CHAPTER 87
PORTAL HYPERTENSION
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Introduction
Portal hypertension (PHT) may be caused by a wide variety of conditions, each with a different natural history. It frequently presents with bleeding from oesophageal varices, which is the commonest cause of serious upper gastrointestinal haemorrhage in children. Precise diagnosis, a sound understanding of the therapeutic options, and a multidisciplinary approach are essential for successful management.

Demographics
Portal hypertension is common in Africa and other developing regions, particularly as a result of endemic hepatitis B–related cirrhosis and, in affected areas, schistosomiasis and some particularly unique toxins that cause veno-occlusive disease.

Portal hypertension in children may be due to:
- primary venous obstruction at a prehepatic (e.g., portal vein obstruction); intrahepatic (e.g., hepatoportal sclerosis); or posthepatic (e.g., veno-occlusive disease and Budd-Chiari syndrome) level (rarely, an arterioportal venous fistula causes portal hypertension in an unobstructed system);
- intrinsic liver disease (e.g., cirrhosis, fibrosis, nodular hyperplasia);
- chronic liver disease, the commonest overall cause of PHT; or
- portal vein occlusion (PVO), the most frequent cause of extrahepatic PHT.

Occasionally, the picture is mixed, as in cirrhosis complicated by portal vein thrombosis.

Aetiology/Pathophysiology
Portal hypertension is defined by an increased hepatic venous pressure gradient (>5 mm Hg), which is the difference between wedged hepatic venous pressure (an indicator of portal venous pressure) and free hepatic venous pressure. A gradient of more than 12 mm Hg is necessary for the development of oesophageal varices. Although the relationship is not linear, the risk of variceal bleeding is increased in larger varices and in those with a higher internal pressure and wall tension. In established cirrhosis, the risk of variceal bleeding is related to the severity of the liver disease.

Portal venous pressure is the product of blood flow from the gut and spleen being increased in cirrhosis due to splanchnic vasodilatation, and vascular resistance. Within the liver, vascular resistance includes both fixed (fibrosis and architectural distortion) and dynamic (sinusoidal vascular tone) components.

A rise in portal pressure leads to splenomegaly and the development of portosystemic collaterals at various sites: the distal oesophagus and gastric cardia (oesophageal and gastric varices), the anal canal (anorectal varices), the falciiform ligament (umbilical varices), and varices in the abdominal wall and retroperitoneum. The junction between mucosal and submucosal varices in the lower 2–5 cm of the oesophagus is the usual site of rupture leading to variceal bleeding.

Clinical Presentation
History
Presentation is typically with acute gastrointestinal haemorrhage (haematemesis and/or malaena) and/or splenomegaly, or as part of the manifestation of chronic liver disease with spider naevi, clubbing, varices, ascites, and bleeding in patients with cirrhosis.

Physical
Children with PVO present with variceal bleeding at a younger mean age than those with cirrhosis (5 years of age versus 8 years), but onset of haemorrhage may occur at any age. The risk of bleeding is often precipitated by an upper respiratory tract infection, but this may reduce with age and the spontaneous development of portosystemic collaterals.

Splenomegaly may be associated with evidence of hypersplenism. However, unlike cirrhotics, humoral immunity is preserved in those with PVO. Ascites usually denotes the presence of chronic liver disease but may occur transiently after a major variceal bleed in those with extrahepatic portal hypertension. Encephalopathy may complicate an episode of bleeding in cirrhotics but is rarely detectable in children with PVO.

Portal hypertension may cause mucosal oedema in the small intestine, leading to malabsorption, protein loss, and failure to thrive. Thus, growth failure is common in cirrhosis and may also be found in children with PVO. In established PHT, dilated cutaneous collateral veins carry blood away from the umbilicus towards the tributaries of the vena cava (caput medusae). In long-standing disease, varices around the common bile duct may cause bile duct dilatation and, rarely, obstructive jaundice. Also rarely, pulmonary hypertension may coexist with portal hypertension—more often in children with cirrhosis than those with PVO. In cirrhotics, 30–50% will have varices and nearly half will have a significant bleed. There is 5–20% mortality during the first bleed, and half of the survivors will bleed again. In PVO, the mortality from the first bleed is <3%, with a lifetime mortality from bleeding of 10–15%.

Investigations
A full blood count may show anaemia, leucopenia, and/or thrombocytopenia from hypersplenism. The prothrombin time is commonly prolonged in patients with intrinsic liver disease or Budd-Chiari syndrome. In PVO, the prothrombin time is often slightly prolonged in association with a reduced factor VII concentration. The presence of reduced procoagulant and anticoagulant protein concentrations in PVO is probably due to reduced portal blood flow and/or portosystemic shunting. In patients with Budd-Chiari syndrome, an underlying myeloproliferative disorder or thrombophilic state should be excluded by bone marrow aspirate, and estimation of protein C, S, factor V Liden, and lupus anticoagulant.

Biochemical liver function tests are essentially normal in PVO but reflect the level of chronic disease in cirrhosis, particularly with low serum albumin. In Budd-Chiari syndrome, both liver and renal function may be disturbed.
Abdominal Ultrasound Scan
An abdominal ultrasound scan confirms nonspecific features of portal hypertension, such as large collateral veins and splenomegaly. Hepatic echotexture may indicate the presence of chronic liver disease. Colour Doppler flow studies provide information on the direction and velocity of flow in the portal vein, hepatic veins, and vena cava.

Gastrointestinal Endoscopy
Endoscopy can be used to evaluate gastro-oesophageal and anorectal varices and mucosal features of portal hypertension at all ages. Oesophageal varices are graded according to severity. Large varices may show “red signs” of recent or impending variceal haemorrhage; these stigmata include “cherry-red spots” and “varices on varices”. Endoscopic ultrasonography assessment of submucosal and para-oesophageal varices is a distinct advantage with diagnostic accuracy. Portal gastropathy is characterized by mucosal hyperaemia and dilated submucosal veins.

Computed Tomography and Magnetic Resonance Imaging
Both computer tomography (CT) and magnetic resonance imaging (MRI) are useful in evaluating local liver lesions associated with portal hypertension and in Budd-Chiari syndrome. In the latter, the findings depend on the duration and degree of venous obstruction; in chronic cases, there is splenomegaly and ascites, and the liver parenchyma shows patchy contrast enhancement and caudate lobe hypertrophy. In PVO, a variable degree of liver atrophy may be seen.

Angiography
Magnetic resonance angiography is being used increasingly as a non-invasive alternative to conventional angiography. It confirms the diagnosis of PVO and assesses the patency and calibre of veins throughout the portomesenteric system. Angiography is particularly important when considering portosystemic shunt surgery, including meso-Rex surgery, and when assessing patients with a thrombosed or abnormal portal vein before liver transplantation. Conventional angiography can be performed by several routes, but the commonest is by indirect portography. Direct splenportography after percutaneous needle puncture of the spleen also enables the measurement of splenic pulp pressure (an index of portal hypertension), which may be of value in assessing anastomotic portal vein strictures posttransplant. Percutaneous transhepatic portography is occasionally used. Hepatic venography shows a typical “spider web” pattern of venous collaterals around hepatic vein thrombosis in Budd-Chiari syndrome. Inferior vena cavography or magnetic resonance venography may be necessary to determine the patency of the inferior vena cava (IVC) or the intrahepatic portal and Rex veins.

Liver Biopsy
If there are no contraindications (poor clotting not corrected by replacement therapy of vitamin K, fresh frozen plasma, or clotting factor concentrates), a biopsy is usually undertaken to diagnose any underlying liver disease. Open or laparoscopically observed biopsy may be a safer option, as postbiopsy bleeding is a real risk. In extrahepatic PVO, the liver architecture is normal, but mild portal fibrosis may be seen. In hepatic vein obstruction, liver biopsy typically shows marked venous congestion around central venules with hepatocyte necrosis; in chronic cases, there is progression to hepatic fibrosis and cirrhosis.

Management

Primary Prophylaxis of Variceal Bleeding

Beta-blockers
Propranolol reduces portal pressure by causing splanchnic vasoconstriction and reducing cardiac output. If there are no contraindications to beta-blockers (e.g., asthma), primary prophylaxis may be worthwhile in children with PVO or cirrhosis and large varices. Therapy should aim to reduce the resting pulse rate by 25%.

Endoscopic therapy
Prophylactic use of injection sclerotherapy or banding is controversial. A small proportion of patients with PVO never bleed. At present, primary endoscopic prophylaxis cannot be recommended except for situations in which a child may be returning to an environment where treatment is limited.

Emergency Management of Variceal Bleeding
Bleeding from oesophageal varices is life threatening and requires hospital admission. Mortality is closely related to the severity of any underlying liver disease.
Octreotide, a long-acting analogue of somatostatin, with a plasma half-life of more than 1 hour, is given as an intravenous infusion and is effective in controlling acute variceal bleeding, particularly when used in combination with endoscopic therapy.

A balloon tamponade may be required to control active variceal bleeding. A Sengstaken-type tube can be inserted by an experienced clinician after securing the airway by endotracheal intubation. Only the gastric balloon need be inflated, and correct positioning must be verified by x-ray. Moderate traction is applied; excessive traction may cause mucosal ulceration or balloon displacement. The balloon is deflated after 12–24 hours at the time of endoscopy. Balloon deflation may be followed by severe bleeding, especially with gastric fundal varices.

Endoscopic Treatment of Oesophageal Varices

Injection sclerotherapy
Endoscopic injection sclerotherapy (EIS) has been a standard technique for inducing variceal thrombosis for many years but has largely been superseded by oesophageal banding in older children. EIS is applicable to all age groups and is best performed under general anaesthesia with an endotracheal tube in place. It is now used only in small infants, in whom it is not possible to pass the endoscope with the banding equipment, as well as where banding equipment is not available. A variety of injection techniques and sclerosants have been used, with 5% ethanolamine oleate being the most widely used. Between 1 and 3 ml of sclerosant are injected into each of the major variceal columns just above the gastrooesophageal junction. Paravariceal injection or a combination of the two is equally efficacious.

Varices should be initially injected every 1 to 2 weeks and then at monthly intervals until sclerosis is complete. Patients are given oral sucralfate for 48 hours and ranitidine for 2 weeks after each injection session to reduce complications from ulceration. Endoscopic review is undertaken after 6 months and then annually, but only large recurrent varices require treatment.

Variceal ligation (banding)
In variceal ligation, the varix is aspirated into a transparent cylinder fitted to the end of a flexible endoscope and an elastic band is released by a trip wire passing through the biopsy channel, causing strangulation of the varix, which then thromboses and sloughs. Treatment begins with ligation of the most distal varix in the oesophagus, just above the cardia. Up to four bands can be applied to the varices at each session; the treatment is repeated after 1 to 2 weeks and then monthly until the varices have been obliterated. Multiband devices allow the application of several bands with one pass of the endoscope.

Gastric Varices
Many gastric varices are fundal and directly contiguous with lower oesophageal varices. Most are present at the initial endoscopy and are eradicated during treatment of oesophageal varices. However, 5–10% of patients develop significant gastric varices after treatment of oesophageal varices by EIS. Bleeding from gastric varices may respond to EIS, but this is much less likely if the gastric varices are isolated and not contiguous with oesophageal varices. Alternative sclerosants, such as bovine thrombin and cyanoacrylate, have been used successfully in adults but have not been evaluated in children. Banding of gastric varices
is associated with a high rebleeding rate. If sclerotherapy is ineffective or inappropriate, then portosystemic shunting or a local devascularization procedure should be considered in those with satisfactory liver function.

**Surgery for Portal Hypertension**

**Surgical shunts**

Shunt surgery (see Figure 87.1) and endoscopic therapy are complementary procedures in the management of portal hypertension.

Indications for surgery include:

- uncontrolled bleeding from oesophageal varices (not responding to at least two sessions of banding or sclerotherapy) in children with PVO or those with chronic liver disease and reasonable liver function;
- bleeding gastric or ectopic varices that cannot be controlled endoscopically;
- massive splenomegaly, causing severe hypersplenism or abdominal pain; and
- lack of access to expert endoscopy.

A case can be made for mesoportal bypass surgery in children with extrahepatic PVO and cavernoma as prophylactic therapy because of the added benefit of not only relieving PHT but also redirecting portal venous blood into the liver.

Many types of portosystemic shunt have been described, but mesocaval and splenorenal shunts have been used most often in children. The distal splenorenal (Warren) shunt is considered to be a selective shunt in that it achieves gastrosplenic variceal decompression while maintaining portal perfusion.

Shunt patency is confirmed by improvement in hypersplenism, as evidenced by an increase in platelet counts, a reduction in splenomegaly, and regression of oesophageal varices observed endoscopically. Shunt thrombosis is a major complication and frequently manifests as recurrent variceal bleeding. It is more likely in children younger than 5 years of age. Shunt patency may be assessed directly by a variety of imaging modalities including colour Doppler ultrasound imaging of the shunt, magnetic resonance angiography, and conventional angiography, or indirectly by ultrasound examination of flow patterns in portomesenteric and systemic veins.

Encephalopathy is a well-recognized complication of portosystemic shunt surgery in cirrhotics but is very rare in children with PVO. Improvement in some areas of cognitive function has been documented after restoration of normal portal blood flow into the liver by means of the mesenterico-left portal (Rex) shunt (Figure 87.2).

The introduction of the Rex shunt has significantly broadened the indications for shunt surgery in PVO. In this shunt, a vein graft is interposed between the superior mesenteric vein and the (intrahepatic) left portal vein, which is located in the Rex recessus adjacent to the falciform ligament. The portal vein occlusion is bypassed, hepatic portal blood flow is restored, and portal hypertension is corrected. The operation demands the presence of an adequate calibre, patent intrahepatic left portal vein and patent splenic and mesenteric veins; this must be established preoperatively by angiography, ultrasound, and/or retrograde hepatic venography. This shunt is a valuable option for selected children with PVO because it restores normal physiology. However, it is not feasible in all cases. Shunt failure is a potential problem, but medium-term follow-up studies indicate that excellent results can be achieved with autologous vein grafts.

Mesocaval shunting has been a successful form of treatment in the past and may be preferred to selective or side-to-side splenorenal shunts because the vessels used are larger and more likely to remain patent. As with all nonselective shunts, there is the long-term risk of encephalopathy.

**Nonshunt surgery**

Other surgical techniques to control variceal bleeding have been disappointing in the long term because of a high rate of rebleeding.

**Liver transplantation**

Liver transplantation is the treatment of choice for most children with variceal bleeding complicating end-stage chronic liver disease.
Surgery for Budd-Chiari syndrome

Rarely, posthepatic portal hypertension has a radiologically or surgically treatable cause, such as a caval web. Many children with hepatic vein thrombosis are successfully managed by medical therapy directed at controlling ascites and preventing progressive venous thrombosis. Portal decompression is necessary for variceal bleeding, deteriorating liver function associated with zonal necrosis on liver biopsy, and intractable ascites. Portosystemic shunting converts the portal vein into a venous outflow tract. Occasionally, more complex shunts are needed in those with IVC obstruction. These procedures are potentially hazardous, and a transjugular intrahepatic stent is a less invasive alternative. In this procedure an expandable wire stent is placed in the hepatic vein after balloon dilatation. Prolonged anticoagulation with warfarin is required. Liver transplantation is indicated for fulminant liver failure or cirrhosis, but recurrence of Budd-Chiari syndrome in the graft is a risk, and patients with thrombophilia usually require long-term anticoagulation.

Transjugular intrahepatic portosystemic stent shunt

A transjugular intrahepatic portosystemic stent shunt (TIPSS) requires sophisticated technology and a skilled interventional endoscopist. It involves the percutaneous insertion of an expandable metal stent via the jugular vein into a hepatic vein and major portal vein. Selected patients with Budd-Chiari syndrome or intractable ascites may also benefit. Portal vein occlusion and uncorrected coagulopathy are contraindications. The major risks include stent occlusion and hepatic encephalopathy. The incidence of stent occlusion increases with time. These and other complications and the technical demands of the procedure have limited its role in children.

Postoperative Complications

Complications after EIS are those of rebleeding, oesophageal ulceration and stricture. Perforation with mediastinitis has occurred only rarely. With occult bleeding (OB), the ulcers tend to be more superficial and the rebleeding rate less. Shunt surgery, if successful, reduces portal pressure and prevents further bleeding, but shunt thrombosis is more frequent in smaller children with a shunt diameter of less than 0.5 cm. Encephalopathy is a real concern, particularly in children shunted for cirrhosis. Selective distal splenorenal shunts generally have a better record. For PVO, the mesenteric left portal bypass is the treatment of choice, but may not be possible in up to 30% of cases.

Prognosis and Outcomes

Prognosis depends on shunt patency and on the severity of liver disease. Those with cirrhosis eventually require liver transplantation before the development of end stage disease. With complimentary medical therapy, endoscopic intervention, and shunt surgery, the ultimate prognosis is excellent.

Prevention

Control of hepatitis B, schistosomiasis, and toxins may prevent liver disease, which subsequently presents as portal hypertension.

Ethical Issues

Where follow-up is poor, early recourse to shunt surgery—if the skills are available—may be preferred to serial endoscopic injection sclerotherapy or banding. Liver transplantation should not be undertaken unless lifelong supervision and immunosuppressive therapy are available.

Evidence-Based Research

Table 87.1 presents a study comparing sclerotherapy and ligation for treating bleeding oesophageal varices in children. Table 87.2 presents a study of endoscopic sclerotherapy for bleeding oesophageal varices in Sudan.

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<th>Title</th>
<th>Endoscopic ligation compared with sclerotherapy for bleeding oesophageal varices in children with extrahepatic portal venous obstruction</th>
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<tr>
<td>Authors</td>
<td>Zargar SA, Javid G, Khan BA, et al.</td>
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<tr>
<td>Reference</td>
<td>Hepatology 2002; 36(3):666–672</td>
</tr>
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Problem: Endoscopic sclerotherapy is an effective treatment for bleeding oesophageal varices, but it is associated with significant complications. Endoscopic ligation, a new form of endoscopic treatment for bleeding varices, has been shown to be superior to sclerotherapy in adult patients with cirrhosis.

| Intervention | To determine the efficacy and safety of endoscopic sclerotherapy and ligation, the two methods were compared in a randomized control trial in 49 children with extrahepatic portal venous obstruction who had proven bleeding from oesophageal varices. |

Comparison/ control (quality of evidence): Twenty-four patients were treated with sclerotherapy and 25 with band ligation. No significant differences were found between the sclerotherapy and ligation groups in arresting active index bleeding (100% each) and achieving variceal eradication (91.7% versus 96%, P = .81). Band ligation eradicated varices in fewer endoscopic sessions than did sclerotherapy (3.9 ± 1.1 versus 6.1 ± 1.7, respectively, P < .0001). The rebleeding rate was significantly higher in the sclerotherapy group (25% versus 4%, P = .049), as was the rate of major complications (25% versus 4%, P = .049).

After eradication, esophageal varical recurrence was not significantly different in patients treated by ligation than in those treated by sclerotherapy (17.4% versus 10%, P = .67).

Outcome/ effect In conclusion, variceal band ligation in children is a safe and effective technique that achieves variceal eradication more quickly, with a lower rebleeding rate and fewer complications compared with sclerotherapy.

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<th>Title</th>
<th>Endoscopic sclerotherapy for bleeding oesophageal varices: experience in Sudan</th>
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<tr>
<td>Authors</td>
<td>Gasim B, Fedial SS, Musaad AM, Ahmed W, Salih SM, Ibn-Ouf M</td>
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</table>

Problem: Bleeding due to oesophageal varices is the commonest cause of upper gastrointestinal tract haemorrhage in Sudan. Endoscopic injection sclerotherapy is a valuable therapeutic modality for the management of variceal bleeding. Other options for treatment, such as variceal banding, are either too expensive or unavailable.

| Intervention | A retrospective study to evaluate the outcome of EST in the management of bleeding oesophageal varices due to portal hypertension in a developing country (Sudan). |

Comparison/ control (quality of evidence): A total of 1070 patients over a period of 10 years (1986–1996) were studied. The inclusion criterion was bleeding oesophageal varices consequent to portal hypertension. EIS was performed using a standard technique. Ethanolamine olate 5% was the sclerosing agent. The procedure was done on a day-case basis.

There were 904 males (84.5%) and 166 females (15.5%). The cause of portal hypertension was schistosomal portal fibrosis (PPF) in 999 (93.3%) patients, liver cirrhosis in 59 (5.5%), mixed PPF and cirrhosis in 5 (0.46%), portal vein thrombosis in 6 (0.64%), and congenital hepatic fibrosis in 1 patient. A total of 100 (9.4%) patients presented with bleeding after surgery. Full obliteration of varices required a mean of 4 sessions with a range of 2–6. Follow-up of 462 patients (43.2%) continued until complete sclerosis of varices.

| Historical significance/ comments | This study provides evidence that endoscopic injection sclerotherapy is an essential component in the management of bleeding oesophageal varices caused by portal hypertension. It is a feasible and cost-effective therapeutic strategy in developing countries. |

| Table 87.1: Evidence-based research. |
| Table 87.2: Evidence-based research. |
Portal hypertension is common in developing regions, and varicose haemorrhage may be lethal.

Noncirrhotic portal hypertension can satisfactorily be treated with a combination of medical, endoscopic, and surgical treatment modalities.

Shunt surgery, particularly the mesenterico-portal bypass operation for PVO, has excellent long-term results and not only cures portal hypertension but also restores normal liver splanchnic blood flow.

Liver transplantation is the treatment of choice for cirrhosis but should be attempted only with lifelong supervision.