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Department of surgical diseases № 2

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Diseases of the liver and spleen. Differential diagnosis of jaundice

Textbook for students of 6 courses
medical faculty of hospital surgery

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This tutorial is devoted to endoscopic and interventional surgery. The authors present modern endoscopic, radiosurgical, radiosurgical methods of research and gave examples of diseases in which they are used.

The textbook "Diseases of the liver and spleen. Differential diagnosis of jaundice" is developed on the discipline "Hospital surgery" in accordance with the requirements of the FSEI HPE, is intended for students of medical Universities and faculties, trained in the specialty 31.05.01 General Medicine.

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Contests:

Anatomy of the liver

The liver is the largest organ in the body, with a weight varying from 1200 to 1600g. It arises from the foregut endoderm as a diverticulum which extends into the septum transversum and connects with the vitelline veins of the yolk sac. The caudal section of the hepatic anlage ultimately forms the biliary tract and gallbladder while the cephalic section forms the hepatic parenchyma. The vitelline veins form the portal and hepatic veins. The left umbilical vein persists as the ductus venosum and diverts oxygenated blood from the placenta around the liver directly into the inferior vena cava. After birth the vestigial ligamentum venosum runs in the free edge of the falciform ligament (round ligament, ligamentum teres). It may recanalize

in patients with portal venous hypertension or can be used after dilatation for exchange blood transfusion or to permit radiological investigation of the portal venous system.

Morphology and topographical anatomy of the liver surfaces

The liver can be regarded as a wedge with rounded edges tapering to the left. It has three surfaces: anterosuperior, inferior and posterior. The anterosuperior surface is marked by the umbilical fissure in the depths of which (recessus of Rex) is inserted the round ligament (obliterated umbilical vein) attached to the cornu of the left portal vein. The umbilical fissure and the falciform ligament are the most conspicuous anatomical landmarks and divide the liver into right and left lobes. The posterior surface of the liver is largely formed of the bare area of the right lobe of the liver attached loosely to the diaphragm and retroperitoneum, and the caval canal that accommodates the retrohepatic vena cava and hepatic veins. The inferior surface of the liver is more complicated. The gallbladder is attached anteriorly some distance to the right of the umbilical fissure. The area between the gallbladder and the umbilical fissure is known as the quadrate lobe. Behind this and the neck of the gallbladder is the transverse hilar fissure that contains the main divisions of the portal vein, hepatic artery and common hepatic duct, and forms the posterior limit of the right lobe. The hepatic parenchyma separating the hilar fissure and the inferior surface of the left lobe from the vena cava forms the caudate lobe.

Relations

In terms of anatomical relations, the anterosuperior surface of the liver is in contact with the diaphragm and its upper margin reaches the level of the fourth interspace on the right and crosses the junction of the xiphisternum and sternum. Inferiorly the tip of the right liver reaches the costal margin, though Riedel's extension commonly extends below the costal margin and can reach the iliac crest. The gallbladder lies in the gallbladder fossa on the undersurface of the liver. There is a layer of fascia between the liver and the gallbladder (which must not be transgressed during cholecystectomy). Inferior relations of the right lobe include the upper pole of the right kidney and the right adrenal gland and more anteriorly the first part of the duodenum as it is overlapped by the gallbladder. The much thinner left lobe overlies the gastro-oesophageal junction. The lesser sac lies below the liver and behind the lesser omentum. It usually communicates with the rest of the peritoneal cavity through the foramen of Winslow lying behind the portal vein, hepatic artery and common bile duct. Occlusion of these structures (by finger, sling or vascular clamp) stops the arterial and portal venous inflow and this manoeuvre first described by Pringle is used to control bleeding during liver surgery and liver trauma.

Ligaments

The coronary and triangular ligaments suspend the liver from the diaphragm. The left triangular ligament is a thin peritoneal fold that is relatively avascular. Its two layers separate medially as the caval canal is reached: one sweeps back to the lesser sac and the other forms the left leaf of the falciform ligament. The coronary ligament is composed of two separate peritoneal folds (superior and inferior) between which lies the 'bare area' of the liver that is connected to the diaphragm by loose relatively avascular areolar tissue. The two leaves of the coronary ligaments join laterally, thus forming a V-shaped attachment to the diaphragm and retroperitoneum. The superior layer is an extension of the right leaf of the falciform ligament and attaches the superior surface to the diaphragm. The inferior leaf of the coronary ligament is a reflection of the peritoneum covering the right perinephric and adrenal region on to the inferior surface of the liver to the right of the infrahepatic vena cava.

Caval canal

This important region is often ignored in accounts of surgical anatomy. It is essentially a gutter in which lies the retrohepatic vena cava and the hepatic veins, all of which are enveloped in a loose fibrous meshwork rather than membranes. The caudate lobe separates the caval canal from the hilar fissure anteriorly and from the left lobe. The caval canal is best exposed during hepatectomy by a combined superior and inferior approach. Superiorly, the caval canal is covered by the diverging layers of the falciform ligament. When these are divided, a loose fibrous packing tissue envelops the vena cava and the right and left hepatic veins. Below, the caval canal is opened by division of the inferior leaf of the coronary ligament. The fibrous tissue covering the vena cava is loose in this region. A variable number of unnamed hepatic veins are encountered and these include veins to the caudate lobe. The retrohepatic vena cava also receives the phrenic veins and below these it is loosely attached to the retroperitoneum and, thus, provided the correct plane is identified, a sling can be passed around it and including the right and left hepatic veins in the immediate suprahepatic region.

Functional or segmental anatomy of The liver

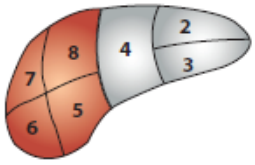
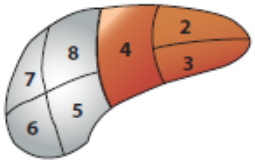
The segmental anatomy of the liver on which modern hepatic surgery is based comes from the anatomical dissections performed by Rex (1888) and Cantlie (1898) more than 100 years ago and subsequently elaborated by Goldsmith and Woodburne (1957), Couinaud (1957), Healy and Schroy (1953) and Elias and Petty (1952). In essence, the liver should be regarded as a paired organ (right and left livers) fused along a line extending from the middle of the gallbladder fossa anteriorly to the left edge of the suprahepatic inferior vena cava posteriorly. Within the liver this corresponds to a vertical plane (the main portal scissura or Cantlie's line) in which lies the middle hepatic vein. The right liver receives the right portal

vein, right hepatic artery and right hepatic duct and the left liver the corresponding left portal vein, left hepatic artery and left hepatic duct. Considerable confusion is often caused by the discrepancy between surface and functional anatomy of the liver, with a portion of the right anatomical lobe (segment IV) effectively belonging to the left functional hemiliver. For this reason, it is advocated that the anatomical division in right and left lobe be left to the anatomists, whereas the terms right and left hemilivers are to be used in all clinical and surgical settings. A further element of confusion is generated by the subdivision of the two hemilivers in sectors and segments, which are effectively fully independent subunits, and by the different terminology used by the influential French school with its followers and the wider international community. A consensus document has recently been produced by the International Hepato- Pancreato-Biliary Association entitled 'IHPBA Brisbane 2000 Terminology of Liver Anatomy & Resections', which is reported in its entirety and whose use is now widely advocated. Because of this segmental liver anatomy, it is possible to resect a single or several segments even in the liver that has been distorted by chronic hepatic disease. A careful identification of the vessels and ducts supplying each segment can be achieved by dissection above the portal hilum or within the liver parenchyma and each segmental or sectorial pedicle may be ligated separately prior to resection of the corresponding portion of liver realizing an 'anatomical resection'.

The right hemiliver

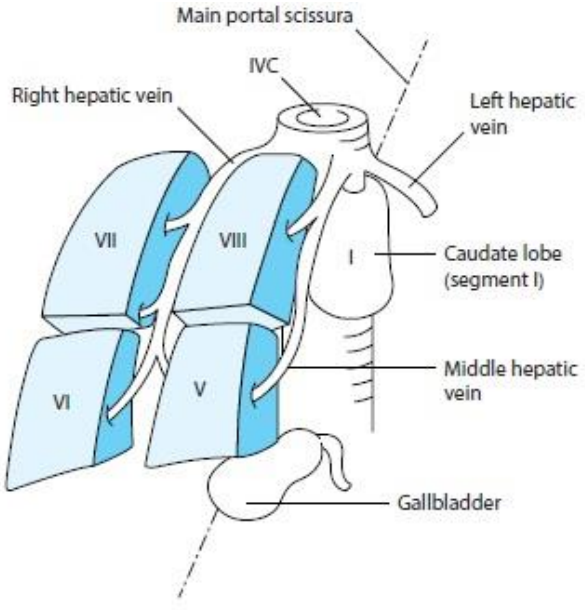
The right hemiliver, situated to the right of Cantlie's line, is further subdivided into two sectors by the vertical right portal scissura in which lies the right hepatic vein. This scissura, which has no surface markings, is a plane that subtends an angle of 40° with a coronal plane conducted through the inferior vena cava (horizontal plane) and on the liver surface corresponds to a line extending from the anterior edge of the liver (midway between its rightmost tip and the right border of the gallbladder fundus) to the confluence of the right hepatic vein with the vena cava. The right posterior sector is situated to the right of the right portal scissura (and of the right hepatic vein) while the right anterior sector (also known as the right paramedian sector) is to the left of it, between the right and middle hepatic veins. The two sectors are further divided in segments by a horizontal plane passing through the hilum of the liver (hilar plane); the anterior sector is therefore composed of segments V (anteroinferior) and VIII (anterosuperior) and the right posterior sector of segments VI (posteroinferior) and VII (posterosuperior). Each segment receives a portal pedicle (a segmental branch of the portal vein and a segmental branch of the hepatic artery) and is drained by a separate bile duct. Thus in the supine patient, segments V and VIII partially overlap segments VI and VII, respectively. The left hemiliver The left hemiliver is divided by the umbilical fissure in the left lateral sector

1 First-order division

Anatomical term	Couinaud segments referred to	Term for surgical resection	Diagram (pertinent area is shaded)
Right hemiliver **OR** *Right liver*	*Sg 5–8(+/–Sg1)*	*Right hepatectomy* **OR** *Right hemihepatectomy (stipulate +/–segment 1)*	
Left hemiliver **OR** *Left liver*	*Sg 2–4 (+/–Sg1)*	*Left hepatectomy* **OR** *Left hemihepatectomy (stipulate +/–segment 1)*	

Border or watershed: The border or watershed of the first-order division which separates the two hemilivers is a plane which intersects the gallbladder fossa and the fossa for the IVC and is called the midplane of the liver.

International Hepato-Pancreato-Biliary Association Brisbane 2000 Terminology of Liver Anatomy and Resections. IVC, inferior vena cava.



Schematic representation of the right liver. The main portal scissura (plane) containing the middle hepatic vein marks the territory between the two livers. It is also known as Cantlie's line and roughly makes an angle of 75° with the horizontal to the left, and extends from the middle of the gallbladder fossa to the left side of the vena cava. The right liver is divided into two sectors by the vertical right portal scissura containing the main trunk of the right hepatic vein. These two sectors are split by a horizontal plane through the right portal vein into two anteroinferior (V and VI) and two posterosuperior (VII and VIII) segments. Thus the right liver is smaller than the right lobe. Unfortunately, the vertical scissurae (planes) are undulating and not straight as shown in the drawing. This precludes a good correlation between radiological and anatomical segmentation (see text). IVC, inferior vena cava.

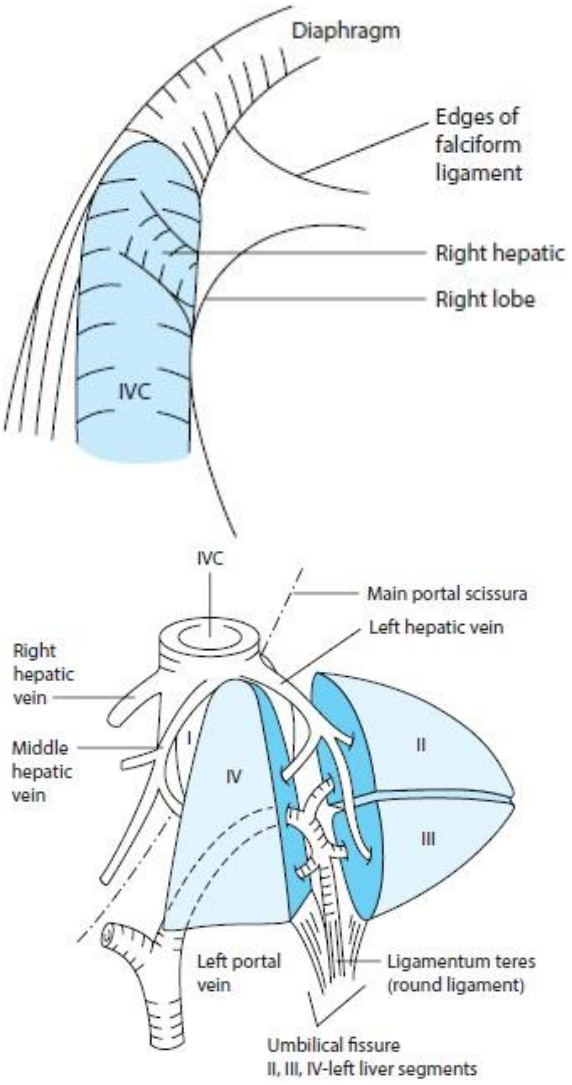
(situated to the left of it) and left medial sector (segment IV also known as the left paramedian sector). The umbilical fissure is easily recognized on the liver surface by the presence of the round ligament (ligamentum teres) and of the falciform ligament. The left portal scissura, in which lies the left hepatic vein, has no surface marking and is said to run from the left margin of the suprahepatic inferior vena cava to the mid-point of the anteroinferior margin of the left lobe of liver. It divides the left lateral sector into an anterior segment (segment III) and a posterior segment (segment II)

Caudate (dorsal, Spigel) lobe

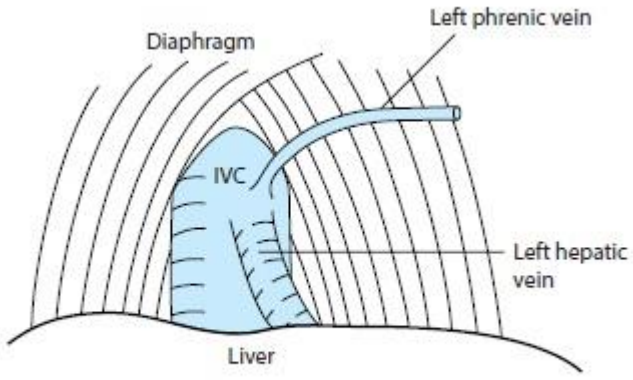
Although this is customarily labelled as segment I, it is really a separate 'liver' because it has its own hepatic veins (Spigelian veins) and bile ducts, although it receives portal and arterial branches from both right and left sides. The caudate lobe is situated behind the hilar fissure and embraces the vena cava from the left forming an L-shaped structure with the horizontal limb separating the hilar fissure from the vena cava and the vertical limb the left liver from the vena cava. Its uppermost part lies posteriorly to the confluence of the hepatic veins and anteriorly to the inferior vena cava.

Main hepatic veins

Each numbered segment contributes hepatic veins that coalesce to form the



Schematic representation of the left hemiliver that is split by the umbilical fissure and by the left portal scissura into segment IV medially and segments II and III laterally. Thus the left liver is larger than the left lobe. IVC, inferior vena cava.

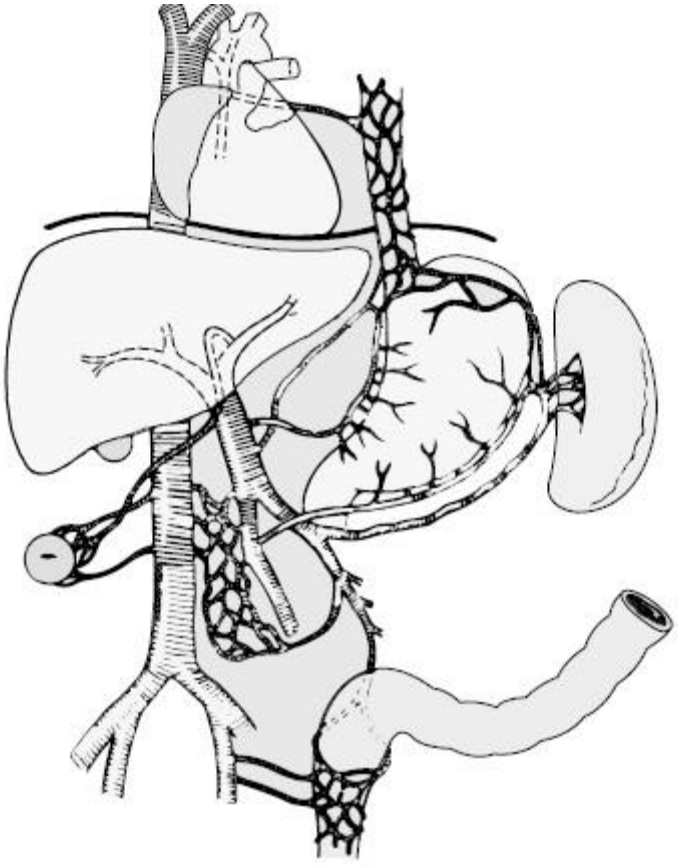


Schematic representation of the left hepatic vein. IVC, inferior vena cava.

main venous drainage of the livers and lie between the segments. There are three main veins of surgical importance: the right hepatic vein drains segments V–VIII by a short vessel directly into the suprahepatic vena cava; the middle hepatic vein drains from both livers (segments IV and V–VIII) and empties either directly into the vena cava in isolation or with a common trunk with the left hepatic vein. The latter vein drains segments II and III. Segment I, the caudate lobe, drains by one or more small hepatic veins directly into the retrohepatic vena cava. In the majority of patients both the right hepatic and the left hepatic veins can be identified and secured extrahepatically within the caval canal, but this manoeuvre is often hazardous for the middle hepatic vein. The left hepatic vein is exposed by complete division of the left triangular ligament. It slopes down from the vena cava to the liver so that its posterior wall is in contact with the vena cava and separated from it by loose fibrous tissue. The right hepatic vein is exposed only after the right lobe is completely mobilized and dislocated to the left. It runs directly posteriorly from the liver in intimate contact with the vena cava before entering it more posteriorly . Again only a loose layer of fibrous tissue separates the medial wall of the right hepatic vein from the vena cava but the fibrous tissue on its outer surface is usually firm and thickened.

Portal hilum

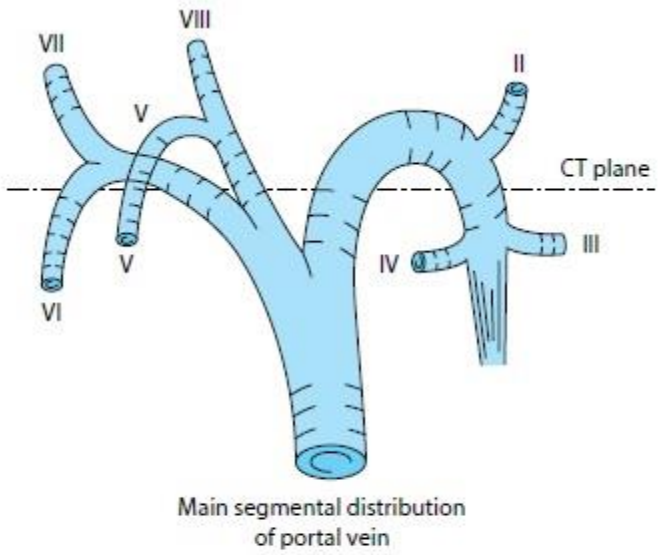
In the portal hilum, the portal vein that has formed behind the head of the pancreas with the confluence of the splenic and superior mesenteric veins passes along the edge of the lesser omentum for 7.5cm. It receives branches from the pylorus and the important left coronary vein from the cardio-oesophageal region. In the axial plane, the two main branches of the portal vein lie in the same plane (sometimes referred to as the transverse scissura). From right to left, segments VI, V, IV and III are below this plane, whereas segments VII, VIII, I (caudate) and II are above it. There are major anastomotic sites between the portal and systemic systems that open up in the presence of occlusion/ obstruction to portal



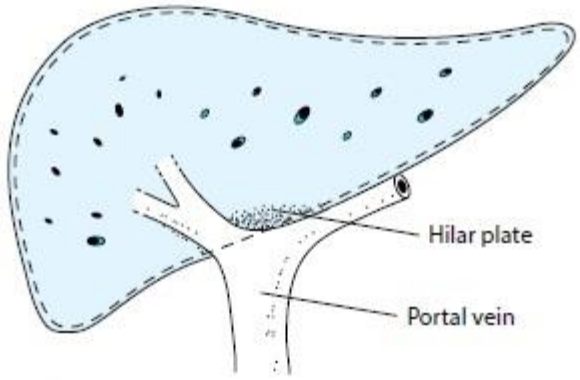
This shows the portal venous drainage from the gastrointestinal tract and demonstrates the major anastomotic sites between the portal and systemic systems: the cardio-oesophageal junction leading up to the azygos system, the retroperitoneum, the umbilicus and the inferior rectal plexus.

blood flow to the liver:

- the cardio-oesophageal junction – left gastric (coronary) vein to the azygos system
- communications with the retroperitoneal veins of Sappey
- umbilicus – recanalized left umbilical vein to abdominal parietal veins – caput medusa
- communications with the inferior rectal plexus. The common hepatic duct draining both livers passes in front of and to the right of the portal vein and receives the cystic duct at a variable point of its course to form the common bile duct. The common hepatic artery runs to the left of the common bile duct giving off the main cystic artery and branches to the common bile duct prior to division into right and left branches. An understanding of the point of the division of the structures in the portal hilum is essential for the surgeon. The vasculobiliary sheath, described originally by Walaeus in 1640 and commonly referred to as the Glissonian sheath, surrounds the main vessels and ducts following them well into the depth of the parenchyma and it is still recognizable around the tertiary ramifications (segmental pedicles). While the portal vein is loosely enclosed, the bile duct and hepatic artery are firmly adherent to the Glissonian sheath. The upper surface of the sheath which is in contact with the liver parenchyma thickens to become the hilar plate. This structure can be released from the liver surface because there are no branches along it and permits the surgeon to isolate the bifurcation of the hepatic pedicle to the right and left hemilivers extrahepatically but *en bloc* (the three elements together, portal vein, hepatic artery and bile duct) and to proceed to liver resection more safely with an extraglissonian approach.



Schematic representation of the usual intrahepatic distribution of the portal vein. Above the transverse line (representing the transverse scissura marking the plane of the right and left portal veins) the upper branches supply segments VII, VIII, I, II and the lower branches VI, V, IV, III.

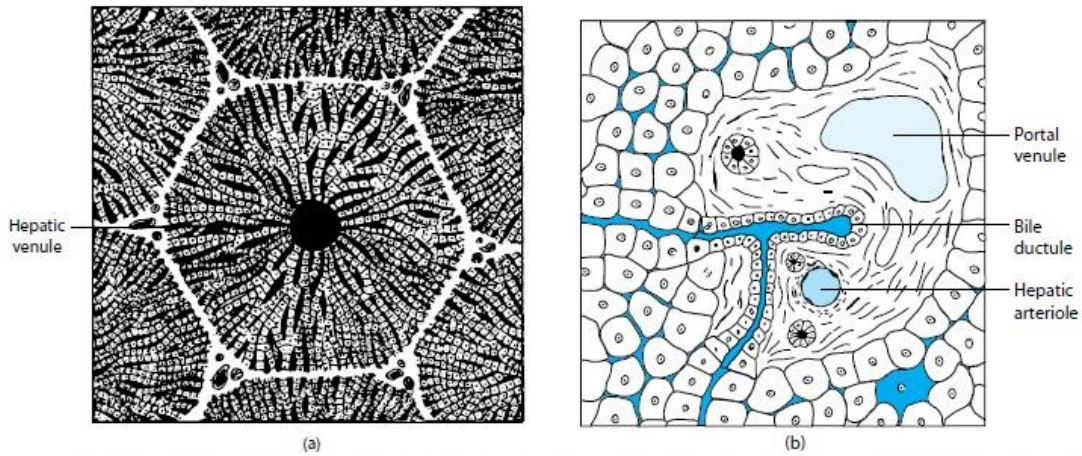


To the undersurface of the liver, the bifurcation of the major hilar structures is secured by a dense fibrous sheath termed the hilar plate. After incising this structure the vessels to the left liver segments run for 1.5 cm before dividing into segmental branches.

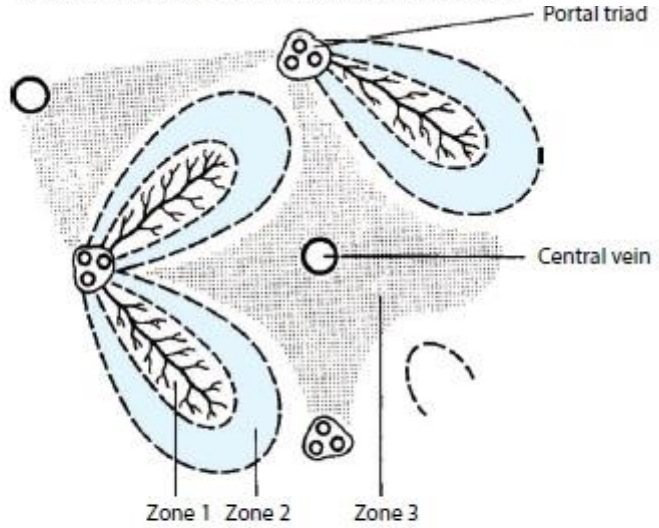
Hepatic architecture

Conventional morphology considers that the liver is composed of pyramidal lobules based on a central vein and surrounded on the periphery by portal trunks with

terminal radicles of bile duct, portal vein and hepatic artery. The two vascular systems of the central vein and portal tract lie on planes at right angles to one another and never interdigitate. Thus the sinusoids are arranged perpendicular to the planes of the central veins and portal blood passes to the central vein along a pressure gradient. The walls of the sinusoids are composed of endothelial and phagocytic cells, termed Kupffer cells. Between the hepatocytes and Kupffer cells is the space of Disse. Bile canaliculi are shown to be channels or grooves in the hepatocyte surface, lined by microvilli. The network of canaliculi drains the liver lobules into the terminal bile ducts. It may help in the understanding of liver injury and its consequences to view the liver morphology somewhat differently. The concept of Rappaport is to regard the liver as a series of acini supplied by a portal triad of structures. Three zones of sinusoids are envisaged in which the peripheral zone of the acini (zone 3) is damaged more severely in any form of injury. Adjacent forms of injury may coalesce to form areas of bridging necrosis and, later, fibrosis, producing the commonpattern of postsinusoidal block; zones 1 and 2 may form the nidus of surviving cells which then regenerate in nodular form.



(a) This demonstrates the normal liver architecture in which a hepatic plate apparently surrounds a hepatic vein through which blood from the hepatic sinusoids drains. (b) In fact it is more appropriate to centre the hepatic plate on the portal tract which contains the elements of the bile ducts into which bile can directly drain from the hepatocytes and branches of the portal vein and hepatic artery together with connective tissue stroma. Zones closest to this portal tract (zone 1) are protected in most circumstances from liver damage. Liver cells surrounding the hepatic vein (zone 3) are more susceptible to all forms of hepatic damage. Regenerative nodules are normally centred on a portal tract.



According to Rappaport, there are three zones of liver parenchyma. Zone 1 adjacent to the portal triad is the best vascularized and least susceptible to injury. Zone 3 is adjacent to the central vein and most susceptible to injury.

Acute liver disease

Viral hepatitis

Acute viral hepatitis presents with nausea, right upper quadrant pain and usually jaundice, so should be included in many differential diagnoses. However, many cases of acute hepatitis are subclinical and will be discovered incidentally on testing of LFTs. It can be caused by hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis E virus (HEV) and by hepatitis C virus (HCV). A milder hepatitis can also be caused by cytomegalovirus, the Epstein–Barr virus and the protozoan Toxoplasma. In some cases of hepatitis, serological testing will be negative, no other aetiology will be evident, and it is assumed that this condition has a viral aetiology, as yet unidentified. It is further assumed that there is more than one agent and the illness is termed seronegative hepatitis. A small subset of these patients develops fulminant hepatic failure (FHF). The management of all these conditions is supportive, with observation for the tiny minority who will develop fulminant liver failure and will need invasive support and consideration of liver transplantation. In surgical practice, universal precautions should always be employed, particular care should be taken in operating on patients who are known to be infected with bloodborne hepatitides, but this should in no way prejudice the care of the patient. HAV and HEV are spread by the faecal–oral route. HAV is becoming much less common but continues to give rise to epidemics. Although the disease is usually benign, complications including prolonged cholestasis and macropapular skin reactions are common. A vaccine developed from killed virus A propagated in fibroblast culture is available. It appears to be particularly effective when combined with recombinant hepatitis B vaccine. HEV is predominant in Asia but is now endemic in the UK, but still more common in patients with a clear travel history to Asia. It has a generally benign course, except in pregnancy where there is a significant mortality. Neither HAV nor HEV infection leads to chronic infection or chronic liver damage. HBV, which was first isolated in 1966, has infected in excess of 350 million individuals worldwide. It is a leading cause of chronic hepatitis, cirrhosis and HCC. The hepatitis B vaccination programme is altering the epidemiology of hepatitis B. Thus infection in healthcare workers and homosexuals (who have accepted the vaccination programme) has fallen. In those countries that have adopted universal vaccination programmes, huge reductions in HBV prevalence have been achieved and a decline in the complications of chronic infection has already been observed. It should be stressed that the infectivity of HBV is much greater (eight times) than that of HIV. Chronic HBV infection is defined as the presence of HBsAg persistent

more than 6 months after infection; spontaneous clearance is still possible at this stage but runs at between 2% and 4% per annum. The risk of chronic infection depends on the age of acquisition: with adult infection less than 10% become chronically infected, whereas infection in the under fives has a greater than 40% risk of chronic infection. The assessment of chronic HBV infection involves HBV serology, but also HBV DNA and an assessment of liver damage by either biopsy or non-invasive markers such as sonoelastography. The recognition of mutant HBV now means that viral load is more important than 'e-antigen' status in predicting prognosis and therefore the need for treatment. The specific therapy of chronic hepatitis B disease is now possible, but is complicated and rapidly evolving and should be undertaken in consultation with expert centres. Therapy has one of two different aims, either viral eradication with defined therapy or viral suppressive therapy long term to prevent complications of cirrhosis or HCC. Currently eradication therapy is based on IЃ-interferon, which inhibits the replication of HBV, and treatment can lead to remission of the disease with clearance of the hepatitis B e-antigen in up to 30% and hepatitis B surface antigen often follows. IЃ}-Interferon is administered subcutaneously in a pegylated formulation weekly for 12 months. Factors associated with better response to IЃ-interferon include:

- HBeAg+
- a raised aminotransferase concentration >100в•›IU/mL
- low values for HBV DNA
- liver biopsy showing moderate to severe inflammatory activity
- age <65 years.

Viral suppressive therapy should only be contemplated in those patients who have significant risk of developing damage from their HBV infection, as it is likely to be lifelong and expensive. The aim of therapy is to depress viral load below the limit of detection, which not only reduces the risk of disease progression but also substantially reduces the risk of viral resistance. Therapy is dependent on nucleoside or nucleotide analogues; there is no synergy between these drug classes but there is a different resistance profile. Older antiviral drugs included the nucleoside analogue lamivudine (3-thiacytidine); although some patients remain on this drug, up to 40% will develop resistant virus within 2 years, with viral escape. Newer drugs with higher genetic barriers to resistance are preferred as front-line therapy. HBV antivirals have revolutionized liver transplantation for HBV with much improved survival rates. Hepatitis C infection becomes chronic in 80% of cases; of these, 20% will progress to cirrhosis within 20 years. Worldwide 200 million people are chronically infected, and in many parts of the world it is now the leading

cause of HCC and the commonest indication for liver transplantation. The commonest routes of transmission are intravenous drug misuse, unscreened blood products (pre-1991 in the UK) and unsterile medical practices. There are six genotypes of the virus with geographical variation: genotypes 1 and 3 are predominant in the UK, Europe and the USA. HCV infection is curable with combination therapy of pegylated Iŕ}-interferon and ribavirin in the majority of cases. Genotype 2 and 3 patients are easiest to treat, needing 6 months' therapy to achieve cure in 70% and 90% respectively. Genotype 1 patients, with a year of combination therapy, have cure rates of 40%; however, very shortly genotype-specific protease inhibitors will increase this to 70%. Following transplantation in those not cured pretransplant, nearly all patients become reinfected and 20% develop cirrhosis in the transplanted liver within 5 years.

Drug-induced liver injury

Since one of the main functions of the liver is to detoxify or to metabolize many pharmaceutical agents, it is perhaps not surprising that an overdose or abnormal response to the agent may lead to problems. It is not usually the drug but a metabolite that causes the liver cell damage, with overt jaundice and in some cases acute hepatic insufficiency (fulminant liver failure). There are many drugs that cause liver damage to varying extents. These may be classified as:

• directly hepatotoxic agents, e.g. carbon tetrachloride, tetracyclines, paracetamol, DDT and benzene derivatives

• drugs that interfe with bilirubin metabolism/transport:

– haemolysis, e.g. para-aminosalicylic acid and phenacetin

– impaired bilirubin excretion, e.g. methyl testosterone and

norethandrone

– interference with uptake and transport of bilirubin, e.g. rifampicin

– interference with bilirubin conjugation, e.g. novobiocin

– interference with bilirubin binding, e.g. salicylates and

sulphonamides

• intrahepatic cholestasis, e.g. phenothiazine derivatives, chlorpromazine

• hepatitis-like disease, e.g. iproniazid, halothane, trichloroethylene

• hepatic fibrosis, e.g. methotrexate.

Damage is maximal in zone 3, where metabolizing enzymes are in the highest concentration and oxygen tension is the lowest. The histological picture may resemble acute hepatitis and, if so, has a poor prognosis. In other cases, light microscopy shows only scattered fatty change and no inflammation. A careful history of both prescribed drugs and self-medication is required for all jaundiced patients or those who have abnormal LFTs. From a clinical standpoint, drug-induced liver injury (DILI) has to be included in the differential diagnosis of most presentations of liver disease:

- cholestatic jaundice
- acute hepatitis
- chronic active hepatitis
- pseudoalcoholic liver disease
- hepatic sclerosis (due to vascular damage)
- hepatic neoplasia
- fulminant liver failure
- hepatic veno-occlusive disease
- vanishing bile duct syndrome.

DILI accounts for 40% of hospitalized cases of 'acute hepatitis'. Over 50% of cases of FHF are caused by drugs such as acetaminophen (paracetamol), halothane, phenytoin and methyl dopa. In surgical practice, hepatic injury induced by antimicrobial drugs is not uncommon, in particular co-amoxiclav (amoxicillin conjugated to clavulanate) can cause a hepatocellular or, more commonly, a cholestatic injury. The mechanism appears to be drug hypersensitivity to the clavulanic acid or a metabolite derived from it. Similar damage can be seen with flucloxacillin. Halogenated anaesthetic agent-induced hepatitis Although rare, halothane hepatitis is most likely to occur postoperatively and deserves mention. Although usually recoverable, severe hepatocellular damage progressing to fulminant liver failure is well documented. The injury appears to be due to hypersensitivity, and the impaired liver function is associated with pyrexia, skin rashes and eosinophilia. Importantly, the condition develops in patients after previous exposure to halothane. An antibody to a hapten metabolite of the anaesthetic agent (trifluoroacetate) is found in 30% of suspected cases of halothane hepatitis. Biochemically, there is elevation of the serum glutathione 5-transferase activity, and this appears to be a more specific and sensitive measure of anaesthetic-induced hepatic injury than the serum aminotransferases. Although there has been only one single case

report implicating isoflurane and the hepatotoxic potential of this agent remains debatable, covalently bound antigens which are recognized by antibodies from patients with previous halothane hepatitis have been reported, indicating the distinct possibility of cross-sensitization with halothane or a common immune-mediated mechanism. Thus the practice of changing halogenated anaesthetics in patients requiring multiple anaesthetics does not guarantee a reduced risk.

Hepatotoxic herbal remedies

The range of DILI is not limited to prescription medication and can occur with over-the-counter medication and alternative remedies. Some herbal remedies are hepatotoxic and the spectrum of the disorders ranges from mild hepatitis to extensive necrosis, prolonged cholestasis, occlusion of the small hepatic veins (venoocclusive disease), chronic hepatitis and cirrhosis. Chinese herbal teas (popular in the treatment of dermatitis) derived from the plants *Dictamnus dasycarpus* and *Paeonia* sp. have been confirmed to have hepatotoxic substances, and cases of severe jaundice and hepatitis have been reported after drinking these teas. Black cohosh used for menopausal symptoms and glucosamine used for joint pain have been associated with liver failure.

Ischaemic hepatitis

This condition, also known as 'shock liver', is the commonest cause of very elevated transaminases in hospital practice. It usually arises in older patients who have had an episode of hypotension. It is characterized by a rapid rise in transaminases into the 1000s within 24–36 hours of the insult and a rapid fall over the following days; often there is a secondary cholestatic phase lasting several weeks. In most patients these abnormalities are asymptomatic compared with the underlying illness, and the abnormalities resolve spontaneously. A small proportion of patients will become jaundiced; of these, some will develop a prolonged prothrombin time and even spontaneous hypoglycaemia. Management is supportive but the prognosis is poor and liver transplantation is usually contraindicated because of comorbidity that leads to shock liver.

Postoperative cholestasis

This is an old term coined more than 100 years ago with the advent of anaesthesia. It still has usefulness describing a syndrome of cholestasis seen in patients after major surgery and major sepsis and multiorgan failure in intensive treatment unit patients, but it is important to exclude drug reactions and ischaemic hepatitis. The aetiology is unclear but can be viewed as a toxic insult to the biliary canalicular system and epithelium from a combination of: bacterial products (from the gut or systemic sepsis), reduced perfusion and toxic bile. The reduced perfusion has been associated with the use of positive

endexpiratory pressure in cardiothoracic procedures. The toxic bile may result from the downregulation of some canalicular transport systems in response to toxins. The clinical syndrome can vary from an asymptomatic biochemical cholestasis to prolonged jaundice or the development of a secondary sclerosing cholangitis.

Chronic liver disease

As described above, chronic liver disease has a duration of greater than 6 months. To some extent, depending on aetiology, it does not cause many symptoms or clinical complications until sufficient loss of liver parenchyma and increase in fibrosis has led to the development of cirrhosis. This and its aetiologies are described below; of course, viral hepatitis, both HBV and especially HCV, can cause chronic disease as described above.

Cirrhosis of the liver

Liver cirrhosis is the end result of hepatocyte death and regeneration with fibrosis. It must be distinguished from hepatic fibrosis, which can occur in the portal regions from chronic bile duct obstruction or congenitally, or around the central veins in chronic cardiac failure. Confluent necrosis of zones 1 and 3 leads to fibrotic bridges, and the regeneration of surviving hepatocytes results in a further distortion of hepatic architecture. There are multiple causes of cirrhosis. In the Western world, alcohol, hepatitis C and non-alcoholic steatohepatitis (NASH) would be the commonest causes. Irrespective of the underlying aetiology of the cirrhosis, the clinical syndrome and complications are very similar or identical, i.e. liver failure and portal hypertension. Not uncommonly, the condition will be unsuspected and comes to light because of a routine estimation of LFTs or found incidentally at laparotomy. Clinical suspicion is aroused by finding stigmata of chronic liver disease such as palmar erythema, spider naevi, or otherwise unexplained peripheral oedema. Alternatively, the patient may present in a later stage of disease with muscle wasting and ascites, with gastrointestinal haemorrhage from varices, jaundice or hepatic encephalopathy. In most patients, liver cirrhosis has a poor prognosis. However, if the underlying cause can be removed, return to normal function is possible with a huge improvement in prognosis, abstinence from alcohol being a typical example. Other diagnoses are less likely to regress, but in some the prognosis may be improved with appropriate management. Thus in the patient with chronic liver disease who presents with a condition requiring surgical intervention, not only is it important to be sure that the patient requires the intervention, but also is this the optimum time? Can the patient's condition be improved. If it can then the correct decision will often be to delay surgery.

Non-alcoholic fatty liver disease

NAFLD is the most common form of liver disease in the Western world. It is considered part of the metabolic syndrome, and as such is closely associated with type 2 diabetes mellitus, obesity, insulin resistance, hypertension and dyslipidaemia. The definition of non-alcoholic varies and in clinical practice a common-sense approach should be taken as to the main driver of liver damage: in general those drinking around 21–28 units of alcohol per week should be regarded as being within NAFLD. NAFLD is an umbrella term encompassing a histological spectrum of disease ranging from simple steatosis to NASH. NASH can progress to the development and propagation of fibrosis leading ultimately to cirrhosis and HCC. The pathology of NAFLD is characterized by excess fat within the liver. The excess fat is predominantly macrovesicular fat and usually seen in a perivenular (zone 3) pattern. Beyond simple fatty change, liver injury in NAFLD includes evidence of hepatocellular injury, most commonly seen as hepatocyte ballooning. Inflammatory changes and the development of fibrosis are also key histological changes seen in progressing NAFLD (or steatohepatitis). To aid histological assessment, numerous scoring systems have been proposed. The most commonly used and widely accepted is the NAFLD activity score (NAS). The NAS is a semiquantitative assessment of the three cardinal histological features of NAFLD – steatosis, lobular inflammation and hepatocyte ballooning. Both steatosis and lobular inflammation are graded 0–3, with ballooning graded 0–2. The unweighted sum of these features constitutes the NAS, with score ≥5 diagnostic of NASH, score ≥3 considered borderline NASH and scores ≤2 labelled ‘not NASH’. Although the NAS system is not widely used in routine clinical practice, it is an essential component of many research studies in the NAFLD arena. Clinical signs and symptoms are uncommon in NAFLD. When seen, the most common complaints are of vague right upper quadrant discomfort and fatigue. Most commonly, mildly abnormal elevations of aminotransferases are found incidentally in patients with some or all of the components of the metabolic syndrome. In patients undergoing obesity surgery, the prevalence of simple steatosis was 91% and 37% for NASH. NALFD is also more commonly found in patients with impaired glucose tolerance and overt type 2 diabetes mellitus, with up to 62% of newly diagnosed type 2 diabetes mellitus patients having coexisting NAFLD. As well as associations with the more commonly recognized features of the metabolic syndrome, NAFLD is also associated with other disease states including polycystic ovarian syndrome, hypothyroidism and colorectal adenomatous polyps. There is currently no specific drug treatment; weight loss with an increase in physical activity is effective if it can be achieved. The prognosis is generally good for patients with steatosis, although they appear to have excess cardiovascular mortality. For those with NASH the prognosis is poorer with many progressing to cirrhosis within 10 years of diagnosis and those that do having an increased risk of developing HCC.

Alcohol-related liver disease

Alcoholic liver disease (ALD) is a major problem, especially in the affluent Western countries. The spectrum of liver damage varies from fatty infiltration to alcoholic hepatitis, hepatic fibrosis and cirrhosis. The last one is the commonest cirrhotic liver disease in some Western countries. The increasing per capita alcohol consumption is not just due to those who drink to excess drinking more but also to an increase in the median level of consumption; as a consequence, there has been a dramatic increase in the amount of alcohol-related liver disease. With the increase in the average amount drunk, many people now drink hazardously without signs of alcohol dependency but can still develop significant liver disease. However, it is important to note that only about 20% of those drinking at hazardous levels develop overt liver disease. Despite intensive research, the exact mechanism responsible for the hepatic damage remains unknown; genetic factors must be important but so far polymorphisms of key genes have not been shown to confer susceptibility to ALD. Dietary deficiencies are not considered a major causal influence, but are highly prevalent as a secondary phenomenon and should be sought and treated. However, oxidative stress is a central mechanism of damage and a failure to adapt to this stress will predispose to alcohol-related liver disease. While the mechanism of activation of the stellate cells in ALD is the subject of much research, once activated they are the central players in the ongoing fibrosis of the liver in a similar manner to other liver diseases. Serum endotoxin levels are known to be increased in patients with ALD and stimulation of the phagocytes by endotoxin with excess production of tumour necrosis factor-IŕŽ has been suggested as a possible mechanism for hepatocyte damage. Acetaldehyde derived by oxidation from ethanol in the liver is involved in the increased synthesis of type I collagen in the liver, hence the fibrosis. Another factor which has been implicated in the fibrosis is the cytokine transforming growth factor (TGF)-b, which is produced in excessive amounts by the Kupffer cells in response to alcohol. The excess TGF-b stimulates the transformation of stellate into active fibroblasts. It is unclear yet which subtype of TGF-b is implicated and although TGF-b1 has been widely reported, it is currently thought that more than one subtype is involved. The presentations of alcohol-related liver disease can be divided into three: fatty liver disease, alcoholic hepatitis and cirrhosis, either compensated or decompensated. Alcohol-related fatty liver disease is now more commonly know as alcoholic steatohepatitis; it usually presents with incidental discovery of abnormal LFTs. Occasionally, there may be right upper quadrant discomfort and sometimes hepatomegaly, which may be tender due to fatty infiltration of the parenchyma. At this stage liver biopsy is not usually needed unless after screening for other liver diseases an alcohol history raises diagnostic uncertainty. If performed, it shows the hepatocytes to be distended with fat and sometimes there is an inflammatory

infiltrate, early fibrosis or hyaline deposits (Mallory's hyaline). Alcoholic hepatitis is an acute severe condition that develops on the background of chronic alcohol use, either in a liver with normal architecture or more usually cirrhosis. The clinical features are of jaundice, often with ascites or encephalopathy, pyrexia and a bounding vasodilated circulation. Laboratory investigations reveal leucocytosis, raised inflammatory markers but only a mild elevation of the transaminases. The syndrome is defined by its poor short-term prognosis with untreated mortality of over 50%. The diagnosis can reliably be made on clinical grounds; some authorities advocate liver biopsy to confirm the diagnosis. The liver biopsy in alcoholic hepatitis shows a cellular infiltrate, liver cell necrosis, cholestasis, variable degree of fatty change and sometimes Mallory's hyaline. These classical features can be seen in patients who are entirely well, adding to the controversy of biopsy. Treatment of alcoholic hepatitis includes cessation of alcohol and most advocate the use of corticosteroids guided by the Maddrey's discriminant function or the Glasgow alcoholic hepatitis score, which both identify high-mortality groups. Ongoing trials are comparing the use of pentoxifylline in combination with steroids or as monotherapy. The differential diagnosis is of end-stage liver disease with no inflammatory components. The final stage is the development of cirrhosis, which is usually of the micronodular variety, but this is no longer a useful concept. The development of cirrhosis occurs some time in advance of clinical consequences, so may not be obvious until a hepatic insult such as surgery causes it to decompensate and manifest as liver failure with jaundice, ascites or encephalopathy. The most important factor in the treatment of ALD is abstinence from alcohol, and considerable improvement is seen both in LFTs and on repeat biopsy. Enteral nutrition imparts significant benefit in patients with alcoholic hepatitis and may improve survival, although this is debatable. The evidence for specific nutritional aids or supplements is poor and the control arm of the studies, if any, often represents inadequate standard hospital nutrition, so ensuring adequate dietary intake is clearly better than starvation for these patients. Transplantation is now performed for advanced alcohol-related chronic liver disease. Minimum periods of 6 months' abstinence before transplantation have previously been applied; however, these are currently being challenged as many patients with most to gain from transplantation do not survive that long. Also, due to the ill health of the patients, the abstinence is less meaningful as the patients are hospitalized for much of the duration. The results to date have been better than predicted and only about 15% of patients have resumed drinking after transplantation. There are no specific laboratory markers of ALD, although the following are suggestive: raised levels of γ-GT, presence of carbohydrate-depleted (sialic acid depleted) transferrin and a specific isoenzyme of

alanine aminotransferase (F-AAT). However, none is specific enough to rely on in an individual case, but they can raise the index of suspicion of an alcoholrelated aetiology.

Cholestatic liver diseases

Cholestasis, impaired bile secretion/excretion, with the development of conjugated hyperbilirubinaemia and raised bile ductular enzymes can be caused by obstructive lesions of the biliary tract such as stones and tumours. In addition, the same pattern can be seen without dilated bile ducts and is described as intrahepatic cholestatsis. The causes of this include drugs, alcohol, viral hepatitis, primary biliary cirrhosis and primary or secondary sclerosing cholangitis. The term 'vanishing bile duct syndromes' is sometimes applied collectively to these disorders; it is a histopathological observation of ductopenia, or a paucity of bile ducts, and is not a specific disease. It can be observed in the conditions listed above and also hepatic sarcoidosis, graft-vshost disease and hepatic transplant rejection, but is only present in a minority of cases.

Primary biliary cirrhosis

This is a disease of unknown aetiology in which the intrahepatic bile ducts are progressively destroyed by an immunological process. It runs a variable course but ultimately ends in primary biliary cirrhosis (as distinct from secondary biliary cirrhosis due to chronic obstruction of the extrahepatic biliary tract, e.g. strictures). Circulating antibodies against mitochondrial constituents (antimitochondrial antibodies) are found in all patients. These antibodies are non-organ and non-species specific and their relationship to the aetiology of the disease remains speculative but they are useful in the diagnosis of the condition. The most widely held immunological hypothesis for the development of the disease is aberrant expression of class II histocompatibility antigens on the epithelium of the bile ducts which induces a T-cell-related progressive immune destruction. There is some evidence that the mitochondrial antigens responsible for the production of antimitochondrial antibodies (e.g. E2 antigen, which is also present in Gram-negative bacteria) may cross-react with the bile duct antigens. The disease is often asymptomatic for long periods. Some cases are discovered accidentally because of abnormal LFTs obtained before blood donation. There is a female preponderance and the mean age at symptomatic presentation is 40 years. The symptoms include itching, weight loss, malaise and icterus. The liver becomes enlarged and, with progression of the disease, portal hypertension with splenomegaly develops. There is deposition of cholesterol in the tissues especially around the orbits and on the extensor surface of the large joints. In advanced disease, intrapulmonary shunting is associated with finger clubbing. The malabsorption secondary to the diminished bile salt pool leads to deficiency of fat-soluble vitamins (A, D, E, K) with the development of osteoporosis. In

addition to biochemical features of cholestasis and presence of antimitochondrial antibodies, the serum IgM is elevated. Smooth muscle antibodies are also present in many patients. There is no effective medical therapy but symptomatic relief is obtained by a variety of drugs. Cholestyramine is used for itching and ursodeoxycholate improves symptoms and the LFTs by replacing the toxic hydrophobic bile acids. Prednisolone seems to reduce fatigue and itching and may improve liver function. Monthly injections of fat-soluble vitamins are administered to counteract the deficiencies caused by the malabsorption. However, the disease process is not influenced by medical treatment and the only effective therapy that imparts a longterm cure is hepatic transplantation. Primary biliary cirrhosis is the second most frequent indication for liver transplantation. Nowadays, this operation is undertaken before the development of end-stage disease and the onset of hyponatraemia or significant bone disease. It is considered in patients whose quality of life has deteriorated or in whom the bilirubin exceeds 100вmmol/L, and in those who develop portal hypertension.

Primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is a chronic inflammatory large duct cholangiopathy, leading to fibrotic strictures of the intra- and extrahepatic bile ducts, of unknown aetiology. It is rare in the UK, but the leading indication for transplantation in Scandinavia. The clinical course of PSC varies considerably between patients, from decades of asymptomatic abnormalities in LFTs to frequent recurrent bouts of cholangitis progressing to liver failure requiring transplantation within a decade. Median survival from diagnosis to death or transplantation is 12 years, but the variability of the natural history makes prognostication difficult for the individual patient. The disease also carries an increased risk of cholangiocarcinoma occurring in 10–15% of cases. The diagnosis of this malignant stricture among the strictures in the biliary tree due to PSC is a significant challenge. The disease is commonly associated with inflammatory bowel disease, with up to 60% of PSC patients having inflammatory bowel disease if this diagnosis is searched for. The only curative treatment is liver transplantation. Ursodeoxycholic acid therapy is used on the basis that this is a cholestatic disease, but this is not recommended in guidelines and lacks any evidence base.

Portal hypertension and complications

Portal hypertension arises as the result of obstruction to portal venous outflow; this may result from extrahepatic compression or thrombosis of the portal, mesenteric or splenic veins, from compression of portal venous radicles within the liver from a wide variety of liver diseases or from obstruction to the outflow from the liver. Rarely, anomalous arterioportal fistulas result in a massive rise in portal venous flow and pressure (see

below). The degree of hypertension depends not only on obstruction to outflow but also on the volume of inflow; for obstructive disease such as portal vein thrombosis the increase in inflow is minimal so the portal hypertension is mild, whereas for cirrhosis there is a massively increased splanchnic blood flow, so even with incomplete obstruction there is significant portal hypertension. The portal pressure is normally estimated in postsinusoidal cirrhosis by performing a wedged hepatic vein pressure and subtracting the inferior vena cava pressure, giving the wedged hepatic venous portal pressure gradient (PPG). A PPG <7mmHg is functionally normal, and at ≥7mmHg ascites and varices can occur, but varices will only bleed at PPG >11mmHg. The measurement of PPG is a useful clinical tool but is not widely performed outside major centres. In sinusoidal and presinusoidal portal hypertension the PPG is normal and portal pressure must be measured by direct methods, such as splenic puncture, which these days are rarely done. Most commonly, portal hypertension is post sinusoidal and results from cirrhosis of the liver. Although a precise diagnosis may not be relevant to the immediate management of a patient with variceal bleeding, it may ultimately indicate prognosis and change the choice of subsequent treatment. Cirrhotic portal hypertension is the result of a combination of increased portal venous resistance and an increased splanchnic blood flow. Increased vascular resistance is both a mechanical consequence of liver architecture distortion and a dynamic process involving active contraction of myofibroblasts, activated stellate cells and venous smooth muscle cells. Vascular resistance may be modified by endogenous factors or pharmacological agents. Endothelin, IЃ-adrenergic stimulus and angiotensin II increase hepatic vascular resistance whereas nitric oxide, prostacyclin and vasodilating medications (e.g. nitrates, calcium channel blockers) reduce resistance. Splanchnic arteriolar vasodilatation is secondary to elevated circulating levels of vasodilator substances (including glucagon, nitric oxide) and decreased sensitivity of the splanchnic vasculature to endogenous vasoconstrictors. Patients have a hyperdynamic circulation with increased cardiac output, hypotension and hypervolaemia from the resulting sodium retention (discussed further under the section Ascites). Portal hypertension sometimes develops in patients with liver disease prior to the onset of cirrhosis. This has been attributed to intrahepatic arterioportal anastomoses, hyperdynamic circulation and the accumulation of vasoactive humoral factors which alter the resistance to flow. About 25% of patients will have an extrahepatic cause for portal hypertension, usually a portal vein thrombosis. A proportion of these patients will also have underlying liver disease or hypercoagulability disorders such as polycythaemia. Chronic pancreaticobiliary disease or pancreatic neoplasms may be precipitating factors for portal or splenic vein thrombosis, but only rarely does neonatal umbilical sepsis seem to be an aetiological factor. Extrahepatic outflow block may result from thrombosis or occlusion of the hepatic veins (Budd–Chiari syndrome). Aetiological factors may be

protein C deficiency, the contraceptive pill and ingested toxins that include *Senecio* or bush tea poisoning (veno-occlusive disease). Other patients have congenital diaphragms in the suprahepatic vena cava or chronic congestive right heart failure. Such patients rarely present with bleeding varices but suffer with intractable ascites, painful hepatomegaly and rapidly deteriorating liver function. Portal hypertension may also follow thrombosis of the splenic vein from pancreatitis or tumour. In this instance the portal hypertension is left sided (sectorial) and the varices affect the short gastric and gastroepiploic veins. Obstruction to portal venous flow is followed by enlargement of natural portosystemic communications (Figure 24.6) and by the development of new collateral channels at surgically constructed mucocutaneous junctions (colostomy, ileostomy). Rarely, portal venous blood is shunted away from the liver by an enlargement of the umbilical vein (Cruveilhier–Baumgarten syndrome) and may be detected by a venous bruit in the midline. Though there is a risk of variceal bleeding from the ileum, colon and haemorrhoidal areas, the major risk of haemorrhage is from the oesophagus and stomach. In the oesophagus the varices are large, tortuous and thin walled with a tendency to rupture. However, in the stomach there is venous engorgement of the gastric mucosa with a tendency to erosive gastritis and a widespread diffuse haemorrhage; there is an additional component of proliferative growth of tiny blood vessels, which together cause the appearance of portal hypertensive gastropathy. The predilection of the gastric cardia to develop varices is probably due to the drainage of the left coronary vein after portal hypertension has developed. Instead of draining towards the liver, blood passes along paraoesophageal veins and then via 'perforator' veins to the submucosa of the oesophagus. Three columns tend to develop and run upwards for a variable length, usually communicating with the azygos system. Blood flow from the spleen may course through the short gastric vessels to the gastric fundus and link with enlarged collaterals at the cardia. Fundal varices are only detectable on retroflexion of the flexible endoscope in the stomach. Colonic varices may occasionally be seen on sigmoidoscopy, but not as commonly as may be expected. Nor is the caput medusa or periumbilical plexus of veins at all common. It is most prominent in patients who develop

Pathogenesis of portal hypertension

- Increased blood flow into portal venous system (no obstruction)
  - Hepatic and splenic arterioportal fistulas (rare)
- Extrahepatic outflow obstruction
  - Hepatic vein thrombosis; Budd–Chiari syndrome, veno-occlusive disease; tricuspid incompetence, right heart failure
- Extrahepatic inflow obstruction
  - Congenital malformation of portal vein
  - Portal vein thrombosis
  - Splenic vein thrombosis (sectorial portal hypertension)
  - Portal vein compression, e.g. nodes
- Intrahepatic obstruction
  - Presinusoidal: periportal fibrosis and schistosomiasis
  - Postsinusoidal: cirrhosis (alcoholic, nutritional, postnecrotic, biliary), veno-occlusive diseases, haemochromatosis, Wilson disease, congenital hepatic fibrosis

a small paraumbilical hernia into which an omental plug provides the portal flow. It has to be recognized that not all patients develop portal hypertension as a result of their chronic liver disease; estimates vary from 15% to 40%. Furthermore, only about one-third of the patients with gastro-oesophageal varices (GOV) ever suffer from gastrointestinal bleeding. This is due both to the age of the patients and to the natural history of the underlying liver disease. In those who do develop portal hypertension, they may present with any combination of four clinical syndromes that can be attributed to portal hypertension:

- hypersplenism
- gastrointestinal bleeding
- ascites
- hepatic encephalopathy.

Hypersplenism

Splenomegaly is frequently associated with portal hypertension; it is due not just to passive venous hypertensive congestion but also to a hypertrophy of splenic tissue. This may lead to sufficient sequestration of formed blood elements in the spleen to cause haemolytic anaemia, leucopenia and thrombocytopenia. Only rarely are these features sufficient to produce major symptoms but they do lead to general debility. After portal vein decompression, hypersplenism improves in approximately 50% of patients.

Gastrointestinal haemorrhage

Approximately 70% of cirrhotics will have GOV at disease presentation. Of these patients, 30% will suffer gastrointestinal haemorrhage within 1 year of diagnosis; the index variceal bleed is associated with a 30–50% mortality rate. Bleeding risk is elevated in patients with larger varices, high portal venous pressure (>12вmmHg) and severe liver disease. The prognosis of a bleed is most dependent on the stage of liver disease prior to haemorrhage and to a lesser but important extent on the duration of the bleed and any hypotension, as this exacerbates decompensation of liver function. The following endoscopic findings are predictive of an increased risk of variceal haemorrhage:

- cherry-red spots
- red wale markings
- blue varices (as opposed to white). Variceal bleeding may present with frank haematemesis, coffee-ground vomitus and/or repeated melaena. Management of

oesophageal varices is divided into treatment of acute bleeding, prevention of recurrent haemorrhage and primary prophylaxis.

Management of acute variceal haemorrhage

Patients should be resuscitated with intravenous fluids and blood products as appropriate; those with known liver disease or stigmata of cirrhosis should receive vasoactive drug therapy (terlipressin or octreotide). Blood volume resuscitation should aim to restore haemodynamic stability but must be undertaken with caution; the recommended target haemoglobin is 8g/dL. Experimental studies have shown that full restitution of lost blood volume results in an elevation of portal pressure above baseline, with increased risk of rebleeding and mortality. Upper gastrointestinal endoscopy should be performed as soon as possible, ideally after the patient has been resuscitated and is haemodynamically stable. On occasion, even with aggressive fluid resuscitation, stability may fluctuate and early endoscopy may stabilize the situation, but this should not slow the resuscitation. Endoscopy should be performed within 12–18 hours of admission. Endoscopic therapy

Oesophageal varices

Endoscopy has the advantage of allowing specific therapy at the time of diagnosis; it is also important to exclude bleeding from other sources (e.g. peptic ulceration). Variceal haemorrhage may be treated endoscopically, either by injection sclerotherapy or by band ligation. Sclerotherapy involves injecting a sclerosant solution such as 5% ethanolamine oleate directly into the varix, producing vessel thrombosis, or into the overlying submucosa to induce inflammation and subsequent fibrosis. Complications include fever (transient), ulceration, stricture, perforation (rare), chest pain, mediastinitis and pleural effusion. Endoscopic variceal ligation (EVL) is achieved by attaching a banding device to the tip of the endoscope. The varix is aspirated into the banding chamber and the band placed over the varix using a trip-wire mechanism, ligating the vessel. One to three bands are applied to each varix, resulting in thrombosis. Chest pain or banding-related ulceration may occur following EVL, but there are fewer associated complications than injection sclerotherapy. It has been demonstrated in a metaanalysis of 10 randomized controlled trials (RCTs) that EVL is superior to sclerotherapy in terms of both rebleeding rates and mortality; injection sclerotherapy had higher complication rates, particularly with regards to oesophageal ulceration and sepsis. Combined endoscopic (either EVL or injection sclerotherapy) and pharmacological (splanchnic vasoconstrictors) therapy has proven superior to endotherapy alone in a meta-analysis of eight trials, with more effective control of initial haemorrhage and 5 day haemostasis without differences in morbidity or mortality. Both the British Society of Gastroenterology and the American

Association for the Study of Liver Diseases (AASLD) recommend combination therapy with initiation of vasoactive drugs at the time of admission, prior to diagnostic upper gastrointestinal endoscopy.

Gastric varices

Bleeding from gastric varices only accounts for 10–36% of all variceal haemorrhages, but the bleeding can be more severe and the management more challenging. Gastric varices are classified according to their distribution and whether they are in continuity with oesophageal varices. GOV type 1 (GOV 1), the most common, are in continuity with oesophageal varices, extending <5cm along the lesser curve. GOV which are in continuity with oesophageal varices but which extend further towards the fundus are classified as GOV type 2 (GOV 2). Isolated gastric varices (IGVs) occur in the absence of oesophageal varices: type 1 are located in the fundus (IGV 1) and type 2 (IVG 2) are located in the body, antrum or around the pylorus. GOV 1, GOV 2 and IGV 1 are most commonly associated with upper gastrointestinal haemorrhage. Fewer clinical trials exist regarding endotherapy for gastric variceal haemorrhage, thus it is difficult to formulate management guidelines in the absence of robust evidence. GOV 1 constitute extensions of oesophageal varices and the recommended management is the same as for oesophageal varices. Haemostasis and rebleeding rates are reportedly similar in GOV 1 and oesophageal variceal haemorrhage. Varices in the cardia and fundus (GOV 2 and IGV 1) tend to be more tortuous and complex; management of haemorrhage from these varices is more challenging and requires different endotherapy to GOV 1. Injection sclerotherapy is not recommended for gastric variceal bleeding following reports of inadequate haemostasis, embolization of sclerosant and ulcer haemorrhage at the site of the injection. Alternative therapeutic options are EVL or variceal obturation by injection of tissue adhesive glue or thrombin. Endoscopic variceal obturation (EVO) using cyanoacrylate injection is the current recommended treatment for fundal variceal haemorrhage, providing better control of initial haemorrhage and lower rebleeding rates than EVL. Two RCTs compared outcomes of EVO and EVL in the management of gastric variceal haemorrhage: the first found EVO to be superior both in the achievement of initial haemostasis and in lowering the rates of repeat haemorrhage; the second found no difference in control of bleeding but demonstrated a significant reduction in recurrent haemorrhage in patients treated with EVO. These studies, however, reported outcomes from all patients presenting with gastric variceal haemorrhage, including those with GOV 1. GOV 1 varices, as reported previously, are as well controlled by EVL as oesophageal varices, making these results difficult to interpret. Future studies limited to the management of GOV 2 and IGV 1 variceal haemorrhage are required. Thromboembolic complications including portal vein embolization (PVE), splenic infarction, myocardial

infarction and stroke have been reported in case studies and a case series reported non-fatal pulmonary emboli in 4.6% of patients. Endotherapy using thrombin injection has also been described in the control of gastric variceal haemorrhage but, as yet, this has not been subjected to RCT. Two small trials (patient numbers of 12 and 13) reported haemostasis rates of 100% and 92% and rebleeding rates of 27% and 0%, respectively. Both studies were limited by small patient numbers and short-term followup. Potential risks of thrombin endotherapy include allergic reactions or thromboembolic complications.

Vasoconstrictor therapy

Vasoactive drugs restrict portal inflow by splanchnic arterial vasoconstriction, resulting in reduced portal pressure. Therapy should be initiated as soon as variceal haemorrhage is suspected, prior to endoscopy. The most commonly used vasoactive drugs are discussed below.

- *Octreotide* – a somatostatin analogue. Administered as a 50mg bolus followed by 50mg/h continuous infusion. Produces splanchnic vasoconstriction without significant systemic vascular effect or complications.

- *Terlipressin* – a synthetic analogue of vasopressin. Administered at an initial bolus dose of 2mg every 4 hours, titrated down to 1mg every 6 hours after haemostasis is achieved. Contraindicated in patients with ischaemic heart disease, terlipressin has longer biological activity and fewer side effects than vasopressin (e.g. arrhythmias, hypertension, digital, gastrointestinal or cardiac ischaemia). A meta-analysis of seven RCTs showed a statistically significant reduction in mortality in patients treated with terlipressin compared with placebo; the number needed to treat to prevent one death was 8.3. Combined vasoconstrictor and endoscopic therapy is superior to endotherapy alone; terlipressin combined with endoscopy showed improved haemostasis and reduced mortality compared with endotherapy plus placebo. UK treatment guidelines recommend initiation of terlipressin therapy in all patients with suspected variceal haemorrhage; treatment should be continued for 48 hours after confirmation of diagnosis. Terlipressin is not yet available for treatment of variceal haemorrhage in North America; somatostatin and its analogues, most commonly octreotide, are administered as recommended by the AASLD. A systemic review identified 21 RCTs studying somatostatin and its analogues; there was no change in mortality but improved rates of initial haemostasis were demonstrated with drug therapy compared with placebo. A meta-analysis of eight RCTs combining endoscopy with somatostatin and its analogues showed combination treatment was superior to endotherapy alone; initial haemostasis and rebleeding rates were significantly lower with combination therapy but there was no

survival benefit. Patients should receive somatostatin and its analogues at initial presentation with variceal bleeding; treatment should continue for 3–5 days following endotherapy. In summary, combined therapy should be the standard of care for acute variceal bleeding with an immediate pharmacological agent when variceal bleeding is suspected; where available terlipressin is probably the agent of choice and this should be combined with early endoscopy and therapy with EVL for oesophageal varices and EVO for gastric varices. Management of uncontrolled variceal haemorrhage Despite urgent pharmacological and endoscopic therapy, uncontrolled haemorrhage or early rebleeding occurs in 10–20% of patients. Initial emergency measures to control massive blood loss should be followed by definitive second-line management of the underlying cause.

Balloon tamponade

This procedure is a temporary salvage treatment for uncontrolled variceal bleeding, two balloon systems are commonly used.

• *Sengstaken–Blakemore tube* – with a gastric balloon of about 60– 100mL capacity, which is meant to anchor the tube at the cardia and an oesophageal balloon which is inflated to 30–40mmHg and compresses the submucosal veins of the oesophagus.

• *Linton tube* – with a large gastric balloon of 300–700вmL capacity which is pulled against the diaphragmatic hiatus with traction and disconnects the high-pressure portal venous system from the thoracic azygous veins. Haemostasis with balloon tamponade is achieved in 80–95% of patients with oesophageal or gastric variceal haemorrhage; it is, however, associated with serious complications such as aspiration pneumonia, mucosal ulceration and oesophageal rupture, which lead to mortality rates of 5–20%. As the use of the oesophageal balloon increases the risk of complications with little evidence of additional haemostatic effect, we should discourage its routine inflation. Haemorrhage of the severity to warrant use of a tamponade tube should also prompt consideration of elective tracheal intubation to prevent aspiration. Balloon tamponade should only be used as a temporizing measure (12–24 hours) in patients with uncontrolled haemorrhage; definitive endotherapy or portosystemic shunting can be performed once the patient is stabilized.

Transjugular intrahepatic portocaval shunt

Transjugular intrahepatic portocaval shunt (TIPS) is performed by interventional radiology and creates a channel between the systemic and portal venous systems to divert portal flow into the hepatic vein, thus reducing portal pressure. A guide wire is passed via the internal jugular vein into the right hepatic vein; the wire then passes via a needle through the liver parenchyma into the portal vein. A metal stent is then deployed

across the intrahepatic parenchymal tract to form a shunt between the portal and hepatic veins. Procedure-related complications include pneumothorax, puncture site haematoma or arteriovenous fistula formation, cardiac arrhythmias, haemorrhage, arterial and bile duct injury. Postprocedure complications include hepatic encephalopathy, shunt-related haemolysis and stenosis or occlusion of the shunt. Acute alterations in cardiac output and central venous and pulmonary wedge pressure immediately post-TIPS insertion may result in cardiac failure or pulmonary oedema and patients must be monitored closely for these complications. TIPS is safer for patients with advanced liver disease, avoiding the risks of general anaesthesia and major surgery. A large retrospective study comparing emergency TIPS insertion to oesophageal transection and devascularization showed improved survival with TIPS (42% vs 79%) and recommended this should be the treatment of choice for torrential variceal haemorrhage. Clinicians tend to have a lower threshold for TIPS insertion in gastric variceal haemorrhage: TIPS is recommended after a single episode of rebleeding or in cases where endotherapy is not possible. TIPS achieves haemostasis rates in excess of 90% in patients with uncontrolled gastric variceal haemorrhage. Additional management of acute variceal haemorrhage

- *Antibiotic prophylaxis* – chronic liver disease patients with acute upper gastrointestinal haemorrhage have a high risk of developing serious bacterial infections such as spontaneous bacterial peritonitis (SBP); severe sepsis is associated with early recurrence of variceal bleeding and increased mortality. A meta-analysis of 12 trials evaluating antibiotic prophylaxis in cirrhotic patients with upper gastrointestinal bleeding demonstrated a significant reduction in infection rates, rebleeding and overall mortality. Short-term (7 days) oral norfloxacin or intravenous ceftriaxone is recommended.

- *Sucralfate* – 1g four times daily is given to prevent mucosal ulceration following EVL or sclerotherapy.

- *Measures to prevent encephalopathy* – PSE may be precipitated by gastrointestinal haemorrhage; the management is described later in this chapter.

Prevention of recurrent variceal haemorrhage

Following the index episode of variceal bleeding, the risk of recurrence is 60–80% within 1–2 years with a mortality of 20– 33%. Secondary preventative measures should be commenced prior to discharge from hospital.

Endoscopic therapy

Repeated courses of endotherapy (at weekly intervals) leads to obliteration of oesophageal varices by fibrous tissue, this usually requires two to four sessions. Once eradicated, patients should undergo surveillance endoscopy every 3–6 months to screen for variceal recurrence. Band ligation (EVL) has been shown to be superior to sclerotherapy in the prevention of variceal recurrence; a meta-analysis of seven trials showed reduced rebleeding rates, mortality and complications with EVL. Complications occur in approximately 14% of patients but are relatively minor, with transient dysphagia and chest discomfort occurring most frequently. Ulceration at the site of EVL is common and treatment with sucralfate and/or esomeprazole is recommended to reduce the risk of banding ulceration and bleeding. There is no current evidence to support repeat courses of endotherapy in patients with gastric varices. A single RCT compared histoacryl glue obliteration with propranolol secondary prevention and found no difference in rebleeding or mortality rates; endotherapy was associated with more complications than beta-blockade.

Vasoactive drug therapy

Propranolol monotherapy was compared to placebo secondary prevention in a meta-analysis of 12 trials and shown to significantly lower the risk of rebleeding and reduce mortality. Combined beta-blockade and endotherapy was demonstrated to be superior to EVL alone in two RCTs, with rebleeding rates of 23% and 14%, respectively, for nadolol plus EVL compared with 47% and 38% for EVL alone. A combination of beta-blocker and nitrate has been shown to be superior to beta-blockade monotherapy and of equal efficacy to EVL. In practice, however, few patients are able to tolerate dual pharmacotherapy because of side effects, and the current recommended practice is combined beta-blockade plus EVL for secondary prevention.

Transjugular intrahepatic portocaval shunt

The use of TIPS for secondary prevention is currently reserved for patients in whom endotherapy and/or pharmacological therapy has failed or cannot be tolerated. A meta-analysis of 22 trials comparing portosystemic shunts (TIPS and surgical shunts) with endotherapy demonstrated a reduction in recurrent haemorrhage, but this was at the expense of an increased incidence of chronic encephalopathy with no survival benefit. Standard practice has recently been challenged by researchers in Barcelona who argued that patients with advanced liver disease and high risk of rebleeding would benefit from early TIPS insertion. Patients with Child's C cirrhosis or Child's B disease with active bleeding at endoscopy were randomized to receive standard medical secondary prevention or early TIPS insertion within 72 hours of admission. The early TIPS group showed significantly lower rates of treatment failure, encephalopathy and mortality than

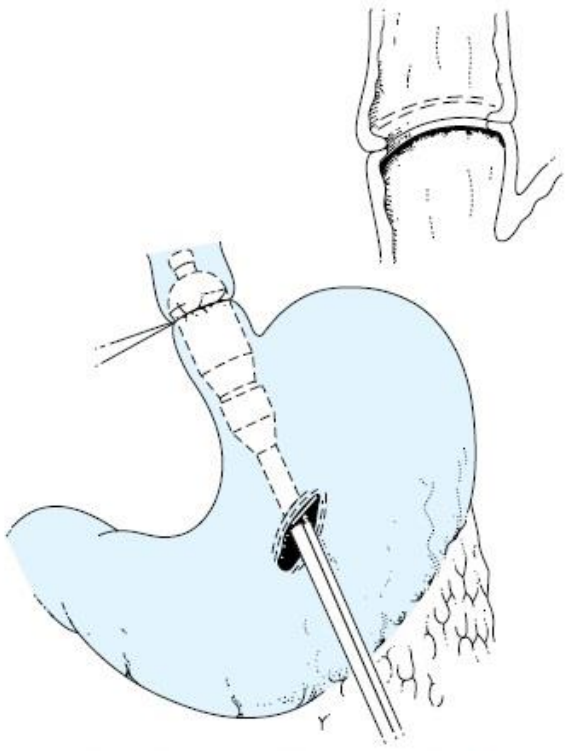
patients managed with EVL and vasoactive drug therapy. Use of more modern polytetrafluoroethylene -covered stents is associated with lower risk of encephalopathy and improved rates in patency and rebleeding. The study is limited, however, by selection bias (e.g. exclusion of patients with Child–Pugh score >13) and low patient numbers.

Primary prophylaxis

All patients with cirrhosis should undergo endoscopic screening to detect varices at the time of diagnosis, and if not present at 3 year intervals thereafter. Beta-blockade is recommended in patients with larger varices or in those with small varices and additional risk factors for haemorrhage (e.g. Child's B/C liver disease, presence of red wale marks on varices). EVL has been shown to be as effective as beta-blockade in primary prophylaxis, but much less cost-effective so is reserved for those intolerant of beta-blockade.

Surgical treatment

More than 85% of patients with bleeding varices can be controlled by non-surgical measures and surgical treatment of refractory variceal bleedings has become even more unusual since the introduction of TIPS and of prophylactic endoscopic sclerotherapy. However patients in whom endoscopic sclerotherapy has failed or the bleeding has recurred early remain problematic. The majority of these patients are high-risk candidates with poor liver function from end-stage liver disease or where liver function has worsened from Child A/B to C as a consequence of the recurrent hypovolaemic episodes. Unless prior information is available on the patient, it is difficult to distinguish between these two categories at the time of emergency presentation. Portosystemic shunting in this group carries a prohibitive mortality and is contraindicated. The aim of surgical management should be to prevent death from exsanguination and not to treat the underlying portal hypertension and therefore an oesophageal transection should be considered instead. This procedure was proposed by Sugiura and Futagawa and consisted of oesophageal transection, extensive oesophagogastric devascularization and splenectomy. Nowadays, the transection and reanastomosis of the oesophagus is performed with a circular stapler



Stapled transection and reanastomosis of the distal oesophagus with a circular stapler (28–31 mm) introduced through a small anterior gastrotomy during a Sugiura procedure. A strong suture is tied around the central axle of the stapler gun before it is closed and fired.

introduced through a service gastrotomy. Some other high-risk patients can be considered for surgical treatment of portal hypertension in an elective setting, such as those in whom variceal bleeding has been temporarily arrested and who have good liver function (Child A/'good' B) but remain at high risk of rebleeding and have had several episodes of sclerotherapy. Elective surgical therapy by portosystemic shunting or oesophageal transection with devascularization may be a sensible, cost-effective and safe management approach. Patients with end-stage liver disease (Child C) who have been definitively controlled by sclerotherapy should be considered for hepatic transplantation. For this reason, surgery should be avoided as it increases the morbidity and mortality of the procedure and TIPSs are more appropriate and successful in achieving portal decompression and thus avoid further bleeding episodes prior to hepatic transplantation. Portosystemic shunts can be total (total deviation of portal blood flow to the systemic circulation), partial (partial deviation of portal blood flow though the placement of a narrow prosthesis in either the portocaval or mesocaval position) and selective (distal splenorenal, coronariocaval, splenocaval). Selective shunt operations are associated with good control of rebleeding and lower rates of encephalopathy but are less successful in controlling acute variceal bleeds. The indications for such an operation are now limited to non-cirrhotic portal hypertension and patients living in areas where newer therapies (TIPS) are not available. The most commonly performed of the selective shunts, and one that still has a role to play nowadays, albeit infrequently, is the distal splenorenal shunt (DSRS or Warren shunt). In this operation, the splenic vein is anastomosed to the left renal vein in an end-to-end fashion with diversion of blood from the cardia via the short gastric veins into the inferior vena cava circulation. The objective is to preserve portal venous flow to the liver and while this is achieved in the postoperative period, it does not seem that it can be maintained in the long term. A multicentre randomized trial of TIPS vs DSRS showed no overall difference in survival and a tendency for TIPS to be more cost-effective in terms of lives saved.

Ascites

Ascites is the commonest complication of hepatic cirrhosis, occurring in 50–60% of patients within 10 years. Ascites is a major cause of hospital admission and its development is an important landmark in the natural history of cirrhosis, being associated with 50% mortality over 2 years. Accumulation of ascites occurs with the development of severe portal hypertension, impaired sodium excretion and water retention. The pathogenesis of ascites has several theories and is not yet fully understood; these have been discussed in great detail in a number of review articles. This chapter will briefly discuss the most accepted mechanisms, the peripheral arterial vasodilatation hypothesis and the forward theory of ascites formation, on which current

treatment recommendations are based. The presence of portal hypertension is essential for the development of ascites; it usually occurs when the wedged hepatic venous portal gradient exceeds 12mmHg but can occur at lower pressures. Portal hypertension disrupts the Starling equilibrium within the splanchnic circulation, resulting in transudation of fluid into the peritoneal cavity.

Peripheral arterial vasodilatation hypothesis

This theory postulates that renal sodium retention occurs as a result of splanchnic arterial vasodilatation secondary to portal hypertension. Nitric oxide is considered to be the putative vasodilator, although other substances (e.g. atrial natriuretic peptide, glucagon calcitonin gene-related peptide and prostaglandins) may also be involved. The reduction in effective arterial blood volume activates the sympathetic nervous system and renin–angiotensin system, thus promoting sodium and water retention. The resultant increase in extracellular fluid volume leads to formation of ascites and oedema. Forward theory of ascites formation According to this theory, splanchnic arterial vasodilatation induces ascites formation by simultaneously impairing the systemic circulation, leading to sodium and water retention, and splanchnic microcirculation, resulting in leakage of fluid into the peritoneal cavity.

Assessment and diagnosis

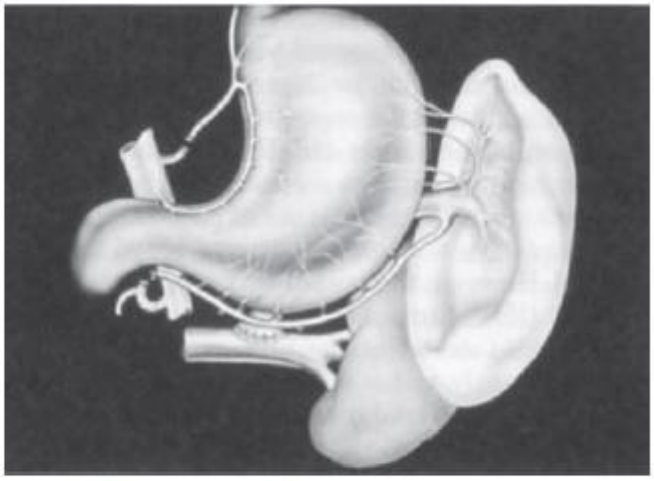
The initial evaluation of the patient presenting with ascites includes a detailed history, physical examination, abdominal ultrasound, laboratory assessment of hepatic and renal function, urine and serum electrolytes and ascitic fluid analysis**.** Diagnostic paracentesis of 10–20mL of fluid should be obtained and the following analyses performed:

- cell count – a neutrophil count >250cells/mm3 is diagnostic of SBP
- Gram stain and culture
- protein and albumin – the serum–ascites albumin gradient (SAAG) helps differentiate ascites due to portal hypertension from ascites due to other causes; a SAAG ≥11g/L is ascribed to portal hypertension with 97% accuracy; total ascitic protein should be measured to assess the risk of SBP, patients with protein <10g/L have a higher infection risk.
- cytology – to assess for malignant cells
- amylase – to exclude pancreatic ascites.

Management

Treatment of ascites aims to restrict dietary salt intake and increase renal sodium excretion; patients with tense ascites will require paracentesis prior to commencement of medical therapy.

Sodium restriction



The Warren distal splenorenal shunt which results in transplenic decompression of the portal circulation.

Negative sodium balance can be achieved by dietary salt restriction alone in 10–20% of patients; in practice it is usually combined with diuretic therapy during initial management. Sodium restriction [2000mg/day (88mmol/day)] is associated with reduced diuretic requirements, more rapid resolution of ascites and shorter hospital stay. Recommended sodium intake for ascitic patients varies between guidelines from 2 to 6.9 g/day; in practice, patients are advised to follow a no added salt diet and to avoid processed foods. This achieves reasonable sodium restriction without impairing nutrition. ***Diuretics*** Spironolactone, an aldosterone antagonist, acts on the distal tubules to promote natriuresis and conserve potassium. It is the drug of choice for the initial management of cirrhotic ascites and is commenced at 100mg daily, increasing to a maximum dose of 400mg. It takes 3–5 days from onset of therapy for the drug to take effect; spironolactone should be increased in 100mg increments every 3 days until adequate natriuresis has been achieved. The aim of diuretic therapy is to increase urinary sodium excretion so that it exceeds 78mmol/day (88mmol intake/day to 10mmol non-urinary excretion/day). A 'spot' urine specimen with sodium concentration more than potassium concentration correlates with a 24-hour sodium excretion greater than 78mmol/day with approximately 90% accuracy. Random testing of the urine sodium–potassium ratio is more convenient than the cumbersome 24-hour collection, and gives an indication of whether diuretic dosage is adequate or requires further titration. Common side effects of spironolactone are hyperkalaemia, renal impairment and those related to the drug's antiandrogenic activity (e.g. reduced libido, gynaecomastia). Amiloride, 10–40mg daily, may be substituted for spironolactone in patients with tender gynaecomastia, but it has been found to be less effective and is more expensive than spironolactone. Furosemide, a loop diuretic, causes marked diuresis and natriuresis in the normal population but has been shown to be less effective in cirrhosis. It is used as an adjunct to spironolactone therapy with initial dosing of 40mg daily, titrating to a maximum 160mg. Higher doses are

associated with electrolyte disturbance and metabolic alkalosis. All patients should be monitored closely in the initial stages of management; overdiuresis may result in volume depletion, renal impairment hyponatraemia or PSE. Spironolactone monotherapy is useful in patients with minimal fluid overload who can be managed in the outpatient setting. Combination therapy is recommended for patients with more marked fluid retention, resulting in faster fluid mobilization and maintenance of normokalaemia.

Refractory ascites

Refractory ascites occurs in patients who fail to respond to sodium restriction and diuretics (diuretic-resistant ascites) or in those who develop complications which preclude the use of effective doses of diuretics (diuretic-intractable ascites). The prognosis is poor in such patients and, if appropriate, referral for liver transplantation should be considered. Other treatment options include paracentesis and portosystemic shunts.

Paracentesis

Patients with refractory ascites are initially managed by serial large volume paracentesis (LVP); total paracentesis is generally safer than repeated smaller aspirations. Volume expansion is given alongside paracentesis to avoid postprocedure circulatory dysfunction, renal impairment and electrolyte disturbance. Several studies have demonstrated the safety and effectiveness of LVP with volume expansion; administration of 8g albumin/L ascites removed (100mL 20% albumin/3 L ascites) is recommended.

Transjugular intrahepatic portocaval shunt

TIPS insertion should be considered in patients in whom frequent LVPs are required; prospective RCTs have shown TIPS to be more effective in controlling ascites than LVP, but there is no difference in survival. Hepatic encephalopathy occurs following TIPS insertion in 25% of patients, with a higher risk in patients over 60. It may precipitate pulmonary oedema and cardiac failure in patients with pre-existing heart disease because of increased cardiac preload. Outcomes are poorer in patients with advanced (Child's C liver disease), and TIPS is not recommended in this group. It is also advisable to avoid TIPS in patients with recurrent hepatic encephalopathy, concomitant infection, progressive renal failure or severe cardiopulmonary disease.

Spontaneous bacterial peritonitis

SBP is a monomicrobial infection of ascites occurring in 10–30% of hospitalized patients with cirrhosis. It is a serious complication of ascites with a mortality rate of 20%, despite improvements in early diagnosis and prompt treatment. Patients with SBP are frequently

asymptomatic; therefore, diagnostic paracentesis is mandatory in all patients presenting to hospital with ascites and in those with worsening decompensation. *Escherichia coli*, Gram-positive cocci (mainly streptococci) and enterococci are the most commonly isolated organisms, accounting for 70% of cases of SBP. Intravenous cefotaxime covers 95% of the flora commonly isolated in SBP and achieves high penetrance of ascitic fluid during therapy. Empirical treatment with cefotaxime is recommended in all patients with ascitic neutrophil count >250cells/mm3 until results from culture and antibiotic sensitivity testing are available. Patients with a negative cell count should receive antibiotic prophylaxis, norfloxacin 400 mg daily, while in hospital.

Hepatorenal syndrome

Hepatorenal syndrome (HRS) is defined as the occurrence of renal failure in patients with advanced liver disease in the absence of an identifiable cause of renal impairment (e.g. hypovolaemia, nephrotoxic drugs). HRS is a functional renal impairment resulting from renal hypoperfusion, the pathophysiology is similar to that producing ascites. There are two types:

• type 1 HRS – characterized by a rapid and progressive impairment in renal function (increase in serum creatinine ≥100% from baseline to >221mmol/L within 2 weeks)

• type 2 HRS – occurs in patients with refractory ascites, characterized by a stable or less progressive impairment in renal function. Type 1 HRS commonly affects patients with severe alcoholic hepatitis or those with end-stage liver disease following an episode of sepsis such as SBP. Development of type 1 HRS has an extremely poor prognosis with 80% mortality within 2 weeks; management involves plasma volume expansion with albumin and vasoconstrictor therapy. Liver transplantation should be considered in all patients with HRS, as post liver transplantation survival is approximately 65% for patients with type 1; optimization of renal function preoperatively improves outcomes after liver transplantation. Terlipressin and albumin therapy has been shown to improve renal function in 50–60% of patients; however, studies to date show no improvement in long-term survival without liver transplantation. TIPS may offer an alternative to pharmacological therapy but there are insufficient data to support this at present; haemodialysis is currently reserved for patients awaiting transplantation who have failed to respond to medical therapy.

Hepatic abscesses

Abscesses of the liver are less common in temperate than in tropical regions. There are also differences in the underlying aetiology between the two regions. There are two types: pyogenic and amoebic.

Pyogenic abscesses

Pathogenesis

The incidence of pyogenic liver abscess has remained relatively constant over the past century despite earlier diagnosis and treatment of underlying causes and more aggressive antibiotic therapies. In recent years, the decrease in cases resulting from haematogenous spread from infected foci has been mirrored by an increase in cases secondary to hepatobiliary pathology. The main aetiological factor is bile duct infection with ascending cholangitis commonly due to *E. coli* and anaerobic Gram-negative organisms. In the UK, biliary sepsis will be the predisposing factor in almost half of the patients reviewed. Hepatic abscesses secondary to ascending cholangitis are often multiple due to the distribution of the infecting organism along the biliary ductal system. Early reports implicated choledocholithiasis as the main causative factor; however, more recent series document malignant biliary obstruction as a more common aetiological factor. Other sources of infection include the following:

- Ascending pylephlebitis. While any inflammatory process within the abdomen may initiate pylephlebitis, it is most commonly the result of complicated diverticulitis.

- Some hepatic abscesses of staphylococcal and streptococcal origin arise as a complication of bacteraemia (haematogenous).

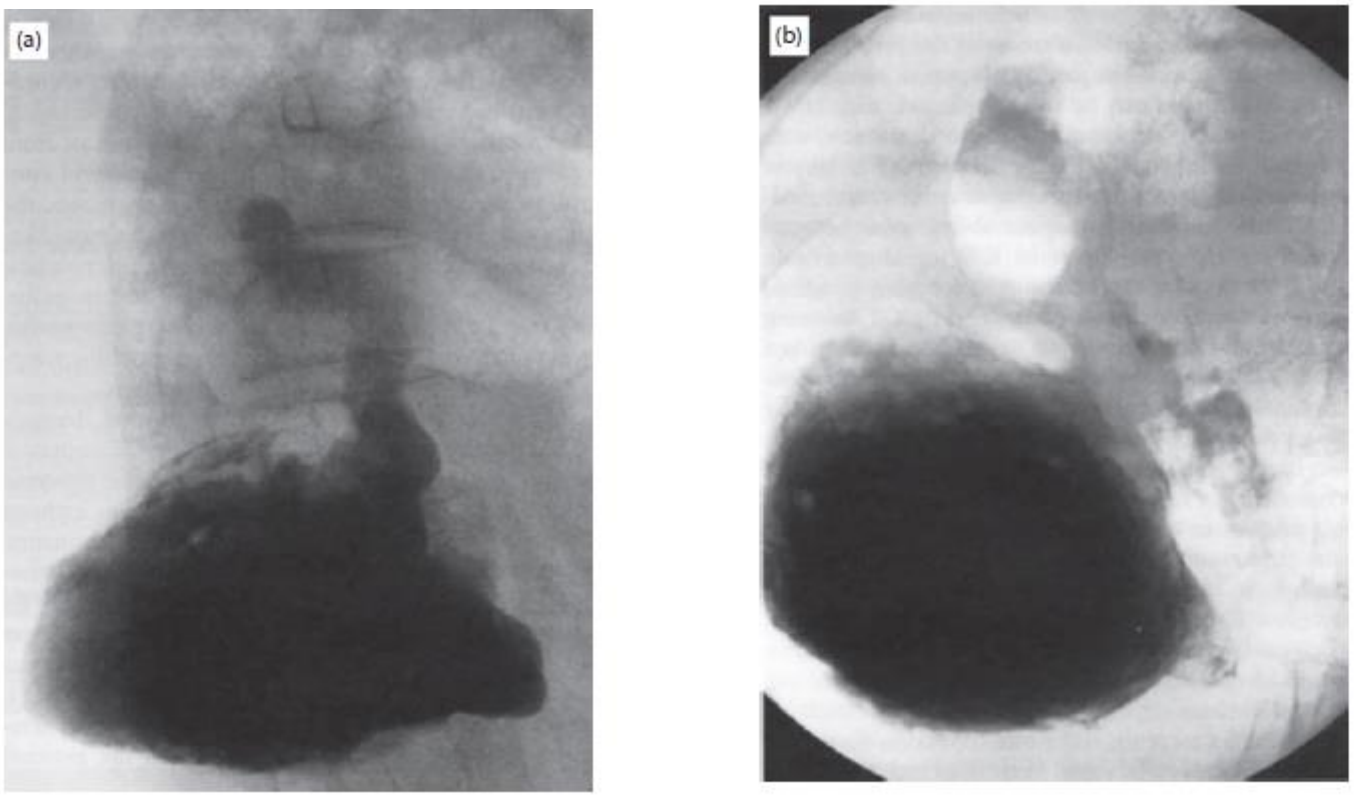
- Direct extension from intra-abdominal suppuration, e.g. gangrenous cholecystitis, penetrating peptic ulcer disease and subphrenic collections.

- Trauma to the liver, both penetrating and non-penetrating, may devitalize liver tissue and subsequent infection produces an abscess.

- A significant group of patients are found in the elderly population. No obvious cause is found in many of these patients (cryptogenic). These often have an insidious onset and non-specific symptoms such that, at the time of diagnosis, the abscess is usually very large. In some cases, the chronic abscess erodes through the diaphragm and bursts into the bronchial tree presenting with chest symptom. The infecting organisms for these abscesses are commonly the *Peptostreptococcus* and *Streptococcus milleri*, but other microbes including *Bacteroides fragilis* may be involved.

- Parasitic infestations – *Ascaris lumbricoides.*

- Tuberculous liver abscesses.



Contrast study showing a fistula between the right hepatic abscess and right basal bronchial tree in an elderly patient initially treated with percutaneous drainage.

• HIV infection – cholangitis/cholangiopathy. HIV infection is now one of the risk factors, and abscesses due to meticillin-resistant *Staphylococcus aureus* appear to be on the increase. The infection is polymicrobial in 45%. *E. coli* and *S. milleri* are the most frequently isolated organisms. In endemic areas of *Ascaris lumbricoides* infestations, e.g. Kashmir, India, up to 15% of pyogenic hepatic abscesses are associated with this infestation. Cholangitis/cholangiopathy associated with HIV infection is characterized by chronic abdominal pain, low-grade fever, cholestasis, and sometimes areas of focal or diffuse dilatation of the bile ducts. The disease appears to be the result of immunosuppression and/or secondary opportunistic infections rather than a direct cytopathic effect of the virus itself. Various opportunistic pathogens, including cytomegalovirus, *Cryptosporidium, Campylobacter fetus* and *Candida albicans*, have been implicated in the aetiology of HIV-associated cholangitis. Pylephlebitis usually occurs secondary to infection in the region drained by the portal venous system, the most common being diverticulitis and appendicitis. Infection is caused by *E. coli* in 54%, followed by *Proteus mirabilis* (23%). The pylephlebitis induces a septic thrombosis of the portal vein and its branches, with multiple microabscess formation in the liver (honeycomb liver). Early recognition of the disease and timely antibiotic therapy are essential for survival. The overall reported mortality is 32%. Irrespective of aetiology, liver abscesses are found much more commonly in the right lobe. All abscesses contain areas of liver parenchymal cell necrosis surrounded by polymorphonuclear leucocytes and lymphocyte infiltration with relatively damaged

parenchyma and viable bacteria on the periphery. Ultimately a fibrous reaction is initiated which may produce a fibrous capsule containing pus.

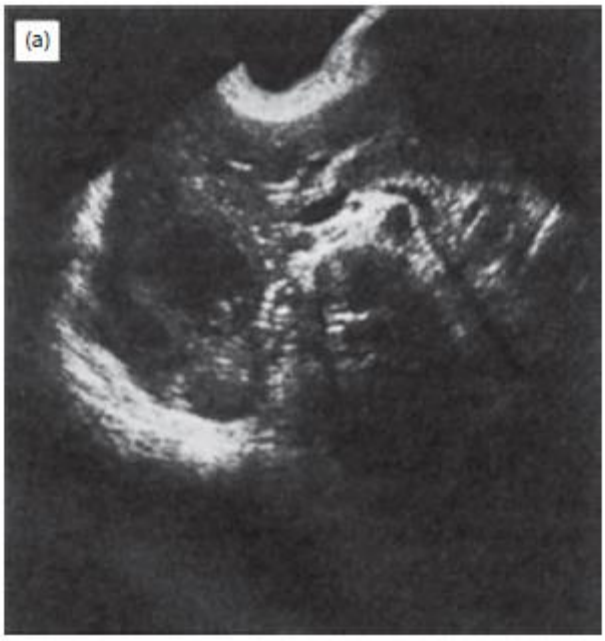
Clinical features of hepatic abscesses

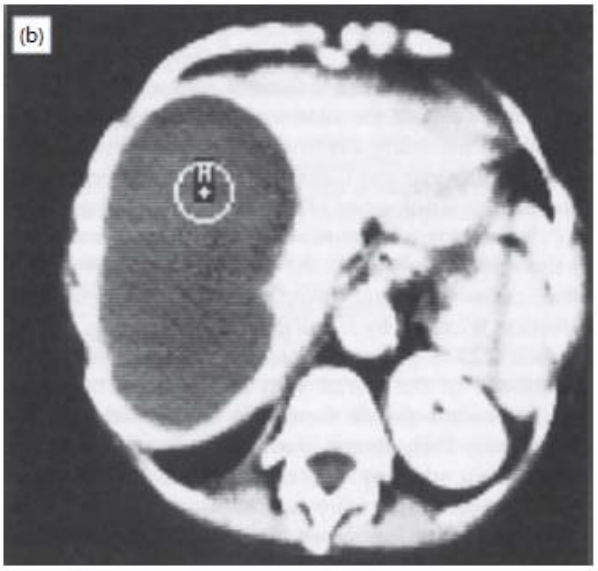
Untreated pyogenic liver abscesses carry a high mortality and 10% are diagnosed only at postmortem. The important determinants of mortality are multiple abscesses, hyperbilirubinaemia and comorbid disease. Since most pyogenic abscesses are secondary to other infective processes, the clinical features may be dominated by the primary disorder. Characteristically there is a high fever, rigors, profuse sweating, anorexia and vomiting, with pain as a relatively late symptom. In elderly people pyogenic liver abscess is commoner in women, and the symptoms may be vague. Thus the patients may have minimal abdominal tenderness on physical examination. The clinical features are also less striking in hepatic amoebiasis where the fever is usually low grade. However, pain is a more common feature with amoebic abscess and is aggravated by movement and coughing. An amoebic abscess may reach a very large size before causing pain if situated posteriorly and pointing to the bare area of the liver. About half the patients with amoebic abscesses will have diarrhoea. Hepatomegaly is common, particularly with amoebiasis. Occasionally with right lobe abscesses there is bulging and pitting oedema of the intercostal spaces. An abscess in the left lobe may present as a painful epigastric swelling. On investigation, anaemia and leucocytosis may be found, and raised levels of acute phase proteins. Disturbances of LFTs are not diagnostic, particularly when complicated by cholangitis, and may be absent in amoebiasis. Blood cultures are usually positive in patients with pyogenic abscesses when taken during the height of pyrexia. Both aerobic and anaerobic cultures are needed. Clinical suspicion of hepatic abscess must be confirmed by ultrasonography or CT scanning. The highest diagnostic yield for both pyogenic and amoebic liver abscess (ALA) is obtained by CT scanning with contrast enhancement. Magnetic resonance cholangiography should be undertaken in patients with biliary symptoms, obstructive LFTs or a dilated common bile duct, and can be combined with cross-sectional MRI to identify any hepatitic parenchymal abnormality. Diagnostic aspiration is a safe and reliable procedure and provides means of identification of the organisms responsible and thus the appropriate antibiotic therapy. Chest radiography is necessary in all cases to outline basal lung changes (consolidation and effusion) and may show direct lung involvement in complicated cases. An elevated immobile diaphragm (radiological screening or ultrasonography) is often encountered, particularly in large abscesses. A plain film of the abdomen may demonstrate gas in the abscess cavity. Barium enema or colonoscopy may be indicated to exclude a colonic source of portal pyaemia.

Complications

Recurrent bacteraemia is the most common complication of pyogenic abscesses. Extension and rupture of the abscess may occur in any direction. Peritoneal rupture results in widespread peritonitis or in the formation of a subphrenic collection. Extension through the diaphragm may lead to thoracic empyema or to a rupture into the bronchus with expectoration of large volumes of 'anchovy paste' pus from amoebic abscesses and bile-stained pus from cholangitic abscesses. Rarely, the abscess ruptures into the pericardium with high mortality.

Treatment



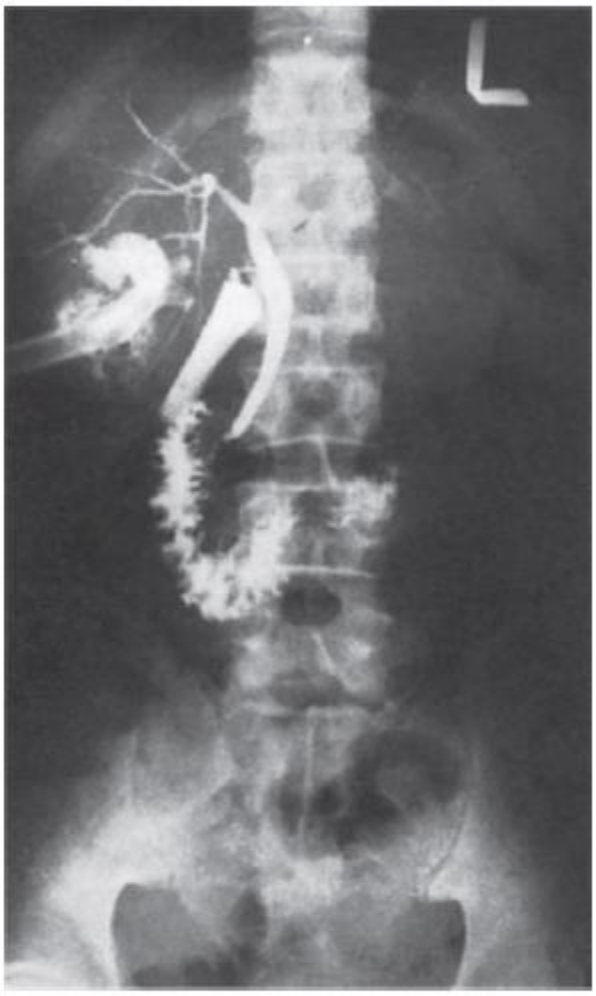


(a) An ultrasound of the liver on coronal section shows a cavity within the liver substance. (b) CT scan demonstrates that the abscess cavity occupies most of the right lobe of the liver. Subsequent drainage of the cavity resulted in complete resolution.

The key to successful management is drainage of the purulent collection combined with appropriate antibiotic therapy. Precise microbiological identification may result from blood cultures or from aspiration of the abscess cavity under ultrasound or CT guidance. In the event of a failure to isolate organisms, the choice of antibiotic should be based on the most likely aetiological factor, i.e. cholangitic and pylephlebitic abscesses are usually infected with *E. coli* and anaerobes and may be appropriately treated with cephalosporins, gentamicin and metronidazole. Microaerophilic *Streptococcus* infections are sensitive to penicillin. Although antibiotic therapy as the sole treatment is rarely successful, prolonged systemic antibiotic administration may be the only option for patients with multiple microabscesses. The introduction and refinement of percutaneous drainage techniques have dramatically altered the management of patients with pyogenic hepatic abscesses. Percutaneous drainage has become the first-line therapeutic option in most centres for patients with single or multiple abscesses. Abscess communication with the intrahepatic biliary tree

does not prevent pyogenic collections being successfully treated by percutaneous techniques, although the periods of drainage may be prolonged. Some groups have advocated the use of percutaneous aspiration combined with systemic antibiotics; however, in the only randomized trial comparing the two techniques, aspiration was successful in only 60% of patients whereas percutaneous catheter drainage was successful in 100% of patients. Regular irrigation of drainage catheters reduces the risk of catheter blockage with necrotic debris. Percutaneous catheter drainage is monitored by serial ultrasound examination to assess the degree of resolution. As the most frequent cause of hepatic abscess is biliary disease, effective decompression of the biliary tree is as important as abscess drainage where obstruction of the bile duct has contributed to the development of the hepatic abscess. The factors indicating failure of initial non-operative management are:

- unresolving jaundice
- renal impairment secondary to clinical deterioration
- multiloculation of the abscess
- rupture on presentation
- biliary communication. Deterioration in the general condition of the patient, repeated episodes of septicaemia or a failure of the abscess to decrease in size are indications for open surgical drainage. Posteriorly placed abscesses may be approached by the retroperitoneal route through the bed of the twelfth rib. Larger abscesses require abdominal drainage with wide-bore sump drains and special care being taken to avoid contamination of the peritoneal cavity. Where a pyogenic abscess is secondary to cholangitis, concomitant drainage of the common bile duct with a T-tube and removal of ductal stones may be necessary. Following successful



Right hepatic abscess communicating with the intrahepatic biliary tree.

drainage of the abscess, antibiotic administration should be continued for a prolonged period (3–6 weeks) to assist in the complete eradication of the infection.

Jaundice

Bilirubin is produced in the reticuloendothelial system from the enzymic breakdown of haem, which is derived from effete red blood corpuscles. As it is water insoluble, bilirubin is carried bound to albumin in the plasma and is taken up by the hepatocytes by means of specific membrane carriers. Within the hepatocytes, the bilirubin is stored bound to specific binding proteins (ligandins Y, Z) and then conjugated by a specific enzyme (glucuronyl transferase) to the watersoluble bilirubin glucuronide (conjugated bilirubin) that is then secreted by means of specific carriers into the bile canaliculi, and finally excreted into the biliary tract and intestine. Bacterial degradation of some of the excreted conjugated bilirubin in the distal small bowel results in the formation of urobilinogen, which is reabsorbed and subsequently excreted in the urine and bile. The normal upper limit of serum bilirubin is 17mol/L. Jaundice (hyperbilirubinaemia) is a syndrome of varied aetiology which may be recognized clinically when the serum bilirubin exceeds 40mol/L. The hyperbilirubinaemia may be either conjugated or unconjugated and may result from:

- excess bilirubin production
- impaired uptake by the hepatocyte
- failure of conjugation
- impaired secretion of conjugated bilirubin into the bile canaliculi
- impairment of bile flow subsequent to the secretion by the hepatocytes – *cholestatic or obstructive jaundice.* The defect may be congenital (benign congenital hyperbilirubinaemias) but much more commonly it is acquired as a result of haemolysis, liver disease, adverse drug reaction and biliary tract obstruction which may be intra- or extrahepatic. The early diagnosis and prompt treatment of patients with jaundice reduces both the morbidity and mortality of the underlying disease. In clinical practice, the largest groups by far are those with hepatocellular and cholestatic jaundice**.**

Hepatocellular jaundice

This is due to parenchymatous liver disease which may be acute (viral hepatitis, liver cell necrosis, acute alcoholic hepatitis, etc.) or chronic (chronic active hepatitis, the various types of cirrhosis, primary biliary, etc.). The principal defect is the failure of secretion of

the conjugated bilirubin into the bile canaliculi. The serum transaminases are grossly elevated especially in acute disease. In patients with alcohol-related liver disease, the γ-glutamyl transpeptidase (γ-GT) is elevated as a result of microsomal induction rather than cholestasis. Acute hepatitis due to viral infection or drugs may also cause a cholestatic picture, in which case the alkaline phosphatase and 5-nucleotidase are elevated. The hyperbilirubinaemia is always (predominantly) of the conjugated variety with the presence of bilirubin in the urine even in the absence of a cholestatic component.

Cholestatic jaundice

This is the result of impaired bile flow to the duodenum subsequent to the secretion of conjugated bilirubin into the bile canaliculi—The block may be intrahepatic when it may be functional (e.g. drugs, hepatitis) or organic (obstruction of theB€intrahepatic biliary tree) or extrahepatic, also known as large bile duct obstruction which constitutes the most important surgical subgroup of cholestatic jaundice as it is always the result of organic disease, e.g. ductal calculi, pancreaticobiliary cancer, etc. The biochemical features of cholestasis are:

• conjugated hyperbilirubinaemia

• elevation of alkaline phosphatase, 5'-nucleotidase and γ-GT; the enzyme 5'-nucleotidase is the most reliable since its level is not influenced by bone disease and the enzyme is not induced by alcohol

• minimal or no elevation of the serum transaminases

• presence of bilirubin in the urine as the conjugated bilirubin is water soluble and is therefore filtered in the glomerulus

• elevation in the serum cholesterol and bile acid levels although these are not routinely measured in patients with cholestatic jaundice. It is important to stress that the above biochemical markers of cholestasis do not distinguish between intra- and extrahepatic obstruction.

Haemolytic jaundice

The unconjugated hyperbilirubinaemia results from excess haemolysis. Bilirubin is not present in the urine as the unconjugated pigment is water insoluble and is carried in the plasma bound to albumin. The excess bilirubin production is accompanied by an increased secretion of the conjugated pigment in the bile and therefore increased

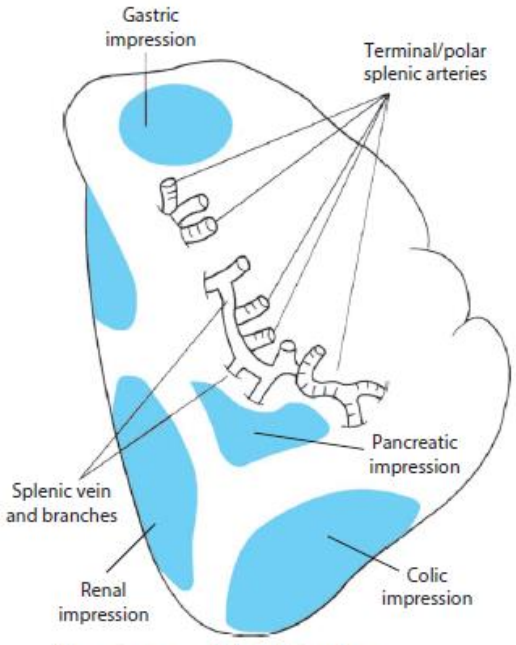
production of urobilinogen by bacterial decomposition in the distal small intestine. The urine, therefore, contains an excess amount of urobilinogen and urobilin. A cholestatic component may develop in patients with prolonged and recurrent haemolysis (e.g. congenital haemolytic anaemias). In some patients excess bilirubin production is present in the absence of overt haemolysis. The excess unconjugated bilirubin is thought to result from breakdown of precursor/ immature red cells in the bone marrow. This form of benign non-familial congenital hyperbilirubinaemia is referred to as *shunt hyperbilirubinaemia.* Benign familial congenital hyperbilirubinaemias This group includes Gilbert disease, Dubin–Johnson syndrome and the Rotor syndrome. All three conditions are congenital and familial. Gilbert disease is due to a defect in the uptake of bilirubin by the hepatocytes and results in mild unconjugated hyperbilirubinaemia. Both the Dubin–Johnson and Rotor syndromes are caused by a secretory defect of conjugated bilirubin by the hepatocytes into the bile canaliculi and therefore lead to a conjugated hyperbilirubinaemia. In addition, patients with the Dubin–Johnson syndrome are unable to excrete contrast medium into the biliary tree and, for this reason, the gallbladder is not visualized by oral cholecystography and intravenous cholangiography. Despite the accumulation of conjugated bilirubin in the blood and its appearance in the urine, there are no other biochemical markers of cholestasis in both conditions.

Anatomy of the adult spleen

The spleen is normally situated in the left upper quadrant tucked under and against the left dome of the diaphragm and overlaid by the lower ninth to eleventh left ribs such that it is impalpable and has to enlarge two to three times before it becomes palpable on examination. It is overlapped anteriorly by the fundus of the stomach with its long axis lying along the line of the tenth rib. The adult spleen has an anterior and posterior extremity (referred to as superior and inferior poles respectively), superior and inferior border and a visceral and diaphragmatic surface. The visceral surface is intimately related to four abdominal organs: stomach (gastric impression), tail of the pancreas, left kidney (renal impression) and the splenic flexure (colic impression). The gastric impression is directly related to the posterior wall of the stomach from which it is separated by the lesser sac. The spleen is intimately related to the tail of the pancreas as this lies in the lienorenal ligament and is liable to injury unless care is taken during splenectomy. Although usually located in the left hypochondrium, abnormal locations are well documented, including the retrorenal space, pelvis and even the scrotum. The normal dimensions of the spleen are 13cm in length (distance between the superior and inferior pole), with a range 9–16cm, breadth (distance from the anterior to posterior border) of 9cm with a range of 6–11cm, and width (distance between the diaphragmatic to the visceral surface at the widest point) of 3cm. Hence size varies considerably between

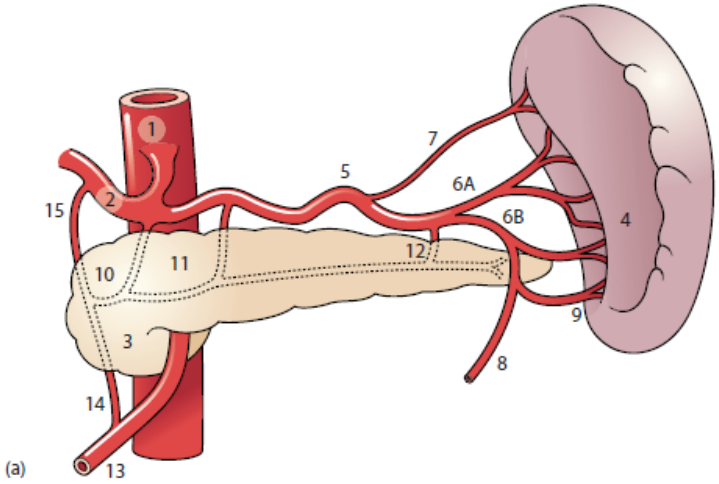
healthy adult individuals. Three distinct morphological types of the human adult spleen are recognized: crescentic, triangular and rhomboid; however, the shape can change with enlargement of the organ by disease. Crescentic spleen refers to organs with regular hila extending from prominent superior to inferior poles. Triangular spleens consist of organs with three borders (anterior, posterosuperior and posteroinferior) and three poles (superior, inferior and posterior). In rhomboid spleens, the poles are expanded into borders, particularly the inferior pole, producing an organ with four unequal sides. The spleen is attached to the diaphragm and retroperitoneal organs by a fascia and peritoneal folds: splenocolic, diaphragmatic and lienorenal. The attachment to the fundus of the stomach is via the gastrosplenic section of the greater omentum that contains the short gastric vessels. Especially in obese subjects, the spleen is often covered with greater omentum, which indeed may be adherent to the surface of the organ. The splenic substance consists of red pulp (80%) made up of sinuses and sinusoids and cellular cords containing macrophages and white pulp consisting of lymphoid tissue (20%). The red pulp is concerned with maturation and the removal of damaged and senescent red cells, whereas the white pulp forms a major component of the cellular immune surveillance and protection of the body.

Splenic vasculature and segmentation

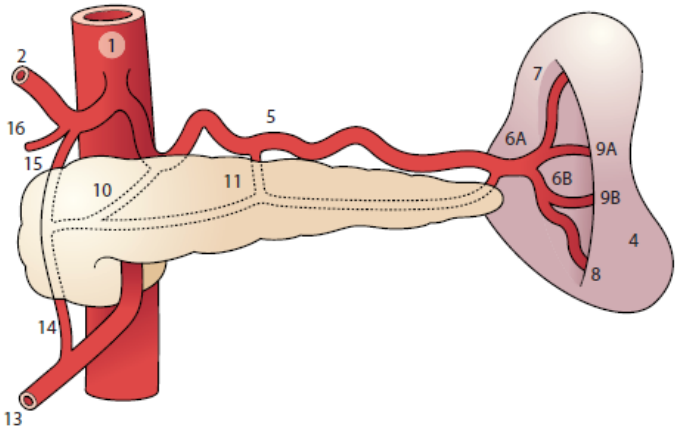


Visceral surface and hilum of the spleen.

The main arterial supply is from the common splenic artery (origin from the coeliac axis) which is tortuous and runs along the upper border of the pancreas and is anatomically divisible into four segments: suprapancreatic (longest segment), pancreatic (looped or coiled segment lying in a groove on the superior border of pancreas), prepancreatic (commonest site of division of the splenic artery particularly with the distributed vascular pattern) and prehilar segment (lies between the tail of the pancreas and splenic hilum). The surgically significant morphological distinction in the blood supply to the spleen is between ‘compact’ (magisteral) and ‘diffuse (distributed)’ as this determines the nature of the terminal branching of the splenic artery. The division of the common splenic artery into its two terminal arteries (superior and inferior) occurs at a variable distance from the spleen. The two terminal arteries give off the segmental arteries to the spleen. The central segmental arteries always arise from the two terminal arteries, but the segmental



1 Aorta
2 Hepatic artery
3 Pancreas
4 Spleen (diffuse, multi-notched)
5 Common splenic artery
6 A Superior and
B Inferior splenic arteries
7 Superior polar artery
8 Left gastro-epiploic artery
9 Inferior polar artery
10 Dorsal pancreatic artery
11 Arteria pancreatica magna
12 Arteria caudis pancreatica
13 Superior mesenteric artery
14 Inferior pancreatic-duodenal artery
15 Superior pancreatic-duodenal artery



(b)

1 Aorta
2 Hepatic artery
3 Pancreas
4 Spleen (compact)
5 Common splenic artery
6 A Superior and
B Inferior splenic arteries
7 Superior polar artery
8 Inferior polar artery
9 A/B Central segmental vessels
10 Dorsal pancreatic artery
11 Arteria pancreatica magna
12 Arteria caudis pancreatica
13 Superior mesenteric artery
14 Inferior pancreatic-duodenal artery
15 Superior pancreatic-duodenal artery
16 Gastroduodenal artery

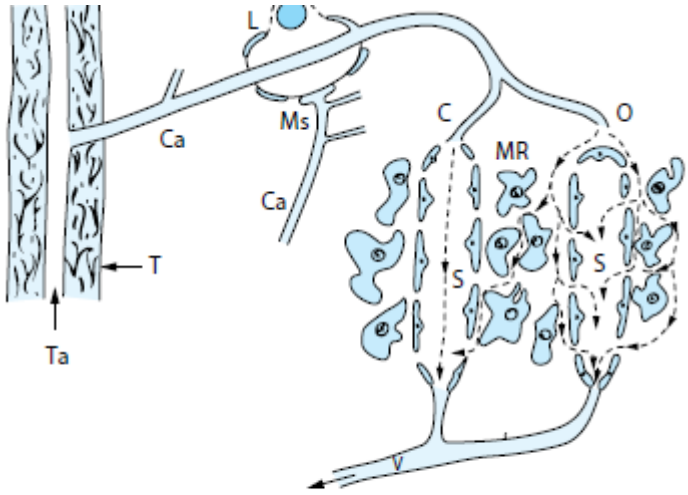
(a) Splenic artery blood supply to the pancreas and spleen (distributed type). (b) Splenic artery blood supply to the pancreas and spleen (magisteral type).

arteries to the poles of the spleen (polar) have very variable origin (directly from the common splenic artery, from the terminal arteries and, in the case of the lower polar artery, from the gastroepiploic artery). The segmental vasculature nature of the spleen is important in relation to partial splenectomy and to splenic preservation. The splenic segments, which are separated by avascular planes, are usually four in number: two central and two polar. The venous drainage mirrors the arterial supply with the splenic vein joining the superior mesenteric vein behind the neck of the pancreas to form the portal vein. The spleen also drains through the short gastric veins and these assume

importance in two situations. In the first instance, they become varicose and lead to gastric varices when there is splenic vein thrombosis. Second, they provide the basis of transsplenic decompression of oesophageal varices by the distal splenorenal shunt (DSRS) of Warren. The microcirculation of the spleen is unique and has two systems: closed and open circulation.

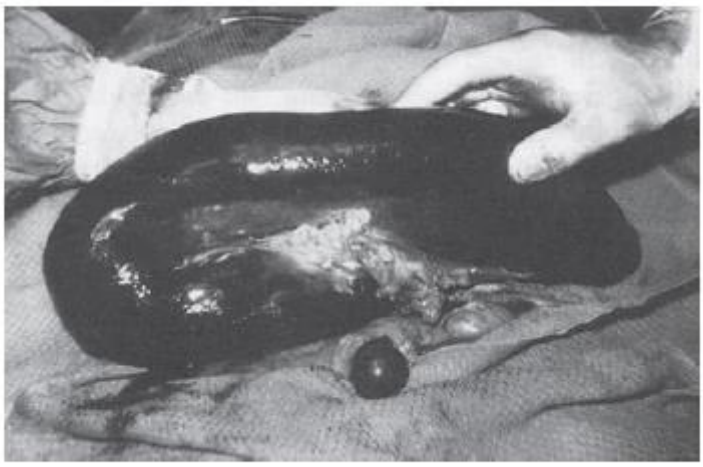
Segmentation

The splenic segments are anatomically distinct areas of splenic tissue, identified by corrosion casting and numbering 3–7 with a mean of 4, which extend from the anterior to posterior borders perpendicular to the long axis of the spleen. Each segment has its own arterial and venous territory, but two morphological types are recognized: central and polar, with the central segments being wedge-shaped and larger than the polar segments. The polar segments are pyramidal and located at either end of the spleen. The individual splenic segments are separated by a relatively avascular plane and are important in conservative splenic surgery. Accessory spleens These are also known as splenunculi and are present in 10% of adults. They can be multiple but rarely exceed 10 and most are situated near the hilum (tail of the pancreas, gastrosplenic ligament, lienorenal ligament and greater omentum). However, they can be located in other sites including the omentum along the greater curvature of the stomach, the mesenteries of the small and large intestine, the broad ligament of the uterus and the pouch of Douglas. They have even been reported in the left testis. The various sites for accessory spleens are grouped as follows:



Splenic microcirculation: T, trabeculum; Ta, trabecular artery; Ca, central artery; L, lymphoid tissue; Ms, marginal sinus; C, closed circulation; O, open circulation; MR, macrophages and reticulum of red pulp; S, sinus; v, collecting vein.

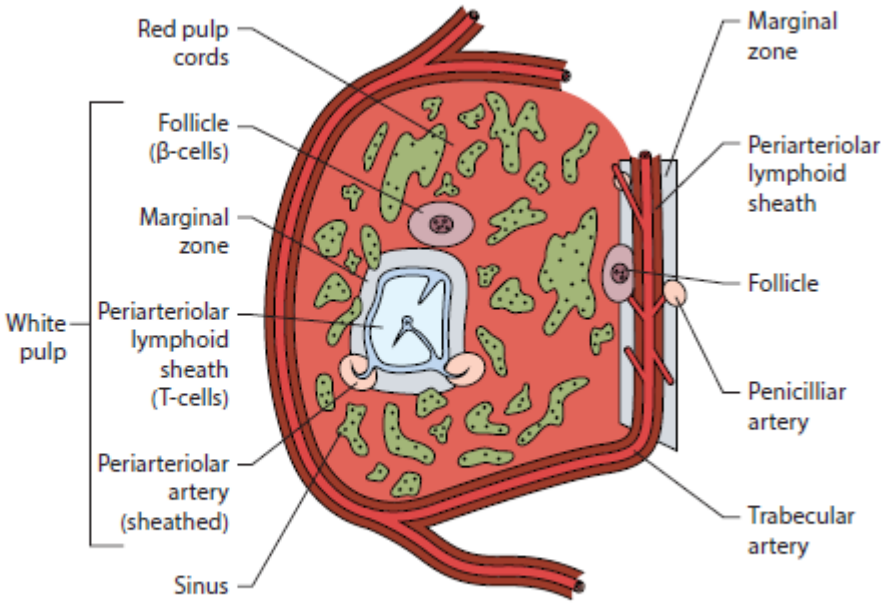
- perisplenic area: hilum, splenic vascular pedicle, tail of pancreas
- greater omentum: along the greater curvature of the stomach



Accessory spleen during open splenectomy.

• mesenteries: small and large bowel

• pelvis/groin: left broad ligament, pouch of Douglas, left testis. There is some evidence that accessory spleens decline in frequency with advancing years presumably secondary to atrophy, and are thus rare in elderly people. Accessory spleens probably result from failure or incorporation of subsegments during embryological development. They have an organized splenic architecture and separate arterial supply, usually from the inferior polar artery. Accessory spleens are important during splenectomy for haematological conditions such as immune thrombocytopenic purpura, for if left behind they may hypertrophy and cause recurrence of the disease. There is some evidence that accessory spleens are less easily identified during laparoscopic splenectomy. The spleen is covered by a capsule which consists of two layers, an external serosal and an internal fibroelastic coat, which extend as trabeculae of mainly fibrous tissue containing some muscle cells. The trabeculae blend with a reticular internal framework forming the stroma of the organ. The splenic pulp is composed of two distinct tissues: the *red pulp*, which occupies 80% and is concerned with elimination of effete red cells, and the white pulp, containing lymphoid tissue and accounting for the remaining 20%. A schematic diagram of the of the red and white pulp of the spleen is shown below:



Histological appearance of the red and white pulp of the spleen. (Adapted from Buckley.)

The spleen together with lymph nodes, tonsils, Peyer's patches, etc., constitute the secondary lymphoid organs of the body as distinct from the primary lymphoid organs (thymus and bone marrow) which are the site of lymphopoiesis. Lymphocytes and antigen-presenting cells are found in all the secondary lymphoid organs.

Cellular components of the spleen

Tissue	Cell type
Red pulp	
Cords	Macrophages
	Reticular cells
Sinuses	Lymphocytes
	Interendothelial cells
White pulp	
Periarteriolar lymphoid sheaths	T lymphocytes (central)
	B lymphocytes (peripheral)
Follicles	Dendritic cells
	Tingible body
	Macrophages
	B lymphocytes
Marginal zone	B lymphocytes
	Marginal zone macrophages

Hypersplenism

Hypersplenism is a syndrome of splenomegaly combined with decreased amounts of one or more circulating blood elements:

- anaemia – in patients with diseased bone marrow
- leucopenia <4–5000/mm3
- thrombocytopenia <100000/mm3.

Early on, hypersplenism was used to describe the essentially normal function of the spleen in destroying the abnormal cells of hereditary spherocytosis. Damashek broadened this definition to include *all conditions of splenomegaly with decreased numbers of one or more of the blood elements.* Although he postulated that the spleen was active in the control of haemopoiesis via humoral mechanisms, this has no current scientific basis. Some distinguish between primary (due to haematological disease) and secondary (e.g. liver disease with portal hypertension) hypersplenism. Work hypertrophy of the spleen occurs when the spleen enlarges due to the constant exposure of the spleen's phagocytic machinery to abnormal cells. This is distinctly different from splenomegaly, where destruction of normal blood elements occurs because of a *primary lymphoreticular* process. The term primary hypersplenism is usually reserved for this latter group of disorders as distinct from hyperactivity following splenic enlargement from other causes, e.g. liver disease – *secondary hypersplenism.* In hypersplenism states, the bone marrow is unable to maintain normal numbers of circulating cells or platelets, and splenic enlargement signals the site of destruction. Splenectomy is potentially curative of the cytopenias that occur in hypersplenic states but there are other alternatives (see below). The exact cause of the cytopenia that

occurs with splenic enlargement is a matter of some speculation. The pooling of blood cells is probably the most important mechanism. With increasing splenic size, up to 50% of the total red cell mass may reside in the spleen. This effectively sequesters red cells in a location 'outside' the circulation. The amount of this isolation of red cells can be estimated by measuring peripheral venous haematocrit and comparing that with the red cell volume obtained by isotope dilution techniques. In a similar fashion, platelets are abnormally sequestered in states of splenomegaly. Approximately 10% of circulating platelets are contained within the spleen in the healthy state. With significant splenomegaly and pooling of blood elements, up to 90% of the circulating platelets are trapped within the spleen. The same can occur with circulating granulocytes and lymphocytes. The overall effect of such congestive splenomegaly is a dynamic balance between the trapping of blood elements and the ability of the bone marrow to compensate. In disorders with a diminished bone marrow reserve, such as myelosclerosis or chronic myeloid leukaemia, severe anaemia, thrombocytopenia and/or neutropenia may result. If the marrow is healthy or minimally diseased, the peripheral smear may be quite normal. Hypervolaemia is also a feature of splenomegaly. Where red cell production is limited, the expanded blood volume is mainly plasma volume, with a resultant dilutional anaemia that can compound the destructive anaemia. It is thought that a hyperkinetic portal circulation from an increased splenic blood flow somehow causes an expansion of the splanchnic blood volume. The exact mechanism is far from clear, however. Because of the expanded circulating volume, transfusion in an attempt to restore appropriate numbers of cellular elements can easily cause circulatory overload.

Destruction of blood cells by the spleen

In addition to pooling and trapping within the spleen, the survival of red cells is probably shortened because of 'metabolic stresses'. These include glucose deprivation, lactate accumulation and cellular acidosis due to abnormally close packing of the red cells. The haemolytic component of this specific type of hypersplenism is mild, however. There is less solid evidence for the thrombocytopenia and neutropenia due to these mechanisms. The spleen routinely destroys abnormal red cells. The cytoskeletal defect manifest as hereditary spherocytosis causes these abnormal red cells to be particularly susceptible to destruction within the spleen. In addition to destroying senescent and diseased red cells, the spleen is active in policing for red cell inclusions such as Heinz bodies (haemoglobin precipitates), via selective membrane disruption and capture of these undesirable intracellular defects. The spleen also maintains surveillance of surface abnormalities of cells and platelets. In this way, red cells coated with antibody are destroyed via macrophage recognition of the constant portion of the IgG, producing

autoimmune haemolytic anaemia. A similar mechanism is probably responsible for the destruction of platelets in certain forms of idiopathic or drug-induced thrombocytopenic states. Additionally, the neutropenia seen in *Felty syndrome* (rheumatoid arthritis and splenomegaly) has an immune basis, probably due to a circulating leucocyte-specific antinuclear factor. The conditions in which splenomegaly can occur with varying degrees of hypersplenism are listed below.

- Infections

– Acute: hepatitis, mononucleosis, salmonellosis, toxoplasmosis, cytomegalovirus, tularaemia, abscess

– Subacute: AIDS, bacterial endocarditis, tuberculosis, brucellosis, malaria, leishmaniasis, trypanosomiasis, histoplasmosis

– Chronic: fungal disease, syphilis, bacterial endocarditis

- Congestive

– Intrahepatic portal hypertension: cirrhosis, Wilson disease, haemochromatosis, congenital hepatic fibrosis

–Prehepatic portal hypertension: portal vein thrombosis, obstruction, cavernoma, atresia

– Posthepatic: Budd–Chiari, congestive cardiac failure

–Segmental (left-sided portal hypertension): splenic vein occlusion by pancreatitis, pancreatic neoplasm, pancreatic pseudocyst, splenic artery aneurysm

- Haematological

– Haemolytic disorders: hereditary cell membrane defects, autoimmune haemolytic states (warm antibodies), thalassaemia, sickle cell disease, haemoglobin C disease

– Myeloproliferative disorders: myeloid metaplasia, polycythaemia vera, essential thrombocythaemia

–Miscellaneous: primary splenic hyperplasia, megaloblastic anaemia, iron deficiency

- Malignant

–Haematological malignancies: acute or chronic leukaemias, leukaemic reticuloendotheliosis, malignant lymphomas, malignant histiocytosis, myelomatosis

– Primary intrinsic malignancies: lymphosarcoma, plasmocytoma, fibrosarcoma, angiosarcoma

– Secondary malignancies: carcinoma, melanoma

– Benign: hamartoma, fibroma, haemangioma, lymphangioma

• Inflammatory or granulomatous

– Felty's syndrome, systemic lupus erythematosus, rheumatic fever, serum sickness, sarcoidosis, beryllosis

• Storage disease

–Gaucher disease, Wilson disease, Niemann

–Pick syndrome, histiocytosis X, Hurler syndrome, Tangier disease

• Miscellaneous

–Cysts: parasitic, pseudocysts, congenital, traumatic

–Others: hyperthyroidism, Osler–Weber–Rendu syndrome, splenic mastocytosis, Albers–Schonberg disease. In practice however 45% of cases of hypersplenism are caused by haematological disease and 40% by liver disease with portal hypertension. Thus all the other causes together account for only 5%.

Management of hypersplenism associated with chronic liver disease

Whereas splenectomy is the recognized treatment for hypersplenism due to haematological disease as it usually normalizes all the components of the cytopenia, the management of hypersplenism associated with chronic liver disease remains non-standardized and currently there are a number of options with no comparative data on efficacy and morbidity. To a large extent, therefore, the treatment depends on local expertise and preferences. Factors that should influence management in the individual case include the severity (Child–Pugh stage) of the disease and the need for treatment of other complications, e.g. bleeding varices, the development of hepatoma in a cirrhotic patient or an end-stage cirrhotic patient requiring liver transplantation. The most important aspect of hypersplenism in patients with chronic liver disease is the thrombocytopenia, and it is this that requires correction in these patients. Active management is considered only in patients in whom the splenic congestion and the thrombocytopenia are severe. In general, open splenectomy is ill advised in patients with liver disease and portal hypertension because it constitutes a major high-risk operation and may be followed by thrombosis of the portal vein. The options for the

treatment of severe thrombocytopenia in patients with liver disease and portal hypertension are:

- DSRS (Warren procedure)
- transjugular intrahepatic portosystemic shunt (TIPSS)
- laparoscopic splenectomy
- partial splenic embolization (PSE). DSRS effectively reverses the profound thrombocytopenia resulting from presinusoidal portal hypertension or stable cirrhosis without sacrificing the spleen, and in some centres is considered the treatment of choice for this condition in children. It is used as the only procedure (Child A/B patients) or before hepatic transplantation (Child C disease). TIPSS improves the hypersplenism in patients with portal hypertension. In one large reported series, the leucopenia was reversed in 50% and thrombocytopenia in 75% of patients. These results indicate that TIPSS is a minimal access intervention that is effective in the treatment of complications of portal hypertension including secondary hypersplenism and has largely replaced the use of DSRS. The problem with TIPSS is its poor long-term patency (beyond 6–12 months). The ideal indication seems to be patients with Child C disease awaiting liver transplantation. In adult patients with end-stage liver disease and hypersplenism awaiting liver transplantation, and in patients with Child A/B disease requiring hepatic resection for small hepatoma, laparoscopic splenectomy prior to the liver resection/transplantation has been performed as an alternative to TIPSS. Others advise concomitant splenectomy at the time of hepatic resection. The fourth option in the management of patients with portal hypertension and hypersplenism is PSE. This has to ablate 50% or more of the splenic parenchyma to be effective. It was initially reported to be successful in reversing the hypersplenism (thrombocytopenia and neutropenia) in 90% of patients undergoing embolization of hepatocellular carcinoma and appears to be safe with a low reported incidence of severe complications including splenic abscess formation. PSE was subsequently extended to Child A or Child B (but not Child C) patients with liver disease, where it is reported to also normalize the levels of cholinesterase, total cholesterol and prothrombin time in addition to haematological improvement of the hypersplenism.

Hyposplenism

The more common causes of asplenism and hyposplenism are:

- splenectomy
- splenic agenesis

• atrophy

• coeliac disease

• inflammatory bowel disease and collagenous colitis

• systemic amyloidosis

• alcoholism

• old age

• dermatitis herpetiformis

• sickle cell anaemia

• systemic lupus erythematosus.

The haematological features of hypo/asplenism are:

• abnormal red cells

–Burr cells

– target cells

–pitted cells

• red cell inclusions

–Howell–Jolly bodies

–siderotic granules

–abnormal platelet morphology

–thrombocytosis

• leucocytosis

– neutrophilia

– lymphocytosis

– monocytosis.

Hyposplenism is confirmed by the appearance of red cell defects (that normally would be culled from the circulation), and the degree of impairment may be qualitatively assessed by 99mTcsulphocolloid scintiscanning. There is some evidence based on the

percentage of pitted cells in the peripheral blood that splenic function is impaired in elderly people and in alcoholics. Pitted erythrocytes are found in 40% of alcoholics and this functional hyposplenism has been attributed to a direct effect of alcohol on the spleen as the pitted erythrocyte count drops in patients who give up the alcohol habit. However, the possibility that the high pitted erythrocyte count is caused by a direct effect of the alcohol on the red cell membrane can equally account for these changes and the controversy remains unresolved. The most frequent cause of hyposplenism is surgical splenectomy. Congenital asplenia (*Ivemark syndrome*) is a truly rare disorder, associated with complex cardiac, gastrointestinal, genitourinary and neuromuscular abnormalities. Survival in such cases is largely determined by the ability to recognize and correct the complex cardiac defects. Gastrointestinal anomalies such as malrotation and situs inversus are frequently seen in congenital asplenia. In surviving infants, a common cause of death is overwhelming sepsis due to encapsulated organisms, particularly pneumococcal. Splenic hypoplasia can also occur from birth as part of the syndrome of *Fanconi's anaemia*, i.e. congenital hypoplastic anaemia. Acquired hyposplenism occurs in about 76% of patients with coeliac disease. The cause is unknown, but may be related to the increased absorption of dietary antigen and subsequent overload of the spleen with circulating immune complexes. The hyposplenic state improves with a gluten-free diet in these individuals. AB€relationship has also been noted between the morphological state of the intestinal epithelium and splenic function. Hyposplenic states have also been described in other disorders involving the gastrointestinal mucosa including Crohn disease, ulcerative colitis, collagenous colitis and intestinal lymphangiectasia. Circulating autoantibodies and immune complexes in clinical autoimmune disorders, e.g. systemic lupus erythematosus, have been noted to cause a functional hypoplastic state secondary to Fc-receptor blockage. The hyposplenism of sickle cell anaemia is related to the degree of splenic infarction. Hyposplenism is also a feature of systemic amyloidosis. Hyposplenism can also occur in patients with full-blown HIV and these patients usually present with the *Mycobacterium avium* complex (infection) complicating HIV-related immune thrombocytopenic purpura. This combination is usually lethal, as the severe thrombocytopenia does not improve with corticosteroids, intravenous immunoglobulin and splenectomy. The peripheral blood smear shows Howell– Jolly bodies. Pathological examination of the spleen shows multiple granulomas with numerous acid-fast organisms.

Postsplenectomy sepsis

There is now uniform consensus that the risk of overwhelming sepsis is increased significantly after splenectomy. There is good evidence that the greatest risk is in infants and children (first 5 years of life), and to some extent the risk in adults may have been

overestimated in the past, although this is debatable. The problem of postsplenectomy sepsis has been compounded by the increasing incidence of penicillin-resistant pneumococci. The risk of postsplenectomy sepsis is also influenced by the nature of the disease for which the spleen is removed, with the lowest incidence of sepsis being reported after splenectomy for trauma as these individuals are otherwise healthy and have no other disease that impairs the immune defence against invading bacteria. Although the absolute lymphocyte count is increased after splenectomy for trauma, the peripheral blood lymphocyte subpopulations of these otherwise healthy subjects are distinctly abnormal. There is a significant reduction in the percentage of CD4+ T-cells due to a selective and long-term decrease in the percentage of CD4+CD45RA+ lymphocytes. These decreased levels of CD4+CD45RA cells are accompanied by an impairment of the primary immune responsiveness in terms of both T-cell proliferation and antibody responses to newly encountered antigens. By contrast, levels of the reciprocal CD45RO+CD4+ T-cell subset, lymphoproliferative responses and interferon γ production to recall antigens remain normal. These findings suggest that the intact spleen is essential for the generation, maintenance and/or differentiation of unprimed T-cells or their precursors and may explain the impaired primary immune responses following splenectomy. Splenectomy for trauma carries the lowest risk and thalassaemia the highest; but even for the lowest risk group, there is still a 40- to 50-fold increase in the incidence of overwhelming sepsis. Some of these estimates have been questioned largely because the majority of reported series have had small numbers, and indeed a substantial cohort of the data (on which estimates are based) are from single case reports of pneumococcal serious infections, often with bacteraemia. It is an undeniable fact that communityacquired pneumococcal pneumonia with bacteraemia is common in patients with normal splenic function and is seldom reported because of its established occurrence in susceptible groups. Because of this, there are some who argue that the risk of postsplenectomy pneumococcal sepsis may have been exaggerated. Although *Streptococcus pneumoniae* is implicated in over 55– 60% of septic episodes in asplenic patients, infections by other encapsulated bacteria, e.g. *Haemophilus influenzae, Haemophilus pertussis* and *Neisseria meningitidis*, are also more commonly reported in these individuals, as indeed are infections by Gramnegative bacteria, e.g. *Escherichia coli.* The functional deficits in asplenic patients are numerous, but impaired filtration, diminished phagocytosis, decreased IgM levels and loss of the opsonic tetrapeptide tuftsin all contribute to the increased risk. The syndrome of overwhelming postsplenectomy infection (OPSI) often begins insidiously. From a non-specific viral-like illness or malaise, the course rapidly turns fulminant. High fever, nausea, vomiting, dehydration, hypotension and obtundation occur with alarming speed, death being the

end result if the course of events is not quickly reversed by effective resuscitation and aggressive antibiotic therapy. Gram stain of the peripheral blood smears will occasionally reveal the causative organism and blood culture is invariably positive. The mortality rate of OPSI is 50– 80% for all cases combined. Postmortem examination often reveals bilateral adrenal haemorrhage (*Waterhouse–Friedrichsen syndrome*). The treatment of suspected episodes of OPSI should be aggressive and without any delay. Broad-spectrum antibiotics effective against encapsulated cocci in the first instance are administered intravenously. Intravenous colloids are used to correct the hypovolaemia using CVP and urine output monitoring within an intensive care setting. Altered haemostasis and disseminated intravascular coagulation can occur, and replacement products (fresh frozen plasma, platelets) are often required. The prevention of OPSI is imperfect at best and is based on vaccination, administration of oral penicillins and patient education. Prophylactic antibiotic therapy is recommended (together with vaccination) in children and some would extend it indefinitely to adults. Although this is sensible for the high-risk groups, there is less of an argument for long-term prophylactic antibiotics in adults undergoing splenectomy for trauma or iatrogenic injury sustained during abdominal surgery. The vaccination should be carried out at least 10–14 days prior to splenectomy for maximum effective immunization. The vaccination programme should always include the polyvalent pneumococcal vaccine and *Haemophilus* vaccines. Unfortunately, the pneumococcal vaccine (against 23 of the most prevalent strains) does not provide immunity against all strains. Not all vaccinated patients develop immunity but the majority do, and the titres of antipneumococcal antibodies remain elevated for up to 42 months. The question of booster immunizations has not been resolved. Immunization after splenectomy (trauma cases) is much less effective but some advise it anyway. Since no form of prophylaxis is completely effective, it is very important that all patients carry 'splenectomy' cards, and close surveillance and specific patient education are mandatory. At the first sign of infection, all patients with hyposplenic states should be strongly advised to seek medical attention and receive antibiotic therapy.

Splenic infarction

Infarction of the spleen is not uncommon and its clinical presentation is variable. Thus some patients have severe acute symptoms and signs, and may develop serious life-threatening complications (splenic rupture, splenic abscess), whereas others (up to 30%) have minor symptoms or are asymptomatic. Aside from the predictable autoinfarction in patients with sickle-cell disease, splenic infarction occurs most commonly with splenomegaly due to congestive disorders such as chronic myeloid leukaemia and myelosclerosis. Thromboembolic disorders may cause splenic infarction,

e.g. atrial fibrillation, arterial embolic (atheromatous) disease, diabetes-associated microvascular disease and acute torsion of an *ectopic* (*wandering*) *spleen.* A variety of other disorders may be complicated with the development of splenic infarction, e.g. falciparum malaria, Q fever, AIDS, severe necrotizing pancreatitis and pancreatic pseudocysts. Splenic infarction has also been reported as a complication of injection of gastric varices with Histoacryl. The splenic infarction in patients with AIDS is associated with the development of high titres of anticardiolipin antibodies, thrombocytopenia and a coagulopathy. Episodes of cerebrovascular infarction may also occur in these patients. The cause of the splenic infarction in these AIDS patients is arterial thrombosis of the coeliac trunk. The age range of splenic infarction varies widely (children to old age) and 70% are symptomatic. The most common symptoms are acute upper left quadrant abdominal pain, fever, chills and malaise. However, some patients are asymptomatic and these are usually patients with non-malignant haematological disorders. Fever and leucocytosis are especially marked in patients with thromboembolism as the cause for the splenic infarction. Physical examination reveals tenderness and guarding maximal in the left upper abdomen. Splenic infarction results in a capsular inflammatory reaction frequently causing irritation of the left diaphragm. This may result in left basal pleurisy/effusion and pain referred to the left shoulder (Kerr's sign). Confirmation of the diagnosis is usually achieved by abdominal angio-CT scan. Initially, the management should be conservative with analgesia and antibiotics. Surgery is indicated if the diagnosis is in doubt or for complications (splenic abscess, bleeding from splenic rupture) when splenectomy is indicated. The morbidity (mainly pulmonary complications) is high and the mortality averages 5% overall.

Splenomegaly

As previously outlined, there are numerous causes of splenomegaly and its relative incidence varies in different parts of the world, but in Western hospital practice, the distribution is as follows:

- patients with hepatic diseases, most commonly cirrhosis – 36%
- patients with haematological disease – 35%
- patients with infectious diseases – 16%, increasingly AIDS
- patients with inflammatory non-infectious disease – 5%
- patients with primary splenic disease – 4%
- others – 3%, e.g. congestive heart failure, endocarditis.

During the past 20 years, AIDS has come to account for 55–60% of patients with splenomegaly caused by infectious disease. The spleen may enlarge transiently in a variety of acute bacterial and viral infections, chronic infections and in subacute bacterial endocarditis. Parasitic infections, e.g. malaria, can result in massive congestive splenomegaly such that rupture is a very real and well-documented risk in those affected. Portal hypertension causes mild to moderate splenomegaly unless it is posthepatic (Budd–Chiari) or follows splenic vein thrombosis (sectorial, left-sided, sinistral portal hypertension) when massive splenomegaly may occur. Splenomegaly accompanies both hereditary and acquired red cell defects. The increasing splenic size predisposes these patients to increased red cell surveillance and hence destruction on a volume basis alone. As such, a vicious cycle is established whereby increased destruction and splenomegaly produces even more rapid red cell destruction. Splenomegaly occurs in about one-third of patients with megaloblastic anaemia, but less frequently in iron-deficiency anaemia. Splenomegaly is unusual in acquired aplastic anaemias, although for unexplained reasons it occurs in a significant number of children with congenital hypoplastic anaemia. It also occurs quite frequently in patients with dyserythropoietic anaemia or 'preleukaemic' states, e.g. sideroblastic anaemia. Splenomegaly regularly accompanies myeloproliferative disorders. Although polycythaemia vera does not commonly exhibit extramedullary erythropoiesis, the process of myeloid metaplasia in myelosclerosis does and splenomegaly is often massive in this condition. Any form of leukaemia or lymphoma can also cause splenomegaly via the same mechanisms. As such, the splenomegaly that accompanies Hodgkin disease or NHL does not necessarily represent tumour involvement of the organ, raising the possibility of a false-positive clinical stage.

Clinical features

A left upper abdominal mass is often not splenomegaly. For this reason, a comprehensive history and good physical examination is necessary in the first instance to minimize the considerable expense and discomfort of a misdirected evaluation. The normalsized spleen is not palpable but, when palpable, the spleen is at least two to three times the normal size. The important questions for history taking reflect the common causes of splenomegaly for the particular region. With the spectrum of diseases in mind, it is important to consider infectious (AIDS in particular) and neoplastic disease. A history of travel is often missed unless specifically questioned. Any suggestion of prior pancreatitis or abdominal pain with alcoholism should raise the suspicion of splenic vein thrombosis. The review of the systems enquiry should include questioning for pruritus, as this frequently accompanies myeloproliferative disorders. The symptoms of splenomegaly itself (irrespective of cause) do not correlate with size, but in practice

they tend to be marked only when the spleen becomes massively enlarged since most are due largely to mechanical displacement of adjacent organs and weight of the congested spleen. The symptoms of splenomegaly, as distinct from the manifestations of the underlying disease, include chronic dragging abdominal pain, or pain when lying on the side, abdominal discomfort and early satiety. In addition patients may complain of attacks of acute (colicky) left upper quadrant pains. In general, the bigger the spleen the worse the cytopenia (from hypersplenism) although there are exceptions to this, e.g. marked thrombocytopenia/ neutropenia and immune (idiopathic) thrombocytopenia purpura where the splenomegaly is invariably mild. Thus the significant correlation between splenic size and blood counts is not always clinically significant. The physical examination of a left upper quadrant mass starts with the examiner's hand well inferior in the right iliac fossa probing gently through each exhaled breath of the patient. In addition, the examiner's left hand is cupped posteriorly on the patient's back and flank so as to produce a 'bimanual' feel to the mass in question. If the mass is an enlarged spleen, it will be impossible to appreciate its superior limit. In contrast to the colon and stomach, the spleen lying against the abdominal wall is dull to percussion. Capsular inflammation of the spleen may produce a rub (with the stethoscope). Finally, the right lateral decubitus position may allow for easier examination of a left upper quadrant mass. A renal mass can usually be distinguished from a splenic mass on physical examination since:

- the kidney moves inferiorly on respiration, whereas the spleen moves medially as well
- the organ shapes are quite different
- the colonic resonance in front of a renal mass is usually not present with splenic masses. Colonic and gastric masses usually move less well with respiration as they are not as intimately attached to the diaphragm, are more irregular than splenic masses and often have a superior limit that is palpable. The physical examination must also include a careful search for lymphadenopathy, including the tissues of the posterior pharynx. A search for the stigmata of chronic liver disease as well as evidence of purpura or bruising mandates a complete head-to-toe examination. Clinically splenomegaly depending on extent of enlargement may be:
- mild – up to 5cm below the left costal margin
- moderate – enlargement up to the umbilicus
- marked (massive)–more than 8cm or below the umbilicus.

Massive splenomegaly is defined as a spleen having a craniocaudal length greater than 18–20cm or weighing more than 600g. Sometimes the term supramassive splenomegaly is used for spleens with a craniocaudal length greater than 22cm or weight more than 1600g but the clinical relevance of this category is moot.

Investigation of splenomegaly

The cause of splenic enlargement can usually be identified by history, physical examination and a few appropriate tests. Those cases associated with haematological disorders are often fully characterized by a peripheral blood smear and a bone marrow biopsy. Lymphoreticular malignancies are defined by appropriate biopsy. Haematological or serological testing can identify most infectious causes of splenomegaly. Mononucleosis, a frequent cause, is diagnosed by the finding of atypical lymphocytes in the peripheral blood smear, a positive Paul–Bunnell test (or similar screen), and a rising anti-Epstein–Barr virus titre. Most patients with AIDS who develop splenomegaly are already known to have the disease, but when suspicion is aroused in previously undiagnosed patients, permission for the appropriate testing should be obtained. Patients with a history of travel or those living in endemic areas of disease should have blood smears looking for malaria or marrow for Leishman–Donovon bodies. Disseminated tuberculosis must be considered in all members of a community where there are also immigrants at risk. Laparoscopy may assist in this elusive diagnosis as the majority will have intestinal tuberculosis. The size, shape and consistency of the spleen can be accurately visualized by CT, MRI or ultrasonography. The determination of splenic size is of crucial importance in determining the surgical approach when splenectomy is indicated in the management of the patient (see below). The spleen's blood vessels can be imaged using either duplex ultrasound, highdose contrast helical CT and MRI or (rarely nowadays) with selective visceral angiography. The last is used almost exclusively for therapeutic embolization. It is no longer necessary to puncture the spleen directly for splenoportography, as other methods are usually sufficiently accurate. Fine ultrasoundguided needle splenic biopsy is carried out for specific lesions but only in specialized centres. Ultrasound is the most widely used imaging modality in the investigation of patients with both acute and chronic disorders of the spleen. It is performed by scanning through the intercostal spaces with both greyscale and colour Doppler or power flow (splenic vasculature). Splenic ultrasound is useful for:

- detection of accessory spleens
- confirmation of splenomegaly but not the cause of the splenomegaly
- differentiation of solid from cystic intrasplenic focal masses

• detection of calcification, wall thickening, internal debris, and gas

within cystic lesions

• detection of splenic cavernous haemangiomas

• diagnosis of splenic infarction

• diagnosis of splenic trauma and monitoring patients with splenic injuries managed conservatively.

An accurate assessment of the spleen's function can be obtained through injection of labelled platelets, cells (red, white) or carrier molecules and radiotracer studies. The splenic uptake rate of Tc–sulphur colloid or Tc–tin colloid provides a sensitive and quantitative function of splenic function and is based on tracer uptake by the spleen (measured splenic uptake rate divided by measured injected activity). The normal splenic tracer uptake rate is 0.0002–0.0006/s. Values lower than 0.0002/s indicate hyposplenism and values greater than 0.0006/s hypersplenism. There is good correlation between high splenic tracer uptake rates and the severity of the neutropenia and thrombocytopenia.

Splenectomy

Indications for splenectomy

There are definite, desirable and debatable indications for splenectomy.

• Definite indications

–non-salvageable spleen injury (see text)

–*en bloc* resection of adjacent neoplasms (usually proximal gastric

cancer)

–neoplasms of the spleen – usually lymphomas

–splenic abscess

–echinococcal cysts

–bleeding gastric varices due to sinistral portal hypertension

–rupture of diseased spleen

• Desirable indications– used selectively

–hereditary spherocytosis

–immune (idiopathic) thrombocytopenic purpura

–AIDS-related thrombocytopenic purpura

– autoimmune haemolytic anaemia

–sickling syndromes (sickle cell disease and sickle-β-thalassaemia)

• Debatable indications

–non-parasitic splenic cysts

–thalassaemia syndromes

–lymphoma with specific cytopenia or pancytopenia

–thrombotic thrombocytopenic purpura

–myeloproliferative disorders.

Definite indications

Neoplasms of the spleen should be removed for accurate diagnosis and staging. Septic emboli to the spleen do not require splenectomy, but, when an abscess has formed, removal of the entire organ is the safest management course. Potential spillage of echinococcal cyst contents requires that the entire spleen be removed for this condition. Bleeding gastric varices resulting from splenic vein thrombosis require splenectomy as does rupture of a splenic artery aneurysm that can occur catastrophically during pregnancy. Splenectomy may be required (*de nŭcessitŭ*) during resection for proximal gastric cancer to obtain the necessary clearance and adequate regional lymphadenectomy. Although spontaneous rupture of the spleen does occur, it is most frequently seen at times of, or following an interval after, minor abdominal trauma; or as the presenting symptom of previously silent splenomegaly in an already diseased spleen, e.g. malaria, mononucleosis, myelosclerosis, etc. Rarely, a rapidly enlarging spleen in the aggressive forms of NHL may rupture spontaneously. Equally rare, a pseudocyst of the tail of the pancreas may cause splenic vein thrombosis, rapid enlargement and congestion of the organ and spontaneous rupture. In otherwise healthy patients, rupture of the spleen much more commonly follows blunt trauma of the chest and abdomen (see section Trauma) or as an iatrogenic injury during abdominal surgery. Because of concerns regarding OPSIs, every reasonable effort should be made to salvage an injured spleen during surgery and emergency laparotomy

(splenic suture, partial splenectomy, etc.). However, there are situations when splenic salvage is ill advised and splenectomy is the sensible option for:

- hilar injuries or a shattered spleen (grade 4 or 5 injuries)
- blast injuries to the organs of the left upper quadrant
- multiple associated injuries where splenic salvage may prolong the

procedure

- haemodynamically unstable and elderly patients
- marked intra-abdominal contamination
- rupture of a pathological spleen.

Non-operative conservative management of a known splenic injury, especially in the paediatric age group, is certainly an acceptable alternative to operative therapy in the first instance. Likewise, in an effort to avoid the many complications of splenectomy in patients with myelosclerosis, a small perisplenic haematoma may be closely observed in hospital, with frequent serial ultrasound examinations. But in either case, with any sign of haemodynamic instability or continued bleeding (need for persistent blood replacement), laparotomy is clearly indicated. The disadvantage of conservative management is that, in the event of failure, the potential for splenic salvage is reduced. Desirable indications In many of these patients, the decision regarding the need for splenectomy is made by the haematologist who refers the patient to the surgeon. It is usually desirable to perform splenectomy for hereditary spherocytosis, refractory immune (idiopathic) thrombocytopenic purpura and AIDS-related thrombocytopenia that have failed to respond to medical therapy (steroids and human IgG), and acquired haemolytic anaemia. Some cases of genetic red cell enzyme defects, such as pyruvate kinase deficiency, respond favourably to splenectomy. Splenectomy may reduce the blood transfusion requirements of haemoglobinopathies, such as the thalassaemia syndromes. It may also be useful in patients with neutropenia secondary to congestive splenomegaly, e.g. tropical or lymphomatous, for the same reason as in those with storage diseases. In patients (usually children) with sickling disorders (sickle cell disease and sickle-β-thalassaemia) splenectomy is beneficial in the management of patients who develop large spleens with hypersplenism, major splenic sequestration crisis, recurrent minor splenic sequestration crises, splenic abscess and massive splenic infarction. A high proportion (25%) of these patients has concomitant gallstones and cholecystectomy may be considered at the time of the splenectomy.

Debatable/controversial indications

Splenectomy in the treatment of myeloproliferative disorders is controversial. Its value in the management of chronic myeloid leukaemia remains unproven. It may be occasionally indicated in myelosclerosis with massive splenomegaly, but only if the sequestration of red cells exceeds the spleen's erythropoiesis as measured by isotope tests. The 'rebound thrombocytosis' often seen after splenectomy is particularly severe in this situation. As myelosclerosis follows an unpredictable course of severity, splenectomy to avoid these complications is highly debated. Staging laparotomy for Hodgkin's and NHLs with splenectomy, lymph node harvest and liver biopsies is no longer performed, as accurate staging is possible with modern imaging tests (helical CT and MRI).

Splenectomy: surgical aspects

The first splenectomy in the human is said to have been done by Zaccarelli of Naples in 1649, for splenomegaly in a 24 year old female. The truth of this report has been questioned, as have reports of splenectomy performed in the sixteenth and seventeenth centuries. The first successful splenectomy in the USA was reported by O'Brien in 1816 for splenic evisceration following a knife wound. In 1866, Spencer Wells performed the first elective splenectomy in the UK. Common knowledge at that time held that the spleen was expendable and splenectomy had no untoward side effects. Laparoscopic splenectomy was first reported in several European and North American centres in 1989–1990. Preoperative management and preparation As previously mentioned, all patients undergoing elective splenectomy should be immunized against *Streptococcus pneumoniae and Haemophilus* spp. and this should be carried out 2 weeks before surgery. Otherwise, preoperative preparation for splenectomy should be routine as for any major abdominal operation and this includes prophylaxis against thromboembolic disease. Special consideration should be given to the patient's haematological findings, clotting parameters and liver enzymes. Patients with bone marrow dysfunction or with immune platelet destruction abnormalities may be markedly thrombocytopenic prior to operation. If the platelet count is low on the basis of bone marrow failure, then platelet transfusion to a level greater than 60в•›000 is indicated both prior to and following operation for the first few days, in an effort to prevent bleeding episodes. If the thrombocytopenia is on the basis of immune disease, e.g. immune thrombocytopenic purpura, then preoperative platelet transfusions will be less useful, whereas human IgG will increase the platelet count. Coagulopathies due to liver disease require replacement therapy with fresh frozen plasma or cryoprecipitate as determined by factor assay. In patients with massive splenomegaly, it may be useful to

consider immediate preoperative radiological embolization of the splenic artery. Otherwise, it is usually possible to ligate the splenic artery at the superior border of the pancreas via the lesser sac at the beginning of the operation. This allows for a period of 'autotransfusion' of the sequestered blood elements during the remaining dissection. As removal of a massive spleen may be accompanied by substantial blood loss, a cell-saver system for autotransfusion should be available. Particular attention should be made during the ligature and division of the splenic hilar vessels to avoid inadvertent damage to the tail of the pancreas. Attention to exact haemostasis is critical for the reduction of postoperative complications. The bed of the spleen, especially the raw surface of the diaphragm, should be meticulously inspected for oozing and bleeders before closure. The use of the argon spray coagulation is very effective in ensuring a dry splenic bed. Drains should not be inserted after splenectomy as they are ineffective and enhance the risk of subphrenic infection.

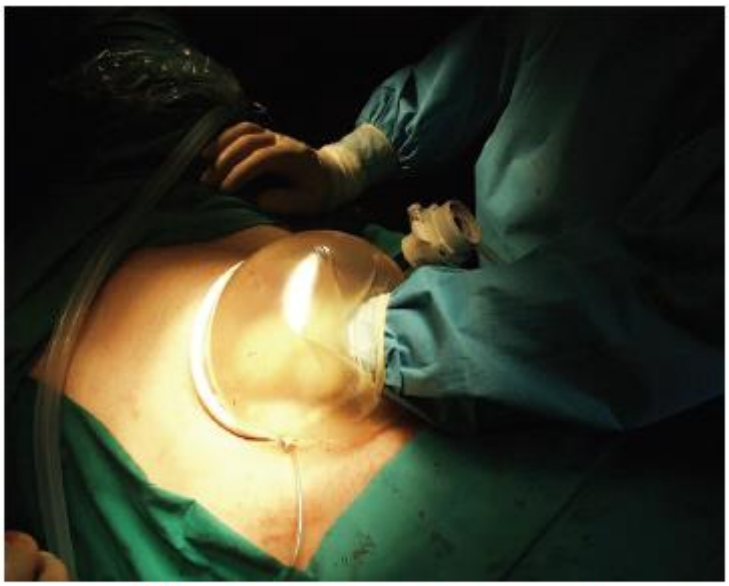
Laparoscopic splenectomy

Because of its advantages (fewer perioperative complications, reduced morbidity and a shorter hospital stay), laparoscopic splenectomy has now replaced open operation for most disorders requiring splenectomy or splenic surgery. There is some evidence, however, that accessory spleens are more difficult to identify laparoscopically. This may result in a recurrence of the thrombocytopenia following laparoscopic splenectomy for idiopathic thrombocytopenia, although there are no comparative studies and the results of laparoscopic splenectomy in reversing the thrombocytopenia and for acquired haemolytic anaemia have been equivalent to those obtained by open splenectomy. Laparoscopic splenectomy has also been performed for isolated traumatic splenic injuries although the reported experience is limited. There are some concerns in relation to laparoscopic splenectomy for neoplastic disease as fragmentation/morcellation of the specimen may promote tumour spillage and implantation and also render pathological examination more difficult. ***Laparoscopic approaches*** A totally laparoscopic approach is used when the diseased spleen although enlarged does not extend significantly below the left costal margin and short of the umbilical plane equivalent to a longitudinal long axis on ultrasound or CT not exceeding 15в•›cm. Above this size and with increasing weight (>1.0kg) splenectomy by the total laparoscopic approach can be difficult and is attended by high conversion rates. Hence until the advent of effective devices that enable hand-assisted laparoscopic surgery (HALS), the correct and appropriate surgical treatment for these patients was open splenectomy. Nowadays, however, the majority of spleens of size ranging from 20 to 40cm (longest diameter) can be safely removed by the HALS approach, which reduces considerably the technical difficulty of the procedure and enhances safe completion

without conversion. It has replaced preoperative percutaneous embolization of the splenic artery. Thus the HALS approach is strongly recommended for all adult patients with massive splenomegaly (>20cm on ultrasound or CT). These large spleens are most often caused by congenital haemolytic anaemias, hypersplenism (primary and secondary) and myeloproliferative disorders. As the HALS technique used differs from the classical splenectomy by the total laparoscopic approach, the two operations are described separately. It should be stressed that the postoperative morbidity of laparoscopic splenectomy is significantly higher in patients undergoing the procedure for massive splenomegaly, although there is some evidence that it is reduced when performed by the HALS approach. The hand access device favoured by the author is the Omniport but there are others such as the Hand Port, the Lap Disk and the Gel Port.

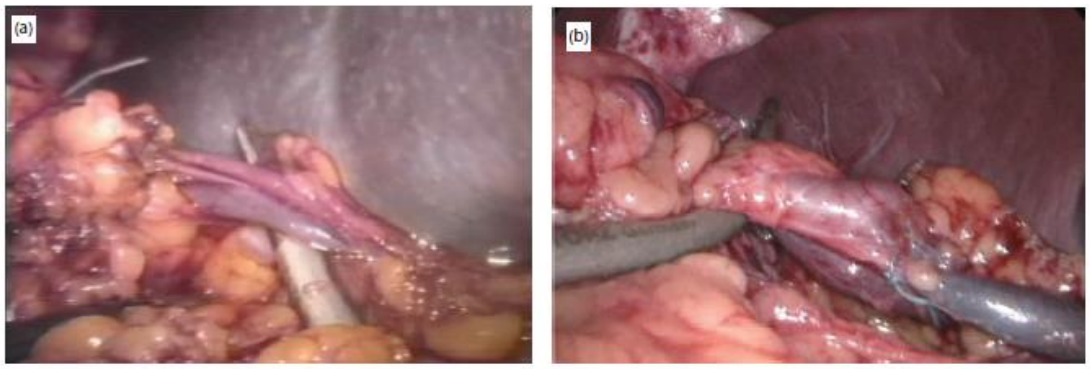
Total laparoscopic splenectomy

The 'hanging spleen' technique is most commonly used with the patient placed just short of the right lateral position (left side up) with the operating table in a slight head-up tilt (20°) facing the surgeon and the camera person on the right, with the scrub nurse on the other side of the table by the patient's back. The operation begins with detachment of the stomach from the spleen and division of the gastrosplenic ligament and short gastric vessels. An avascular window of the gastrosplenic ligament is identified for opening the lesser sac by scissors or ultrasonic dissection. The next step of the operation consists of dissection of the main splenic vascular pedicle which is made easier if the peritoneum overlying the pancreas is divided to expose the areolar tissue plane beneath the main splenic artery and the splenic vein. Careful dissection in this plane enables separation of the tail of the pancreas, which is at times closely applied to the main splenic vessels and risks being injured if cross stapling is carried out. Whenever possible, the author prefers to isolate the pancreatic segment of the common splenic artery along the upper border of the pancreas using curved coaxial scissors and duckbill forceps; the artery is ligated in continuity intracorporeally or with an external slip knot. The ligature in continuity of the pancreatic segment of the splenic artery achieves one important immediate benefit

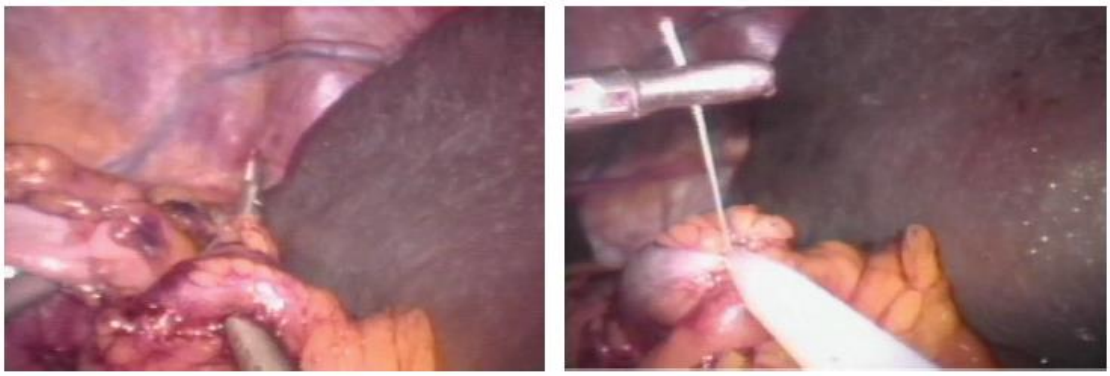


Omniport hand assist device for hand-assisted laparoscopic surgery splenectomy

especially in large/massive spleens – reduction of the splenic volume aside from increase in the circulating blood volume as the splenic red pulp drains via the intact splenic vein. Additionally, it reduces the risk of major bleeding. The splenic vein is mobilized further down together with the now collapsed prehilar segment of the splenic artery. The vein is then tied together with the collapsed prehilar artery. Alternatively no attempt is made to dissect and separate the artery from the vein. Instead the curved duckbill forceps or Maryland forceps is used to create the necessary space underneath the splenic pedicle lateral to the tail of the pancreas for the insertion of the linear cutting stapler mounted with vascular cartridges. To ensure accurate placement of the stapler limbs completely across the vessels, it is wise to insert a vascular sling which is

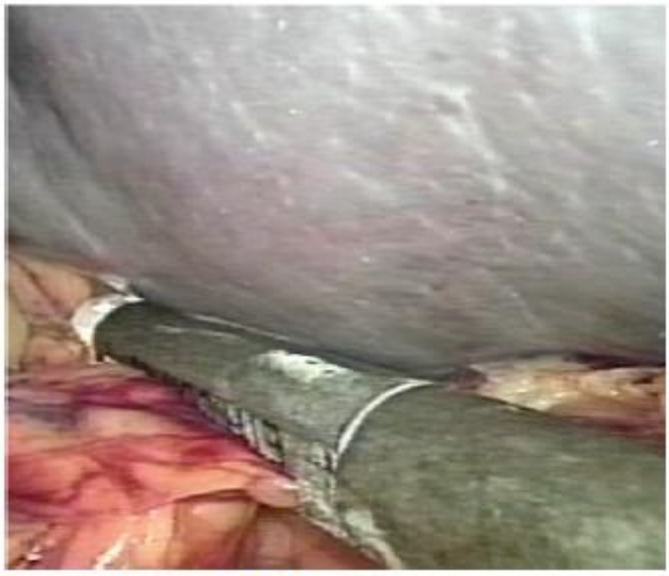


(a,b) Dissection and ligature of the splenic vein with the collapsed prehilar splenic artery.



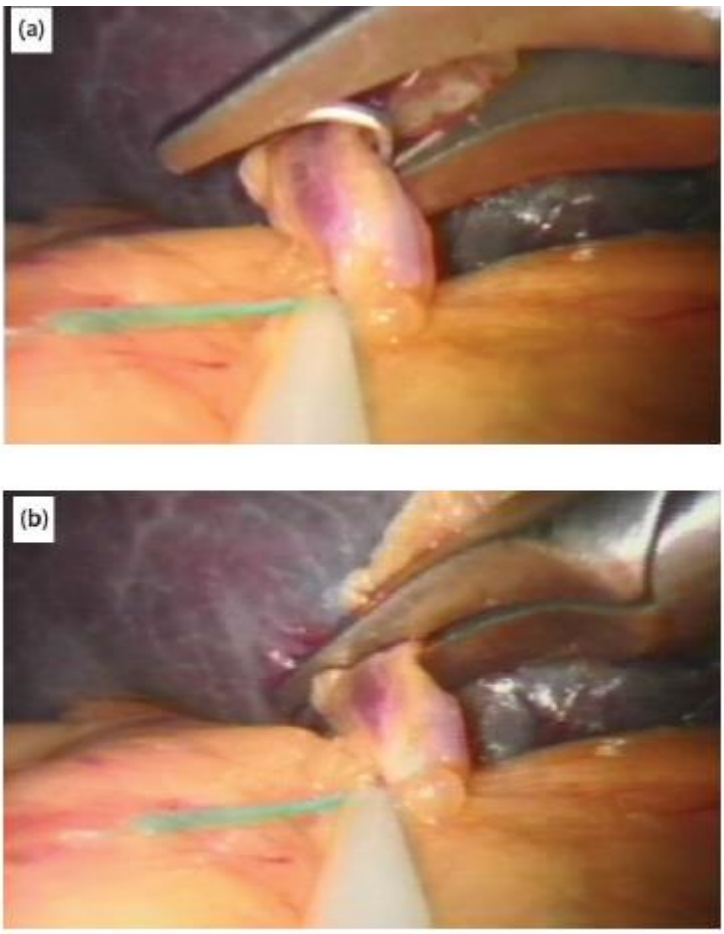
The curved coaxial duckbill forceps is under the dissected artery which is ligatured in continuity with an external slip knot. The pancreatic segment of the splenic artery may be clipped instead unless it is atherosclerotic, when clipping may be dangerous as the artery may with major bleeding requiring immediate emergency conversion.

then used to open the space. The stapling technique is obviously much quicker but may



Stapling of splenic hilar vessels.

carry a risk of atriovenous fistula. Problems may be encountered with the stapling technique in spleens with a wide diffuse (magistral) pedicle such that more than one stapler application is necessary to secure it. Bleeding may then be encountered after the first stapler application is released. The best option to deal with this problem is suction with minimal delay before the second stapler application. The other potential problem with stapler transection of the splenic hilar vessels is risk of damage to the tail of the pancreas. Following ligature/stapling of the vessels, the spleen is inspected closely. It should assume a uniformly dusky appearance. If not and segments are seen that are still relatively 'pink', careful search must be made for accessory/segmental vessels, the most common of which arises from the left gastroepiploic artery. The next step following splenic devascularization is division of the superior leaf of the lienorenal ligament. A fan or equivalent retractor is then placed on the dorsal surface of the spleen and used to displace the organ gently downwards to expose the superior peritoneal leaf of the lienorenal ligament. This is then divided with ultrasonic shears, scissors, electrosurgical hook knife or LigaSure starting at the lower pole of the spleen and including the splencolic peritoneal fold. This is followed by separation of the posterior areolar attachments of the spleen. The fully mobilized spleen is captured in a bag such as the Endo Catch or equivalent. It usually requires finger morcellation. The neck of the bag is then exteriorized through the port wound after removal of the port. The rim of the opened bag is surrounded by



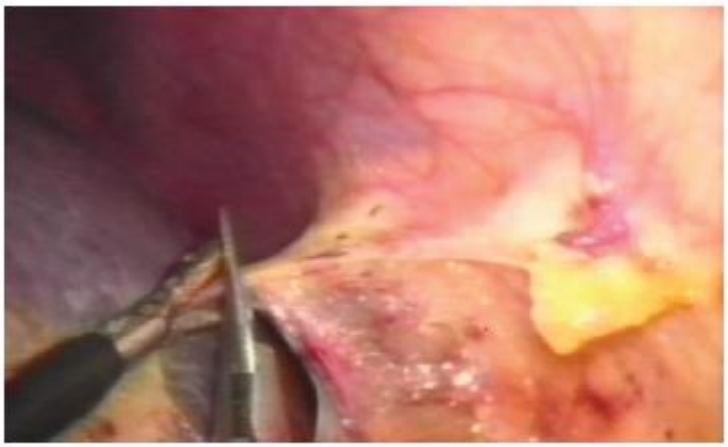
(a,b) Proximal ligation and distal clipping of a segmental polar artery arising from the left gastroepiploic artery.

Betadine swabs and the spleen fragmented by sponge forceps inside the bag and removed piecemeal.

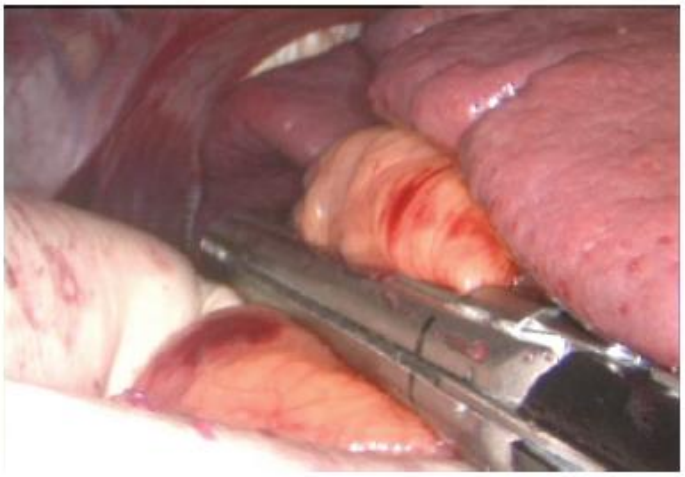
HALS splenectomy

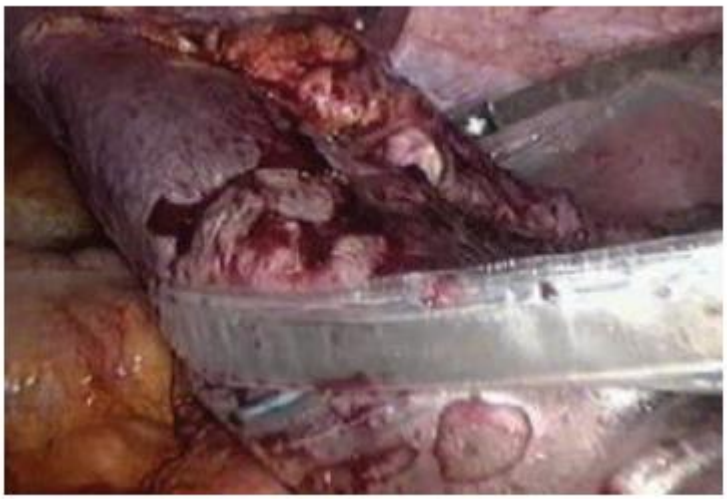
The incision for the placement of the HALS device is vertical along the linea alba at a variable distance from the umbilicus depending on the size of the spleen. The non-dominant hand is then inserted through the HALS device into the peritoneal cavity. The internal hand is used to elevate the hilar surface of the spleen to enable the insertion and deployment of a fan retractor which is then fixed to and held in position by the Martin's arm clamped to the rail along the left side of the operating table. The internal hand is then used to stretch the gastrosplenic ligament and an avascular window is identified for opening the lesser sac by scissors or ultrasonic dissection. Once inside the lesser sac, the splenic artery is identified running sinuously along the upper border of the pancreas towards the hilum of the spleen. The stomach is then detached from the spleen by LigaSure/ultrasonic division of the gastrosplenic ligament and short gastric vessels. Whatever technique is used, the detachment of the top end of the gastrosplenic ligament can be difficult because of the enlarged splenic pole with resulting foreshortening of the ligament such that the stomach wall approximates the splenic parenchyma and can be damaged unless extreme care is taken. The pancreatic segment of the splenic artery is exposed by division of its peritoneal and fascial coverings with the electrosurgical hook knife, and the artery then separated from the pancreas by curved duckbill or Maryland's forceps. The mobilized pancreatic segment of the splenic artery is then clipped or tied in continuity. The division of the peritoneum overlying the pancreas and the areolar tissue attaching the spleen to the Gerota's fascia, perinephric fat and pancreas (inferior layer of the lienorenal ligament) is a crucial technical point in HALS splenectomy as it identifies the areolar tissue plane and avoids all the major branches of the splenic artery and tributaries of the splenic vein. This step is best carried out with the electrosurgical hook knife. Although largely avascular, occasional small vessels may cross this areolar plane but these are easily secured with ultrasonic dissection or clips. The separation of the inferior border and surface of the spleen from the pancreas and perinephric fat is continued through the areolar tissue separating the peritoneal leaf reflected down from the hilum of the spleen (inferior leaf of the lienorenal ligament) to the perinephric fat and pancreas This separation must be sufficient to ensure that the pancreatic tail is not damaged when the main hilar vessels are ligated. The space created should enable the passage of a curved coaxial grasper or Maryland forceps behind the

hilar vessels (arteries and veins), followed by the tip of the index finger of the dissecting hand. The splenic vessels are best tied intracorporeally. Alternatively, the vessels may be secured using external slip knots of braided 1/0 polyester.

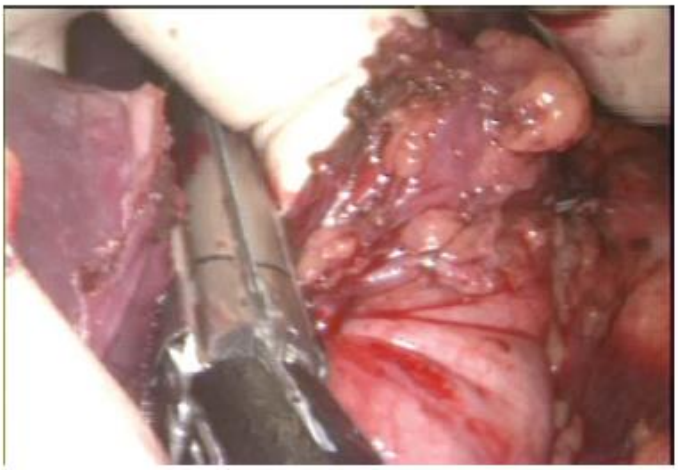


Division of the superior leaf of the lienorenal ligament starts at the lower pole and includes the suspensory ligament.

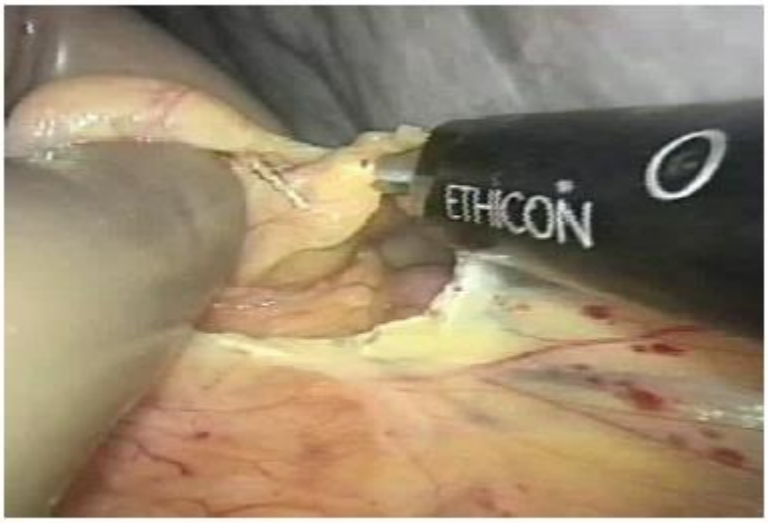




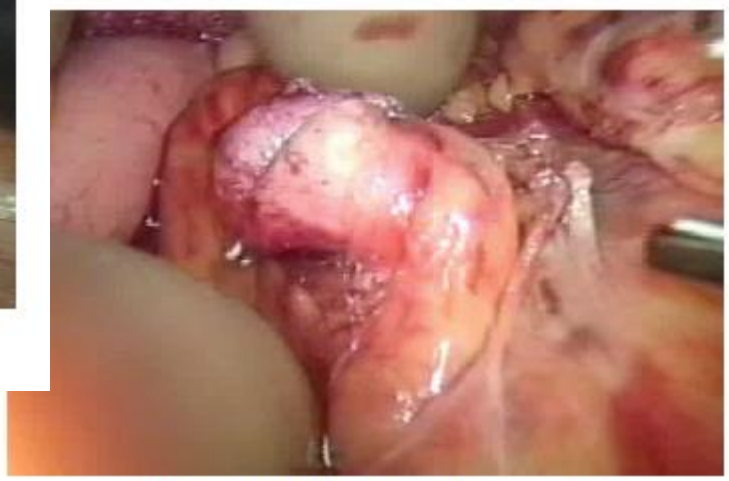
Capture of the spleen by an End Catch bag.



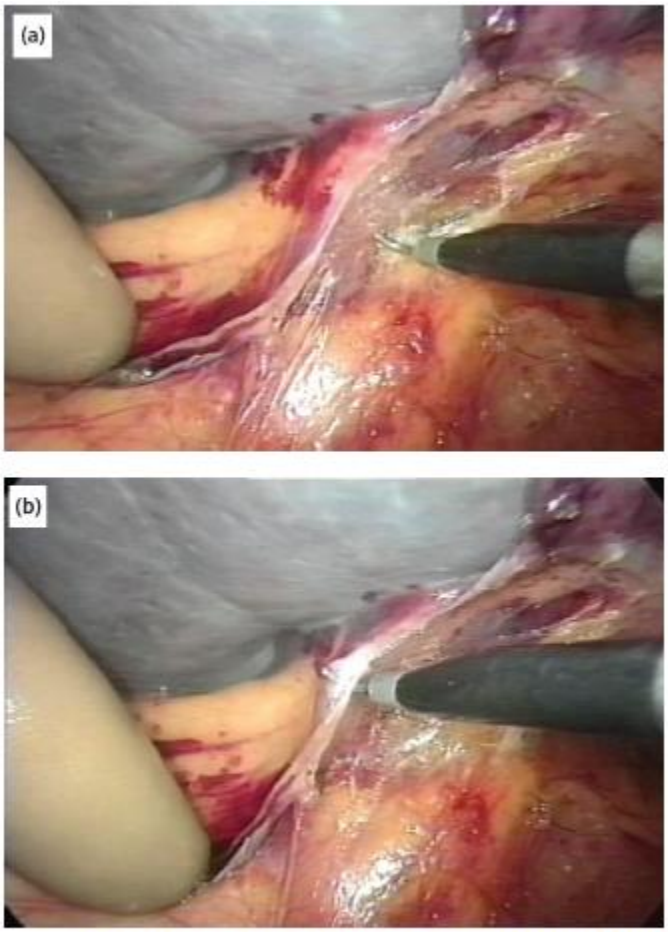
Detachment of the gastrosplenic ligament and short gastric vessels by a linear cutting angulated endostapler using a vascular cartridge. This step can be done by LigaSure (Atlas) or ultrasonic dissection.



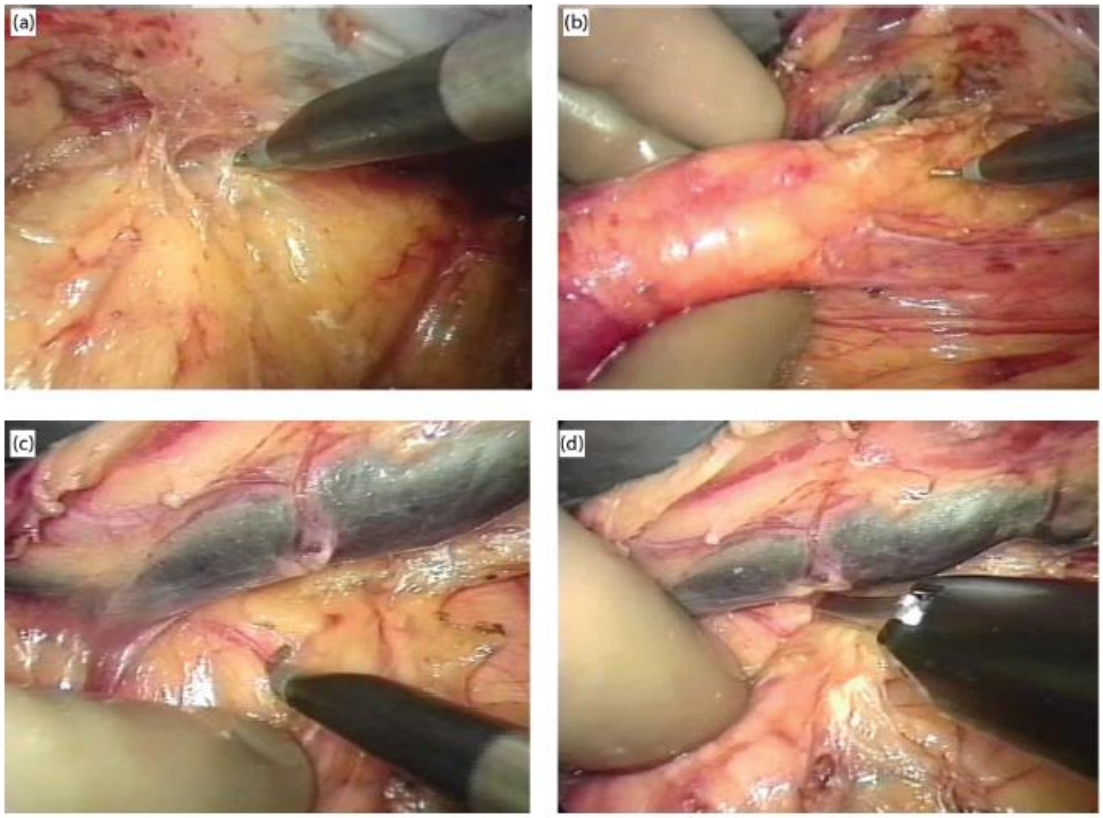
Opening the lesser sac.



Ligature/clipping of the splenic artery in continuity.



(a,b) Division of the inferior leaf of the lienorenal ligament and the areolar tissue plane binding it to the perinephric fat and pancreas.



(a–d) Separation of the inferior surface of the spleen from the perinephric fat and pancreas.

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All the illustrated materials are taken from «Essential Surgical Practice. Higher Surgical Training in General Surgery. Fifth Edition. Edited by Alfred Cuschieri and George B Hanna»

Tests

1. What is not characteristic of the jaundice caused by choledocholithiasis:

a) Urobilinuria
b) High alkaline phosphatase
c) Normal or low blood protein
d) High blood bilirubin
e) Normal or moderately high transaminase

2. The stone transfer from the cholecyst to the choledoch doesn/'t cause:

a) Biliary colic
b) Jaundice
c) Purulent cholangitis
d) Cholangiolithiasis
e) Budd-Chiari syndrome

3. The patient with jaundice caused by cholecholithiasis needs:

a. Urgent surgery
b. Conservative treatment
c. Urgent surgery after the preoperative preparation
d. Catheterization of the celiac arteries
e. Plasmapheresis

4. Courvoisier`s symptom is not characteristic of:

a. Acute calculous cholecystitis
b. Cancer of the head of pancreas

c. Indurative pancreatitis
d. Tumours of the large duodenal papilla
e. Tumours of choledoch

5. What symptoms are not characteristic of obstructive jaundice conditioned by cholangiolithiasis:

a. Hyperthermia
b. High conjugated blood bilirubin
c. High alkaline phosphatase
d. Sharp increase in plasma transaminase level
e. Absence of stercobilin in feces

6. What methods are not used to detect the character and causes of jaundice:

a. Computer tomography
b. Intravenal cholecystocholangiography
c. Percutaneous transhepatic cholangiography
d. X-ray endoscopic examination of pancreatobiliary zone
e. Ultrasonic scanning

7. Intermittent jaundice is called:

a. Impacted stone of the choledoch terminal portion
b. Choledoch tumour
c. Cystic duct stone
d. Valvular duct stone
e. Choledoch structure

8. Courvoisier`s symptom is not observed in the cancer of:

a. Head of pancreas
b. Supraduodenal part of the choledoch
c. Retroduodenal part the common bile duct
d. Large duodenal papilla
e. Cholecyst

9. What combination of clinical symptoms cooresponds to Courvoisier`s symptom:

a. Enlarge painless cholecyst, jaundice
b. Enlarged liver, ascites, anteroventral vein dilatation
c. Jaundice, palpable painful cholecyst, local peritoneal phenomena
d. Absence of stool, cramp-like pain, palpable lump in the abdominal cavity

e. Evident jaundice, tuberous liver, cachexia

10. The combination of symptoms characteristic of cholangitis is:

1. Jaundice;
2. Shiver;
3. Anaemia;
4. Leukocytosis;
5. Ascites.

Right variants:

a) 1, 2, 3
b) 1, 2, 4
c) 3, 4, 5
d) 2, 5
e) 2, 3, 5

Situational task 1

The 41-year-old patient entered the clinic complaining of vomiting unchanged blood, dizziness, weakness, suffered malaria 10 years ago. In the last 3 years – periodic pain in the right hypochondrium. Objectively: the state of moderate severity. Pallor of the skin and mucous membranes. Slight jaundice of the sclera, vascular asterisks on the skin. Pulse 110 beats/min, rhythmic. Blood PRESSURE 90/50 mmHg. Tongue is dry, overlaid with a brown coating. The abdomen is enlarged, flattened. The liver protrudes from under the costal arch, dense with a pointed edge. The spleen performs on Percussion is determined 8 see ascites. In the General analysis of blood: erythrocytes 2,3 * 1012/l, hemoglobin 72 g/l, hematocrit 0,29.

1. Your preliminary diagnosis?
2. What diseases should be differentiated?
3. What special and instrumental studies are needed to make a final diagnosis, the expected results.
4. Specify the treatment tactics.
5. Prescribe treatment.
6. List the operative methods of treatment in case of failure of conservative therapy.

Situational task 2

Patient C, 62 years old, taken by ambulance to the emergency Department. On the street suddenly emerged a sharp pain in the left hypochondrium, briefly has lost consciousness. Blood PRESSURE 90/60 mmHg.article Pulse 100 beats per min., weak filling. The abdomen is soft, moderately painful along the left lateral canal, there is also a dulling of the percussion sound and questionable symptoms of peritoneal irritation. Additionally, the patient reported that about 2 weeks ago she was injured, hit her left side on a chair in the tram, and then noted moderate pain in the left hypochondrium.

1. Make a preliminary diagnosis.
2. With what diseases is it necessary to differentiate this disease?
3. What additional instrumental methods of research will help to make a final diagnosis? Expected result.
4. What is the therapeutic tactics of this patient?
5. What are the principles of treatment in the postoperative period?

Situational task 3

A patient of 38 years was taken to the surgical Department with complaints of vomiting scarlet blood, weakness, dizziness. From anamnesis established-about 7 years ago suffered acute pancreatitis. On examination, the skin and visible mucous membranes are pale. The vesicular breathing, heart sounds are muffled. Pulse 112 beats per minute, rhythmic. Blood PRESSURE 110/60 mmHg.my Tongue is wet. The abdomen is soft, the spleen is palpated, protruding beyond the edge of the costal arch at 6 cm. splenomegaly is determined By ultrasound. The liver is not enlarged, its tissue is without features. Portal vein is within normal limits. Pancreatic fibrosis is determined, calcifications in its tissue, the splenic vein is not clearly visualized. In the clinical analysis of blood: er. 2.8 * 1012 / l., hemoglobin 78 g / l, hematocrit 0.32.

1. What preliminary diagnosis is most likely?
2. What diseases should be carried out differential diagnosis?
3. What instrumental methods can help in the final diagnosis and expected results?
4. Determine the degree of blood loss and therapeutic tactics in various States of hemostasis.
5. Specify the main components of preoperative preparation and the amount of surgery for various States of hemostasis.

Check yourself

Tests

1	2	3	4	5	6	7	8	9	10
a	e	c	a	d	b	d	e	a	b

Situational task 1

1. Cirrhosis of the liver, bleeding from varicose veins of the esophagus and stomach.
2.

- stomach ulcer, complicated by bleeding,
- stomach cancer complicated by bleeding
- liver tumor,
- pulmonary and nasal bleeding.

3. Radioscopy of the esophagus and stomach-multiple rounded and oval filling defects in the esophagus.

Fibroesophagoscopy-varicose veins of the lower third of the esophagus and the cardiac part of the stomach.

4. Conservative therapy with the use of a Blakemore tube.

Introduction of vikasol 1% - 1 ml, in / in 5-10 ml of 10% R-RA calcium chloride, 1 ml of pituitrin on 5% R-re glucose.

5. Erythrocyte mass with replacement purpose, fresh frozen plasma with hemostatic purpose, colloidal, crystalloid solutions to fill the deficit of circulating blood volume.

6. Transgastric ligation of varicose veins of the esophagus and cardia. The imposition of the vascular selective portocaval anastomosis after stopping the bleeding and the lack of activity of hepatitis.

Situational task 2

1. Closed injury of abdominal cavity organs. Two-stage rupture of the spleen. Intra-abdominal bleeding.
2. Closed injury of the liver. Retroperitoneal hematoma. Perforation of the hollow organ.

3. Ultrasound of the abdominal cavity: - uneven contour of the spleen capsule, the presence of free fluid in the peritoneal cavity. Laparocentesis: the presence of blood in the abdomen. Diagnostic laparoscopy:

- the presence of blood with clotting in the abdominal cavity,
- violation of the integrity of the spleen.

4. Surgical treatment under General anesthesia for emergency indications. Splenectomy.

5. Painkillers, antibacterial therapy, solutions of crystalloids, colloids, infusion of erythrocyte mass in order to eliminate anemia. Take food after recovery of bowel function.

Situational task 3

1.Thrombosis of the splenic vein. Selective portal hypertension.

Peptic ulcer of the stomach and duodenum.

Stomach cancer.

2. Mallory-Weiss Syndrome.

Hemorrhagic gastritis.

Hemangioma of the stomach.

3. Fibrogastroscopy will determine the source of bleeding and the state of hemostasis. With selective (left-sided) portal hypertension, dilated veins of the esophagus and predominantly the arch of the stomach are determined.

4. Moderate blood loss. With continued bleeding, emergency surgery is indicated, with stopped bleeding – planned.

5. With continued bleeding, splenectomy is indicated against the background of preoperative and operative hemostatic therapy (freshly frozen plasma, 10% p-R of calcium chloride, dicinnon, vikasol), transfusion of erythrocyte mass with a replacement purpose, infusion of crystalloid, colloidal solutions. When bleeding stops, it is necessary to eliminate anemia, and planned surgery is indicated.