced as spontaneous bacterial peritonitis is prevented compared to no treatment [186]. Mechanisms may include increased intestinal transit and decreased mucosal congestion [187]. Abstention reduces HVPG and improves liver function [188]. Complications other than bleeding are also reduced by lowering HVPG [189,190]. Simvastatin lowers HVPG with or without beta-blockers; long-term studies may show further reduction in bleeding [191].

Summary
Variceal bleeding still has a high mortality, particularly if patients have more severe liver function or they have developed previous jaundice, ascites or encephalopathy. However, survival has improved steadily over the past decades, through use of prophylactic antibiotics, better use of specific therapies and better general care of the patient. Bleeding as a direct cause of death is rare. Rebleeding has been reduced by about 40–50%, and first bleeding by a similar proportion. Reduction in HVPG reduces complications and improves survival. Practice guidelines are based on many dozens of randomized trials (second only to the number in viral hepatitis) [138].

The hepatic veins
The hepatic veins begin in zone 3. They join the sublobular veins and merge into large hepatic veins, which enter the inferior vena cava while it is still partly embedded in the liver. The number, size and pattern of hepatic veins are very variable. Generally, there are three large veins, one draining segments 2, 3 and 4, and the other two draining segments 5, 6, 7 and 8 (Fig. 9.63). There are variable numbers of small accessory veins, particularly from the caudate lobe [192].

In the normal liver there are no direct anastomoses between the portal vein and hepatic vein, which are linked only by the sinusoids (Fig. 9.64). In the cirrhotic liver there are anastomoses between the portal and hepatic veins so that the blood bypasses the regenerating liver cell nodules (see Fig. 9.46). There is no evidence, either in the normal or cirrhotic liver, of anastomoses between the hepatic artery and the hepatic vein.

Functions
The pressure in the free hepatic vein is approximately 6mmHg.

The hepatic venous blood is only about 67% saturated with oxygen.

Dogs have muscular hepatic veins near their caval orifices which form a sluice mechanism. The hepatic veins in man have little muscle.

The hepatic venous blood is usually sterile since the liver is a bacterial filter.

Visualizing the hepatic vein
Hepatic venography. This is performed by injection of contrast into a hepatic vein radicle with a wedged
Chapter 9

Vein anastomoses and may be outlined. In cirrhosis the sinusoidal pattern is coarsened, beady and tortuous, and gnarled hepatic radicles may be seen. The extent of filling of the main portal vein may indicate the extent to which the portal vein has become the outflow tract of the liver.

Scanning. The main hepatic veins may be visualized by ultrasound, colour Doppler imaging, enhanced CT scan and MRI. A CT scan without contrast enhancement in a patient with a fatty liver shows excellent hepatic venous anatomy well (Fig. 9.65).

Catheter or occluded with a balloon catheter and results in filling of the sinusoidal area draining into the catheter and also in retrograde filling of the portal venous system in that area. The portal radicle then carries the contrast medium to other parts of the liver and so other hepatic vein branches become opacified. Cirrhotic nodules and tumour deposits are surrounded by portal vein–hepatic vein anastomoses and may be outlined. In cirrhosis the sinusoidal pattern is coarsened, beady and tortuous, and gnarled hepatic radicles may be seen. The extent of filling of the main portal vein may indicate the extent to which the portal vein has become the outflow tract of the liver.

Scanning. The main hepatic veins may be visualized by ultrasound, colour Doppler imaging, enhanced CT scan and MRI. A CT scan without contrast enhancement in a patient with a fatty liver shows excellent hepatic venous anatomy (Fig. 9.65).
Experimental hepatic venous obstruction

The usual method is to constrict the inferior vena cava by a band placed above the entry of the hepatic veins, and so obstruct the venous return from the liver [193]. Zone 3 haemorrhage and necrosis with fibrosis follow. The hepatic lymphatics dilate and lymph passes through the capsule of the liver forming ascites with a high protein content.

Budd–Chiari (hepatic venous obstruction) syndrome [194]

This condition is usually associated with the names of Budd and Chiari although Budd’s description [195] omitted the features, and Chiari’s paper [196] was not the first to report the clinical picture. The syndrome comprises hepatomegaly, abdominal pain, ascites and hepatic histology showing zone 3 sinusoidal distension and pooling. It may arise from obstruction to hepatic veins at any site from the efferent vein of the acinus to the entry of the inferior vena cava into the right atrium (Fig. 9.66). It occurs in 1/100 000 of the general population [197]. A similar syndrome may be produced by constrictive pericarditis or right heart failure.

Myeloproliferative diseases, particularly polycythaemia rubra vera, are associated in up to 50% of cases [198]. These may be covert and diagnosed only by the erythroid bone marrow colony test, although the JAK2 mutation is found in 80% of cases with polycythaemia rubra vera and 50% of idiopathic myelofibrosis patients [199]. The patient is often a young female. Multiple thrombophilic conditions may be present in the same patient [198].

The Budd–Chiari syndrome has been associated with systemic lupus erythematosus [200] and with circulating lupus anticoagulant [200], sometimes with disseminated intravascular coagulation. The antiphospholipid syndrome may be primary or secondary to systemic lupus [201]. Idiopathic granulomatous venulitis is another cause, which is treated successfully with corticosteroids [202].

Paroxysmal nocturnal haemoglobinuria in up to 35% of cases may be associated with Budd–Chiari syndrome, the severity varying from the asymptomatic to a fatal syndrome [203].

The Budd–Chiari syndrome is associated with deficiency of anticoagulant factors and impairment of fibrinolysis [204]. These include antithrombin III deficiency, whether primary or secondary to proteinuria [205], protein S and protein C deficiency [194], which may be difficult to diagnose due to poor hepatic synthesis. A normal factor II concentration together with a 20% or more reduction in protein C or S confirms a true deficiency; factor V Leiden mutation occurs in 20% [194,205,206]. Thromboelastography can detect hypercoagulability even if specific defects are not found [207].

Hepatic vein thrombosis complicating Behçet’s disease is a sudden event, usually related to extension of a caval thrombosis to the oestome of hepatic veins [208].

The risk in users of oral contraceptives is about the same as other thrombotic complications [209]. Oral contraceptives may act synergistically in those predisposed to clotting [210].

Hepatic vein thrombosis has been reported in pregnancy (Chapter 27) [211]. Trauma may lead to membranous obstruction to the inferior vena cava in those with a hypercoagulable state [212].

The hepatic veins may be mechanically compressed by severe, polycystic liver disease [213].

Obstruction to the inferior vena cava is secondary to thrombosis in malignant disease, for instance an adrenal or renal carcinoma or invasion by a hepatocellular cancer [214] or angiosarcoma [215]. Rare tumours include leiomyosarcoma of the hepatic veins [216]. Wilms’ tumour metastases may involve the inferior vena cava and hepatic veins [217].

Myxoma of the right atrium and metastases to the right atrium can cause hepatic outflow obstruction. Invasion of hepatic veins by masses of aspergillus and compression by amoebic abscesses has been reported.
Chapter 9

The Budd–Chiari picture also follows central hepatic vein involvement in the alcoholic and in veno-occlusive disease (Chapter 24).

Liver transplantation may be followed by small hepatic vein stenosis with some of the features of veno-occlusive disease. It is usually associated with azathioprine and with cellular rejection [218]. Small for size syndrome also has features of venous outflow obstruction [219].

*Membranous obstruction* of the suprahepatic segment of the inferior vena cava by a web is usually a sequel to thrombosis. It may be associated with infection or with a hypercoagulable state [220]. The web varies from a thin membrane to a thick fibrous band. It is particularly frequent in Japan where it has a strong association with hepatocellular carcinoma [221] and in South Africa and, to a lesser extent, in India and Nepal [222]. It may affect children. Its incidence is falling in India [223]. The clinical picture is milder than for classical Budd–Chiari syndrome. Markedly enlarged subcutaneous veins over the trunk are conspicuous. The picture has been termed *obliterative hepatocavopathy* [224].

The Budd–Chiari syndrome is being diagnosed more frequently and in milder forms, probably due to the routine use of imaging, especially ultrasound [194].

**Pathological changes**

The hepatic veins show occlusion at points from the ostia to the smaller radicles. Thrombus may have spread from an occluded inferior vena cava. Thrombus may be purulent or may contain malignant cells, depending on the cause. In chronic cases, the vein wall is thickened and there may be some recanalization. In others it is replaced by a fibrous strand; a fibrous web may be seen.

Involvement of large hepatic veins is usually thrombotic. Isolated obstruction to the inferior vena cava or small hepatic veins is usually non-thrombotic [194].

The liver is enlarged, purplish and smooth. Venous congestion is gross and the cut surface shows a ‘nutmeg’ change. Hepatic veins proximal to the obstruction and, in the acute stage, subcapsular lymphatics, are dilated and prominent.

In the chronic case, the caudate lobe is enlarged and compresses the inferior vena cava as it passes posterior to the liver (Fig. 9.67). Areas less affected by obstruction form nodules. The fibrosis and regenerative nodules continue to evolve after the first hepatic vein thrombosis and often progress to involve the portal venous system. The spleen may enlarge and a portal–systemic circulation develops. Mesenteric vessels may thrombose.

Histology shows zone 3 venous dilatation with haemorrhage and necrosis (Figs 9.68, 9.69). The parenchymal response depends on the distribution of vascular obstruction [224]. Persisting hepatic venous obstruction

*Fig. 9.67.* Vertical section of the liver at autopsy in hepatic venous obstruction. The pale areas represent regeneration and the dark areas are congested. Note the marked hypertrophy of the caudate lobe (C).

*Fig. 9.68.* Hepatic venous occlusion (Budd–Chiari syndrome). Hepatic histology showing marked zone 3 haemorrhage (C). The liver cells adjoining the portal zones (P) are spared. (H & E, ×100.)
results in venocentric cirrhosis, so-called reverse lobulation. Portal vein involvement leads to venoportal cirrhosis and mixed forms exist. Large regenerative nodules are usual and are related to a new arterial supply. Nodular regenerative hyperplasia is frequent with longstanding arterialization [225].

Clinical features

These depend on the speed of occlusion, severity of liver dysfunction, anatomical sites of thrombosis and aetiology [194]. The picture varies from a fulminant course, the patient presenting with encephalopathy (and usually with ascites) and dying within 2–3 weeks, to a presentation as chronic hepatocellular disease, with ascites (often not responding to diuretics), and causing confusion with other forms of cirrhosis. The differing presentations are due to sudden massive thrombosis, or repeated thromboses overtime with variable recanalization [194].

In the most acute form the picture is of an ill patient, often suffering from some other condition—for instance renal carcinoma, hepatocellular cancer, thrombophlebitis migrans or polycythaemia. The presentation is with abdominal pain, vomiting, liver enlargement, ascites and mild icterus. Watery diarrhoea, following mesenteric venous obstruction, is a terminal, inconstant feature. If the hepatic venous occlusion is total, delirium and coma with hepatocellular failure and death occurs within a few days.

In the more usual chronic form the patient presents with pain over an enlarged tender liver and ascites developing over 1–6 months. Jaundice is mild or absent, unless zone 3 necrosis is marked. Pressure over the liver may fail to fill the jugular vein (negative hepatojugular reflux). As portal hypertension increases, the spleen becomes palpable. The enlarged caudate lobe, palpable in the epigastrium, may simulate a tumour.

Asymptomatic patients, who account for up to 15% of cases, may have no ascites, hepatomegaly or abdominal pain [226]. Hepatic outflow is diagnosed fortuitously, either by imaging or by the investigation of abnormal liver function tests. It may be explained by remaining patency of one large hepatic vein or development of a large venous collateral.

If the inferior vena cava is blocked, oedema of the legs is gross and veins distend over the abdomen, flanks and back. Albuminuria is found.

The condition may develop over months as ascites and wasting.

Serum bilirubin rarely exceeds 2mg/100mL (34μmol/L). The serum alkaline phosphatase level is raised and the albumin value reduced. Serum transaminase values increase and, if very high, concomitant blockage of the portal vein is suggested. The prothrombin time is markedly increased, especially in the acute type. Hypoproteinaemia may be due to protein-losing enteropathy.

The protein content of the ascites should, theoretically, be high (total protein >25g/L) but this is not always so.

Hepatic venous outflow obstruction is classified according to the site of obstruction and the presence or absence of portal vein thrombosis (PVT) [194]: (1) hepatic vein thrombosis or obstruction without obstruction or compression of the inferior vena cava (IVC); (2) hepatic vein thrombosis or obstruction with IVC obstruction (as a result of compensatory hypertrophy of the caudate lobe, or thrombosis); (3) isolated hepatic vein webs; and (4) isolated IVC webs. Diagnosis of portal vein thrombosis and/or IVC thrombosis and measurement of infrahepatic and suprahepatic caval pressures are needed to plan therapeutic options [194].

Ultrasound shows hepatic vein abnormalities, caudate lobe hypertrophy, increased reflectivity and compression of the inferior vena cava. The appearances are hypoechogenic in the early stages of acute thrombosis and hyperechogenic with fibrosis in the later stages. Ascites is confirmed.

Doppler ultrasound shows abnormalities in the direction of flow in the hepatic vein and retrohepatic inferior vena cava. The blood flow in the inferior vena cava and hepatic veins may be absent, reversed, turbulent or continuous. Colour Doppler imaging shows abnormalities in the hepatic veins, portal vein and inferior vena cava and correlates well with venographic appearances [227].

Detection of intrahepatic collateral vessels is important in the distinction from cirrhosis or where hepatic veins are inconspicuous on ultrasound [227].

CT scan (Fig. 9.70) shows enlargement of the liver with diffuse hypodensity before and patchy enhancement after contrast. Heterogeneous hepatic parenchymal patterns are related to regional differences in portal flow.
Areas with complete hepatic vein obstruction remain hypodense after contrast, probably due to portal flow inversion. Subcapsular areas may enhance.

In the unenhanced scan, the caudate lobe appears dense with surrounding underperfused parenchyma (Fig. 9.70).

Thrombi in the inferior vena cava and/or hepatic vein may be seen as intraluminal filling defects that are not changed by contrast [228].

The CT appearances are easily confused with those of hepatic metastases.

MRI shows absence of normal hepatic venous drainage into the inferior vena cava, collateral hepatic veins and signal intensity alterations in the hepatic parenchyma (Fig. 9.71). The caudate lobe can be seen deforming the inferior vena cava.

Early diagnosis depends on Doppler ultrasound and MRI [197,229,230].
From needle liver biopsy speckled zone 3 areas can be distinguished from the pale portal areas. Histologically, the picture is of zone 3 congestion (Figs 9.68, 9.69). Alcoholic hepatitis or phlebitis of the hepatic veins should be noted.

Hepatic venography may fail or show narrow occluded hepatic veins. Adjacent veins show a tortuous, lace-like spider-web pattern (Fig. 9.72) [197]. This probably represents abnormal venous collaterals. The catheter cannot be advanced the usual distance along the hepatic vein and wedges 2–12 cm from the diaphragm.

Inferior vena cavography establishes the patency of the inferior vena cava. The hepatic segment may show side-to-side narrowing due to distortion from the enlarged caudate lobe (Fig. 9.73). Pressure measurements should be taken in the inferior vena cava along its length to confirm its patency and to quantify the extent of any membranous or caudate lobe obstruction.

From selective coeliac arteriography the hepatic artery appears small. Branches appear stretched and displaced, producing the appearance of multiple space-occupying lesions simulating metastases. The venous phase shows delayed emptying of the portal venous bed.

### Diagnosis

The condition should be suspected if a patient with a tendency to thrombosis, or with malignant disease in or near the liver, or on oral contraceptives, develops tender hepatomegaly with ascites (Table 9.7). Diagnosis, prognosis and correct treatment are only possible if the disease is staged by imaging [194].

Heart failure and constrictive pericarditis must be excluded. Tense ascites *per se* can elevate the jugular venous pressure and displace the cardiac apex.

### Table 9.7. Hepatic vein occlusion (Budd–Chiari syndrome)

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Abdominal pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td></td>
<td>Ascites</td>
</tr>
<tr>
<td></td>
<td>Liver biopsy</td>
</tr>
<tr>
<td></td>
<td>Zone 3 congestion</td>
</tr>
<tr>
<td>Imaging</td>
<td>MRI (contrast enhanced)</td>
</tr>
<tr>
<td></td>
<td>Doppler ultrasound</td>
</tr>
<tr>
<td>Aetiology</td>
<td>Myeloproliferative diseases</td>
</tr>
<tr>
<td></td>
<td>Anticoagulant deficiency</td>
</tr>
<tr>
<td></td>
<td>Paroxysmal nocturnal haemoglobinuria</td>
</tr>
<tr>
<td></td>
<td>Malignant disease</td>
</tr>
<tr>
<td>Management</td>
<td>Cause</td>
</tr>
<tr>
<td></td>
<td>anticoagulants, venesection</td>
</tr>
<tr>
<td></td>
<td>cytotoxic drugs</td>
</tr>
<tr>
<td></td>
<td>Ascites (Chapter 10)</td>
</tr>
<tr>
<td></td>
<td>Surgical</td>
</tr>
<tr>
<td></td>
<td>portacaval shunt</td>
</tr>
<tr>
<td></td>
<td>TIPS</td>
</tr>
<tr>
<td></td>
<td>orthotopic transplant</td>
</tr>
</tbody>
</table>
Cirrhosis must be distinguished and liver biopsy is helpful. The ascitic protein is usually lower in cirrhosis.

Portal vein thrombosis rarely leads to ascites. Jaundice is absent and the liver is not very large.

Inferior vena caval thrombosis results in distended abdominal wall veins but without ascites. If the renal vein is occluded, albuminuria is gross. Hepatic venous and inferior vena caval thrombosis may, however, coexist.

Hepatic metastases are distinguished clinically and by the liver biopsy.

A thrombophilia screen must be performed on all patients and myeloproliferative disorder requires screening of the V617F mutation in Janus tyrosine kinase-2 gene of granulocytes in blood [231]; if this is negative a bone marrow should be performed. Paroxysmal nocturnal haemoglobinuria requires flow cytometry of peripheral blood cells for detection of CD55 and CD59 deficient clones for diagnosis.

**Prognosis**

In symptomatic untreated patients, 90% will die by 3 years [232]. With treatment mortality rates have fallen over recent years [226,232], and survival has reached 75% at 5 years. However, specific therapy may have less beneficial effect than previously thought [232]. Severity of liver and renal dysfunction are important as predictors of survival [194]. If liver function is reflected in a low Child–Pugh score and renal function is normal, 5 year survival is over 95% [226,233]. Hepatocellular carcinoma develops in about 10%, during a mean follow-up of 5 years [234].

The fulminant form is usually fatal unless liver transplantation is carried out. Variceal haemorrhage can occur, as well as extension of the thrombus. Histopathological features do not help to determine prognosis [235]; in fact almost 60% of patients with an acute presentation have features of chronic disease [236]. Japan patients with obliteratorative cavopathy have a 25% mortality rate over 15 years, dying from variceal bleeding and hepatocellular carcinoma [237].

**Treatment**

Early treatment of an underlying haematological disorder improves long-term survival [238,239]. This can include anticoagulants in those with hypercoagulation or reduction of haemoglobin and platelets by venesection, cytotoxic drugs in those with polycythaemia and thrombocytosis and molecular therapies for such as ecu-lizumab for paroxysmal nocturnal haemoglobinuria. Progressive loss of hepatic veins can be halted as large intrahepatic and portal–systemic collaterals develop [226]. Long-term anticoagulation is given for all patients irrespective of whether a thrombophilic condition is diagnosed. It can be sufficient to control disease in about 10% [194].

Ascites is treated with a low sodium diet, diuretics and paracentesis. Severe cases demand ever increasing doses of potent diuretics and eventually the patient is overtaken by inanition and renal failure, unless a TIPS is placed. Some milder cases, however, respond slowly and require less treatment with time.

The timing of radiological or surgical intervention is difficult. On the one hand, some revascularization may continue. On the other hand, the long-term results of medical therapy are so poor that as time passes, radiological or surgical treatment becomes mandatory [194].

**Percutaneous transluminal angioplasty**

This has been used to dilate webs (Fig. 9.74) and also for hepatic vein obstruction after liver transplant. It is particularly useful if the suprahepatic portion of the inferior vena cava is involved. As for hepatic vein webs, multiple dilatations are usually necessary [240].
Intravascular metallic stents may be introduced after the dilatation [241]. Stents are usually reserved for those in whom angioplasty has failed. Together with anticoagulation this treats Budd–Chiari syndrome in up to 30% of cases in series from Western countries.

**Transjugular intrahepatic stent shunt**

If anticoagulation and percutaneous angioplasty, if performed, fail, TIPS is the next step [194]. The aim is to decompress the liver and reverse portal venous flow, in effect acting as a side-to-side portal caval shunt. TIPS has greatly improved treatment for Budd–Chiari syndrome. It avoids laparotomy, overcomes caudate lobe compression and occlusion of the IVC, with less mortality than surgical shunting. It does not hinder further surgical management [242] and, in fulminant Budd–Chiari syndrome, if emergency transplantation is not available it may rescue some patients [242]. Survival at 5 years is currently 70% or more [243]. If the hepatic vein cannot be entered a trans caval approach is used, and even if the portal vein is occluded a TIPS placement is possible [244].

Long-term patency (with anticoagulation) should be improved by PTFE-covered stents. An estimate suggests about 60% of patients in Western countries will need to undergo TIPS [194].

**Surgical portal–systemic shunts**

Surgical shunts are indicated only if TIPS is not available or cannot be fashioned, and liver transplantation is not feasible. It should be avoided in acute Budd–Chiari syndrome as liver failure may be precipitated requiring salvage transplantation [194,245,246]. Results on the whole are unsatisfactory due to thrombosis of the shunt, especially in those with haematological disorders or where stents have been used. If the shunt remains patent, 5-year survival is 87%, falling to 38% if the shunt thromboses [247]. No survival benefit has been clearly shown when taking into account the initial severity of disease [194]. Life-long anticoagulation is essential, but may not be sufficient to maintain patency [191].

Liver function usually deteriorates slowly and the patient becomes a candidate for transplant [246]. Morbidity for transplantation is greater with a previous shunt.

The enlarged caudate lobe increases pressure in the infrahepatic inferior vena cava so that it may exceed the portal venous pressure. If it exceeds 20 mmHg shunting is precluded [194] unless an inferior vena caval stent is placed [248]. The anatomical bulk of the caudate lobe makes a technical approach to the portal vein difficult [194].

If the portal vein is also occluded, shunts will not function.

Clinically, shunts such as side-to-side portacaval or mesocaval are technically difficult. Interposition grafts are often needed, increasing the likelihood of thrombosis [194,246]. A mesocaval interposition shunt has given good results and does not affect the subsequent hepatic transplantation. Mesoatrial shunt is used rarely when the inferior vena cava is obstructed. Posterocranial liver resection can render liver transplantation impossible and is a redundant intervention due to advances in interventional radiology [249].

**Liver transplantation**

This is indicated when the patient deteriorates despite aggressive medical and radiological therapy. The patient has usually progressed to cirrhosis with hepatocellular failure [246]. The transplant may have been preceded by a TIPS, so allowing more time to procure the donor liver. Surgical shunt may have failed [191,239,240]. The 1-year survival is 85% and 5 year survival of 80% [250,251]. Post-transplant thrombosis remains a problem and early anticoagulation is essential [252]. In the case of an underlying thrombotic condition, anticoagulation must be lifelong despite curing protein C [253], S and antithrombin III deficiency, multiple, including as yet unknown, thrombotic conditions may co-exist, so anticoagulation must still be used [94]. After transplantation, obstruction to hepatic venous drainage can be improved by balloon angioplasty [254].

**Veno-occlusive disease**

See Chapter 24.

**Spread of disease by the hepatic veins**

The hepatic veins link the portal and systemic venous systems. Malignant disease of the liver is spread by the hepatic veins to the lungs and hence to other parts. Liver abscesses can burst into the hepatic vein and metastatic abscesses may result. Parasitic disease, including amebiasis, hydatid disease and schistosomiasis, is spread by this route. The portohepatic venous anastomoses developing in cirrhosis may allow intestinal organisms to cause septicemia.

**Circulatory failure**

A rise in pressure in the right atrium is readily transmitted to the hepatic veins. Liver cells are particularly vulnerable to diminished oxygen supply, so that a failing heart, lowered blood pressure or reduced hepatic blood
flow are reflected in impaired hepatic function. The left lobe of the liver may suffer more than the right.

**Hepatic changes in acute heart failure and shock**

Hepatic changes are common in acute heart failure and in shock. Ischaemic changes follow cessation of hepatic blood flow during the course of hepatic transplantation or tumour resection.

Some patients show mild icterus. Cardiac causes accounted for 1% of referrals for jaundice to a special access clinic [255]. Jaundice has been recorded in severely traumatized patients. Serum transaminase levels increase markedly and the prothrombin time rises.

*Light microscopy* shows a congested zone 3 with local haemorrhage (Fig. 9.75). Focal necrosis with eosinophilic hepatocytes, hydropic change and polymorph infiltration is usual. The reticulin framework is preserved within the necrotic zone. With recovery, particularly after trauma, mitoses may be prominent. Diffuse hepatic calcification can follow shock [256]. This might be related to the disturbance of intracellular Ca²⁺ homeostasis as a result of ischaemia.

**Mechanisms of the hepatic changes**

The changes can be related to duration. The fall in blood pressure leads to reduction in liver blood flow and hepatic arterial vasoconstriction. The oxygen content of the blood is reduced. The cells in zone 3 receive blood at a lower oxygen tension than zone 1 cells and therefore more readily become anoxic and necrotic. Intense selective splanchnic vasoconstriction follows.

The hepatocyte injury is largely hypoxic. Insufficient substrates and accumulation of metabolites contribute. The mechanisms are multiple. The absence of available oxygen results in loss of mitochondrial oxidative phosphorylation. Impaired membrane function and reduced protein synthesis contribute. There are alterations in hepatocellular ion homeostasis [257].

*Hypoxia* can induce hydrogen peroxide in hepatocytes and this induces apoptosis in sinusoidal endothelial cells [258]. Much of the tissue damage develops during reperfusion, when there is a large flux of oxygen-derived ‘free’ radicals [259]. These initiate lipid peroxidation with disruption of membrane integrity. Experimentally, superoxide, formed during reperfusion, may combine with nitric oxide (NO) to cause hepatocellular injury [260]. Free radical peroxynitrate may be responsible. Lysosomal membranes may be peroxidized with the release of enzymes into the cytoplasm. Treatment is unsatisfactory. ‘Free’ radical trapping agents such as vitamin E, glutathione and ascorbic acid are being evaluated.

**Hypoxic or ischaemic hepatitis**

This term is defined as marked and rapid elevation of serum transaminases in the setting of an acute fall in cardiac output. *Acute hepatic infarction* is a term sometimes used. The picture simulates acute viral hepatitis.

The patient usually suffers from cardiac disease, often ischaemic or a cardiomyopathy and less often chronic respiratory failure, and toxic septic shock [261]. It is particularly frequent in patients in coronary care units where it affects 22% of those with a low cardiac output, a decreased hepatic blood flow and passive venous congestion [261]. Zone 3 necrosis, without inflammation, results. Clinical evidence of hepatic failure is absent. Congestive cardiac failure is inconspicuous. True circulatory shock may be absent except in cases associated with sepsis. It may be associated with renal impairment and hyperglycaemia [262].

Ischaemic hepatitis may complicate variceal haemorrhage in patients with cirrhosis [263]. Severe arterial hypoxaemia due to obstructive sleep apnoea may be causative [264].

Serum bilirubin and alkaline phosphatase values increase slightly, but serum transaminases and lactic dehydrogenase values rise rapidly and strikingly [265]. Values return speedily towards recovery in less than 1 week. Mortality is high (58.6%) and depends on the underlying cause and not the liver injury [265]. If the liver has been previously damaged by chronic congestive heart failure, acute circulatory failure may lead to the picture of fulminant hepatic failure and the cardiac cause misdiagnosed [266,267].
Postoperative jaundice

Jaundice developing soon after surgery may have multiple causes. Increased serum bilirubin follows blood transfusion, particularly of stored blood. Extravasated blood in the tissues gives an additional bilirubin load.

Impaired hepatocellular function follows operation, anaesthetics and shock. Severe jaundice develops in approximately 2% of patients with shock resulting from major trauma [268]. Hepatic perfusion is reduced particularly if the patient is in incipient circulatory failure and the cardiac output is already reduced. Renal blood flow also falls.

Anaesthetics and other drugs used in the operative period must be considered. Sepsis, per se, can produce deep jaundice which may be cholestatic.

Rarely, a cholestatic jaundice may be noted on the first or second postoperative day. It reaches its height between the fourth and tenth day, and disappears by 14–18 days. Serum biochemical changes are variable. Sometimes, but not always, the alkaline phosphatase and transaminase levels are increased. Serum bilirubin can rise to levels of 23–39mg/100mL. The picture simulates extrahepatic biliary obstruction. Patients have all had an episode of shock, and have been transfused. Hepatic histology shows only minor abnormalities. The mechanism of the cholestasis is uncertain. This picture must be recognized and, if necessary, needle biopsy of the liver performed.

Severely ill patients in intensive care following severe trauma or postoperative intra-abdominal sepsis may develop jaundice, which reflects severe multiple organ failure and a poor prognosis [269]. The jaundice is usually of cholestatic type with raised conjugated serum bilirubin and alkaline phosphatase levels and only slightly increased transaminases.

Endotoxaemia and sepsis may activate inflammatory mediators leading to vascular damage, increased permeability and oedema and impaired oxygen transport [270].

Bile flow falls following the reduction in hepatic arterial perfusion (ischaemic cholangitis) [271].

Ischaemia in the rat liver is followed by ATP depletion in the cholangiocytes with changes in membrane and membrane–skeletal structures [272].

Jaundice after cardiac surgery

Jaundice develops in 20% of patients having cardiopulmonary bypass surgery [273,274]. It carries a bad prognosis. The jaundice is detected by the second postoperative day. Serum bilirubin is conjugated and the level returns to normal in 2–4 weeks in those who survive. Serum alkaline phosphatase may be normal or only slightly increased and transaminases are raised, often to very high levels. Older patients are particularly at risk. Jaundice is significantly associated with multiple valve replacement, high blood transfusion requirements and a longer bypass time.

Many factors contribute. The liver may have already suffered from prolonged heart failure. Operative hypotension, shock and hypothermia contribute. Infections, drugs (including anticoagulants) and anaesthetics must be considered.

Liver blood flow falls. The serum bilirubin load is increased by blood transfusion. The pump may contribute by decreasing erythrocyte survival and by adding gaseous microemboli and platelet aggregates and debris to the circulation.

Virus B and C hepatitis are rare nowadays. Cytomegalovirus hepatitis may develop.

The liver in congestive heart failure

Pathological changes [275]

Hepatic autolysis is particularly rapid in the patient dying with heart failure [276]. Autopsy material is therefore unreliable for assessment.

Macroscopic changes. The liver is enlarged, and purplish with rounded edges. Nodularity is inconspicuous but nodular masses of hepatocytes (nodular regenerative hyperplasia) may be seen. The cut surface (Fig. 9.76)
Endotoxins diffusing through the intestinal wall into the portal blood may augment this effect [278]. The liver attempts to compensate by increasing the oxygen extracted as the blood flows across the sinusoidal bed. Collagenosis of Disse’s space may play a minor role in impairing oxygen diffusion.

Necrosis correlates with a low cardiac output [278]. The hepatic venous pressure increases and this correlates with zone 3 congestion [279]. Thrombosis begins in the sinusoids and may propagate to the hepatic veins with secondary local, portal vein thrombosis, ischaemia, parenchymal loss and fibrosis [280].

**Clinical features**

Mild jaundice is common but deeper icterus is rare and associated with chronic congestive failure. In hospital in-patients, cardiorespiratory disease is the commonest cause of a raised serum bilirubin level. Oedematous areas escape, for bilirubin is protein-bound and does not enter oedema fluid with a low protein content.

Jaundice is partly hepatic, for the greater the extent of zone 3 necrosis the deeper the icterus (Fig. 9.79) [276].

Bilirubin released from infarcts or simply from pulmonary congestion, provides an overload on the anoxic liver. Patients in cardiac failure who become jaundiced with minimal hepatocellular damage usually have pulmonary infarction [276]. The serum shows unconjugated bilirubinaemia.

The patient may complain of right abdominal pain, probably due to stretching of the capsule of the enlarged liver. The firm, smooth, tender lower edge may reach the umbilicus.

A rise in right atrial pressure is readily transmitted to the hepatic veins. This is particularly so in tricuspid incompetence when the hepatic vein pressure tracing resembles that obtained from the right atrium. Palpable systolic pulsation of the liver can be related to this transmission of pressure. Presystolic hepatic pulsation occurs shows prominent hepatic veins which may be thickened. The liver drips blood. Zone 3 is prominent with alternation of yellow (fatty change) and red (haemorrhage) areas.

**Histological changes.** The hepatic venule is dilated, and the sinusoids entering it are engorged for a variable distance towards the periphery. In severe cases, there is frank haemorrhage with focal necrosis of liver cells. The liver cells show a variety of degenerative changes but each zone 1 is surrounded by relatively normal cells to a depth that varies inversely with the extent of the zone 3 atrophy. Biopsy sections show significant fatty change in only about a third of cases. This contrasts with the usual post-mortem picture. Cellular infiltration is inconspicuous.

Zone 3 degenerating cells are often packed with brown lipochrome pigment. As they disintegrate, pigment lies free. Bile thrombi, particularly in zone 1, may be seen in the deeply jaundiced. Zone 3 PAS-positive, diastase-resistant hyaline globules may be seen [277].

Zone 3 reticulin condenses. Collagen increases and the central vein shows phlebosclerosis. Eccentric thickening or occlusion of the walls of zone 3 veins and perivenular scars extends into the lobule [268]. If the heart failure continues or relapses, bridges develop between central veins so that the unaffected portal zone is surrounded by a ring of fibrous tissue (*reversed lobulation*) (Fig. 9.77). Later the portal zones are involved and a complex cirrhosis results. A true cardiac cirrhosis is extremely rare.

**Mechanism** (Fig. 9.78)

Hypoxia causes degeneration of the zone 3 liver cells, dilatation of sinusoids and slowing of bile secretion.

Endotoxins diffusing through the intestinal wall into the portal blood may augment this effect [278]. The liver attempts to compensate by increasing the oxygen extracted as the blood flows across the sinusoidal bed. Collagenosis of Disse’s space may play a minor role in impairing oxygen diffusion.

Necrosis correlates with a low cardiac output [278]. The hepatic venous pressure increases and this correlates with zone 3 congestion [279]. Thrombosis begins in the sinusoids and may propagate to the hepatic veins with secondary local, portal vein thrombosis, ischaemia, parenchymal loss and fibrosis [280].

**Clinical features**

Mild jaundice is common but deeper icterus is rare and associated with chronic congestive failure. In hospital in-patients, cardiorespiratory disease is the commonest cause of a raised serum bilirubin level. Oedematous areas escape, for bilirubin is protein-bound and does not enter oedema fluid with a low protein content.

Jaundice is partly hepatic, for the greater the extent of zone 3 necrosis the deeper the icterus (Fig. 9.79) [276].

Bilirubin released from infarcts or simply from pulmonary congestion, provides an overload on the anoxic liver. Patients in cardiac failure who become jaundiced with minimal hepatocellular damage usually have pulmonary infarction [276]. The serum shows unconjugated bilirubinaemia.

The patient may complain of right abdominal pain, probably due to stretching of the capsule of the enlarged liver. The firm, smooth, tender lower edge may reach the umbilicus.

A rise in right atrial pressure is readily transmitted to the hepatic veins. This is particularly so in tricuspid incompetence when the hepatic vein pressure tracing resembles that obtained from the right atrium. Palpable systolic pulsation of the liver can be related to this transmission of pressure. Presystolic hepatic pulsation occurs
Possible mechanisms of the hepatic histological changes in heart failure.

Fig. 9.79. Possible mechanisms of the hepatic histological changes in heart failure.

Contrast-enhanced CT shows retrograde hepatic venous opacification on the early scans and a diffusely mottled pattern of hepatic enhancement during the vascular phase [284].

Cardiac cirrhosis should be suspected in patients with prolonged, decompensated mitral valve disease with tricuspid incompetence or in patients with constrictive pericarditis. The prevalence has fallen since both these conditions are relieved surgically.

Biochemical changes

The biochemical changes are small and proportional to the severity of the heart failure.

In congestive failure the serum bilirubin level usually exceeds 1 mg/dL and in about one-third it is more than 2 mg/dL [276]. The jaundice may be deep, exceeding 5 mg/dL and even up to 26.9 mg/dL. Patients with advanced mitral valve disease and a normal serum bilirubin concentration have a normal hepatic bilirubin uptake but diminished capacity to eliminate conjugated bilirubin related to reduced liver blood flow [285]; this contributes to postoperative jaundice.

Serum alkaline phosphatase is usually normal or slightly increased. Serum albumin values may be mildly reduced. Protein loss from the intestine may contribute.

Serum transaminases are higher in acute than chronic failure and are proportional to the degree of shock and the extent of zone 3 necrosis. The association of very high values with jaundice may simulate acute viral hepatitis.

Prognosis

The prognosis is that of the underlying heart disease. Cardiac jaundice, particularly if deep, is always a bad omen.

Cardiac cirrhosis per se does not carry a bad prognosis. If the heart failure responds to treatment, the cirrhosis compensates.

The liver in constrictive pericarditis

The clinical picture and hepatic changes are those of the Budd–Chiari syndrome.

Marked thickening of the liver capsule simulates sugar icing (zuckergussleber). Microscopically, the picture is of cardiac cirrhosis.

Jaundice is absent. The liver is enlarged and hard and may pulsate [286]. Ascites is gross.

A differential diagnosis must be made from ascites due to cirrhosis or to hepatic venous obstruction [287]. This is done by the paradoxical pulse, the venous pulse,
the calcified pericardium, the echocardiogram, the electrocardiogram and by cardiac catheterization.

Treatment is that of the cardiac condition. If pericardectomy is possible, prognosis as regards the liver is good although recovery may be slow. Within 6 months of a successful operation, liver function tests improve and the liver shrinks. The cardiac cirrhosis will not resolve completely, but fibrous bands become narrower and avascular.

References

35. Scandalis N, Archimandritis A, Kastanas K et al. Colonic findings in cirrhosis with portal hypertension. A prospec-
The Hepatic Artery, Portal Venous System and Portal Hypertension

41 Sogni P, Moreau R, Gadano A et al.
43 Bhathal PS, Grossman HJ. Reduction of the increased Iwakiri Y, Groszmann RJ. Vascular endothelial dysfunc-
44 Wheatley AM, Zhang X-Y. Intrahepatic modulation of Gerbes AL, Bilzer M, Gulberg V. Role of endothelins.
The Hepatic Artery, Portal Venous System and Portal Hypertension


129 Groszmann RJ. Beta-adrenergic blockers and nitrovasodilators for the treatment of portal hypertension: the good, the bad, the ugly. Gastroenterology 1997; 113: 1794–1797.


177 Ho K-S, Lashner BA, Emond JC et al. Prior esophageal variceal bleeding does not adversely affect survival after


study in patients admitted to an intensive care unit with severe trauma or with septic intra-abdominal complications following surgery and without evidence of bile duct obstruction. J. Hepatol. 1988; 7: 111–117.


