

INTRODUCTION

Surgery of the liver and portal circulation is based on a clear understanding of the detailed anatomy of the liver, its arterial and portal blood supply, as well as the biliary and venous drainage.

ANATOMY

The liver is the largest abdominal organ, weighing approximately 1500g and extends from the fifth intercostal space to the right costal margin. It is wedge shaped, its apex reaching the left midclavicular line in the fifth intercostal space. The liver is attached to the undersurface of the diaphragm by suspensory ligaments which enclose a “bare area”, the only part of its surface without a peritoneal covering.

Topographically the liver is divided by the attachment of the falciform ligament into right and left lobes; fissures on its visceral surface demarcate two further lobes, the quadrate and caudate. (Fig 1)

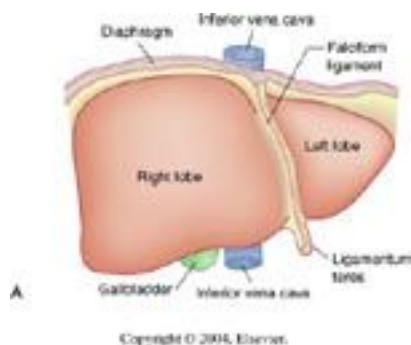


Figure 1: Liver Anatomy

The obvious surface markings of the liver which divide it into the anatomical right and left lobes conceal a functional system of liver segments divided vertically by the scissurae demarcated by the planes of the right, middle and left hepatic veins. Within each of the resulting four liver sectors there is a segmental arrangement defined by the portal and arterial blood

supply. This system of eight structurally and functionally independent liver segments has now been universally adopted (Figure 2).

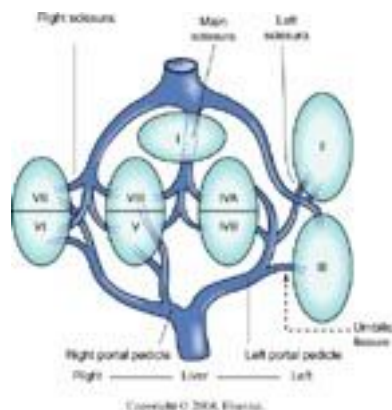


Figure 2: Schematic diagram of the segmental anatomy of the liver. Each segment receives its own portal pedicle (triad of portal vein, hepatic artery, and bile duct).

The right liver has four segments (5, 6, 7, 8) and the left liver three (2, 3, 4). The caudate lobe, which has a separate venous drainage to the inferior vena cava, constitutes segment 1. Each segment contributes hepatic veins that join to form the three main veins; the right hepatic drains segments 5-8, the middle hepatic drains from both livers (segments 4 and 5); and the left hepatic drains segments 2-4 (Figure 3).

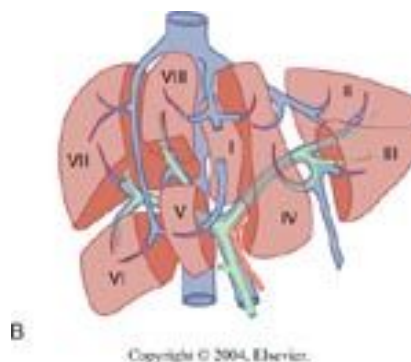


Figure 3: Segmental anatomy of the liver.

Major resections of the liver are possible provided whole segments with their associated blood supply, biliary and venous drainage are left intact. Identification of segmental anatomy is mandatory in patients with focal lesions being considered for surgery, as this aids planning of liver resections.

Accurate localisation of individual lesions by preoperative imaging and intraoperative ultrasound may allow segmental anatomic resections that reduce blood loss and loss of hepatic functional reserve.

Blood Supply

The liver normally receives 1500 mL of blood per minute and has a dual blood supply: 65% comes from the portal vein and 35% from the hepatic artery. Because of its better oxygenation the hepatic artery supplies 50% of the oxygen requirements.

The venous drainage of the liver comprises three main hepatic veins that drain into the suprahepatic inferior vena cava, and smaller accessory hepatic veins that drain into the retrohepatic vena cava. The right hepatic vein is single in 90 per cent of cases. The middle hepatic vein runs in the principal portal fissure and forms a common trunk with the left hepatic vein in 85 per cent of cases. The left hepatic vein arises from the confluence of a transverse vein which drains segment II, and a sagittal vein which drains segment III and has contributions from segment IV.

The portal vein divides at the hepatic hilum into right and left pedicles on which the right and the left lobes of the liver respectively are based (Figure 4).

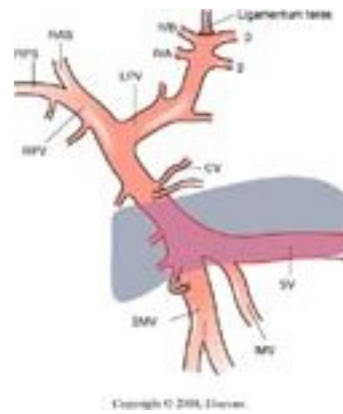


Figure 4: Portal Venous Anatomy

A theoretical plane, the main portal fissure, separates the two lobes. The right portal vein, the shorter of the two, lies anterior to the caudate process and enters the liver through the hilar plate to divide into anterior and posterior branches. The anterior branch divides into segments VIII and V. The posterior branch supplies segments VII and VI. The left portal vein is longer than the right and runs transversely in the hilum and then superiorly in the base of the umbilical fissure to supply segments II, III, IV and the caudate lobe. The anatomy of the left portal venous system is remarkably constant.

The common hepatic artery, usually a branch of the coeliac trunk but occasionally of the superior mesenteric artery, supplies the liver with arterial blood through its right and left hepatic branches. The right hepatic artery passes behind the common bile duct and right hepatic duct to enter the liver parenchyma. The left hepatic artery runs along the inferior margin of the quadrate lobe, with the left hepatic duct and left portal vein before entering the left lobe in the umbilical fissure (Figure 5).

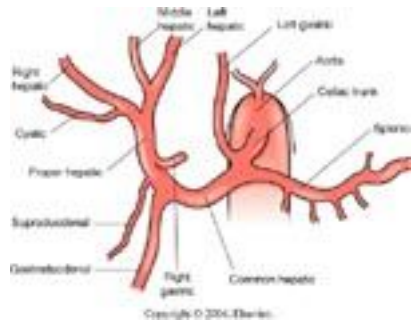


Figure 5: Hepatic Arterial Supply

LIVER PHYSIOLOGY

The liver has a key role in a wide spectrum of complex and critical functions. These include metabolism of carbohydrates, lipids, proteins and vitamins, production of bile, detoxification of both exogenous and endogenous blood-borne substances, and immune function via the fixed reticuloendothelial system of Kupffer cells. There is no single comprehensive test of 'liver function' and the term 'liver function tests' ('LFTs') covers a wide variety of investigations used for different purposes. The most commonly performed blood tests include the serum bilirubin which is a measure of conjugation and excretion of bile pigment, alkaline phosphatase, an enzyme associated with cholestasis and the transaminases, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are elevated by liver cell injury. γ -glutamyl transpeptidase (or γ -glutamyl transferase, GGT) provides a sensitive measure of enzyme induction, including that associated with alcohol abuse. Albumin concentration is a measure of hepatocellular protein synthesis, as is the prothrombin time. These basic tests give a broad assessment of underlying liver pathology, and are considered in more detail below.

Jaundice becomes clinically apparent when plasma bilirubin exceeds $50\mu\text{mol/l}$, which is three times the upper limit of normal. Routine bilirubin levels reflect total bilirubin, but in some circumstances it is useful to measure conjugated and unconjugated bilirubin separately. Unconjugated hyper-

bilirubinaemia is caused by an overproduction of bilirubin, usually as a result of haemolytic diseases such as congenital spherocytosis. It may also be caused by decreased hepatocyte uptake in sepsis or decreased conjugation caused by drug reactions, jaundice of prematurity, cirrhosis, hepatitis or Gilbert's syndrome. An increase in conjugated bilirubin may be the result of decreased secretion caused by drug reactions, cirrhosis, hepatitis, cholestasis of pregnancy or Dubin-Johnson syndrome, but more often is the result of biliary obstruction. Excess conjugated bilirubin in the urine resulting from extra- or intrahepatic biliary obstruction, produces the dark urine and pale stool of obstructive jaundice. In contrast, excessive urobilinogen in the urine implies an increased load or failure of extraction.

An increase in serum alkaline phosphatase in hepatobiliary disease is a sensitive marker of biliary obstruction and is also elevated in patients with space-occupying lesions in the liver. γ GT activity is induced by a variety of drugs, including ethanol, and may be markedly elevated even after a single episode of excessive alcohol intake. In combination with raised transaminase levels and increased mean corpuscular volume (MCV), it is a sensitive though non-specific indicator of chronic alcohol abuse. 5'-nucleotidase is less commonly used, but is more specific than alkaline phosphatase in detecting liver disease.

Some elevation of AST and ALT is found in almost all forms of liver disease. Both are significantly elevated in the presence of hepatocyte necrosis, though there is no direct relationship with the degree of functional liver impairment. High values are found in acute hepatitis, but high levels without a raised alkaline phosphatase suggest a hepatocellular rather than an obstructive cause for jaundice.

Albumin is one of the most important plasma proteins produced by the liver. Patients with cirrhosis and ascites frequently have low plasma albumin levels. Albumin levels are affected not only by liver disease but also by nutrition, osmotic pressure, acute phase reaction stimuli and alcohol. Thus the serum albumin concentration per se is not an accurate prognostic indicator in liver disease although it is a useful component of the Child-Pugh scoring system.

The liver is the major synthetic site for all coagulation proteins except von Willebrand's factor. The synthesis of factors II, VII, VIII and X is dependent on normal liver function and on adequate vitamin K levels. As vitamin K is fat soluble, deficiency develops in the presence of biliary obstruction with fat malabsorption. The prothrombin time must always be checked before invasive procedures are undertaken in patients with suspected liver disease. Parenteral administration of vitamin K usually corrects deficiencies caused by biliary obstruction, but is not effective in patients with prolonged or severe hepatocellular disease in whom fresh frozen plasma or cryoprecipitate should be given.

The above tests are static indicators of individual components of liver function. More sensitive information may be obtained by quantitative or semi-quantitative dynamic tests, including antipyrine, aminopyrine, lignocaine and galactose clearance tests. Arterial ammonia levels are sometimes measured in patients with suspected liver failure and portal systemic encephalopathy. The indocyanine green dye clearance test is used in some specialist units to predict complications after hepatic resection and rejection after liver transplantation.

Other tests used in liver disease

Specific tests for liver disease include screening for hepatitis A, B and C. Antimitochondrial, smooth muscle and antinuclear antibodies are used to investigate suspected primary biliary cirrhosis and autoimmune chronic active hepatitis. Iron, iron-binding

capacity and serum ferritin are used in the diagnosis of haemochromatosis. Caeruloplasmin and urinary copper levels are used to diagnose Wilson's disease. α 1-antitrypsin is measured when a deficiency of this enzyme is suspected. Specific markers for neoplasms include alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) levels. Infectious serologic markers include cytomegalovirus (CMV), Epstein-Barr virus antibodies, leptospiral agglutination tests and amoebic and hydatid complement fixation tests.

Scoring systems in liver disease

Scoring systems have been used to monitor the progression of conditions such as primary biliary cirrhosis and sclerosing cholangitis, and to predict the need and timing of transplantation. The most commonly used is the Child's grading system, modified by Pugh. Originally designed to predict mortality and encephalopathy following portal-systemic shunting, the Child-Pugh classification has been extended to grade liver function and assess risk in patients with liver disease. A new system is the Model for End-stage Liver disease (MELD) which measures 3 factors, bilirubin, INR and creatinine.

DIAGNOSIS OF LIVER DISEASE

The clinical history, physical examination, urine investigation and stool and haematology tests are important and combined with the liver biochemical tests and radiographic examinations allow an initial differential diagnosis and direct triage and supplementary investigations.

Details of any anorexia, nausea, jaundice, pruritus, fever and pain, as well as previous operations, drugs (especially alcohol), toxins and exposure to infection should be sought. Fever and pain are common in alcoholic hepatitis; rigors and sudden severe pain suggest cholangitis. Relentless progression of jaundice with weight loss, pruritus and pale stools point to malignant extrahepatic obstruction. Prior biliary surgery directs attention to the bile

duct. Transfusion, injections, polypharmacy, promiscuity, contact with dialysis patients or jaundiced persons, intravenous drug use and tattooing raise the possibility of hepatitis.

Stigmata of chronic liver disease including palmar erythema, spider naevi, finger clubbing, white nails, gynaecomastia, muscle wasting, spontaneous bruising and scratch-marks from pruritus should be specifically excluded. Skin bruising may be present, reflecting the clotting defects characteristic of vitamin K deficiency in severe liver disease. Testicular atrophy, gynaecomastia, parotid enlargement and Dupuytren's contracture suggest an alcoholic aetiology. Intellectual deterioration, flapping tremor and foetor hepaticus indicate marked liver decompensation. Liver size, consistency and tenderness should be noted. Greater enlargement tends to occur with extrahepatic biliary obstruction. Jaundice and a palpable gallbladder suggest periampullary cancer (Courvoisier's law). A cirrhotic liver may be large, medium-sized or small with blunt, lobulated and firm edges. A liver with hepatocellular cancer is often large, hard and nodular. A systolic bruit over the liver may indicate hepatocellular cancer or alcoholic hepatitis. Dilated abdominal wall veins draining away from the umbilicus signify portal hypertension. Splenomegaly and ascites should be noted.

IMAGING

X-rays

Liver size may be indicated by bowel displacement. Calcification in gallstones (10-15%) and chronic pancreatitis or mass effects of tumours, or hydatid cysts can sometimes be seen. Gas in intrahepatic bile ducts or abscess cavities can aid in diagnosis.

Ultrasound

Ultrasound (US) is the first line radiological test used for hepatobiliary disease, especially jaundice. US is

quick, cheap and patient-friendly and can be used to guide invasive procedures such as drainage of fluid collections and biopsies. Intrahepatic duct dilatation is usually indicative of biliary obstruction and US establishes the presence and level of biliary obstruction in over 90% of cases, similar to computed tomography scans. Parenchymal liver disease or sclerosing cholangitis may prevent biliary dilatation and obesity and bowel gas can limit visibility. Use in ICU and theatre (including laparoscopic) extends its role. Duplex doppler combines US and doppler to evaluate blood flow in vessels, tumours and shunts.

Computed tomography (CT) scanning

CT scanning is extremely helpful in evaluating liver disease and masses, often complementing ultrasound. Spiral CT allows the rapid acquisition of high quality images during various intravenous contrast phases. Lipiodol, an iodized oil suspension, has some value in detecting small primary hepatocellular carcinomas.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) images hydrogen nuclei in water using magnetic fields and radiowaves. Different sequences may provide valuable information for the surgeon in evaluating the nature of liver tumours.

Biliary imaging

Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) can both be used to depict biliary strictures, tumours or calculi.

Hepatic angiography

Hepatic angiography is particularly useful prior to liver resection to detect arterial anomalies. Arterial portography with Digital Subtraction Angiography (DSA) is used in patients with portal hypertension.

Arterial embolization

Selective transcatheter arterial embolic occlusion with a variety of materials including metal coils and gelfoam allows treatment of arterial injuries. Shrinkage of tumours by occlusion or chemo-embolisation of the arterial blood supply is used in selected cases. Transhepatic portal venous embolization is used to produce atrophy of a liver lobe and allow hypertrophy of the remaining liver before resection.

Isotope scanning

Nuclear medicine studies may be of value in diagnosing certain liver masses, the causes of postoperative jaundice, and in evaluating the success of biliary drainage procedures. Positron emission tomography (PET scanning) is a new investigation which may enable better detection of hepatic primary and secondary tumors, due to increased glucose metabolism in neoplasms.

ASSESSMENT OF A LIVER MASS

This common problem merits separate consideration. The objectives in assessing a liver mass are:

- to establish a diagnosis
- to determine whether surgery is indicated
- to judge whether resection is possible (i.e. the extent of the lesion and relation to vascular and biliary anatomy)

The importance of a careful history and examination has already been emphasized. Particular attention is given to details of previous surgery, malignancy or liver disease. The clinical features and organ of origin of the mass should be assessed. Large right adrenal or kidney tumours may mimic liver tumours. Liver function tests, serum tumour markers (α -foetoprotein, carcinoembryonic antigen, CA 19-9) should be obtained. Gastrointestinal hormones and urinary 5-hydroxyindoleacetic acid for carcinoid tumours are measured when appropriate. Patients with primary

fibrolamellar liver tumours often do not express AFP, but the presence of neurotensin and elevated vitamin B12-binding capacity in the serum are relatively specific for this type of tumour. Rapid recourse to percutaneous biopsy of a liver mass without careful diagnostic evaluation and planning of possible treatment is often inappropriate, may be dangerous and is often not necessary.

Imaging

Radiological imaging is the cornerstone of diagnosis for focal liver lesions. Various algorithmic approaches have been described, all starting with an ultrasound scan. The initial questions to determine are whether lesion(s) are single or multiple, or solid or cystic. Cystic lesions of the liver are considered later in this chapter. The solitary or potentially resectable liver 'tumour' is best evaluated by CT and, when appropriate, MRI scanning. Each of the benign and malignant tumour types has typical but seldom diagnostic appearances. The CT evaluation of the tumour appearance and behaviour during the various phases of contrast injection may be helpful. It should be possible to distinguish most cavernous haemangiomas from other tumours by this means, though some vascular tumours may create difficulty. It is important to remember that chest radiographs (and possibly CT scans of the lungs) may avoid unnecessary investigations by demonstrating that the patient has metastatic disease, rendering further investigation and surgery futile. Solid lesions which are multiple and bilobar are unlikely to be treated by liver resection and may reasonably be biopsied under ultrasound guidance, provided there are no other contraindications. Biopsy of a liver mass may be performed percutaneously (with or without CT or ultrasound guidance), laparoscopically, or at laparotomy. The biopsy may be for cytology only (fine-needle aspiration [FNA]) or for histology (larger-bore core biopsy). Early biopsy of a solitary lesion, or

lesions likely to be resected is not advised. Not only is there a risk of bleeding from vascular tumours, but tumour dissemination into the peritoneal cavity and along the needle track following percutaneous needle biopsy may occur⁸. Sampling and interpretational errors and infection can also occur. Fine-needle aspiration cytology is safer, but is more difficult to interpret and has a higher false-negative rate for diagnosing tumours. Hypervascular masses, coagulopathy, and ascites are contraindications to percutaneous core biopsy. FNA biopsy is generally safe under these circumstances. In the evaluation of any liver mass, percutaneous biopsy should be performed only if it can reasonably be expected to obviate the need for exploratory laparotomy. Most patients with symptomatic masses would be considered for laparotomy, making preoperative histology superfluous. Biopsy of an irresectable suspected primary or metastatic malignancy can spare the patient an unnecessary laparotomy. Laparoscopic biopsy can also be used to evaluate liver masses and to avoid laparotomy.

PYOGENIC LIVER ABSCESS

Liver abscesses are caused by bacterial, parasitic or fungal infection. Pyogenic abscesses account for three-quarters of hepatic abscess in developed countries. Elsewhere, amoebic abscesses are more frequent and, world-wide, are the commonest cause of liver abscesses.

Aetiology

Most pyogenic liver abscesses occur secondary to infection originating in the abdomen. Cholangitis due to stones or strictures is the commonest cause (Table 1). Abdominal infection due to diverticulitis or inflammatory bowel disease may spread through the portal vein to the liver. Less commonly bacteraemia occurs via the hepatic artery from a distant site such as dental sepsis or endocarditis. Other routes of spread are by direct extension from an adjacent

inflammatory process such as an empyema of the gallbladder or a perinephric abscess, or as a result of penetrating trauma. In 15% of cases no cause can be found ("cryptogenic abscesses"). Compromised host defenses have been implicated in the development of cryptogenic abscess and may play a role in the aetiology of most hepatic abscesses. Liver abscess occur in children with leukaemia and other immune disorders. Diabetes mellitus has been noted in 15% of adult patients with pyogenic liver abscess. Uncommon causes are due to secondary bacterial infection of an amoebic abscess or hydatid cyst.

Bacteriology

In most pyogenic liver abscesses a polymicrobial infection is present with predominantly endogenous gram negative aerobic and anaerobic organisms. Most organisms are of bowel origin. *Escherichia coli*, *Klebsiella pneumoniae*, *Bacteroides*, enterococci, anaerobic streptococci and microaerophilic streptococci are most common. Staphylococci, haemolytic streptococci, and *Streptococcus Milleri* are usually found if the primary infection is bacterial endocarditis or dental sepsis. Immunosuppression due to AIDS, intensive chemotherapy and transplantation has resulted in an increase of involvement by fungal and opportunistic organisms.

TABLE 1 Causes and origin of Pyogenic liver abscess

Biliary tract
<ul style="list-style-type: none"> • Stones • Cholangiocarcinoma • Strictures • Sclerosing cholangitis
Hepatic artery
<ul style="list-style-type: none"> • Dental infection • Bacterial endocarditis • Intravenous drug abuse

Portal vein
<ul style="list-style-type: none"> • Appendicitis • Diverticulitis • Crohn's disease • Pelvic sepsis
Direct extension
<ul style="list-style-type: none"> • Gall bladder empyema • Perforated peptic ulcer • Perinephric abscess
Trauma
Iatrogenic
<ul style="list-style-type: none"> • Liver biopsy • Percutaneous biliary stent drainage
Cryptogenic
Secondary infection of liver cyst

Clinical Features

The classic presentation is with abdominal pain, swinging pyrexia and nocturnal sweating, vomiting, anorexia, malaise and weight loss. The onset may be insidious or occult in the elderly. Single abscesses tend to be gradual in onset and are often cryptogenic. Multiple abscesses are associated with more acute systemic features and the cause is more often identified. Clinically the liver is enlarged and tender. Percussion over the lower ribs aggravates the pain. The spleen may be palpable in chronic cases. Ascites is uncommon. Clinical jaundice occurs only in the late stage unless there is suppurative cholangitis. Some patients do not have right upper quadrant pain or a hepatomegaly and an initial diagnosis is a fever of unknown origin.

Laboratory Investigations

In two-thirds of patients there is a marked leucocytosis, although the white count may be normal in seriously ill patients. The ESR is usually markedly raised with an anaemia of chronic infection. The alkaline phosphatase is generally raised with hypoalbuminaemia. The serum

aminotransferases are marginally elevated. On plain abdominal film, hepatomegaly may be seen, sometimes with an air fluid level in the abscess cavity (Figure 6). The right diaphragm is usually elevated with a pleural reaction or pneumonic consolidation.



Figure 6: CXR with Air Fluid Level in Liver Abscess

Ultrasound is the preferred first line scan as it is non-invasive, cost-effective and accurate. A CT scan is useful to identify other intra-abdominal abscesses (Figure 7). ERCP is used to define the site and cause of biliary obstruction. Identification of the organism by ultrasound guided aspiration is an essential diagnostic step.



Figure 7: CT with multiple Cholangitic Abscesses

Treatment

Treatment of pyogenic liver abscess includes antibiotic therapy and

evacuation of the abscess by percutaneous aspiration, or catheter or surgical drainage. Antibiotics should be started promptly. The appropriate selection is based on the spectrum of organisms likely to be isolated. Initial empiric broad-spectrum parenteral broad-spectrum antibiotic therapy should include penicillin, an aminoglycoside and metronidazole which are adequate for *E coli*, *K pneumoniae*, *Bacteroides*, enterococcus and anaerobic streptococci. In the elderly and those with impaired renal function a third-generation cephalosporin should be used instead of an aminoglycoside. Metronidazole is effective against both anaerobes and amoebiasis. Penicillin is the drug of choice for *Strep milleri* infections which are usually resistant to metronidazole. In patients allergic to penicillin, the combination of vancomycin, an aminoglycoside, and metronidazole will provide appropriate and effective cover. Ampicillin should be added if *Strep faecalis* is cultured. The regimen may be modified later according to the results of cultures.

The length of antibiotic therapy is based on the number of abscesses, the clinical response, and the potential toxicity of the chosen regimen. Patients with multiple biliary abscesses should receive 4 weeks of antibiotic therapy. A shorter antibiotic course may suffice for a small, solitary abscess that has been adequately drained. Initially, antibiotic therapy is given parenterally. In patients requiring a prolonged course of antibiotics, appropriate oral agents may be used after 2 weeks of systemic therapy.

Antibiotic therapy alone is effective only in a small number of cases and most pyogenic liver abscesses initially require ultrasound or CT scan guided percutaneous aspiration or catheter drainage. The advantages of percutaneous drainage include avoiding general anaesthesia and an operative procedure, shorter hospitalization, easier nursing and

better patient acceptance. Open surgical drainage is used when antibiotic therapy and percutaneous aspiration or catheter drainage have failed because of radiologically inaccessible abscesses, or very large, multiloculated abscesses, or where there is underlying intra-abdominal disease such as biliary tract stones or intra-abdominal sepsis that requires surgery. In all cases an underlying cause should be sought and treated. Acute biliary obstruction with cholangitis must be relieved urgently and can usually be done via endoscopic papillotomy and if necessary, insertion of a temporary biliary stent.

Early diagnosis, treatment with appropriate antibiotics and selective drainage have substantially reduced mortality. Adverse prognostic factors increasing mortality include the presence of shock, adult respiratory distress syndrome, disseminated intravascular coagulation, immunodeficiency states, severe hypo-albuminaemia, diabetes, ineffective surgical drainage and associated malignancy.

AMOEBIC LIVER ABSCESS

Some 10% of the world's population are chronically infected with *Entamoeba histolytica*. Amoebiasis constitutes the third leading parasitic cause of death, surpassed only by malaria and schistosomiasis. *Entamoeba histolytica* is ubiquitous with a worldwide distribution. The prevalence of infection varies widely, and is most frequently encountered in tropical and subtropical climates. Overcrowding and poor sanitation are the major environmental predisposing factors and the brunt of disease is borne by the poor and lower socioeconomic groups within developing nations.

Pathogenesis

Parasite transmission is via the faeco-oral route with the ingestion of viable

protozoal cysts. The cyst wall disintegrates in the small intestine and motile trophozoites are released which migrate to the large bowel where pathogenic strains may cause invasive disease. Mucosal invasion results in flask-shaped ulcers through which amoebae gain access to the portal venous system. The abscess is usually solitary and involves the right lobe in 80% of cases. The abscess contains sterile pus and reddish-brown ("anchovy paste") liquefied necrotic liver tissue. Amoebae are occasionally present at the periphery of the abscess.

Clinical Presentation

The duration of symptoms ranges from a few days to several weeks before presentation. Pain is a prominent feature and the patient appears toxic, febrile and chronically ill. Fever (38-39°C) is characteristically intermittent with night sweats and weight loss, nausea, vomiting, cough and dyspnoea. The liver is enlarged with maximal tenderness over the abscess.

Diagnosis

The diagnosis is based on clinical, serological and radiological features. The patient is usually resident in or has visited an endemic area recently, although there may be no history of preceding diarrhoea. A leucocytosis with 70-80% polymorphs (eosinophilia is not a feature), a raised ESR and moderate anaemia are common. In severe disease with multiple abscesses, elevated alkaline phosphatase and bilirubin levels occur. Stool examination may reveal cysts, or in the case of dysentery, haematophagous trophozoites. Radiological imaging is essential. Chest x-ray shows a raised, poorly moving, right diaphragm with atelectasis or pleural effusion. After rupture through the diaphragm, a pleural effusion, lung abscess, consolidation or, rarely, bronchopleural fistula, may be present. Ultrasound shows the size and position of the

abscess and is useful when aspiration is necessary to establish the diagnosis. Ultrasound is also used to assess the response to therapy.

Serological tests provide a rapid means of confirming the diagnosis, but may be misleading because of previous infection in endemic areas. Indirect haemagglutination titres for *Entamoeba* are elevated in over 90% of patients. In areas where amoebiasis is uncommon, delay in diagnosis may occur because the disorder has not been considered. Pain or tenderness in the right upper quadrant may lead to a suspicion of other liver, gall bladder, duodenal or pancreatic disease. A history of travel abroad to an endemic area and a raised right diaphragm on X-ray should lead to the diagnosis. Major complications occur either as a result of secondary infection or rupture into adjacent structures such as pleural, pericardial or peritoneal spaces. Two-thirds of ruptures occur intraperitoneally and one-third intrathoracically.

Treatment

Supportive measures such as adequate nutrition and pain relief are important. The mainstay of drug therapy is metronidazole 800 mg three times a day for 5 days, which has a cure rate of 95%. Clinical symptoms usually improve dramatically within 24 hours. Lower doses of metronidazole are often effective in invasive disease but may fail to eliminate the intraluminal infection and so clinical relapses can occur. After the amoebic liver abscess has been treated diloxanide furonate 500 mg 8 hourly for 7 days is used to eliminate intestinal amoebae.

Most uncomplicated abscesses resolve with metronidazole treatment alone. Ultrasound guided needle aspiration is performed if serology is negative, or the abscess is large (>10 cm), if there is no satisfactory response to treatment, or there is

impending peritoneal, pleural or pericardial rupture. The conservative regimen described above has been adopted in most endemic areas. Surgical drainage is required only if the abscess has ruptured with amoebic peritonitis or if there is no response to medical treatment in spite of needle aspiration or catheter drainage.

HYDATID DISEASE

Hydatid disease in man is caused by the dog tapeworm, *Echinococcus granulosus*. Dogs are the definitive host, shedding ova in the faeces, which infect the natural intermediate hosts such as sheep or cattle. Hydatid disease is endemic in many sheep-raising countries. Increasing migration and world travel have made hydatidosis a global problem of increasing importance.

Echinococcus is the smallest of all adult tapeworms, measuring 6 mm in length. Several closely related species of *Taenia echinococcus* have the potential of causing disease in man. *Granulosus* is cosmopolitan, *multilocularis* is limited to the northern hemisphere while *vogeli* and *oligarthrus* are indigenous to Central and South America. The life-cycle typically involves 2 hosts. The definitive host is a carnivore, the adult worm living in the host small bowel attached to mucosa and shedding its eggs in the gut. The ova are resistant to drying and remain viable for several weeks after being passed. The intermediate host is a herbivore, which ingests the ova while grazing. The ova hatch in the bowel, enter the portal circulation and develop in the liver. The life-cycle is completed when the dog eats contaminated offal. Man is an unwitting accidental intermediate host and contracts the disease when ova are swallowed after contact with an infected dog. Preventative campaigns depend on interrupting this life-cycle. *E. multilocularis* is uncommon; the primary host is usually

a fox or wolf and the intermediate host a vole or lemming.

Human infection follows accidental ingestion of ova passed in dog faeces. The ova penetrate the intestinal wall and pass through the portal vein to the liver, lung and other tissues. Hydatid cysts can develop anywhere in the body but two-thirds occur in the liver, and one quarter involve the lungs. The mature cyst has 3 layers, an inner germinal lining, and a middle acellular laminated layer, which is surrounded by an outer fibrous host pericyst layer. In older cysts the laminated and pericyst layers may become calcified. The germinal layer produces daughter cysts and brood capsules containing scoleces capable of spreading the disease.

A liver hydatid may present either with liver enlargement and right upper quadrant pain due to cyst pressure or acutely with a complication. Hydatid cysts progressively enlarge. Complications include cyst rupture into the peritoneal cavity, resulting in urticaria, anaphylactic shock, eosinophilia and implantation into omentum and other viscera. Cysts may compress or erode into a bile duct causing pain, jaundice or cholangitis or the cyst may become infected secondary to a bile leak. Perforation through the diaphragm and communication with the lung and bronchus ("coughing up grape-skins") is uncommon. Ultrasound and CT scan demonstrate the size, position and number of liver cysts (Figure 8).

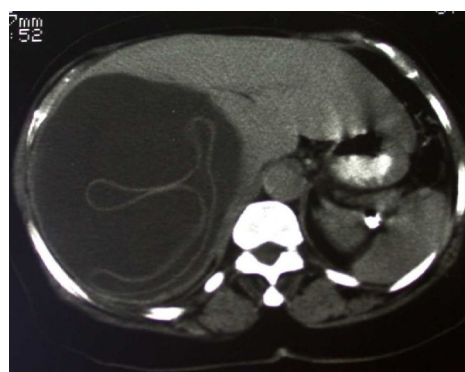


Figure 8: CT showing Right Lobe Liver Hydatid

The scan should examine the entire abdomen for extrahepatic cysts. In 10% of patients the chest X-ray will also show a lung hydatid. Eosinophilia is present in 40% of patients. The diagnosis is confirmed by serologic haemagglutination and complement fixation tests. ERCP is used to demonstrate a cyst communication with the bile ducts if the patient is jaundiced or if the serum alkaline phosphatase, gamma GT or bilirubin are elevated.

All symptomatic cysts require surgery to prevent complications. Small densely calcified cysts ("golf-ball" appearance) signify death of the parasite and require no further treatment. Surgery requires careful isolation of the operative field by abdominal swabs soaked in scolical fluid to prevent spillage and implantation. Because the cyst wall is fragile, care must be taken to avoid rupturing the cyst. If scoleces spill into the peritoneal cavity, the parasite will form new cysts. During operation the cyst fluid is aspirated and replaced by a scolical agent such as 0.5% sodium hypochlorite or 0.5% silver nitrate solution. Scolical solutions are not injected if there is a bile leak because of possible chemical injury to biliary epithelium. Once the cyst is decompressed, the cyst and contents are carefully shelled out by peeling the endocyst off the host ectocyst layer along its cleavage plane. The fibrous host wall of the residual cavity is carefully examined for bile leakage from biliary-cyst communications and these are sutured closed. The cavity is drained and filled with omentum. Conservative surgery is effective in most cysts and liver resection is seldom necessary. Albendazole is given for 2 weeks postoperatively to prevent recurrence. Drug therapy is also used in patients unfit for surgery, in those with disseminated, recurrent or inoperable disease and or as an adjuvant in complex surgery. These drugs must be used cautiously and the patients carefully monitored for side-

effects which are bone-marrow depression, liver and renal toxicity. New radiologically guided aspiration techniques are being assessed in selected patients.

LIVER TUMOURS

Tumours of the liver may be cystic or solid, benign or malignant. The majority are asymptomatic, with normal liver function tests and increasingly are discovered as incidental findings during ultrasound or computed tomography. Many require no treatment, but it is important for non-specialists to identify lesions that require further investigation and to avoid unnecessary biopsy, which is now rarely indicated.

Cystic liver lesions

Cystic lesions of the liver are easily identified by ultrasound scan. The majority (>95%) are simple cysts which are estimated to be present in 1% of the population. These are thin walled, containing clear fluid without septa or debris and are surrounded by normal liver tissue. Asymptomatic simple cysts are regarded as congenital malformations and require no further investigation or treatment, as complications are rare. Aspiration and injection of sclerosants should be avoided as it may result in bleeding and infection, and does not result in resolution of the cyst. Rarely simple cysts can grow very large and produce compressive symptoms that are managed by limited surgical excision of the cyst wall (cyst fenestration).

Two or more cysts are present in 50% of patients with simple cysts. True polycystic liver disease is seen as part of adult polycystic kidney disease (APKD), an uncommon autosomal dominant disease that progresses to renal failure (Figure 9). Multiple renal cysts are always present and usually precede liver cyst development. Liver function is normal and most patients are asymptomatic. Occasionally pain

due to liver capsule distension requires cyst fenestration.

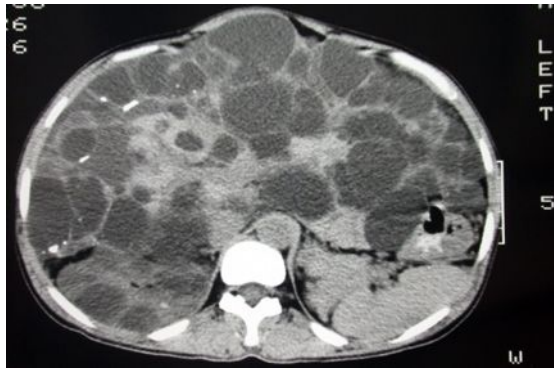


Figure 9: Polycystic Disease of the Liver

Thick walled cysts, those containing septae or nodules or echogenic fluid, may represent cystic tumours (cystadenoma, cystadenocarcinoma) or infective cysts (hydatid cysts and abscesses), and should be referred for specialist surgical opinion.

BENIGN TUMOURS OF THE LIVER

Benign liver tumours are common, usually asymptomatic and the importance of most is only in differentiation from malignant lesions.

Haemangiomas

These are the commonest benign solid tumours of the liver with a reported incidence in the general population of around 3%. Those over 10cm in diameter occasionally produce non-specific symptoms of abdominal discomfort and fullness, and rarely fever thrombocytopenia and hypofibrinogenaemia. Malignant transformation and spontaneous rupture rarely, if ever, occur. CT is usually sufficient to diagnose most haemangiomas and in equivocal cases magnetic resonance imaging (MRI) or ⁹⁹Tc-labeled red blood cell scintiscanning are diagnostic. Angiography and biopsy are now rarely required (Figure 10, 11)



Figure 10 CT showing haemangioma of liver

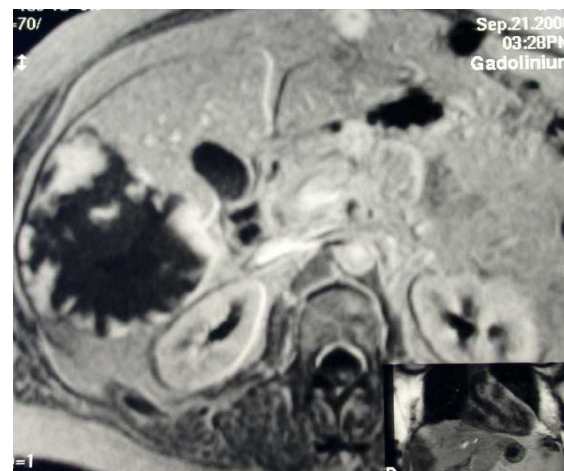


Figure 11 MRI Scan of Liver Haemangioma

Liver Cell Adenoma (LCA) and Focal Nodular Hyperplasia (FNH)

These uncommon tumours both occur predominantly in women of childbearing age. LCA became more prevalent with the widespread usage of oral contraceptive medication (OCM) in the 1960's but is now less common with the reduced oestrogen content of modern contraceptives. Most patients present with pain due to rapid tumour growth, intratumour haemorrhage or the sensation of a mass. LCA has a 10% risk of rupture and malignant transformation is found in 10% of resected specimens. FNH is not related to OCM usage, is usually asymptomatic and is not premalignant. FNH classically demonstrates a central stellate scar on CT and MRI

and does not require treatment unless symptomatic. Patients with LCA require liver resection to prevent the risks of haemorrhage and malignant transformation.

There remains a small proportion of patients in whom a firm radiological diagnosis cannot be made and in which distinction from a malignant hepatic tumour is uncertain. Symptomatic patients require surgical resection, which in specialist centres has a mortality of <5%. Surgical excision should also be the management of choice in most asymptomatic patients rather than liver biopsy, since the latter may yield inadequate samples and carries the risks of haemorrhage and tumour seeding. Furthermore histological distinction between FNH and cirrhosis, and LCA from well-differentiated hepatocellular carcinoma (HCC) may be very difficult with tru-cut biopsy or fine needle aspiration samples.

MALIGNANT TUMOURS

Hepatocellular carcinoma

Although uncommon in the UK, accounting for only 2% of all cancers, worldwide there are over 1 million new cases per annum with annual incidence rates of 100 per 10⁵ males in parts of Southern Africa and SE Asia. The incidence of HCC is closely related to areas with high carrier rates of hepatitis B and C and >80% of HCC's occur in cirrhotic livers. Once viral infection is established it takes approximately 10 years for patients to develop chronic hepatitis, 20 years to develop cirrhosis and 30 years to develop HCC. In African and Asian countries Aflatoxin, produced as a result of contamination of imperfectly stored staple crops by *Aspergillus flavus*, appears to be an independent risk factor in the development of HCC, probably through mutation of the p53 suppressor gene.

In patients with cirrhosis, the diagnosis should be suspected when there is

deterioration in liver function, an acute complication (ascites, encephalopathy, variceal bleed, jaundice) or development of upper abdominal pain and fever. Ultrasound is capable of demonstrating most tumours, and demonstration of a discrete mass within a cirrhotic liver together with an alpha-fetoprotein (AFP) level of >500ng/ml is diagnostic, and liver biopsy is unnecessary. Surgical resection is the only treatment that can offer cure. However due to local tumour spread and severity of pre-existing cirrhosis, such treatment is feasible in less than 20% of patients even in experienced centres. Five year survival similar to those for surgery. For larger tumours, transarterial embolisation may have some survival advantage. Iodised oil (lipiodol) and cytotoxic drugs (cisplatin or doxorubicin) are injected into the hepatic artery via a catheter inserted in the femoral artery (Figure 12). The lipiodol is rapidly cleared by normal hepatocytes but not by tumour cells and is concentrated in the tumour. Tumour necrosis undoubtedly occurs but it remains to be seen if this results in a prolonged survival advantage.



Figure 12: Hepatic Angiogram of HCC

In patients without cirrhosis, HCC's usually present late with an abdominal mass and have normal liver function. CT has a greater sensitivity and specificity than ultrasound, particularly in tumours smaller than 1cm (Figure 13). AFP is elevated in 80% of patients but may also be elevated in patients with other tumours (testicular, gastric

and pancreatic). Fibrolamellar carcinoma is an important subtype of HCC, occurring in non-cirrhotic livers in patients without hepatitis B or C. It accounts for 15% of HCC in the Western Hemisphere and is important because of the favourable prognosis, with a 5 year survival of 50% following resection.



Figure 13: CT of Right Lobe HCC

Metastatic tumours

Liver metastases are common and are found in 40% of all patients dying with carcinoma. They are most frequently associated with carcinomas of the gastrointestinal tract (colo-rectal, pancreas and stomach) but are nearly as common in carcinomas of the bronchus, breast, ovary and lymphoma. With the exception of colorectal liver metastases, tumour deposits are usually multiple and seldom amenable to curative resection.

Colorectal liver metastases

Around 8-10 % of patients undergoing curative resection of colorectal tumours have isolated liver metastases suitable for liver resection, equivalent to around 1000 patients in the UK per annum. Half will have metastases present at the time of diagnosis of the primary (synchronous) and most of the rest will develop within the next 3 years (metachronous metastases).

Without surgical resection the 5 year survival rate for all patients with liver

metastases is zero, compared with an overall 5 year survival following resection of 30%. Tumours need not be solitary nor even confined to a single lobe, although outcome is worse in patients with resectable bilateral disease. The only limitation to liver resection for colorectal metastases is the ability to leave enough tumour-free liver to function, which depends on the extent and distribution of the tumour burden and the general fitness of the patient and their liver. The capacity of the liver to regenerate is legendary and a fit patient with a healthy liver can undergo a 60% resection that will completely regenerate in three months.

Liver resection

Liver resection has advanced rapidly over the last two decades due to a number of key developments. First was the anatomical description by Couinaud in 1957 of the segmental anatomy of the liver with its division into eight segments each, supplied by its own branch of the hepatic artery, portal vein and bile duct. It is now possible to safely remove each of these segments individually when required, reducing the amount of normal liver unnecessarily removed. Subsequently surgical techniques have been developed to dissipate the liver parenchyma, either by crushing with a clamp or by ultrasonic dissection, allowing the vascular and biliary radicals to be individually ligated. Occlusion of the vascular inflow (Pringle manoeuvre) and where possible the appropriate hepatic vein, together with lowering of the central venous pressure during survival is around 15%, with average operative mortality rates of 12%.

For patients with non-operable HCC less than 5cm in diameter, injection with 95% alcohol under ultrasound guidance has minimal morbidity and has been shown to result in 5 year survival figures

Resection, have reduced blood loss making blood transfusion unnecessary in 80% of liver resections. Improvements in postoperative care including epidural anaesthesia to reduce postoperative chest infections, and the ability to manage postoperative fluid or bile collections by radiological or endoscopic drainage, have resulted in a median hospital stay of 7-10 days and mortality of <3%. As a result liver resection has evolved from a hazardous bloody procedure, into a routine operation.



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