OPEN ACCESS TEXTBOOK OF GENERAL SURGERY

PORTAL HYPERTENSION

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INTRODUCTION

The portal vein carries approximately 1 500ml/min of blood from the small and large bowel, spleen and stomach to the liver. Any obstruction or increased resistance to flow, or, rarely, pathological increases in portal blood flow, may lead to portal hypertension. The causes of portal hypertension are categorised as prehepatic, intrahepatic and posthepatic. Although the differential diagnosis is extensive, alcoholic and viral cirrhosis are the leading causes of portal hypertension in the West, liver disease due to schistosomiasis is the main cause in other areas of the world and portal vein thrombosis the commonest cause in children.

With increasing portal pressure, a portosystemic collateral circulation develops with resultant compensatory portosystemic shunting and disturbed intrahepatic circulation. These factors are in part responsible for the important complications of chronic liver disease, including variceal bleeding, hepatic encephalopathy, ascites, hepatorenal syndrome, recurrent infection and coagulation abnormalities. The clinically most important portosystemic venous collaterals occur in the lower oesophagus and present as oesophageal varices. Variceal bleeding is the most serious complication of portal hypertension and a main cause of death in patients with cirrhotic liver disease. Patients with oesophageal varices have a 30% chance of bleeding from varices and of those who bleed, one-third die. Patients who have bled once from oesophageal varices have a 70% chance of bleeding again, and about one-third of further bleeding episodes are fatal.

ACUTE OESOPHAGEAL VARICEAL BLEEDING

The possibility of variceal bleeding should be considered in any patient with known risk factors for chronic liver disease or clinical evidence of portal hypertension. In Western countries variceal bleeding accounts for approximately 7% of gastrointestinal bleeding episodes, although this varies [11% in the USA, 5% in the UK] according to the prevalence of alcohol-related liver disease.

Choice of therapy

Several techniques are available to control variceal bleeding including drug treatment (octreotide, somatostatin, vasopressin, terlipressin), balloon tamponade, endoscopic therapy using sclerosant such as 5% ethanolamine oleate, tissue adhesives, or cyano-acrylate ("superglue") injection, rubber band ligation, transjugular intrahepatic portosystemic shunt (TIPS) and emergency surgery.

TABLE 1: CAUSES OF PORTAL HYPERTENSION

1. **INCREASED RESISTANCE TO FLOW**
   - **A: Prehepatic (portal vein obstruction)**
     1. Congenital atresia or stenosis
     2. Thrombosis of portal vein
     3. Thrombosis of splenic vein
     4. Extrinsic compression of portal vein
   - **B: Hepatic**
     1. Cirrhosis
        a. Portal cirrhosis
        b. Postnecrotic cirrhosis
        c. Biliary cirrhosis
        d. Other
     2. Acute alcoholic liver disease
     3. Portal fibrosis
     4. Idiopathic portal hypertension
     5. Schistosomiasis
   - **C: Posthepatic**
     1. Budd-Chiari syndrome
     2. Veno-occlusive disease
     3. Constrictive pericarditis
2. **INCREASED PORTAL BLOOD FLOW**
   - **A: Arterial-portal venous fistula**
   - **B: Increased splenic flow**

Several important considerations influence choice of therapy and prognosis in individual patients; these include the natural history of the disease causing portal hypertension, location of the bleeding varices, residual hepatic function, presence of associated systemic disease, continuing drug or alcohol abuse, patency of major splanchnic veins and response to specific treatment. The modified Child-Pugh risk classification identifies 3 risk categories (A = good; B = moderate; C = poor). (Table 2.)

TABLE 2 CHILD-PUGH CLASSIFICATION

	Number of points		
	1	2	3
Bilirubin (μmol/L)	<34	34-51	>51
Albumin ($g1/L^{-1}$)	>35	28-35	<28
Prothrombin time	<3	3-10	>10
Ascites	None	Slight	Mod - severe
Encephalopathy	None	Slight	Mod - severe

Grade A: 5-6 points

Grade B: 7-9 points

Grade C: 10-15 points

General measures

All patients with suspected acute variceal bleeding require urgent hospitalisation. The immediate aims of emergency medical treatment involve haemodynamic stabilization, blood-volume replacement, supporting of vital organ function and prevention of complications due to hypovolaemic shock and impending liver failure. Patients should be nursed in an intensive or high care unit and standard resuscitation for major haemorrhage instituted. Although variceal bleeding stops spontaneously in 60% of patients, it is not possible to predict who will continue to bleed and require further emergency therapy. Patients should be transferred to a centre with appropriate facilities and expertise as soon as they have been adequately resuscitated, because subsequent management is difficult if bleeding continues or recurs and may require advanced multidisciplinary investigations and therapy.

Initial measures

Many patients with acute variceal haemorrhage have liver decompensation with encephalopathy, ascites, coagulopathy, bacteraemia and malnutrition. The aim of treatment is to resuscitate the patient effectively and to control the bleeding as quickly and reliably as possible using methods with the fewest possible side effects. The extent and urgency of initial therapy depends on the severity of bleeding. Stable patients with intermittent bleeding are candidates for endoscopic therapy whereas exsanguinating bleeding may require balloon tamponade to control bleeding before endoscopy is performed.

Prompt resuscitation and restoration of circulating blood volume is vital and precedes any diagnostic studies. Intravenous access is obtained via a central venous cannula. While blood is being cross-matched, crystalloid solution is rapidly infused until blood pressure is restored and urine output, measured with a Foley catheter, is adequate. Saline infusions may aggravate ascites and must be avoided. Overzealous expansion of circulating volume may precipitate further bleeding. Central venous pressure should be maintained at 2 to 5 cm H_2O measured from the sternal angle. Patients who are haemodynamically unstable, elderly or have concomitant cardiac or pulmonary disease should be monitored using a pulmonary artery catheter as injudicious administration of crystalloids, combined with vasoactive drugs, may lead to the rapid onset of oedema, ascites and hyponatraemia. Clotting factors are often deficient and fresh blood, fresh frozen plasma and Vitamin K_1 should be given. Platelet transfusions may be necessary. Sedatives should be avoided. Haloperidol is useful if the patient has alcohol withdrawal symptoms.

TABLE 3 MANAGEMENT OF ACUTE VARICEAL BLEEDING: TREATMENT OPTIONS

1. **Pharmacologic Agents**
   a. Vasopressin
   b. Terlipressin
   c. Somatostatin
   d. Octreotide
2. **Endoscopic Therapy**
   a. Band Ligation
   b. Injection Sclerotherapy
      i. Sclerosants
      ii. Cyano-acrylate ("superglue")
      iii. Thrombin
3. **Balloon tamponade**
4. **TIPS**
5. **Surgical Therapy**
   a. Shunt procecures
   b. Oesophageal transection

Pharmacological control

Pharmacological therapy, aimed at controlling the acute bleed and facilitating diagnostic endoscopy and emergency sclerotherapy, should be started when variceal bleeding is suspected. Octreotide [50ug/hr] a synthetic somatostatin analogue given intravenously as a constant infusion is safe and effective and is used widely before endoscopy in patients with active bleeding. vasopressin at 0,4 u/min, combined with glyceryl trinitrate administered intravenously or transdermally using a skin patch is also used but has more side effects than octreotide. Glyceryl trinitrate reduces the peripheral vasoconstriction caused by vasopressin and has an additive effect in lowering portal pressure. Glypressin, a synthetic analogue of vasopressin, has a longer duration of action, but is expensive and is no more effective than vasopressin (Table 3).

Emergency endoscopy

Emergency diagnostic endoscopy is essential to confirm that oesophageal varices are present and are the source of bleeding. Most patients will have stopped bleeding before endoscopy either spontaneously or after receiving pharmacological therapy. Emergency endoscopy should be done in a well-equipped endoscopy unit or in an operating theatre with full resuscitative facilities and adequate assistance. Protection of the airway is essential during endoscopy. Endotracheal intubation may be necessary during endoscopy, especially in a patient who is actively bleeding, is encephalopathic or unstable despite vigorous resuscitation. Skilled placement of the endotracheal tube is critical to avoid aspiration during intubation. Intravenous analgesia and sedation, when required, should be administered in the smallest effective doses. In 90% of patients variceal bleeding originates from a 5 cm area above the gastrooesophageal junction. Most of the remaining 10% will be bleeding from gastric varices, either on the lesser curve or in the fundus of the stomach. At endoscopy, actively bleeding oesophageal varices are either injected with sclerosant or elastic bands applied.

Sclerotherapy

Emergency sclerotherapy is effective in controlling acute variceal bleeding and provides definitive treatment but requires an experienced endoscopist. A 23-gauge needle and catheter is passed through the endoscopic channel and sclerosant solution (ethanolamine oleate or STD) is injected into the bleeding varix to obliterate the lumen by thrombosis or into the submucosa overlying the varix to produce inflammation followed by fibrosis (Figure 1). Control of bleeding is successful in 80% after the initial injection. . If bleeding recurs, injection is repeated. Complications are related to sclerosant toxicity and include transient fever, dysphagia and chest pain, ulceration, stricture and rarely perforation. Bleeding from gastric varies are more difficult to inject and superglue or thrombin is used.

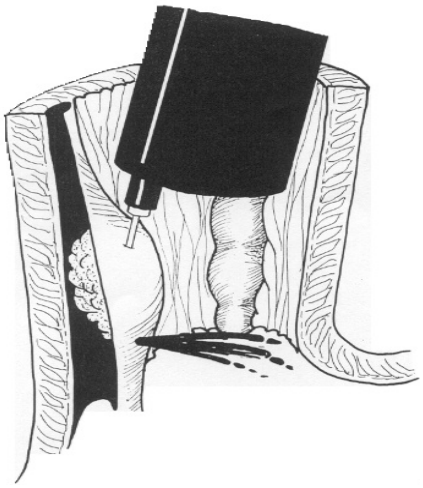

FIGURE 1. INTRAVARICEAL INJECTION SCLEROTHERAPY FOR ACUTE BLEEDING VARICES

After emergency endoscopic treatment patients are nursed in an intensive or high care unit for 24 hours. Oral fluids are allowed during the first 24 hours and there after a normal diet is instituted. Standard therapy is instituted for the underlying liver disease.

Variceal Band Ligation

The attachment of a simple ligating device to the end of an endoscope provides a mechanism for applying a rubber band around the base of an ensnared oesophageal varix. The technique is similar in principle to rubber band ligation of internal haemorrhoids. After confirming that varices are the cause of bleeding the endoscope is removed and the banding device attached to the tip. The endoscope is reinserted, the varix identified and aspirated into the banding chamber. A trip wire dislodges the rubber band carried on the banding chamber which ligates the entrapped varix. One to three bands are applied to each varix. Band ligation eradicates oesophageal varices with fewer treatment sessions and less complications than sclerotherapy.

If immediate endoscopic injection or banding therapy fails, major bleeding should first be controlled by balloon-tube tamponade before the patient has further endoscopic treatment. Any patient who rebleeds after two emergency endoscopic treatments during a single hospital admission for acute variceal bleeding, should have the bleeding temporarily controlled with balloon tube tamponade and should then be evaluated for a TIPS shunt.

Balloon tube tamponade

Balloon tube tamponade is highly effective in providing temporary control of variceal bleeding and allows time for resuscitation and planning of subsequent management. The balloon tube may be life-saving in patients with active variceal bleeding where emergency sclerotherapy or banding is not available or not technically possible because visibility is obscured.

In patients with active bleeding, an endotracheal tube should first be inserted to protect the patient's airway before attempting to place the oesophageal balloon tube.

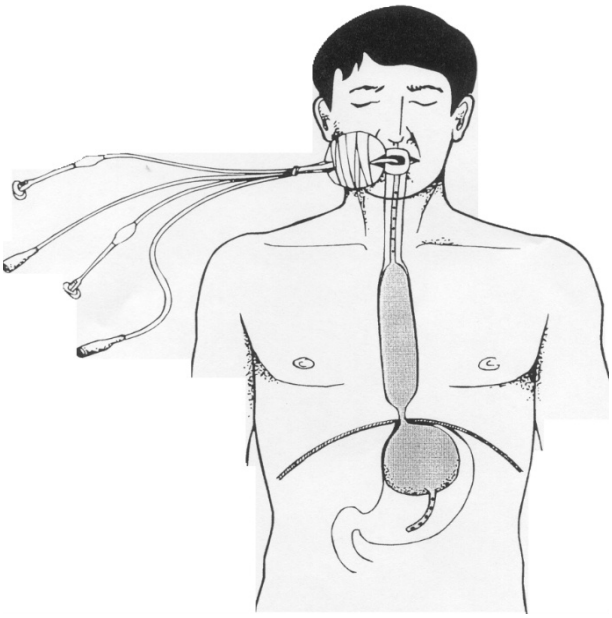

FIGURE 2. BALLOON TUBE TAMPONADE TO CONTROL ACUTELY BLEEDING VARICES

The Minnesota balloon tube has four lumens, one for gastric aspiration, one each to inflate the gastric and oesophageal balloons and one opening above the oesophageal balloon for suction of secretions to prevent aspiration. A new tube should be used on each occasion and the integrity of the gastric and oesophageal balloons tested by inflating under water prior to insertion through the patient's mouth. The correct siting of the tube in the stomach is checked by auscultation while injecting air through the gastric lumen and the position confirmed on abdominal X-ray. The gastric balloon is inflated with 200ml of air in 50ml increments. Difficulty with insufflation or pain is an indication that the tube may be incorrectly sited. Once fully inflated, the gastric balloon is pulled up snugly against the oesophagogastric junction, producing compression of the submucosal varices. Tension is maintained by strapping a split tennis ball to the tube at the patient's mouth (Figure 2). . The main complications are gastric and oesophageal ulceration, aspiration pneumonia and oesophageal perforation. The patient is nursed in an intensive care unit and particular attention is paid to the airway. Continued bleeding during balloon tamponade indicates an incorrectly positioned tube or bleeding from another source. After resuscitation, within 12 hours, the tube is removed and endoscopic therapy repeated.

Alternative management

Transjugular Intrahepatic Portasystemic Shunt (TIPS)

TIPS is now the salvage procedure of choice for patients whose bleeding is not controlled by endoscopy (Figure 3). The radiological placement of an intrahepatic shunt has significant advantages over major invasive surgical techniques. TIPS is performed via the internal jugular vein under local anaesthesia with sedation by cannulating a hepatic vein and creating a tract through the liver parenchyma, from hepatic to portal vein, using a needle under ultrasound and fluoroscopic guidance. The tract is dilated and an expandable metal stent placed creating an intrahepatic portosystemic shunt (Figure 3).

Technical success rate for the procedure is excellent and haemodynamic effects are similar to surgical shunts, without the morbidity and mortality associated with major surgery. TIPS is the preferred procedure for patients who are candidates for subsequent liver transplantation. TIPS is an effective salvage procedure for stopping acute variceal haemorrhage, controlling bleeding from gastric varices and congestive gastropathy after failure of medical and endoscopic therapy. However, because encephalopathy occurs in up to 25% of cases and up to 50% of shunts may occlude by 1 year, its primary role is to rescue failed endoscopy or as a bridge to subsequent liver transplantation.

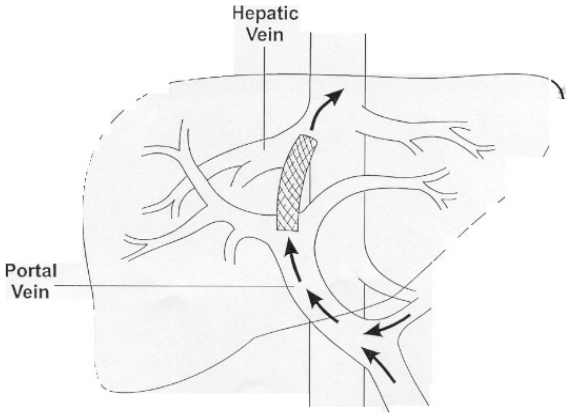

FIGURE 3 TIPS STENT

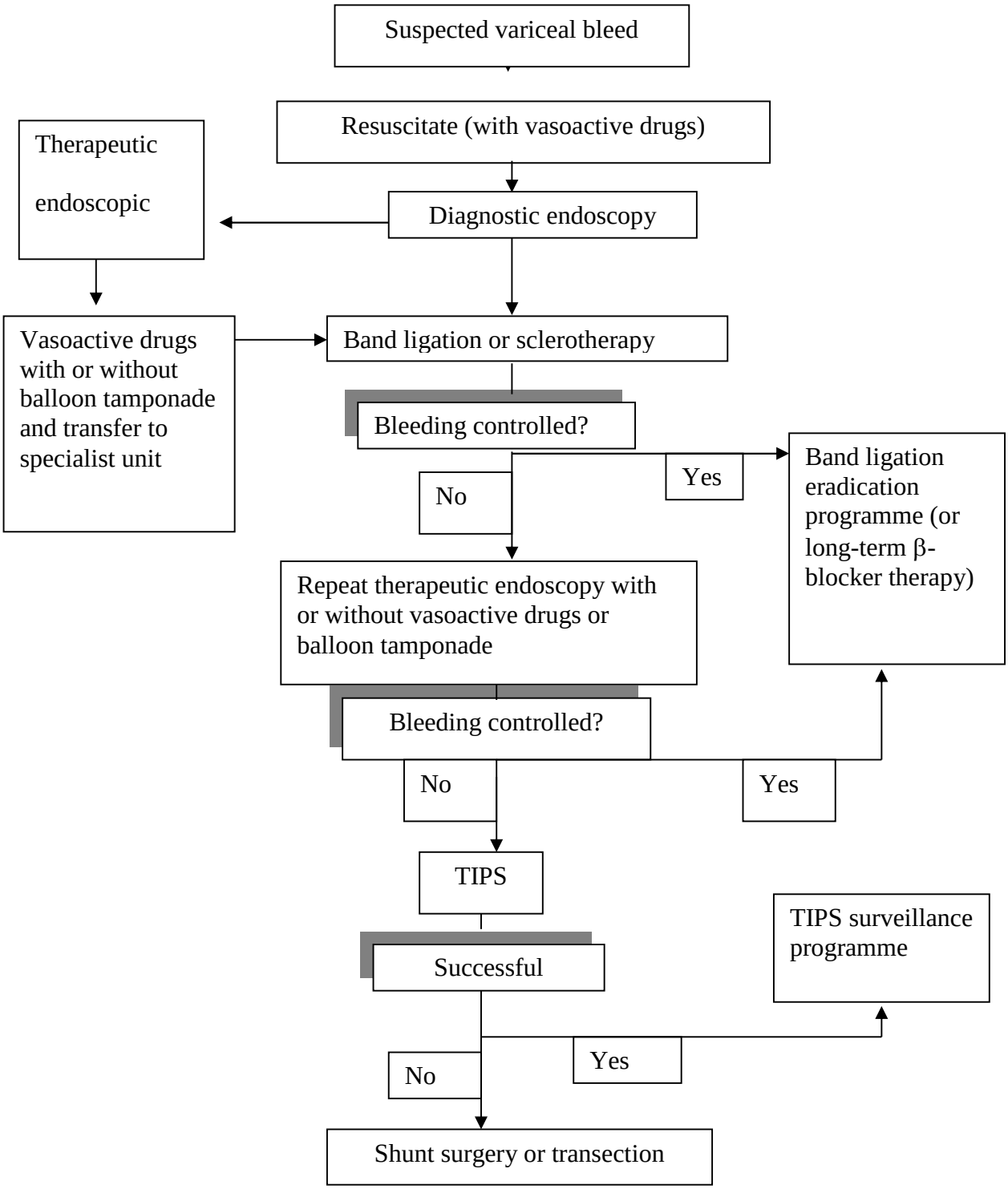

FIGURE 4. ALGORITHM FOR MANAGEMENT OF ACUTE VARICEAL HAEMORRHAGE

Operative Shunts

The standard side-to-side portacaval shunt using an H-graft is the preferred shunt used in emergencies. Successful shunting stops acute variceal bleeding and prevents recurrent bleeding. However, operative mortality for emergency surgical shunt is high. The major disadvantages are a progressive liver decompensation and unpredictable postoperative encephalopathy. Shunts are now seldom used because of the efficacy of endoscopic therapy and the availability of TIPS which is a safer option in high risk patients.

Oesophageal transection

Oesophageal transection using an automatic anastomotic staple gun is the simplest emergency operation for patients who do not respond to endoscopic therapy and are unsuitable for TIPS or an operative shunt. An extended procedure combining gastric devascularisation and oesophageal transection may provide better long-term results but increases the operative risk and has been discontinued as an emergency therapy.

Long-term management after variceal bleeding

After the acute variceal haemorrhage has been controlled, treatment should be initiated to prevent rebleeding, which occurs in most patients. The options are repeated endoscopic therapy, longterm β blockers or surgery (Table 4).

Repeated endoscopic therapy

Repeated endoscopic therapy has distinct advantages when compared with more major surgery. It is the simplest and most direct method of dealing with oesophageal varices and procedure-related morbidity and mortality are low, which is important in poor-risk patients. Endoscopic therapy does not affect liver function or increase the incidence of encephalopathy. Repeated endoscopic therapy eradicates oesophageal varices in most patients, and once eradicated, with adequate follow-up, major recurrent variceal bleeding is uncommon. Because the underlying portal hypertension persists, patients remain at risk of developing recurrent varices and therefore require life-long follow-up with regular surveillance endoscopy. Recurrent varices usually appear as single channels and are easily re-eradicated. Repeated injections or banding, however, increase the cumulative risk of endoscopic-induced complications in the individual patient.

TABLE 4 LONG-TERM MANAGEMENT TO PREVENT VARICEAL BLEEDING

1.	**Endoscopic Therapy**
	Injection Sclerotherapy
	Variceal band ligation
2.	**Pharmacotherapy**
	β-blockers
3.	**Surgery**
	a. Shunt
	i) DSRS
	ii) Portacaval
	b. Non-Shunt
	i) Oesophageal transection and gastric devascularisation
	ii) Splenectomy for gastric varices due to splenic vein thrombosis
4.	**Liver Transplantation**

Surgical shunts

Patients with good liver function who fail endoscopic management or live far from centres where endoscopic sclerotherapy services are available are candidates for surgical shunt procedures. A successful portal systemic shunt effectively prevents recurrent variceal bleeding. However, portal systemic shunts are major operations with substantial morbidity and mortality rates in poor-risk patients. Shunts may cause further impairment of liver function in patients with diminished liver reserves and with the exception of the distal splenorenal shunt [DSRS], are associated with an increased and largely unpredictable incidence of encephalopathy.

The DSRS is the most widely performed selective shunt worldwide and selectively decompresses oesophageal varices while preserving portal venous flow and liver perfusion thereby preventing post-shunt liver atrophy and encephalopathy. However, DSRS is a difficult and time-consuming operation which is not feasible in all patients, especially those at high risk. Good long-term survival has been reported in non-alcoholic cirrhotics, but results in alcoholic cirrhotic patients are not superior to standard portacaval shunts. Partial portacaval shunts using 8-mm interposition grafts have been popularized in the last decade. These have given results comparable to other shunts for control of rebleeding with a low encephalopathy rate. The choice of shunt depends on venous patency, the individual centres experience and the rapidity with which a decompressive shunt must be performed.

Devascularisation procedures

These are important in unshuntable patients with portal and splenic vein thrombosis who continue to have significant gastric and oesophageal variceal bleeding despite endoscopic and pharmacological therapy. As with most operative approaches in portal hypertension, quality of outcome is in large part dependent on the surgeon's expertise. Extensive gastric devascularization and oesophageal transection reduces the risk of subsequent bleeding.

Liver transplantation

Transplantation is the treatment of choice in advanced liver disease and hepatic decompensation and is the ultimate decompressive shunt for portal hypertension, also restoring liver function. Transplantation treats other complications of portal hypertension and has one year and 5 year survival rates of 80% and 60%.

Long-term pharmacological therapy

The use of β-blockers should be reserved for selected compliant patients, who are unable to undergo endoscopic treatment and who have no contra-indications and develop no complications from β-blockers [2,5]. Difficulty with resuscitation if patients bleed, transient increases in portal pressure with increased risk of bleeding on abrupt withdrawal of β-blockers, potential deleterious effects on the renal and systemic circulation, and aggravation of hepatic encephalopathy, are problems associated with the use of β-blockers. Compliance may be poor, especially in alcoholic cirrhotics, and the expense of lifelong therapy needs to be considered before usage.

Prophylactic management

Patients with varices who have never had bleeding are at risk of bleeding. The magnitude or timing of this risk is unpredictable. Currently only patients with large varices should receive prophylactic therapy. The best indicators on endoscopy are the presence of cherry red spots on the varices and the size of the varices.

Gastric varices and portal hypertensive gastropathy

Gastric varices are the source of bleeding in 5-10% of patients with variceal haemorrhage. Higher rates are reported in patients with left-sided portal hypertension due to splenic vein thrombosis. Endoscopic control of gastric varices is difficult unless these are located on the proximal lesser curve in continuation with oesophageal varices. Endoscopic control with cyanoacrylate monomer ("superglue") is useful for treating gastric varices.

Bleeding from portal hypertensive gastropathy accounts for 2-3% of bleeding episodes in cirrhosis. Although major bleeding from these sources is uncommon, when it occurs, its diffuse nature precludes the use of endoscopic therapy and treatment options are β blockers, TIPS, or surgery dependent on the severity of bleeding and the degree of liver impairment.

ASCITES

Ascites, variceal bleeding and hepatic encephalopathy are the most common major complications of cirrhosis. The formation of ascites in cirrhosis is due to a combination of abnormalities in both renal function and portal and splanchnic circulation. The main pathogenic factor is sodium retention. Approximately 50% of patients with cirrhosis develop ascites during 10 years of observation. The development of ascites is an important event in the natural history of chronic liver disease as half of cirrhotic patients with ascites die within two years. Cirrhosis accounts for 75% of cases of ascites, malignancy for 10%, cardiac failure for 5%, and a variety of other causes for the remaining 10% (Table 5). In most patients the history and examination will yield valuable clues to the cause of the ascites e.g. signs of chronic liver disease suggest cirrhosis of the liver, evidence of cardiac failure points to a cardiac cause, and pelvic examination may detect an ovarian mass.

TABLE 5 CAUSES OF ASCITES

1. Portal Hypertension
- Cirrhosis of liver
- Congestive heart failure
- Constrictive pericarditis
- Budd-Chiari Syndrome
- Inferior vena cava obstruction

2. Hypoalbuminaemia
- Nephrotic Syndrome
- Protein losing enteropathy

3. Neoplasms
- Peritoneal carcinomatosis
- Pseudomyxoma

4.Miscellaneous
- Pancreatic ascites
- Nephrogenic ascites (associated with maintenance haemodialysis
- Myxoedema
- Meigs's Syndrome

Diagnosis

Ascites may not be clinically detectable when present in small volumes. In larger volumes, the classic findings of ascites are a distended abdomen with a fluid thrill or shifting dullness. Ascites must be differentiated from abdominal distension due to obesity, pregnancy, gaseous distension of the bowel, bladder distension, cysts and tumours. Tense ascites may cause marked discomfort, difficulty in breathing, eversion of the umbilicus, herniae, and scrotal oedema. Rapid onset of ascites may be due to gastrointestinal haemorrhage, infection, portal venous thrombosis or the development of a hepatocellular carcinoma. Ascites may also develop during a period of heavy alcohol abuse or excessive sodium intake in food or medication. Ultrasonography is of value in confirming the presence of minimal ascites and in guiding diagnostic paracentesis. Successful treatment depends on an accurate diagnosis of the cause of ascites. Paracentesis with ascitic fluid analysis is the most rapid and cost-effective method of diagnosing the cause of ascites and should be obtained in patients with recent onset ascites, cirrhotic patients with ascites admitted to hospital, or those with clinical deterioration. Most important are quantitative cell counts, fluid culture, and calculation of the serum-to-ascites albumin gradient (SAAG) which reflects differences in oncotic pressures and correlates with portal venous pressure. Normal portal pressures have a SAAG less than 1.1 g/dL, whereas ascites associated with portal hypertension usually has a SAAG greater than 1.1 g/dL (Table 6). The traditional classification of transudative and exudative ascites based on ascitic fluid protein concentrations of less than or greater than 2.5 g/dL is less useful than the SAAG, because diuresis can affect the ascitic total protein concentration.

Treatment

The principal aim of treatment of symptomatic ascites in the cirrhotic patient is to improve general comfort and quality of life. Treatment includes restriction of sodium and, sometimes, water intake, the promotion of sodium

and water excretion by diuretics and the correction, where possible, of precipitating factors. Most patients will respond to these measures, but other treatments are available for those who do not. Treatment does not necessarily improve the prognosis for patients with cirrhosis and may cause complications. It is not necessary, therefore, to treat minor amounts of ascites which are asymptomatic. A crucial first step in treating ascites is to convince patients with alcoholic cirrhosis to abstain from alcohol. In a period of months, abstinence can result in a substantial improvement in the reversible component of alcoholic liver disease. Dietary salt restriction is the most important initial treatment. A low sodium diet of 1-1.5 g of salt (40-60 mmol per day) usually produces a net sodium loss which may be sufficient in patients with mild ascites. Fluid restriction is not a necessity when treating most patients with cirrhotic ascites, however marked hyponatraemia (serum Na <120 mmol /L) does warrant fluid restriction. Although conventional recommendations suggest bed rest, its value is not supported by controlled trials.

Most patients need dietary restrictions combined with diuretic therapy. The usual diuretic regimen consists of single morning doses of oral spironolactone (an aldosterone antagonist) and furosemide (a loop diuretic) beginning with 100 mg of spironolactone and 40 mg of furosemide. The dose of both oral diuretics can be increased simultaneously, maintaining the 100 mg:40 mg ratio, if weight loss and natriuresis are inadequate on the lower doses. Maximum doses are 400 mg/day of spironolactone and 160 mg/day of furosemide. Dietary sodium restriction and dual diuretic therapy is effective in 90% of patients. The patient's weight, electrolytes and renal function should be carefully monitored. Treatment should always be approached cautiously because of the dangers of aggressive therapy and iatrogenic complications. Patients with ascites and peripheral oedema may tolerate 1-2 kg weight loss per day whereas loss of 0.5 kg should be the goal in patients without oedema. Potential complications during diuresis are encephalopathy, hypokalaemia, hyponatraemia, hypochloraemic alkalosis and azotaemia.

TABLE 6 ANALYSIS OF ASCITIC FLUID

- Evaluate macroscopic appearance (straw coloured, turbid, bloody, chylous)
- Cell count and differential
- Chemistry profile (protein, albumin, amylase)
- Cytology
- Gram stain and bacterial culture

Tests to consider ordering

- Adenosine deaminase (if tuberculosis is suspected)
- pH, lactate, lactate dehydrogenase (if bacterial peritonitis suspected)

Patients with tense ascites should have a single 4 to 6 L abdominal paracentesis, followed by sodium restricted diet and oral diuretics. Options for patients refractory to routine medical therapy include 1) serial therapeutic paracentesis, 2) peritoneovenous shunt, 3) TIPS and 4) liver transplantation. Serial therapeutic paracentesis should be performed as required approximately every 2-3 weeks. Albumin infusion is unnecessary for paracentesis of <5 L. Peritoneovenous shunts are seldom used and are reserved for diuretic resistant patients who are not transplant candidates and unsuitable for paracentesis because of abdominal scars.

HEPATIC ENCEPHALOPATHY

Hepatic encephalopathy is a reversible state of impaired cognitive function or altered consciousness which occurs in patients with liver disease or portal systemic shunts. The typical features of hepatic encephalopathy include monotonous speech, flat effect, metabolic tremor, muscular incoordination, impaired handwriting, asterixis, fetor hepaticus, coma, upgoing plantar responses, hypo- or

hyperactive reflexes and decerebrate posturing. The diagnosis of hepatic coma, especially in alcoholic patients, should only be made once intracranial space-occupying and vascular lesions, trauma, infection, metabolic, endocrine, drug-induced and post-epileptic coma have been excluded.

TABLE 7 EVENTS PRECIPITATING HEPATIC ENCEPHALOPATHY IN CIRRHOTIC PATIENTS

Electrolyte imbalance
- diuretics
- vomiting
- diarrhoea

Gastrointestinal bleeding
- oesophageal and gastric varices
- gastroduodenal erosions

Drugs
- alcohol withdrawal
- benzodiazepines

Infection
- spontaneous bacterial peritonitis
- urinary
- chest

Constipation
- dietary protein overload

Hepatocellular insufficiency and portal systemic shunting may act separately or in combination to cause encephalopathy. Almost all cases of clinically apparent hepatic encephalopathy occur in patients with cirrhosis. Fewer than 5% occur in non-cirrhotic forms of portal hypertension. However, a disproportionately large proportion of patients with surgical and radiological portal systemic shunts develop severe, frequently intractable, hepatic encephalopathy. The combination of impaired hepatic and renal function is frequently associated with hepatic encephalopathy. Roughly half of these patients have diuretic-induced renal impairment and half have functional renal failure. Drugs are implicated in one quarter of patients with hepatic encephalopathy. Most common are benzodiazepines, barbiturates, analgesics and other sedatives. Another quarter of cases of encephalopathy are precipitated by gastrointestinal tract haemorrhage. This is frequently associated with deep and prolonged coma. The combination of gastrointestinal haemorrhage and hepatic encephalopathy indicates a poor prognosis. A small proportion of cases are precipitated by dietary protein excess, hypokalaemic alkalosis, constipation and deterioration of liver function secondary to drugs, toxins, viruses or hepatocellular carcinoma.

The treatment of hepatic encephalopathy is empirical and relies largely on establishing the correct diagnosis, identifying and treating precipitating factors, emptying the bowels of blood, protein and stool, attending to electrolyte and acid-base imbalance and the selective use of benzodiazepine antagonists. Non-absorbable disaccharides, such as lactulose or lactitol, are the mainstay of therapy. Antibiotics and protein restriction (40 g/day) may be advised if there is no response. In intractable cases, closure of surgical shunts and liver transplantation should be considered.

HEPATORENAL SYNDROME

The hepatorenal syndrome (HRS) is an acute oliguric renal failure resulting from intense intrarenal vasoconstriction in otherwise normal kidneys. It occurs in patients with chronic liver disease, usually with cirrhosis, portal hypertension and ascites or with acute liver failure; a clinical cause is often not found, treatment is often ineffective and prognosis is poor. HRS is prevented by carefully avoiding excessive diuresis and by early recognition of electrolyte imbalance, bleeding or infection. Potentially nephrotoxic drugs such as aminoglycosides should be avoided. Blood cultures are taken and bacteraemia treated. The majority of patients with liver disease who develop azotaemia will have pre-renal failure or acute tubular necrosis. The diagnosis of HRS is one of exclusion, and should not be made until all potentially reversible causes of renal failure have been excluded. All patients suspected of having HRS

should have an intravenous colloid infusion in an attempt to exclude intravascular hypovolaemia as a cause of pre-renal azotaemia. Liver transplantation, if otherwise appropriate and feasible, is the only truly effective therapy in these patients who have a very poor prognosis.

SPONTANEOUS BACTERIAL PERITONITIS

SBP is an infection of ascites that occurs in the absence of a local infectious source. It is mainly a complication of cirrhotic ascites, with a prevalence of 15% to 20% (when culture-negative cases are included). Gram-negative enteric bacteria are the causative agents in more than 70% of cases. SBP is usually the consequence of bacteraemia due to defects in the hepatic reticuloendothelial system and in the peripheral destruction of bacteria by neutrophils, with secondary seeding in ascitic fluid deficient in antibacterial activity. Patients with advanced liver disease and low ascitic fluid protein concentrations have an increased susceptibility to SBP. A diagnostic paracentesis should be performed in any cirrhotic patient who suddenly deteriorates or presents with fever or abdominal pain. Clinical signs however may be minimal in SBP. Some patients manifest only vague abdominal discomfort or worsening encephalopathy. A PMN count >500/mm^3 is indicative of SBP. Optimal culture techniques include bed-side inoculation of blood culture bottles with 5 ml of ascitic fluid. Treatment with intravenous broad-spectrum antibiotics should be started immediately. Although the mortality of an acute episode of SBP decreases with early therapy, it is still high (approximately 50%), and patients who survive an episode of SBP have a high frequency of recurrence. Mortality is related to the severity of the underlying liver disease, because only a third of patients die from sepsis and prophylactic antibiotics decrease the frequency of SBP but do not improve long-term survival.