

CHAPTER 12

Gallstones and Benign Biliary Diseases

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Learning points

- Presentation of benign biliary disease is often non-specific; imaging is central in management, ultrasonography being the first approach used.
- Gallstone formation is multifactorial, though lifestyle has an important influence. Genetic markers of increased risk are now recognized in humans.
- Laparoscopic cholecystectomy is the standard surgical approach for patients with cholecystitis. Open cholecystectomy is still needed in some cases, and because of the comorbidities in this selected patient group has a higher complication rate and mortality.
- Bile duct damage at cholecystectomy occurs in around 1 in 200 patients; management requires a multidisciplinary team approach (radiologist, endoscopist, surgeon).
- Biliary tract intervention has a greater risks in patients with cirrhosis.

The spectrum of benign biliary disease is wide (Table 12.1), although the majority of clinical events are due to gallstones, either in gallbladder or bile duct. Symptoms and laboratory tests are likely to be suggestive but non-specific, but this does not obviate the careful assessment of history, examination findings and blood tests. An orderly work-up usually starts with ultrasonography. For the hepatologist, there will be the added complication of benign biliary disease coexisting or developing in a patient with primary hepatic disease, which may complicate normal approaches to management. Less difficult to recognize are the biliary complications of cholecystectomy and liver transplantation, although their management may be complex.

Gallbladder disease is in the differential diagnosis of right upper quadrant pain, some features of which particular suggest this origin. However, there are many other sources of similar pain or discomfort, emphasizing the need for collateral evidence from scanning.

Cholestatic liver function tests with or without jaundice, itching, pain or fever focus attention on possible bile duct disease, although again these features are not specific for bile duct obstruction.

Examination may be useful in showing characteristic pain or tenderness in the right upper quadrant, or a large nodular liver suspicious of malignancy. Jaundice and scratch marks suggest cholestasis. Splenomegaly raises the question of chronic liver disease, although haematological and other causes need to be remembered.

Liver function tests (bilirubin, transaminases, alkaline phosphatase, γ -glutamyl transpeptidase) will generally be normal in gallbladder disease, although there may be mild abnormalities with sepsis. However, abnormalities have to raise the possibility of bile duct disease. Characteristically, serum alkaline phosphatase and γ -glutamyl transpeptidase, with or without bilirubin, are high when bile drainage is impaired. However a sudden rise (and usually fall) of transaminases may be seen when acute obstruction occurs due to a stone, leading to an initial search for a hepatitis. Polymorph leucocytosis will relate to underlying infection.

In these situations, as in most liver-related algorithms, ultrasonography is the first imaging approach of choice. It is effective in showing gallbladder disease, and bile duct dilatation. It may show all that is required; if not, other modalities are used. A single flow chart for all clinical scenarios is not appropriate. Direct cholangiography (percutaneous cholangiography (PTC), endoscopic retrograde cholangiopancreatography (ERCP)) are now done with a specific purpose, therapeutic or to obtain tissue, such is the effectiveness of modern scanning. These techniques compliment management approaches where surgery is an alternative, and this emphasizes the need for a multidisciplinary team.

Cholestatic jaundice without or with pain may be due to malignant disease of the biliary system, described in Chapter 13.

Table 12.1. Benign biliary diseases

Gallbladder	
Stones	
Cholecystitis	
	calculous
	—acute
	—chronic
	acalculous
	—acute
	—chronic
	—gallbladder dyskinesia
	empyema
Polyps	
	inflammatory
	neoplastic
Miscellaneous	
	adenomyomatosis
	cholesterolosis
	porcelain
	xanthogranulomatous
	congenital anomalies
	associated with infections (e.g. HIV related, Salmonella)
Bile duct	
Stones	
	Common duct
	—asymptomatic
	—without cholangitis
	—with cholangitis
	Intrahepatic
Strictures	
	Postoperative
	—cholecystectomy
	—transplantation (Chapter 36)
	—anastomotic
	Primary sclerosing cholangitis (Chapter 16)
	Chronic pancreatitis
Others	
	Sphincter of Oddi dysfunction
	Autoimmune pancreatitis
	Haemobilia
	Mirizzi syndrome
	Parasites

Imaging

Gallbladder

Ultrasonography (US) after fasting is the most effective investigation. It is quick, does not involve radiation and is 95% accurate in the demonstration of gallbladder stones [1] (Fig. 12.1). US will also show whether the gallbladder is tender, whether the gallbladder wall is thickened and whether there is pericholecystic fluid, all features of acute cholecystitis (Fig. 12.2). Failure to show a gallbladder may also be an important finding.

Scintigraphy with technetium-labelled iminodiacetic acid derivatives (which track bile flow) also has an accu-

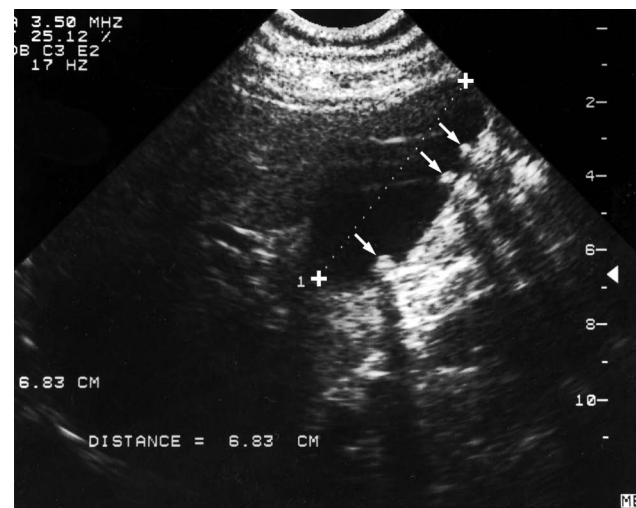


Fig. 12.1. Ultrasound scan of gallbladder showing three stones (arrowed) which cast acoustic shadows.

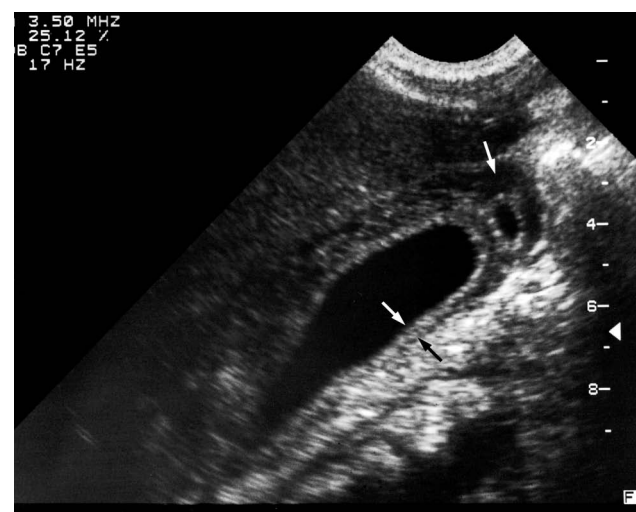


Fig. 12.2. Ultrasound scan in acute cholecystitis. Note the thickened wall of the gallbladder (between black and white arrows) with some pericholecystic fluid (single arrow).

Fig. 12.3. Cholescintigraphy (^{99m}Tc Iodida). (a) Normal scan. At 30 min the gallbladder (g) has filled. Isotope has already entered the bowel (B). (b) Acute cholecystitis. Gallbladder has not filled by 60 min.

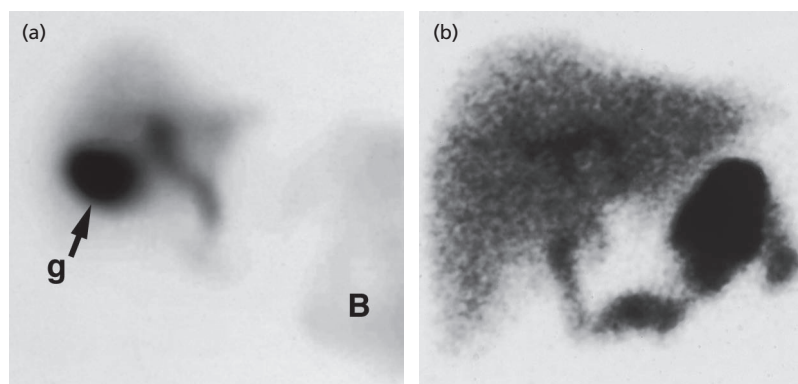


Fig. 12.4. Ultrasound scan showing dilated intrahepatic ducts (arrowed) and common bile duct (marked ++).

racy of 95% for acute cholecystitis (non-filling of gallbladder) (Fig. 12.3), but it may be more difficult to arrange quickly, takes longer and involves radioisotope. US takes precedence as the diagnostic approach.

CT and MRI scanning can show stones, but are most complementary in showing gallbladder size, wall thickness and evidence of inflammation as in acute cholecystitis [1]. They are second-line approaches after US.

Bile duct

US is also the method of choice in patients with cholestatic features where the primary question is whether there is evidence of bile duct dilatation or disease. The major intrahepatic bile ducts are normally 2 mm in diameter, the common hepatic duct less than 4 mm and the common bile duct less than 5–7 mm. Dilated bile ducts usually (but not always) characterize large bile duct obstruction (Fig. 12.4). US is 95% accurate in diag-

nosis of bile duct obstruction if the serum bilirubin level exceeds $170\ \mu\text{mol/L}$ ($10\ \text{mg/dL}$). False negatives occur if obstruction is of short duration or intermittent. US diagnoses the correct level and cause of obstruction in about 60% and less than 50% of cases, respectively, largely due to failure to visualize the complete biliary tree, particularly the periampullary region. Thus the sensitivity of US for showing common bile duct stones has been reported at 63% [2].

CT scanning may follow US, particularly if there is suspicion of malignant disease (see Chapter 13). It is more likely than US to show the level and cause of disease, and conventional CT has been reported to be around 70% sensitive in showing duct stones [2]. Helical CT-cholangiography is more sensitive but involves intravenous contrast and has no advantage over MRCP.

Magnetic resonance cholangiopancreatography (MRCP) allows excellent non-invasive cholangiography. Overall, it has an accuracy of greater than 90% in showing common bile duct stones [3] (Fig. 12.5). The sensitivity is lower for stones less than 6 mm in diameter. MRCP also has a high accuracy in showing bile duct strictures and is as sensitive as ERCP in detecting pancreatic carcinoma. It also shows changes of primary sclerosing cholangitis (Fig. 12.6) (see Chapter 16). MRCP is particularly useful in patients who are poor candidates for ERCP such as the elderly with comorbidity.

Endoscopic ultrasound (EUS) has a sensitivity and accuracy for choledocholithiasis of 96% and 99%, respectively, and is more accurate than transabdominal US [2]. However, the performance of EUS is not statistically better than MRCP [3]. Thus although EUS has been found to be valuable in specific situations, for example the patient with recent acute pancreatitis in whom a stone cannot be seen with non-invasive imaging [4], other techniques come first for most patients. EUS has, however, a role in the evaluation for malignant biliary tract disease (Chapter 13), and in difficult diagnostic situations to help to differentiate between benign and



Fig. 12.5. Magnetic resonance cholangiopancreatography in a 39-year-old woman with right upper quadrant discomfort. Ultrasound showed a bile duct of 1 cm but no stones were seen. Gallbladder was normal. Liver function tests were normal apart from marginally abnormal γ -glutamyl transpeptidase. The MRCP shows filling defects in the mid bile duct and stones were removed after endoscopic sphincterotomy.

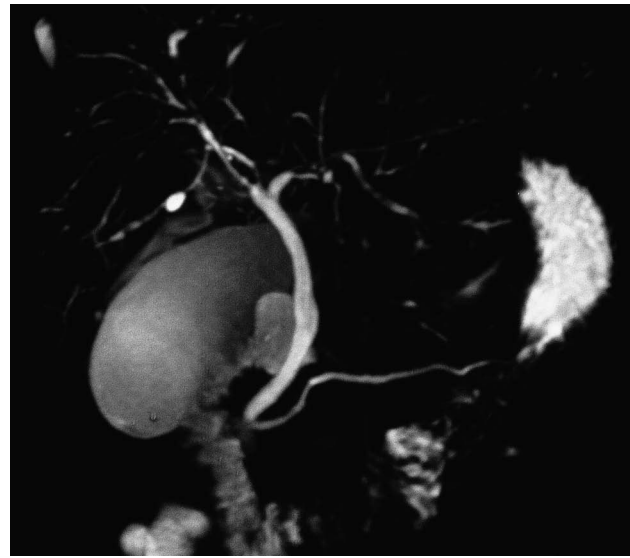


Fig. 12.6. Magnetic resonance cholangiopancreatography in a 40-year-old woman with chronic cholestasis of unknown aetiology. There are dilations and strictures of the intrahepatic and perihilar bile ducts. Diagnosis: sclerosing cholangitis.

malignant periampullary stricture—with the option of fine needle aspiration cytology or biopsy.

Oral cholecystography (OCG) and intravenous cholangiography have been superseded by other techniques for showing gallbladder stones and bile duct disease. On the rare occasion when it is necessary to show whether patients are appropriate for non-surgical treatment of gallbladder stones, however, OCG is valuable (see below).

Scintigraphy has a limited role for bile duct diseases, but can be valuable to demonstrate a biliary leak, as after cholecystectomy (Fig. 12.7), or non-invasively to document the degree of functional obstruction to intra- or extrahepatic bile ducts.

Endoscopic retrograde cholangiopancreatography (ERCP) is now widely available (Fig. 12.8). It may be performed in out-patients with only selected patients being admitted afterwards for observation [5]. The development of CT, MRI and MRCP, and EUS has led to the majority of ERCPs being planned therapeutic procedures. Sphincterotomy, stone removal, stent insertion, cytological sampling, balloon dilatation and manometry are all feasible. However, ERCP is an invasive procedure and carries the risk of complications. These include pancreatitis (generally ranging between 1 and 7%), cholangitis, bleeding and perforation (after sphincterotomy), as well as the risks of sedation and cardiovascular events in susceptible patients.

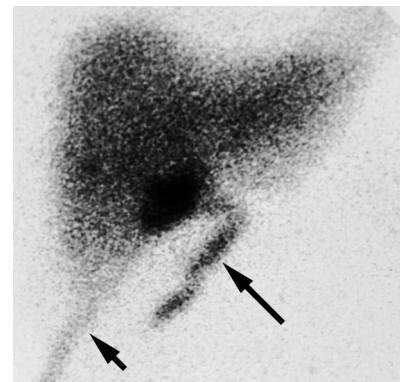


Fig. 12.7. Cholescintigraphy (^{99m}Tc Iodida). Postcholecystectomy bile leak. Isotope tracks laterally from gallbladder bed (short arrow) and T-tube track (long arrow).

The overall complication rate is around 4–7% with a mortality of 0.1–0.4% [6–8]. Complications are related to several factors including the underlying pathology, the difficulty of the procedure and the skill and experience of the operator. One particular focus of discussion currently is around approaches to reduce the risk of post-ERCP pancreatitis, particularly with consideration of placement of a temporary pancreatic duct stent in selected high-risk patients [9–11]. A selective rather than global prophylactic antibiotic policy is reported as being equally effective in preventing septic complications [12]. Despite the associated risks, ERCP rather than PTC is usually the first choice for direct cholangiography.

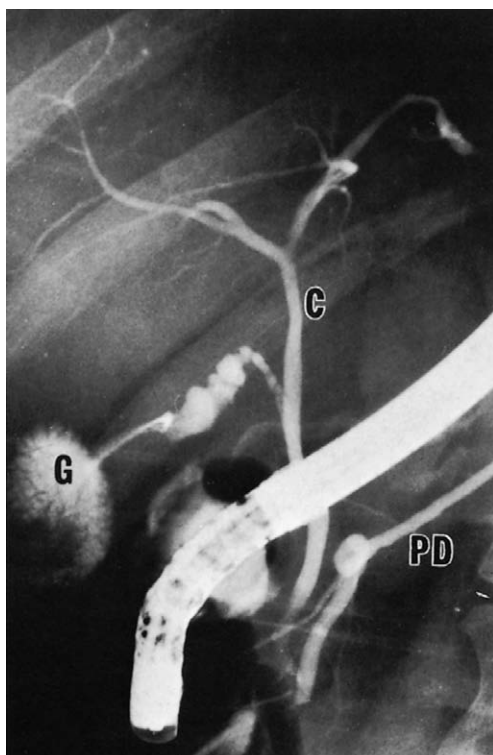


Fig. 12.8. Endoscopic retrograde cholangiopancreatography, normal appearances. C, common bile duct; G, gallbladder; PD, pancreatic duct.

Percutaneous transhepatic cholangiography (PTC) is done by passing a fine-gauge needle through the liver under fluoroscopic control and injecting contrast to identify and fill the biliary system (Fig. 12.9). Most PTC procedures are interventional and the biliary system is then entered with a catheter (PT drainage, PTD). Usually this is prior to insertion of an internal/ external biliary drain, or an internal endoprosthesis for malignant disease. However, PTC/D may be used for a combined procedure after failed ERCP access. A wire is passed down the bile duct, through the ampulla and retrieved by the endoscopist. Also, PTD can be done for acute cholangitis when ERCP and drainage has failed.

PTC, however, carries a potentially greater risk than ERCP since catheters are passed through the vascular liver. Haemorrhage, bile leakage with peritonitis and cholangitis may follow. It is rarely used in patients with benign bile duct disease, unless ERCP has failed or previous surgery (e.g. hepaticojejunostomy) has made the ampulla inaccessible.

The nature of biliary tract disease is such that it presents to general physicians and surgeons as well as hepatologists and hepatobiliary surgeons. Cases are often straightforward, but a multidisciplinary approach with physician, radiologist, pathologist and surgeon is optimal to avoid inappropriate diagnostic and therapeutic approaches.



Fig. 12.9. Percutaneous transhepatic cholangiogram showing normal right and left intrahepatic ducts and common bile duct, and free flow of contrast into duodenum. The gallbladder is beginning to fill.

Composition of gallstones

There are three major types of gallstone: cholesterol, black pigment and brown pigment (Fig. 12.10, Table 12.2). In the Western world most are cholesterol stones. Although these consist predominantly of cholesterol (51–99%) they, along with all types, have a complex content and contain a variable proportion of other components including calcium carbonate, phosphate, bilirubinate and palmitate, phospholipids, glycoproteins and mucopolysaccharides. The nature of the nucleus of the stone is uncertain—pigment, glycoprotein and amorphous material have all been suggested.

Formation of cholesterol stones

Three major factors determine the formation of cholesterol gallstones. These are: altered composition of hepatic bile, nucleation of cholesterol crystals and impaired gallbladder function (Fig. 12.11).

The complexity is demonstrated by the finding that although cholesterol supersaturation is a prerequisite for gallstone formation, it does not alone explain the pathogenesis. Other factors must be important since bile supersaturated with cholesterol is frequently found in individuals *without* cholesterol gallstones [13].

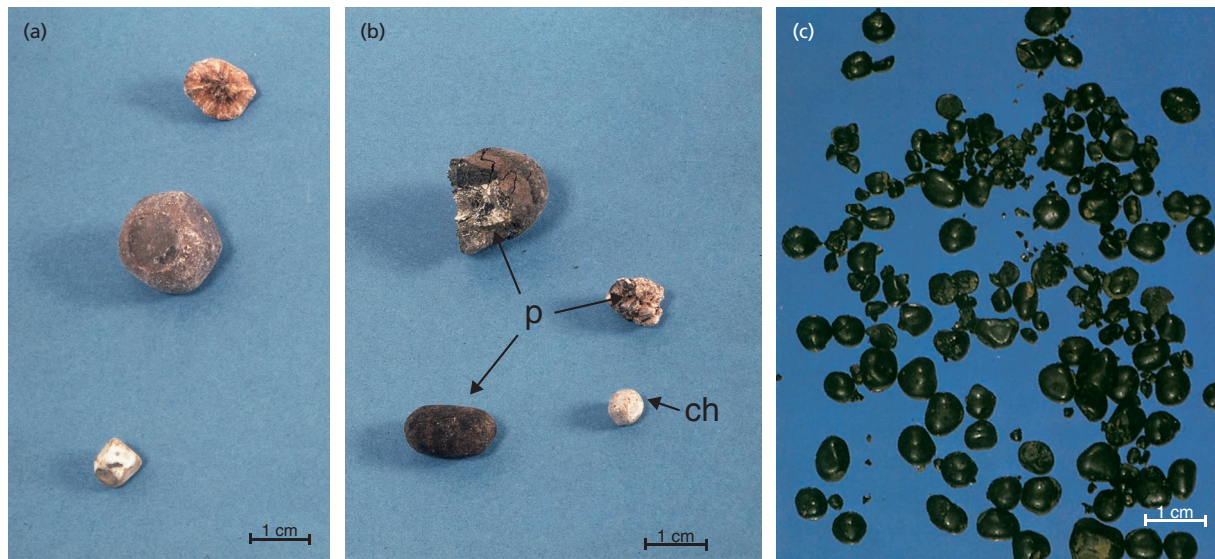


Fig. 12.10. (a) Two faceted cholesterol gallstones. The fragment above shows the concentric structure formed as layer upon layer of cholesterol crystals aggregate.

(b) Stones removed from the common bile duct (ch, cholesterol gallstone; p, brown pigment stone). (c) Black pigment gallstones.

Table 12.2. Classification of gallstones

	Cholesterol	Black pigment	Brown pigment
Location	Gallbladder, ducts	Gallbladder, ducts	Ducts
Major constituents	Cholesterol	Bilirubin pigment polymer	Calcium bilirubinate
Consistency	Crystalline with nucleus	Hard	Soft, friable
% Radio-opaque	15%	60%	0%
Associations			
Infection	Rare	Rare	Usual
Other diseases	See Fig. 12.11	Haemolysis, cirrhosis	Chronic partial biliary obstruction

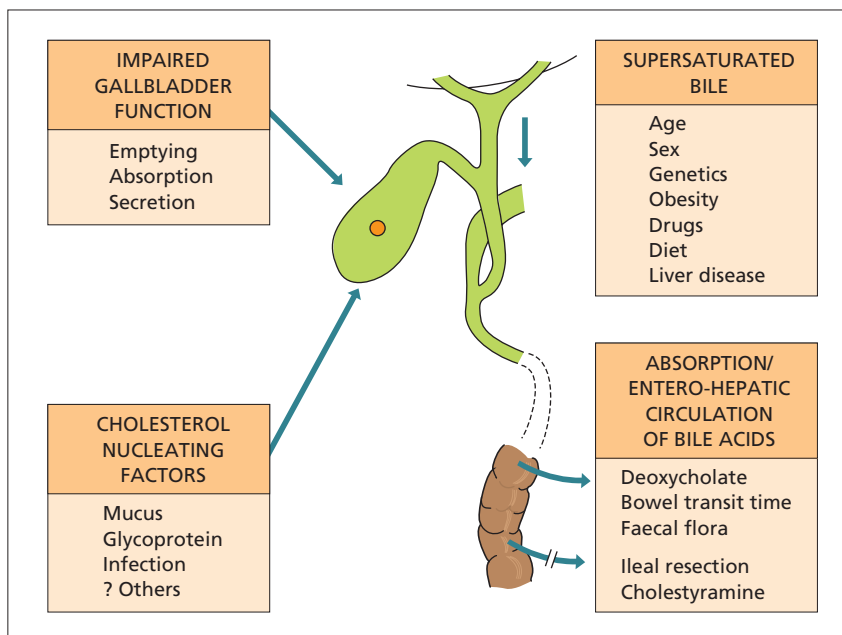


Fig. 12.11. Major factors in cholesterol gallstone formation are supersaturation of the bile with cholesterol, increased deoxycholate formation and absorption, cholesterol crystal nucleation and impaired gallbladder function.

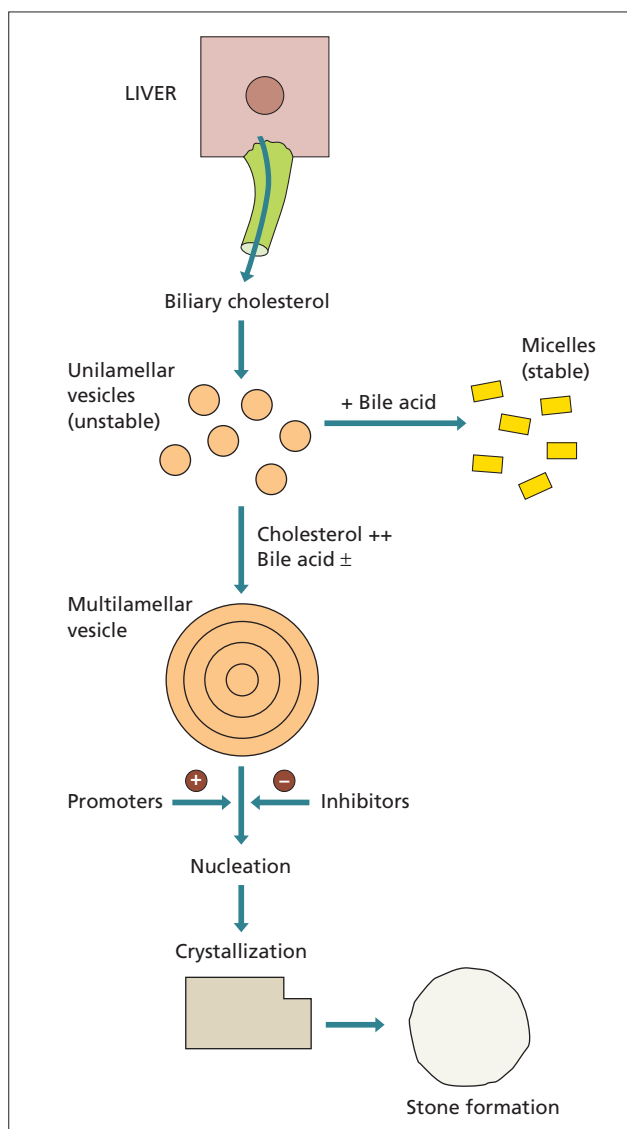


Fig. 12.12. Pathway for cholesterol crystallization in bile.

Altered hepatic bile composition

Bile is 85–95% water. Other components are cholesterol, phospholipids, bile acids, bilirubin, electrolytes and a range of proteins and mucoproteins.

Cholesterol is insoluble in water. It is secreted from the canalicular membrane in unilamellar phospholipid vesicles (Fig. 12.12). Solubilization of cholesterol in bile depends upon whether there is sufficient bile salt and phospholipid (predominantly phosphatidylcholine (lecithin)) to house the cholesterol in mixed micelles (Fig. 12.13). If there is excess cholesterol or reduced phospholipids and/or bile acid, multilamellar vesicles form and it is from these that there is nucleation of cholesterol crystals and ultimately sludge and stone formation (Fig. 12.12).

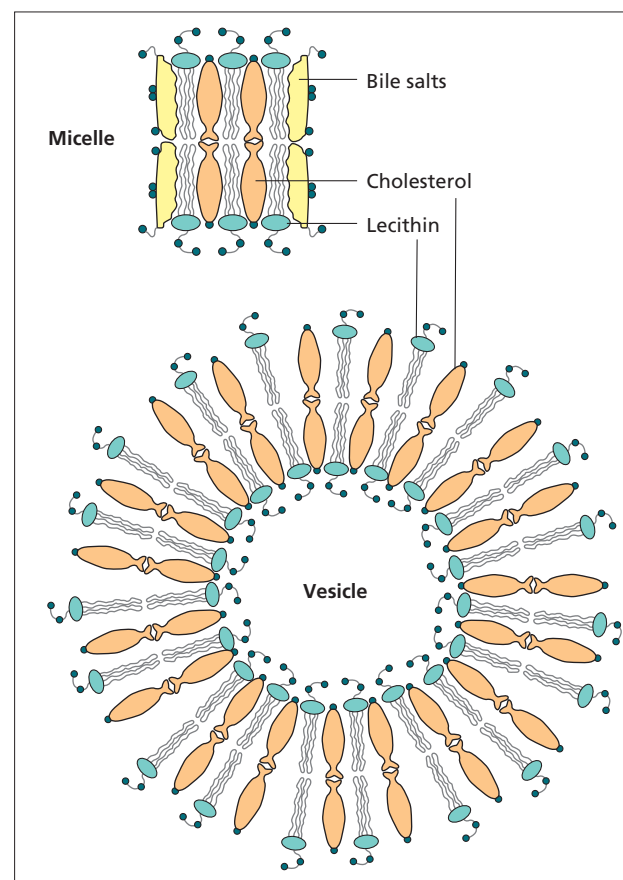


Fig. 12.13. Structure of mixed micelles and cholesterol/phospholipid vesicles.

Biliary cholesterol concentration is unrelated to serum cholesterol level and depends only to a limited extent on the bile acid pool size and bile acid secretory rate.

Changes in bile acid type also reduce the capacity for cholesterol solubilization. A higher proportion of deoxycholate (a secondary bile acid produced in the intestine and absorbed) is found in gallstone patients. This is a more hydrophobic bile salt and when secreted into bile extracts more cholesterol from the canalicular membrane, increasing cholesterol saturation. It also accelerates cholesterol crystallization.

Cholesterol nucleation

Nucleation of cholesterol monohydrate crystals from multilamellar vesicles is a crucial step in gallstone formation (Fig. 12.12).

One distinguishing feature between those who form gallstones and those who do not is the ability of the bile to promote or inhibit nucleation of cholesterol. The time taken for this process ('nucleation time') is significantly shorter in those with gallstones than in those without and in those with multiple as opposed to solitary stones

[14]. Biliary protein concentration is increased in lithogenic bile. Proteins that accelerate nucleation (pronucleators) include gallbladder mucin and immunoglobulin G. Cholesterol gallstones have bilirubin at their centre, and a protein pigment complex might provide the surface for nucleation of cholesterol crystals from gallbladder bile.

Factors that slow nucleation (inhibitors) include apolipoprotein A1 and A2 [15] and a 120-kDa glycoprotein [16]. Ursodeoxycholic acid, as well as decreasing cholesterol saturation, also prolongs the nucleating time [17]. Aspirin reduces mucus biosynthesis by gallbladder mucosa which explains why this drug and other non-steroidal anti-inflammatory drugs inhibit gallstone formation [18].

Gallbladder function

The gallbladder fills with hepatic bile during fasting, concentrates the bile and contracts in response to a meal, resulting in the passage of bile into the duodenum. The gallbladder must be capable of emptying so as to clear itself of microcrystals, sludge and debris that might initiate stone formation.

The concentration of bile salts, bilirubin and cholesterol, for which the gallbladder wall is essentially impermeable, may rise 10-fold or more as water and electrolytes are absorbed. The concentration of these constituents does not, however, rise in parallel and the cholesterol saturation index may decrease with concentration of bile because of the absorption of some cholesterol.

Gallbladder contraction is under cholinergic and hormonal control. *Cholecystikinin* (CCK), derived from the intestine, contracts and empties the gallbladder and increases mucosal fluid secretion with dilution of gallbladder contents. *Atropine* reduces the contractile response of the gallbladder to CCK [19]. Other hormones found to have an influence on the gallbladder include *motilin* (stimulatory) and *somatostatin* (inhibitory).

Immune processes and inflammation in the gallbladder also appear to effect contraction and promote the production of pronucleators [20].

That gallbladder stasis has a role clinically in the formation of gallstones is suggested by the relationship between impaired gallbladder emptying and the increased incidence of gallstones in patients on long-term parenteral nutrition, and in pregnant women [21].

Biliary sludge

Biliary sludge is a viscous suspension of a precipitate which includes cholesterol monohydrate crystals, calcium bilirubinate granules and other calcium salts/

sludge. It usually forms as a result of reduced gallbladder motility related to decreased food intake or parenteral nutrition. After formation, sludge disappears in 70% of patients [22]. Twenty per cent of patients develop complications of gallstones or acute cholecystitis. Whether treatment of sludge would reduce the incidence of complications is not known.

Epidemiology [23]

The prevalence of gallstones varies considerably between and within populations studied. However there are broad differences which are consistent. The highest known prevalence is among American Indians with up to 60–70% of females having cholelithiasis or gallbladder disease in some studies. The prevalence in Chilean Indians is also high. The lowest frequencies are in Black Africans (<5%). In the Western world the prevalence of gallbladder stones is about 5–15%, for example in White Americans and in the UK and Italy, around twofold greater in women than in men. Studies suggest a slightly greater prevalence in Norway and Sweden, but lower in China and Japan. The prevalence is likely to rise as lifestyles change.

Factors in cholesterol stone formation

Genetics

Studies have shown genetic risk and have implicated genes, with a clear link to physicochemical changes in cholesterol and phospholipids.

Analysis of mono- and dizygotic twins suggests that genetic factors account for 25% of the difference in the prevalence of gallstones [24]. In an American family study, around 29% of the chance of having symptomatic gallstones was inherited [25].

Candidate gallstone genes have been identified in mouse models, and recent human studies in sib pairs and cohorts identified a common variant (p.D19H) of the hepatocanalicular cholesterol transporter *ABCG5/ABG8* to be a risk factor for gallstone formation (sevenfold in homozygotes). This variant appears to contribute up to 11% of the total gallstone risk [26].

In a group of individuals with indicators of a risk of cholesterol stones (and also cholestasis), point mutations in *ABCB4* (the transporter for phosphatidyl choline) were found in over 50% of patients [27]. Since ursodeoxycholic acid may reduce the risk in such patients, it has been suggested that checking for mutations in this gene in high-risk patients may be appropriate [28].

Variants in a nuclear receptor (farnesoid X, FXR or NR1H4), which induces *ABCB11* and *ABCB4*, also relate to gallstone formation [29].

Lifestyle

Lack of physical activity [30] is also an association. There also is an association with the metabolic syndrome, and related conditions of obesity, type 2 diabetes and dyslipidaemia [31]. At the molecular level this appears to relate to insulin resistance leading to biliary cholesterol hypersecretion and impaired synthesis of bile acids [32].

Obesity

This seems to be more common among gallstone sufferers than in the general population [33] and is a particular risk factor in women less than 50 years old. Obesity is associated with increased cholesterol synthesis. There are no consistent changes in postprandial gallbladder volume. Fifty per cent of markedly obese patients have gallstones at surgery.

Dieting (2100 kJ/day) can result in biliary sludge and the formation of symptomatic gallstones in obese individuals [34].

Gallstone formation during weight loss following gastric bypass surgery for obesity is prevented by giving ursodeoxycholic acid [35].

Dietary factors

Epidemiological studies show that chronic over-nutrition with refined carbohydrates and triglycerides increases the risk [36].

Increasing dietary cholesterol increases biliary cholesterol but there is no epidemiological or dietary data to link cholesterol intake with gallstones.

In Western countries, gallstones have been linked to dietary fibre deficiency and a longer intestinal transit time [37]. This increases deoxycholic acid in bile, and renders bile more lithogenic. Deoxycholate is derived from dehydroxylation of cholic acid in the colon by faecal bacteria. There is an enterohepatic circulation. Gallstone patients have significantly prolonged small bowel transit times [38] and increased bacterial dehydroxylating activity in faeces [39].

A diet low in carbohydrate and a shorter overnight fasting period protects against gallstones, as does a moderate alcohol intake in males [40]. Vegetarians get fewer gallstones irrespective of their tendency to be slim [41].

Age

There is a steady increase in gallstone prevalence with advancing years, probably due to the increased cholesterol content in bile. By age 75, around 20% of men and 35% of women in some Western countries have

gallstones. Clinical problems present most frequently between the ages of 50 and 70.

Sex and oestrogens

Gallstones are twice as common in women as in men, and this is particularly so before the age of 50.

The incidence is higher in multiparous than in nulliparous women. Incomplete emptying of the gallbladder in late pregnancy leaves a large residual volume and thus retention of cholesterol crystals. Biliary sludge occurs frequently but is generally asymptomatic and disappears spontaneously after delivery in two-thirds [42]. In the postpartum period gallstones are present in 8–12% of women (nine times that in a matched group) [43]. One-third of those with a functional gallbladder are symptomatic. Small stones disappear spontaneously in 30%.

The bile becomes more lithogenic when women are placed on birth control pills. Women on long-term oral contraceptives have a twofold increased incidence of gallbladder disease over controls [44]. Postmenopausal women taking oestrogen-containing drugs have a significant increase frequency (around 1.8 times) of gallbladder disease [45]. In men given oestrogen for prostatic carcinoma the bile becomes saturated with cholesterol and gallstones may form [46].

Serum factors

The highest risk of gallstones (both cholesterol and pigment) is associated with low HDL levels and high triglyceride levels, which may be more important than body mass [47]. High serum cholesterol is not a determinant of gallstone risk.

Cirrhosis

About 30% of patients with cirrhosis have gallstones. The risk of developing stones is most strongly associated with Child's grade C and alcoholic cirrhosis with a yearly incidence of about 5% [48]. The mechanisms are uncertain. All patients with hepatocellular disease show a variable degree of haemolysis. Although bile acid secretion is reduced, the stones are usually of the black pigment type. Phospholipid and cholesterol secretion are also lowered so that the bile is not supersaturated.

Cholecystectomy in patients with cirrhosis carries an increased morbidity and mortality [49,50]. In Child's group A and B the laparoscopic approach is preferred to open cholecystectomy because of lower morbidity and mortality. In Child C patients and those with a higher MELD score the risk of cholecystectomy is particularly

high, making management decisions more difficult [49,50]. In such patients with symptomatic gallbladder and bile duct stones, non-surgical techniques have to be considered as alternatives to surgery.

Infection

Although infection is thought to be of little importance in cholesterol stone formation, bacterial DNA is found in these stones [51]. Conceivably, bacteria might deconjugate bile salts, allowing their absorption and reducing cholesterol solubility.

Diabetes mellitus

Diabetics have a higher prevalence of gallstones (or a history of cholecystectomy) than non-diabetics, particularly females (42 versus 23%) [52]. The older diabetic tends to be obese, and this may be the important factor in gallstone formation.

Patients with diabetes may have large, poorly contracting and poorly filling gallbladders [53]. A 'diabetic neurogenic gallbladder' syndrome has been postulated.

Patients with diabetes mellitus undergoing cholecystectomy, whether emergency or elective, have an increased risk of complications. These are probably related to associated cardiovascular or renal disease and to more advanced age.

Other factors

Hepatitis C is associated with a higher incidence of gallbladder stones than patients with hepatitis B, or those without hepatitis B or C (11.7 vs. 5.4 vs. 6.0% respectively [54]), but the reason for the link is not known.

Ileal resection breaks the enterohepatic circulation of bile salts, reduces the total bile salt pool and is followed by gallstone formation. The same is found in subtotal or total colectomy [55].

Gastrectomy increases the incidence of gallstones [56].

Long-term cholestyramine therapy increases bile salt loss with a reduced bile acid pool size and gallstone formation.

Parenteral nutrition leads to a dilated, sluggish gallbladder containing stones.

Endoscopic sphincterotomy improves gallbladder emptying and decreases the lithogenicity of bile in patients with gallstone disease [57]. Patients with gallbladder stones have significantly higher sphincter of Oddi tone [58].

Pigment gallstones

This term is used for stones containing less than 30% cholesterol. There are two types: black and brown (see Table 12.2).

Black pigment stones are largely composed of an insoluble bilirubin pigment polymer mixed with calcium phosphate and carbonate. There is no cholesterol. The mechanism of formation is not well understood, but supersaturation of bile with unconjugated bilirubin, changes in pH and calcium, and overproduction of an organic matrix (glycoprotein) play a role [59]. Overall, 20–30% of gallbladder stones are black. The incidence rises with age. They may pass into the bile duct. Black stones accompany chronic haemolysis, usually hereditary spherocytosis or sickle cell disease, and mechanical prostheses, for example heart valves, in the circulation. They show an increased prevalence with all forms of cirrhosis, particularly alcoholic [48]. Patients with ileal Crohn's disease may form pigment stones because of increased colonic absorption of bilirubin due to failure of ileal absorption of bile acid [60].

Brown pigment stones contain calcium bilirubinate, calcium palmitate, and stearate, as well as cholesterol. The bilirubinate is polymerized to a lesser extent than in black stones.

Brown stones are rare in the gallbladder. They form in the bile duct and are related to bile stasis and infected bile. They are usually radiolucent. Bacteria are present in more than 90%. Stone formation is related to the deconjugation of bilirubin diglucuronide by bacterial β -glucuronidase [59]. Insoluble unconjugated bilirubinate precipitates.

Brown pigment stones form above biliary strictures in sclerosing cholangitis and in the dilated segments of Caroli's disease. There is an association with juxtapaillary duodenal diverticula [61]. In Oriental countries, these stones are associated with parasitic infestations of the biliary tract such as *Clonorchis sinensis* and *Ascaris lumbricoides*. These stones are frequently intrahepatic.

Natural history of gallbladder stones

(Fig. 12.14)

Gallstones can be dated from the atmospheric radiocarbon produced by nuclear bomb explosions. This suggests a time lag of about 12 years between initial stone formation and symptoms culminating in cholecystectomy [62].

However, gallbladder stones are usually asymptomatic and diagnosed by chance by imaging or during investigation for some other condition. A small proportion develop symptoms. Around 8–10% of patients with asymptomatic gallstones developed symptoms within 5 years and only 5% required surgery [63,64]. Only about half the patients with symptomatic gallstones come to cholecystectomy within 6 years of diagnosis. Patients with gallstones seem to tolerate their symptoms for long periods of time, preferring this to cholecystectomy. If

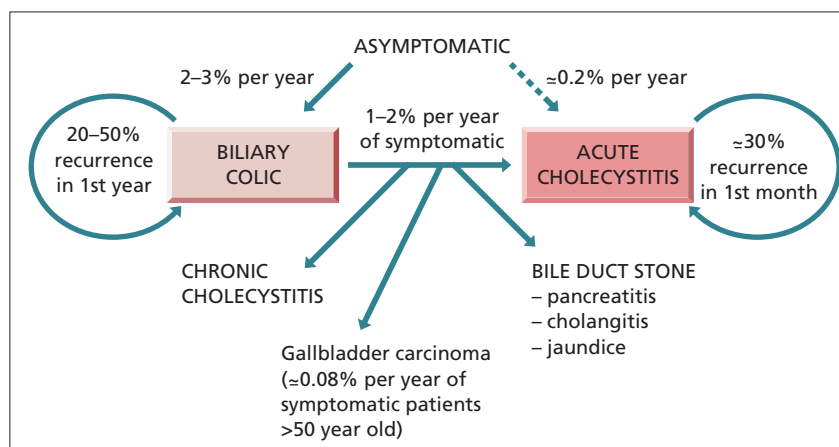


Fig. 12.14. The natural history of gallstones.

symptoms develop, they are unlikely to present as an emergency.

Data suggest that elective cholecystectomy is an appropriate choice for patients with biliary colic [65].

Prophylactic cholecystectomy should not be performed for asymptomatic gallbladder stones [66]. It should not be done to prevent gallbladder cancer since the risk is small and less than that of cholecystectomy [67].

Migration of a stone to the neck of the gallbladder causes *obstruction of the cystic duct* and a rise in gallbladder pressure. There is chemical irritation of the gallbladder mucosa by the retained bile, followed by bacterial invasion. According to the severity of the changes, *acute* or *chronic cholecystitis* results. Empyema may follow; perforation, fistula formation and emphysematous cholecystitis are rare.

Migration of a stone into the bile duct may present with pain, jaundice, cholangitis or pancreatitis.

Possible association of stones with gallbladder and bile duct cancer

Population surveys have investigated the link between stones and malignancy of the gallbladder and extrahepatic bile ducts.

The relative risk of gallbladder carcinoma is 2.4 if gallbladder stones are 2.0–2.9 cm in diameter, and greater with larger stones [68]. The issue is whether this is causative or an association, meaning that there is a common factor(s) that predisposes to both stones and carcinoma. This remains a possibility [69] and difficult to rule in or out.

There appears to be a lower risk of extrahepatic bile duct carcinoma during follow up of patients who had cholecystectomy, raising the question of a link between gallbladder stones or gallbladders containing stones with extrahepatic bile duct malignant changes [70].

Acute calculous cholecystitis

Aetiology

In 95% of patients the cystic duct is obstructed by a gallstone. The imprisoned bile salts have a toxic action on the gallbladder wall. Lipids may penetrate the Rokitansky–Aschoff sinuses and exert an irritant reaction. The rise in pressure compresses blood vessels in the gallbladder wall; infarction and gangrene may follow.

Pancreatic enzymes may also cause acute cholecystitis, presumably by regurgitation into the biliary system when there is a common biliary and pancreatic channel.

Bacterial inflammation is an integral part of acute cholecystitis. Bacterial deconjugation of bile salts may produce toxic bile acids which can injure the mucosa.

Pathology

The gallbladder is usually distended, but after previous inflammation the wall becomes thickened and contracted. There may be vascular adhesions to adjacent structures.

Histology shows haemorrhage and moderate oedema reaching a peak by about the fourth day and diminishing by the seventh day. As the acute reaction subsides it is replaced by fibrosis.

Bacteriology. Cultures of both gallbladder wall and bile usually show organisms of intestinal type, including anaerobes. Common infecting organisms are *Escherichia coli*, *Streptococcus faecalis* and *Klebsiella*, often in combination. Anaerobes are present, if sought, and are usually found with aerobes. They include *Bacteroides* and *Clostridium sp.*

Clinical features

These vary according to whether there is only mild inflammation or more severe disease such as

fulminating gangrene of the gallbladder wall. The acute attack is often an exacerbation of underlying chronic cholecystitis.

The sufferers are often obese, female and over 40, but no type, age or sex is immune.

Pain often occurs late at night or in the early morning, usually in the right upper abdomen or epigastrium and is referred to the angle of the right scapula, to the right shoulder [71], or rarely to the left side. It may simulate angina pectoris.

The pain usually rises to a plateau and can last 30–60 min without relief, unlike the short spasm of biliary colic. Attacks may be precipitated by late-night, heavy meals or fatty food.

Distension pain coming in waves is due to the gallbladder contracting to overcome the blocked cystic duct.

Peritoneal pain is superficial with skin tenderness, hyperaesthesia and muscular rigidity. The fundus of the gallbladder is in apposition to the diaphragmatic peritoneum, which is supplied by the phrenic and last six intercostal nerves. Stimulation of the anterior branches produces right upper quadrant pain and of the posterior cutaneous branch leads to the characteristic right infra-scapular pain.

Examination

The patient appears ill. The temperature rises with bacterial invasion. Jaundice usually indicates associated stones in the common bile duct.

The gallbladder is usually impalpable; occasionally a tender mass of gallbladder and adherent omentum may be felt. *Murphy's sign* is positive.

The *leucocyte count* may be raised with a moderate increase in polymorphs. In the febrile patient blood cultures may be positive.

For the patient with acute abdominal pain of uncertain cause, a plain X-ray will be taken during the work-up, but if acute cholecystitis is suspected scanning is indicated. Only about 10% of gallstones are radio-opaque, compared with 90% of renal calculi.

Imaging

The diagnosis of gallbladder disease depends upon scanning because of the overall lack of power of any specific symptom [72]. As described earlier, ultrasound is the test of choice. Scintigraphy is also accurate but second line.

Gallstones cast intense echoes with obvious posterior acoustic shadows (see Fig. 12.1). They change in position with turning of the patient. Stones 3 mm or more in size are usually seen. Diagnostic accuracy is 96% but less experienced operators may not achieve this success.

Acute calculous cholecystitis is suggested by the finding of stones with:

- a thickened gallbladder wall (>5 mm) (see Fig. 12.2);
- a positive sonographic Murphy sign—the presence of maximum tenderness, elicited by direct pressure of the transducer, over a sonographically localized gallbladder;
- gallbladder distension;
- pericholecystic fluid;
- subserosal oedema (without ascites);
- intramural gas;
- a sloughed mucosal membrane.

Cholescintigraphy. Technetium-labelled iminodiacetic acid derivatives (IDA) are cleared from the plasma by hepatocellular organic anion transport and excreted in the bile (see Fig. 12.3a).

Hepatic IDA scanning may be used to determine patency of the cystic duct in suspected acute cholecystitis. If the gallbladder fails to visualize, despite common bile duct patency and intestinal visualization (Fig. 12.3b), the probability of acute cholecystitis is 80–90%. False-negative results are more common the later the gallbladder fills [73].

CT and MRI scanning are not indicated as the initial assessment of a patient with suspected acute cholecystitis.

Differential diagnosis

Acute cholecystitis is liable to be confused with other causes of sudden pain and tenderness in the right hypochondrium. Below the diaphragm, acute retrocaecal appendicitis, intestinal obstruction, a perforated peptic ulcer or acute pancreatitis may produce similar clinical features.

Myocardial infarction should always be considered.

Referred pain from muscular and spinal root lesions may cause similar pain.

Prognosis

Spontaneous recovery follows disimpaction of the stone in 85% of patients. Recurrent acute cholecystitis may follow—approximately a 30% chance over the next 3 months [74].

Rarely, acute cholecystitis proceeds rapidly to gangrene or empyema of the gallbladder, fistula formation, hepatic abscesses or even generalized peritonitis. The acute fulminating disease is becoming less common because of earlier antibiotic therapy and more frequent cholecystectomy for recurrent gallbladder symptoms.

Treatment

Medical. This depends upon the clinical severity for which a grading has been described [75,76]. This is based on the white cell count, clinical findings, duration and features of systemic/ multisystem signs or complications. General measures during the acute phase include intravenous fluids, nothing given orally, analgesia and antibiotics. Tokyo guidelines recommend management depending upon the severity [75,76].

Antibiotic(s) are given if there is clinical evidence of sepsis, and should have a spectrum to cover the likely micro-organisms. Choice is according to hospital policy, but a second or third-generation cephalosporin or combination of a quinolone with metronidazole are usually adequate for the stable patient with pain and mild fever. Patients with features of severe sepsis require broader-spectrum antibiotics such as piperacillin/ tazobactam, combined if necessary with an aminoglycoside. The elderly, and those with diabetes or immunodeficiency, are at particular risk of severe sepsis.

Cholecystectomy (see below). For those with mild acute cholecystitis, early cholecystectomy is recommended [75,76]. Meta-analysis of randomized controlled trials shows that this approach (within 1 week) is superior to delayed cholecystectomy (2 to 3 months later) because of avoidance of gallstone-related complications during the waiting period [65,77]. These could lead to emergency surgery which is known to carry a higher risk than elective operation, particularly in elderly patients over 75 years old and in the diabetic patient where early elective cholecystectomy is preferred once symptoms have developed [78].

For moderate acute cholecystitis there may be early or delayed cholecystectomy, but if early laparoscopic surgery is done, it should be by a highly experienced surgeon so that decisions to alter the approach can be made and carried out if the operation becomes complicated [75,76].

For severe acute cholecystitis, based on the Tokyo guidelines, initial intensive medical treatment with antibiotics is recommended with, if needed, percutaneous cholecystostomy [75,76]; surgical decisions are then customized for individual patients according to the clinical course and degree of surgical risk.

Empyema of the gallbladder

If the cystic duct remains blocked by a stone and infection sets in, empyema may develop. Symptoms may be of an intra-abdominal abscess (fever, rigors, pain), although the elderly patient may appear relatively well.

Treatment is with antibiotics and surgery. There is a high postoperative rate of septic complications [79]. Percutaneous cholecystostomy is considered if the patient is unfit for surgery.

Emphysematous cholecystitis

The term is used to denote infection of the gallbladder with gas-producing organisms (*Escherichia coli*, *Clostridium welchii*) or anaerobic streptococci. The primary lesion is occlusion of the cystic duct or cystic artery. Infection is secondary [80]. The condition classically affects male diabetics who develop features of severe, toxic, acute cholecystitis. An abdominal mass may be palpable.

On a plain abdominal X-ray the gallbladder may be seen as a sharply outlined pear-shaped gas shadow. Occasionally air may be seen infiltrating the wall and surrounding tissue. Gas is not apparent in the cystic duct, which is blocked by a gallstone. In the erect position, a fluid level is seen in the gallbladder. However, plain abdominal X-ray may not show the characteristic changes. Ultrasound is diagnostic in around 50% of cases. CT may also show characteristic features.

Standard treatment is with antibiotics and emergency cholecystectomy. In the severely ill patient percutaneous cholecystostomy is an alternative [81].

Chronic calculous cholecystitis

This is the commonest type of clinical gallbladder disease. The association of chronic cholecystitis with stones is almost constant. Aetiological factors therefore include all those related to gallstones. The chronic inflammation may follow acute cholecystitis, but usually develops insidiously.

Pathology

The gallbladder is usually contracted with a thickened, sometimes calcified, wall. Stones are seen lying loosely embedded in the wall or in meshes of an organizing fibrotic network. One stone is usually lodged in the neck. Histologically, the wall is thickened and congested with lymphocytic infiltration and occasionally complete destruction of the mucosa.

Clinical features

Chronic cholecystitis is difficult to diagnose because of the ill-defined symptoms. Episodes of acute cholecystitis punctuate the course.

Abdominal distension or epigastric discomfort, especially after a fatty meal, may be temporarily relieved by belching. Nausea is common, but vomiting is unusual unless there are stones in the common bile duct. Apart from a constant dull ache in the right hypochondrium and epigastrium, pain may be experienced in the right scapular region, substernally or at the right shoulder. Postprandial pain may be relieved by alkalis.

Local tenderness over the gallbladder and a positive Murphy sign are very suggestive.

Investigations

The temperature, leucocyte count, haemoglobin and erythrocyte sedimentation rate are within normal limits. A plain abdominal X-ray may show calcified gallstones. However, the imaging technique of first choice is ultrasound, which may show gallstones within a fibrosed gallbladder with a thickened wall. Non-visualization of the gallbladder is also a significant finding. CT scan may show gallstones but this technique is not usually appropriate in the diagnostic work-up. Endoscopy may be necessary to rule out gastric or duodenal inflammation or ulceration.

Differential diagnosis

Fat intolerance, flatulence and postprandial discomfort are common symptoms. Even if associated with imaging evidence of gallstones, the calculi are not necessarily responsible since stones are frequently present in the symptom-free.

Other disorders producing a similar clinical picture must be excluded before cholecystectomy is advised, otherwise symptoms persist postoperatively. These include peptic ulceration or inflammation, hiatus hernia, irritable bowel syndrome and functional dyspepsias.

Since approximately 10% of young to middle-aged adults have gallstones, symptomatic gallbladder disease may be over-diagnosed. Conversely, ultrasound is only about 95% accurate and symptomatic gallbladder disease may therefore sometimes be unrecognized.

Prognosis

This chronic disease is compatible with good life expectancy. However, once symptoms, particularly biliary colic, are experienced, the patients tend to remain symptomatic with about a 40% chance of recurrence within 2 years [82]. Gallbladder cancer is a rare, later development (see above).

Treatment

Medical measures may be tried if the diagnosis is uncertain and a period of observation is desirable. This

is especially so when indefinite symptoms are associated with a well-functioning gallbladder. The general condition of the patient may contraindicate surgery. The infrequent place of medical dissolution and shock-wave lithotripsy of radiolucent stones is discussed later.

Obesity should be addressed. A low-fat diet is advisable.

If the patient is symptomatic, particularly with repeated episodes of pain, cholecystectomy (see below) is indicated.

Acalculous cholecystitis

Acute

About 5–10% of acute cholecystitis in adults and about 30% in children occurs in the absence of stones. The most frequent predisposing cause is an associated critical condition such as after major non-biliary surgery, multiple injuries, major burns, recent childbirth, severe sepsis, mechanical ventilation and parenteral nutrition.

The pathogenesis is unclear and probably multifactorial, but bile stasis (lack of gallbladder contraction), increased bile viscosity and lithogenicity, and gallbladder ischaemia are thought to play a role. Administration of opiates, which increase sphincter of Oddi tone, may also reduce gallbladder emptying.

Clinical features should be those of acute calculous cholecystitis with fever, leucocytosis and right upper quadrant pain but diagnosis is often difficult because of the overall clinical state of the patient who may be intubated, ventilated and receiving narcotic analgesics.

There may be laboratory features of cholestasis with a raised bilirubin and alkaline phosphatase. Ultrasound and CT are complementary and useful in showing a thickened gallbladder wall (>5mm), pericholecystic fluid or subserosal oedema (without ascites), intramural gas or a sloughed mucosal membrane. The sensitivity of ultrasound varies widely between studies (30–100%), but prospective studies have suggested that this is a useful technique [83,84]. Cholescintigraphy is reported to have a sensitivity of 60–90% for acalculous cholecystitis [85,86], but moving patients to the imaging unit for the time required for scanning may not be practical.

Because of the difficulties of diagnosis a high index of suspicion is needed, particularly in patients at risk. Gangrene and perforation of the gallbladder are common. The mortality is high, 41% in one series [85], often due to delayed diagnosis.

Treatment is emergency cholecystectomy. In the critically ill patient percutaneous cholecystostomy under ultrasound guidance may be life saving (see below).

Chronic (including gallbladder dyskinesia)

This is a difficult diagnosis as the clinical condition resembles others, particularly irritable bowel syndrome and functional dyspepsias. A description of biliary-like pain has been endorsed by the Rome committee on functional biliary and pancreatic disorders [87]: an episodic, severe, constant pain, in epigastrium or right upper quadrant, lasting at least 30 min, severe enough to interrupt daily activities or lead to consultation with a physician. Laboratory investigations (liver enzymes, conjugated bilirubin, amylase, lipase) are normal; routine transabdominal ultrasound scan shows a normal gallbladder.

Cholescintigraphy with measurement of the gallbladder ejection fraction 15 min after CCK infusion has been used to try and identify patients who have putative gallbladder pathology and would benefit from cholecystectomy. Normal individuals have an ejection fraction of around 70%. In those with a low ejection fraction (usually regarded as less than 35–40%) or who develop pain during the infusion, symptom relief after cholecystectomy is reported in between 70 and 90% of patients [88–90]. However, decisions on management based on the results of a single isotope scan alone may not appear appropriate. There are many issues regarding the actual technique used (e.g. dose and rate of CCK infusion) and that a low ejection fraction is not specific for functional gallbladder disease [91]. Results of scanning should be taken in the context of the other clinical features of the patient. Of note is that EUS may detect small gallbladder stones missed by transabdominal US and in these patients cholecystectomy resulted in loss of pain [92].

In patients with acalculous gallbladder disease undergoing cholecystectomy, chronic cholecystitis, cholesterosis, muscle hypertrophy and/or a narrowed cystic duct have been shown in patients in whom symptoms were relieved [89,90].

Cholecystectomy

Laparoscopic cholecystectomy, introduced in the late 1980s, is the current standard treatment for symptomatic gallbladder stones, and mild and moderate acute cholecystitis, based on superior outcomes compared with open cholecystectomy [93–95]. *Open cholecystectomy* is still required where the laparoscopic approach fails, or is not possible. Thus expertise is still needed for the open operation.

Operative approach for laparoscopic cholecystectomy

Under general anaesthesia the abdominal cavity is insufflated with CO₂ and the laparoscope and operating channels inserted. Cystic duct and vessels to the gall-

bladder are carefully identified and clipped. Haemostasis is achieved by electrocautery or laser. The gallbladder is dissected from the gallbladder bed on the liver and removed whole. When necessary large stones are fragmented while they are still within the gallbladder to allow its delivery through the anterior abdominal wall.

Results

Systemic reviews and meta-analyses show that there is no overall difference in outcome measures of mortality and complications between open, small-incision and laparoscopic cholecystectomy [93,96]. However, the minimally invasive methods (laparoscopic and small incision) were associated with a significantly shorter postoperative hospital stay (around 3 days) compared with open cholecystectomy, and convalescence was shortened (around 22 days). The results from laparoscopic and small incision cholecystectomy were similar. The smaller incision approach interestingly had a shorter operative time and possible lower cost than laparoscopic cholecystectomy.

The Cochrane review raises the question of why laparoscopic rather than mini-incision cholecystectomy has become the standard approach for patients with symptomatic disease, and suggests that to address this other outcomes need more concerted analysis, such as symptom relief and complications. One study involving minilaparotomy and laparoscopic cholecystectomy evaluated pain scores, physical function and psychological health 1 week after operation and found that the laparoscopic approach gave a significantly better outcome [97] (Fig. 12.15). The wide use of laparoscopic cholecystectomy also appears to reflect patient preference and the overall pattern of practice available. Thus practitioners of mini-incision surgery are in the minority, because of its technical difficulty and the fewer opportunities for training.

Laparoscopic cholecystectomy is successful in about 95% of patients. In the remainder, the operation has to be converted to open cholecystectomy. This is more likely if there is acute cholecystitis, particularly with empyema [98]. In these cases, initial laparoscopic assessment is appropriate and conversion to open operation made if indicated. In experienced hands laparoscopic cholecystectomy for acute and gangrenous cholecystitis is as safe and effective as open cholecystectomy although there is a moderately high conversion rate (16%) to the open procedure [99].

Complications

The perioperative mortality lies between 0 and 0.3% [65,96]. The complication rate is around 5% [96], and includes bile duct injury, biliary leak, postoperative

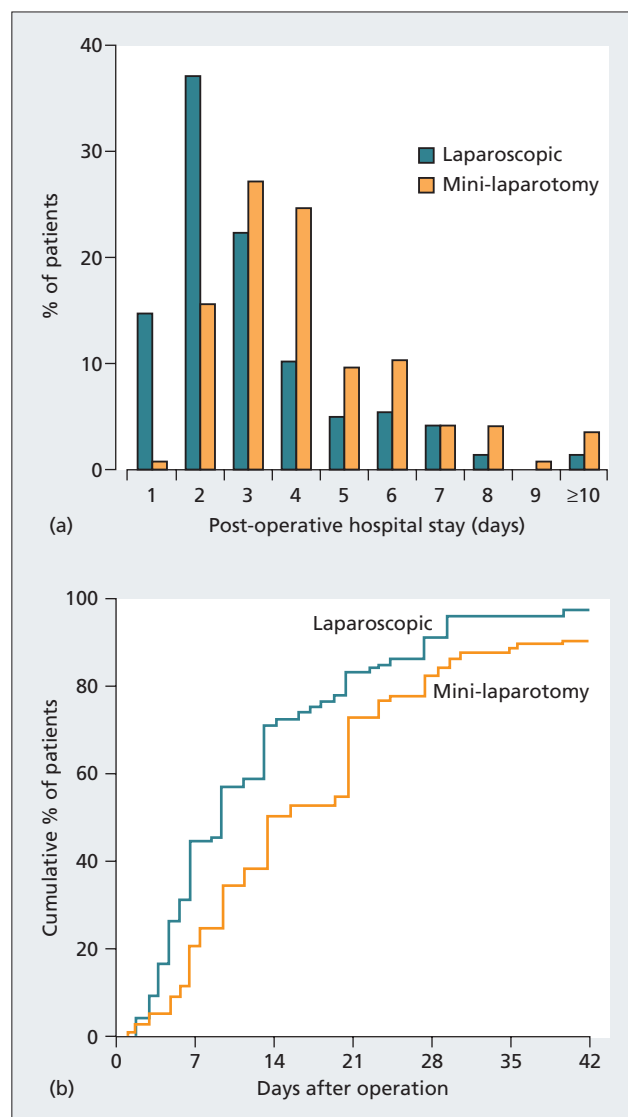


Fig. 12.15. Laparoscopic versus minicholecystectomy. (a) Postoperative hospital stay. (b) Return to work in the home. (From [97] with permission.)

bleeding and wound infection. Complication rates have been reported to be associated with patient characteristics (age, comorbidities) rather than surgeon or hospital operative volume [100]. Bile duct injury occurs in around 0.4–0.6% of patients [101,102], and this is considered as being higher than in the era of open cholecystectomy (0.2–0.3%)[101]. This emphasizes the need for caution at surgery and for rigorous training. Duct injury may occur even with an experienced surgeon.

The reported risks of open cholecystectomy (collected recently) are now greater than laparoscopic, but this predominantly reflects the patient characteristics of those chosen for open operation preoperatively, and those converted from laparoscopic to open at the time of surgery. Thus differences in 30-day morbidity (18.7% vs. 4.8%; open versus laparoscopic respectively) and

30-day mortality (2.4% vs. 0.4%) reflect these patient factors, including ASA (American Society of Anesthesiologists) class, patient comorbidities, functional status, age, previous abdominal surgery, emergency status and albumin [103].

Cholangiography

Of patients having cholecystectomy, 10–15% have common duct stones. Preoperative ERCP is appropriate for patients with criteria suggestive of a duct stone—recent jaundice, cholangitis, pancreatitis, abnormal liver function tests or duct dilatation on ultrasound. If the data raise the question of a duct stone but are not considered enough for ERCP, MRCP is indicated. If there is a duct stone it is removed after sphincterotomy.

Intraoperative cholangiography at laparoscopic cholecystectomy needs experience. Some advocate its routine use to define bile duct anatomy, anomalies and stones, but this prevents only the minority of bile duct injuries [104].

Laparoscopic common bile duct exploration

In experienced hands duct stones can be removed in 90% of patients [105]. However, this technique is not routine because of lack of expertise and the need for special equipment. Laparoscopic removal of common duct stones is as effective and safe as endoscopic sphincterotomy [106]. Management should be customized according to local expertise, resources and patient considerations.

Percutaneous cholecystostomy

This has a particular place in the elderly patient with acute complicated cholecystitis with comorbid disease [107]. The method can either be done under ultrasound control or fluoroscopy after initial opacification using a skinny needle. A drainage catheter can be left to drain the gallbladder, or aspiration of the fluid and pus can be done without continued drainage [108]. Both methods are combined with intensive antibiotic therapy. Bile/pus is sent for culture. There is usually rapid relief of clinical symptoms.

In the severely ill patient, percutaneous transhepatic cholecystostomy is effective. Resolution of sepsis has been recently reported in 87% of 23 patients, with a 30-day mortality of 8.7%, and one procedure-related death (4.3%) [109].

This technique may allow the patient to be brought to elective surgery in a better clinical condition. In the inoperable patient, after recovery, if a percutaneous catheter has been left in place, it can be removed and

the patient treated conservatively, often without recurrence [107].

In the situation of the patient not being a surgical candidate, and/or having a coagulopathy or ascites that precludes cholecystostomy, ERCP with selective cannulation of the cystic duct and nasobiliary tube or stent placement in the gallbladder is possible [110], although technically difficult. A systematic review reported over 90% technical and 80–90% clinical success, with complications in 1–4% [111].

Postcholecystectomy bile duct damage

Bile duct damage occurs in around 0.4–0.6% of patients [101,102]. Injuries include bile leak from cystic duct or gallbladder bed, complete transection of the duct and complete or partial stricture due to clips or damage during dissection.

Several factors contribute to duct injury. There may be mistaken interpretation of the anatomy due to oedema or haemorrhage around an inflamed gallbladder, anomalies of the cystic duct or right hepatic duct (Fig. 12.16), or lack of operator experience.

Risk factors for *laparoscopic bile duct injury* include obesity, bleeding, acute cholecystitis and scarring in Calot's triangle (the area between the cystic duct and common hepatic duct). Uncertain anatomy, inexperience

and a long procedure are also associated with damage [112,113]. The threshold at which the decision is made to convert from laparoscopic to open surgery is also important.

Clinical features

Complete ligation, clipping or transection will become clear clinically in the immediate perioperative period. With partial injury, the occlusion develops slowly. About 60% of patients with bile duct injury present within 3 months of operation, and 80% within 1 year [114].

If unrecognized at the time of cholecystectomy, presentation depends upon the degree of damage. Postoperative anorexia, nausea, vomiting, pain, abdominal distension, ileus and delayed recovery should raise the possibility of damage [112], although the presentation is usually more obvious.

The appearance of bile-stained fluid in the surgical drain raises the possibility of duct damage. Complete transection of the main bile duct usually gives pain (bile peritonitis), fever and cholestatic jaundice 3–7 days postoperatively. Alternatively, an external biliary fistula develops. The fistula may drain intermittently with episodes of jaundice when it is closed. Subhepatic abscesses may develop.

Ligation or clipping the main duct, or a later stricture, gives escalating cholestatic jaundice with or without cholangitis.

With current awareness of the complications of laparoscopic cholecystectomy, and the availability of ERCP and other imaging techniques, patients should not develop the chronic complications of biliary obstruction. Biliary cirrhosis with portal hypertension and splenomegaly will develop with time if the obstruction is not recognized and relieved effectively.

Patients unfortunate enough to suffer bile duct damage at cholecystectomy may become increasingly introspective as the months pass. Some keep the most detailed notes of their symptoms and, understandably, become querulous and suspicious of their medical advisors. They need considerable support.

Investigations

The history of recent cholecystectomy, the postoperative features and the biochemical and imaging data should lead to cholangiography and the correct diagnosis.

Liver function tests may show cholestasis, but may be normal.

Radiology. The first step is scanning with ultrasound or CT. Where duct damage has led to a bile leak, ultrasound or CT will show an intra-abdominal collection which may be drained under scanning control. Bile



Fig. 12.16. Benign bile duct stricture following laparoscopic cholecystectomy (arrow). Note anomalous right-sided bile duct (a).

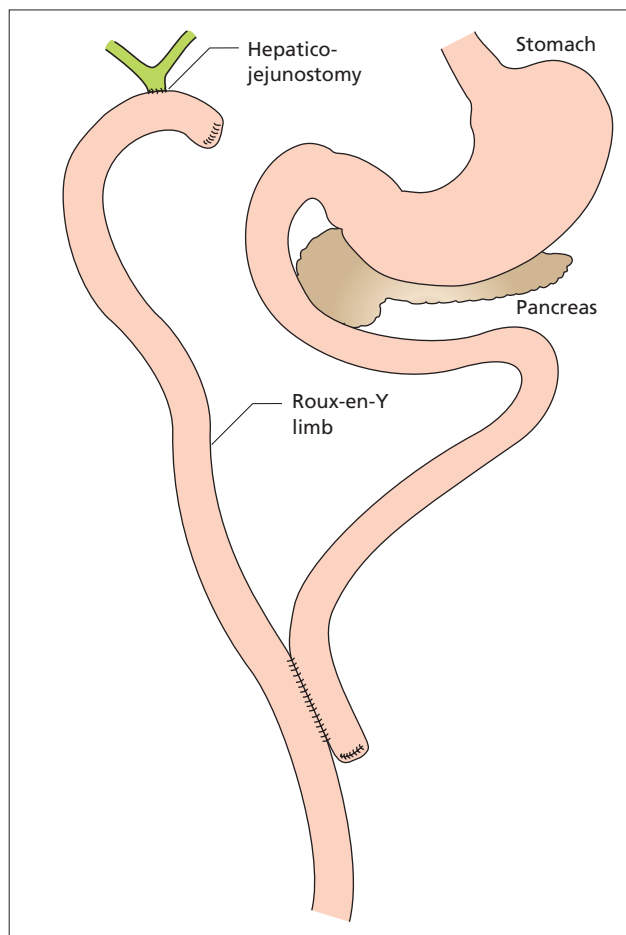


Fig. 12.17. Repair of a high biliary stricture by Roux-en-Y hepaticojejunostomy.

ducts may not be dilated. Biliary scintigraphy detects around 50% of leaks (see Fig. 12.7) [115]. When there is a stricture without a leak, dilated intrahepatic bile ducts are seen.

The route of cholangiography depends upon the clinical data. If bile leakage from a cystic duct or a partial low duct stricture are suspected then ERCP is the first choice (see Fig. 12.16). MRCP may be valuable depending upon the type of injury. For duct transection and discontinuity or a high stricture, percutaneous cholangiography and drainage are appropriate as part of the preoperative work-up and management. *CT or MR angiography* is indicated if vascular injury is suspected, and may be done as a road map for patients with high duct damage.

Classifications

There are many classifications of types of injury, in an attempt to define different patterns and facilitate management decisions [116]. Bergman *et al.* [117] separate

injuries into four major categories and this more often used by biliary endoscopists:

- Type A: cystic duct leak, or leakage from aberrant or peripheral hepatic radicals;
- Type B: major bile duct leak with or without a concomitant bile duct stricture;
- Type C: bile duct stricture without bile leakage;
- Type D: complete transection of the duct, with or without excision of some portion of the biliary tree.

Other classifications are more detailed, such as that by Strasberg *et al.* [118], and are used for planning of surgical repair.

Treatment

Prevention. The majority of strictures would be prevented if: (1) cholecystectomy was only performed by experienced surgeons; (2) the top-down approach was used with thorough dissection at the junction of the gallbladder infundibulum and cystic duct; and (3) there was an appropriate threshold for conversion from laparoscopic to open surgery. This is particularly so in the presence of acute cholecystitis.

Medical. Fluid and electrolyte balance must be maintained, particularly in the jaundiced septic patient and those with a biliary fistula. Antibiotic therapy, based if possible on blood and bile culture, will improve septicaemia but, if there is bile duct obstruction or a leak, bile duct catheterization and drainage by the endoscopic or percutaneous route is essential to treat sepsis. Bile collections may need percutaneous drainage under scanning control.

The overriding principle is the importance of early referral to a specialist hepatobiliary centre where there will be a multidisciplinary approach by surgeon, radiologist and endoscopist [119].

Interventional endoscopy and radiology; surgical repair. Bile leakage from a cystic duct stump or tiny ducts in the gallbladder bed can usually be managed endoscopically by stent insertion [116]. This is the first-choice procedure.

For the incomplete stricture, endoscopic balloon dilatation and stenting, using repeat procedures with graduated increase in balloon diameter and number of stents, over a year gives a successful outcome in 80–90% of postcholecystectomy strictures [120–122]. Success with strictures at the hilar confluence is lower.

An analysis of mesh metal stents in this scenario suggests that they should not be used unless life expectancy is less than 2 years, because of occlusion [123]. Whether removable covered mesh metal stents have any role awaits outcome analysis.

For the completely obstructed or transected bile duct, surgery is necessary after investigation and preparatory percutaneous bile drainage, as appropriate to the individual patient. The endoscopic route is likely to be of no value. These are complex patients requiring a specialist multidisciplinary team.

Preoperative percutaneous transhepatic biliary drainage is performed. Intra-abdominal collections are drained. Other preoperative investigations are done, including angiography to detect vascular damage. Surgery may then be performed electively in the subsequent weeks under optimal conditions.

The operation chosen will depend mainly on two factors—the site and length of the stricture and the amount of duct available for repair. Any operation must provide excision of the stricture with mucosal apposition between the duct lining and the intestinal mucosa. The anastomosis must be as large as possible and not under tension.

Even if sufficient duct is available proximally, excision of the stricture and end-to-end anastomosis of the duct is rarely performed. Differences between the calibre of the duct above and below the stricture are too great for a satisfactory anastomosis. Recurrent stricture occurs in 60% of cases.

The usual operation is between the bile duct and a Roux-en-Y segment of jejunum (*choledochojejunostomy*). In the case of high stricture, the hepatic duct is used (*hepaticojejunostomy*) (Fig. 12.17).

Successful long-term results of hepaticojejunostomy (mean 5 years) have been reported in 50 of 54 patients in one series [124]. Predictors of poor outcome were peritonitis at the time of reconstruction, combined vascular and bile duct injuries and injury at or above the level of the biliary bifurcation. Another series also analysed associations with a poor outcome which included three or more attempts at operative repair before referral, hypoalbuminaemia, high serum bilirubin, the presence of liver disease and portal hypertension [125].

Stenosis of a hepaticojejunostomy done either as the primary repair, or after failed other approaches, may be managed by interventional radiological approaches, or by surgical revision (see below).

Postcholecystectomy syndromes

About 90–95% of those *with gallstones* are freed of symptoms or improved postoperatively. The absence of stones questions the original diagnosis. These patients may have been suffering from a psychosomatic or some other disorder including non-visceral pain [126]. Results of surgery are poor when done for vague symptoms such as abdominal bloating or dyspepsia, or in patients using psychiatric medication [127,128]. A biliary cause is likely

if stones are found at cholecystectomy and if a period of relief follows the operation. The colon and pancreas are common alternative culprits.

Postoperative symptoms may be related to technical difficulties at the time of surgery. These include traumatic *biliary stricture* and *residual calculi* (see below).

Ampullary neuromas can be demonstrated in some patients but removal offers no relief and this seems unlikely to be the cause of the symptoms.

Chronic pancreatitis, a common association of *choledocholithiasis*, may persist postoperatively.

US is the first test to image the bile duct. Depending on the result and the clinical features MRCP may be indicated. Despite all these, ERCP is usually necessary. Residual calculi, stricture, ampullary stenosis or normal appearances are significant findings.

Sphincter of Oddi dysfunction [129,130]

This has been an area of controversy but now appears to be a cause of postcholecystectomy pain in some patients. Two forms exist.

Papillary stenosis is defined as narrowing of all or part of the sphincter of Oddi. There is fibrosis. It may follow injury due to stones [131], operative instrumentation, biliary infection or pancreatitis. There may be episodes of pain associated with abnormal liver function tests. On ERCP the bile duct is dilated and drains slowly. The basal sphincter tone is raised on manometry and is not reduced by smooth muscle relaxants. Endoscopic sphincterotomy is helpful [132].

Sphincter of Oddi (biliary) dyskinesia is a more difficult area. Biliary manometry shows a range of abnormalities including sphincter spasm, increased phasic contraction frequency (tachyoddia), paradoxical contraction response to CCK and abnormal propagation of phasic waves.

Clinical features (Table 12.3) are valuable in management decisions. Group I benefit from sphincterotomy in around 90% of cases. In group II manometry is important. Patients with an elevated basal sphincter pressure have had greater benefit from sphincterotomy than those with a normal pressure (91 vs. 42%) [133], although a recent expert review suggests a lower success rate (50–70% vs. 30%) based on manometry result [130]. Studies continue in group III. Duodenal distension reproduces the symptoms in most patients [134]. Sphincterotomy in those with abnormal manometry may be beneficial in only 20–30% of patients [130]. This is a difficult group of patients, and it has been suggested that such patients should first have a trial of medical therapy (including proton pump inhibitors and/or calcium channel blockers (nifedipine)) before considering ERCP and manometry, with the attendant risks, in those without a response [135].

Table 12.3. Sphincter of Oddi dysfunction: classification (modified according to [130])

<i>Group I (definite)</i>	
Biliary-type pain	
Abnormal liver function tests (serum transaminases or alkaline phosphatase $> 1.5 \times$ normal) documented on two or more occasions, with normalization between attacks	
Dilated common bile duct $> 8\text{mm}$	Manometry unnecessary
<i>Group II (presumptive)</i>	
Biliary-type pain and one of other group I criteria	
	Manometry essential
<i>Group III (possible)</i>	
Biliary-type pain only. No other abnormalities	
	Manometry essential if intervention contemplated

Non-surgical treatment of gallstones in the gallbladder

The widespread availability and acceptance of laparoscopic cholecystectomy has markedly reduced the use of non-surgical treatments for gallbladder stones. However, a small group of patients remain where these approaches need to be considered, including those unfit for or refusing surgery.

Dissolution therapy with ursodeoxycholic acid [136]

Ursodeoxycholic acid decreases biliary cholesterol secretion as well as cholesterol absorption and increases solubility of cholesterol by the formation of liquid crystals [28]. Ursodeoxycholic acid also prolongs nucleation time.

Indications

The patient must be compliant and prepared for at least 2 years of treatment. Symptoms must be mild to moderate and silent stones should not be treated. On oral cholecystography the cystic duct must be patent ('functioning gallbladder') and stones radiolucent, preferably floating. They should be less than 15 mm in diameter. Best results are for stones less than 5 mm diameter.

Unfortunately, no imaging technique accurately determines the composition of gallstones and therefore solubility. Ultrasound is of little value. CT can be useful and, because of the expense of bile acid therapy, cost-effective in assessing stones. Stones with an attenuation value of less than 100 Hounsfield units (reflecting low calcium content) are more likely to dissolve [137].

Results

The dose of ursodeoxycholic acid is at least 10 mg/kg per day with more being needed if the patient is mark-

edly obese. The overall success rate for oral bile acid therapy is approximately 40%, rising to 60% with careful patient selection [138]. Stones of 5 mm or less in diameter that float dissolve more quickly (80–90% complete dissolution by 12 months). Larger non-floating stones take longer or never disappear.

The effect of bile acid therapy on symptoms is variable. Biliary pain is less frequent in those patients on long-term ursodeoxycholic acid therapy [139]. Stone recurrence develops in 25–50% of patients at a rate of 10% per year. They are most likely in the first 2 years and unlikely after the first 3 years. Recurrence is higher in those with multiple rather than solitary stones.

Side effects are absent. During treatment the stones may undergo surface calcification [140], but this is probably of little significance.

Extracorporeal shock-wave therapy [141]

Gallbladder stones can be fragmented by shock waves generated extracorporeally using the same principle as that developed for kidney stones. Ultrasound is usually used to target stones. Oral bile acid therapy is given to dissolve those fragments remaining in the gallbladder, although when pulverization is achieved bile acid therapy is not necessary [141]. The gallbladder shows bruising and oedema after the shock waves but these are reversible.

Results

These vary from one machine, centre and protocol to another. Only 20–25% of patients referred satisfy the treatment criteria which included: three or fewer radiolucent gallbladder stones with a total diameter of less than 30 mm, in a functioning gallbladder (on cholecystography), in a symptomatic patient who is otherwise healthy.

Studies have shown overall complete clearance rates at 12 months of 70–90%. However, long-term results are disappointing with recurrence rates of more than 40% after 5 year [142]. Because of this and the development of laparoscopic cholecystectomy, this method is now used rarely.

Other gallbladder pathology [143]

Gallbladder polyps

Polypoid lesions of the gallbladder are seen in around 5% of patients scanned by ultrasound (Fig. 12.18). The majority of these are pseudopolyps—that is cholesterol polyps, inflammatory polyps and adenomyomas, but some (15 of 130 in one series) are neoplastic polyps [144]. Of these most are adenomatous, but dysplasia and malignant change are seen, so that carcinoma of the gallbladder is a risk. Most patients with polyps do not have symptoms. Ultrasound does not differentiate the potentially malignant polyp.

Most studies have recommended cholecystectomy for symptomatic patients, and/or for solitary sessile polypoid lesions greater than 10 mm. Surveillance by ultrasound at set (but not well defined) intervals has been recommended for ‘polyps’ less than 10 mm, with cholecystectomy done when enlargement is detected, or the threshold of 10 mm reached. These recommendations have been recently questioned, mainly because neoplasia, with in some cases a risk of malignancy, has been found in ‘polyps’ less than 10 mm diameter [144,145]. The rationale is that the threshold for removal may have to be lowered, because development of malignancy (carcinoma of the gallbladder) in general has a poor prognosis. The data from a recent study found that reducing the threshold diameter to 6 mm gave an 18.5% positive and 100% negative predictive value for neoplastic change, and dropped the false negative rate to 0% [144].

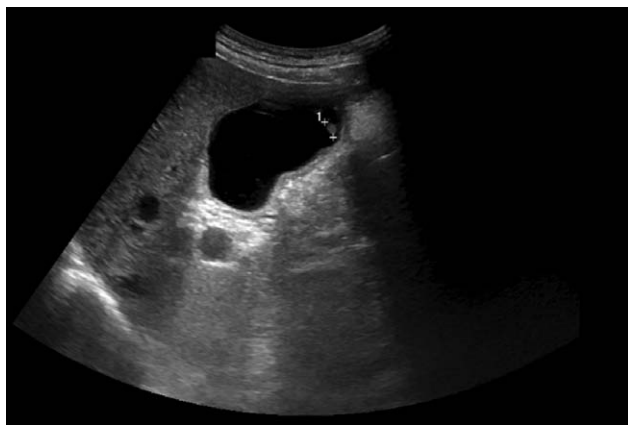


Fig. 12.18. Ultrasound showing 4 mm gallbladder polyp, which does not move on repositioning and does not cast an acoustic shadow.

On the other hand, a study showing no change during follow up (5 years) in 91% of polypoid lesions advised a ‘wait and see policy’. Histology, however, was not done in this study (no patient had cholecystectomy) [146]. These recent papers do raise re-examination of the previous recommendation based on a threshold of 10 mm diameter for intervention. However, the use of a lower threshold recognizes that in some patients no lesion is found in a proportion of patients, 27% in the series quoted [144].

Cholecystectomy in polyps is recommended in lesions that show growth, vascularity, invasion, as well as those that are symptomatic, and in those where surveillance is not possible. Age (>50) and the presence of gallstones are also factors to take in account in the decision [147]. To what extent EUS would be able to separate those with and without a malignant potential is unclear.

The risk of malignancy in polyps is considered greater in patients with primary sclerosing cholangitis, and thus cholecystectomy has been recommended in all such patients [148].

Thus, for asymptomatic patients with lesions seen on US less than 6 mm diameter, surveillance is the agreed approach. For polypoid lesions larger than this, there is agreement that those enlarging or greater than 10 mm diameter be removed by cholecystectomy. Whether the threshold for removal is better reduced below 10 mm is conjectural. The presence of other risk factors may favour removal.

Adenomyomatosis

This may affect the gallbladder wall profusely or locally. There is epithelial proliferation with muscular hypertrophy and mural diverticulae (Rokitansky–Aschoff sinuses), which may be seen as spots of contrast medium outside the lumen of the gallbladder on oral cholecystography after a fatty meal. The changes may also be shown by US, CT and MRI. Demonstration of Rokitansky–Aschoff sinuses is important so as to make the diagnosis—and differentiate the thickened gallbladder wall from other causes. Adenomyomatosis may cause chronic symptoms, which are relieved by cholecystectomy.

Cholesterosis

There is accumulation of cholesterol and triglyceride in the gallbladder wall. It is present in 50% of patients with gallstones, and 35% of symptomatic patients without stones having cholecystectomy for polyp or adenomyomatosis [149].

Cholesterol esters and other lipids are deposited in the submucosal and epithelial cells as small, yellow, lipid specks. As more lipid is deposited, it projects into the lumen as polyps which may become pedunculated.

The change is confined to the gallbladder and never extends to the ducts.

The cholesterolosis is related to the biliary, not blood, cholesterol concentration.

The aetiology is uncertain. The gallbladder mucosa may simply be taking up excess cholesterol from bile. Other possibilities are a defect in submucosal macrophages, impaired transport of cholesterol out of the mucosa [149] or increased cholesterol ester synthesis by the gallbladder mucosa [150].

There is controversy concerning the relation of cholesterolosis to symptoms. However, cholesterolosis may sometimes cause right upper quadrant pain and features causing confusion with the irritable bowel syndrome. Diagnosis is from histology since the changes are generally not shown radiologically.

Xanthogranulomatous cholecystitis

This is an uncommon inflammatory disease of the gallbladder characterized by a focal or diffuse destructive inflammatory process with lipid-laden macrophages. Macroscopically, areas of xanthogranulomatous cholecystitis appear as yellow masses within the wall of the gallbladder. The gallbladder wall is invariably thickened and cholesterol or mixed gallstones are usually present.

The pathogenesis is uncertain, but an inflammatory response to extravasated bile, possibly from ruptured Rokitansky–Aschoff sinuses, is likely.

Symptoms often begin with an episode of acute cholecystitis which persist. There is extension of yellow tissue into adjacent organs. US and/or CT may show hypochoic or low attenuation areas or bands in the gallbladder wall [143]. Because of the difficulty in pre- and perioperative differentiation from carcinoma of the gallbladder in some cases, extended resection as for malignant disease has been reported [151].

Porcelain gallbladder

This rare condition (0.4–0.8% at cholecystectomy) is due to extensive calcification of the gallbladder wall. Circumferential calcification is seen on abdominal X-ray or CT [143]. Ultrasound is helpful in showing the extent of involvement of the gallbladder wall. It was thought that porcelain gallbladder has a relationship to gallbladder carcinoma, although this is conjectural. Particular patterns of calcification may be relate to risk (see Chapter 13).

Typhoid cholecystitis

Circulating typhoid bacilli are filtered by the liver and excreted in the bile. The biliary tract, however, is infected

in only about 0.2% of patients with typhoid fever. Colonization may be facilitated by biofilm formation on cholesterol gallstones [152].

Acute typhoid cholecystitis is becoming very rare. Signs of acute cholecystitis appear at the end of the second week or even during convalescence, and are sometimes followed by perforation of the gallbladder.

Chronic typhoid fever cholecystitis and the typhoid carrier state. The typhoid carrier passes organisms in the faeces derived from a focus of infection in the gallbladder or biliary tract. Chronic typhoid cholecystitis is symptomless. The carrier state is not cured by antibiotic therapy. Cholecystectomy is successful if there is no associated infection of the biliary ducts. Chronic typhoid cholecystitis is not an important cause of gallstones, but carries an increased risk of gallbladder carcinoma [153].

Biliary carriers of other salmonellae have been reported and treated with ampicillin and cholecystectomy.

Acute cholecystitis in AIDS

This is thought to occur because of gallbladder stasis and increased bile lithogenicity in the critically ill patient, opportunistic pathogens such as cytomegalovirus (CMV) and cryptosporidium, or vascular insufficiency due to oedema or infection. Calculous and acalculous cholecystitis are seen.

Patients present with fever, right upper quadrant pain and tenderness. The white cell count is often normal but with a left shift of neutrophils. Ultrasound shows features of acute cholecystitis.

Treatment is by cholecystectomy. In the late 1980s, this carried a mortality of around 30% due to sepsis [154]. However, a mortality of 2% was reported in a series of 53 patients with acute cholecystitis in 1999 from the same group, thought due to improvement in medical treatment [155]. Highly active antiretroviral therapy (HAART) is associated with a reduction in post-operative complications after cholecystectomy [156].

Acute cholecystitis is one part of the spectrum of hepatobiliary disease seen in patients with HIV. There may be parenchymal liver disease (see Chapter 22). Pancreatitis may be seen from HIV-related medications or less often opportunistic infections. AIDS-related diseases include not only acalculous cholecystitis, but also Kaposi's sarcoma, gallstones and AIDS cholangiopathy [157,158].

AIDS cholangiopathy has several patterns: papillary stenosis with bile duct dilatation above; a sclerosing cholangitis-like appearance of intra- and extrahepatic ducts; a combination of the two; or segmental extrahepatic strictures. Patients may be asymptomatic, or present with malaise, fever or right upper quadrant pain. US and CT may be useful, but the combination of

MRI and MRCP is valuable [159]. ERCP allows biopsies and bile to be taken, and if appropriate sphincterotomy to be done. Since the introduction of HAART, the incidence of AIDS cholangiopathy has declined (as with other AIDS-related diseases), and survival with this entity has improved significantly [157]. A worse outcome is associated with opportunistic infections (especially *Cryptosporidia*) and an alkaline phosphatase of greater than eight times normal.

Other associations including infection

Diseases involving the *cystic artery*, such as polyarteritis nodosa, may lead to cholecystitis [160].

The gallbladder may be involved in *Crohn's disease*.

Actinomyces can very rarely involve the gallbladder, as may *Vibrio cholerae* [161] and *Leptospirosis* [162], which have been associated with acalculous cholecystitis. The pathological significance of *Helicobacter* spp. in the biliary tree still seems uncertain.

Congenital gallbladder anomalies (see Chapter 14)

Possible gallbladder anomalies include absence, double, left-sided, intrahepatic and folded. Accessory bile ducts and anomalous cystic duct are seen. All are rare, as is floating gallbladder with torsion [163] which may present with pain.

Although these congenital defects seem rarely related to symptoms the range of case reports show that awareness of them is of importance to the radiologist and to the biliary and hepatic transplant surgeon.

Perforation of the gallbladder

Acute calculous cholecystitis may lead to complete necrosis of the gallbladder wall and perforation. The gallstone may erode the necrotic wall; alternatively, dilated infected Rokitansky–Aschoff sinuses may provide a weak point for rupture.

Rupture usually takes place at the fundus which is the least well-vascularized part of the gallbladder. Discharge into the free peritoneal cavity is rare and, more usually, adhesions form between adjacent organs with local abscess formation. Rupture into adjacent viscera leads to internal biliary fistula.

The patient presents with nausea, right upper quadrant pain and vomiting. A right upper quadrant mass is palpable in 50%, and a similar number are febrile. The diagnosis is often overlooked. CT and ultrasound are of value in showing peritoneal fluid, abscess and gallstones.

There are three clinical types:

1 Acute with bile peritonitis. A history of gallbladder disease is rare. Associated systemic conditions include

vascular insufficiency or immunodeficiency such as atherosclerosis, diabetes mellitus, collagen diseases, corticosteroid use or decompensated cirrhosis. The diagnosis should be suspected in any immunocompromised patient, such as a patient with AIDS with an acute abdomen. Prognosis is poor with a mortality of about 30%. Treatment is by massive antibiotics and restoration of the fluid balance. The gangrenous gallbladder wall is removed or drained percutaneously or surgically. Any abscess must also be drained.

2 Subacute with pericholecystic abscess. These patients have chronic gallstone disease and the picture is intermediate between the acute and chronic types.

3 Chronic with cholecystenteric fistula formation, such as between the gallbladder and colon (see below and Fig. 12.19).

Biliary fistulae

External

These follow procedures such as cholecystotomy, transhepatic biliary drainage or T-tube choledochotomy, after the tube or catheter has been removed.

Because of the sodium and bicarbonate content of bile, patients with large leaks run a risk of hyponatraemic acidosis and impaired renal function.

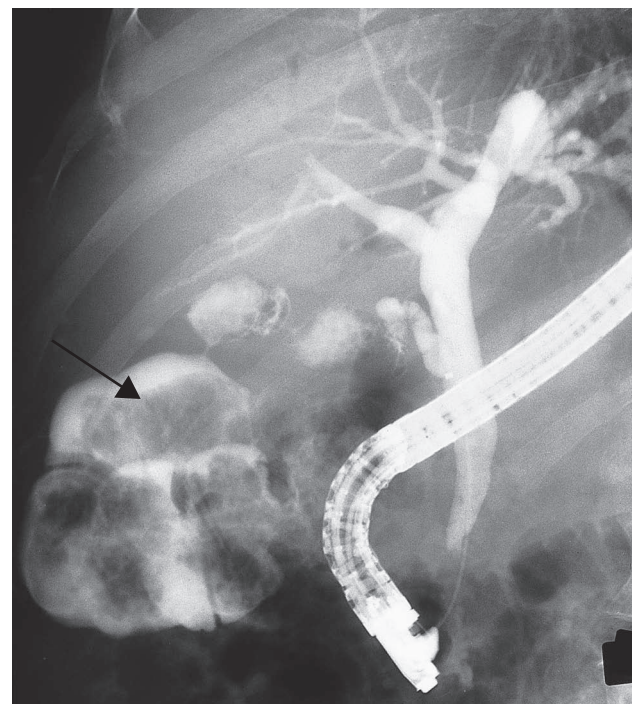


Fig. 12.19. Endoscopic retrograde cholangiopancreatography showing a fistula between the gallbladder and colon (large arrow).

Distal bile duct obstruction may contribute to the failure of a fistula to heal and the placement of an endoscopic stent is likely to be beneficial.

Internal

In 80% these are due to long-standing calculous cholecystitis. The inflamed gallbladder, containing stones, adheres and ruptures into a segment of the intestine, usually the duodenum and less often the colon (Fig. 12.19). The ejected gallstones may be passed or cause intestinal obstruction (*gallstone ileus*), usually in the terminal ileum.

Biliary fistulae may also follow rupture of a chronic duodenal ulcer into the gallbladder or common bile duct. Fistulae may also develop between the colon and biliary tract in ulcerative colitis or Crohn's disease.

Clinical features

The fistula may be symptomless and, when the gallstones have discharged into the intestine successfully, the fistula closes. Such instances are often diagnosed only at the time of a later cholecystectomy.

About one-third give a history of jaundice or are jaundiced on admission. Pain may be absent or as severe as biliary colic. The features of cholangitis may be present. In cholecystocolic fistula the common bile duct may be filled with calculi, putrefying matter and faeces, which cause the severe cholangitis. Bile salts entering the colon produce severe diarrhoea.

Radiological features

These include gas in the biliary tract and the presence of a gallstone in an unusual position. The biliary tree may be filled from barium meal in the case of a cholecystoduodenal fistula, or at barium enema, in the case of a cholecystocolic fistula. ERCP should be diagnostic (Fig. 12.19).

Treatment

Fistulae due to gallbladder disease are treated surgically.

Endoscopic treatment of common duct stones can result in closure of cholecystocolic and bronchobiliary fistulae [164].

Gallstone ileus

A gallstone over 2.5cm in diameter entering the intestine causes obstruction, usually of the ileum, less often of the duodenojejunal junction, duodenal bulb, pylorus

or colon [165]. The impacted gallstone may excite an inflammatory reaction in the intestinal wall, or cause intussusception. Gallstone ileus is very rare but is a cause of non-strangulated intestinal obstruction.

The patient is usually an elderly, afebrile female, possibly with a preceding history suggestive of chronic cholecystitis. The onset is insidious, with nausea, occasional vomiting, colicky abdominal pain and a somewhat distended but flaccid abdomen. There is obstruction to the bowel, and 'ileus' is a misnomer.

A plain X-ray of the abdomen may show loops of distended bowel with fluid levels and possibly the obstructing stone. Gas may be seen in the biliary tract and gallbladder, indicating a biliary fistula.

The plain film on admission is diagnostic in about 50% of patients. Ultrasound, barium studies and CT provide diagnostic information in a further 25%.

Preoperative diagnosis is made in about 70% of cases [165].

Treatment

The intestinal obstruction should be relieved surgically. Whether fistula repair and cholecystectomy are done at the time of the first operation to relieve intestinal obstruction is debated [166]. The decision may be based on the clinical state of the patient and the operative feasibility [165]. If not done at the initial operation, subsequent cholecystectomy is not mandatory. Recurrent gallstone ileus has been reported at 17% with such treatment [165]. Surgical mortality in series is reported from 10 to 30%.

Bile peritonitis

Aetiology

Postcholecystectomy. Bile may leak from small bile channels between the gallbladder and liver or from an imperfectly ligated cystic duct (see also pg 274). If the biliary pressure is raised, perhaps by a residual common duct stone or papillary stenosis, leakage is facilitated and the subsequent paraductal bile accumulation favours the development of biliary stricture.

Post-transplantation. Leakage of bile from the bile duct anastomosis is a recognized complication of liver transplantation (see Chapter 36).

Rupture of the gallbladder. Empyema or gangrene of the gallbladder may lead to rupture and the formation of an abscess; this is localized by previous inflammatory adhesions.

Trauma. Crushing or gunshot wounds may involve the biliary tree. Needle biopsy of the liver or percutaneous cholangiography may rarely be complicated by puncture of the gallbladder or of a dilated intrahepatic bile duct in a patient with deep cholestasis. Oozing of bile rarely follows operative liver biopsy.

Spontaneous. Biliary peritonitis may develop in patients with prolonged, deep obstructive jaundice without demonstrable breach of the biliary tree. This is presumably due to bursting of minute superficial intrahepatic bile ducts.

Common bile duct perforation is exceedingly rare. The factors concerned are similar to those for perforated gallbladder. They include increases of intraductal pressure, calculous erosion and necrosis of the duct wall secondary to thrombosis [167].

Spontaneous perforation of the extrahepatic bile ducts is a rare cause of jaundice in infancy, the most common site being at the confluence of the cystic and common hepatic duct. The pathogenesis is unknown (see Chapter 14).

Clinical picture

This depends on whether the bile is localized or free in the peritoneal cavity, sterile or infected. Free rupture of bile into the peritoneal cavity causes severe shock. Due to the irritant effect of bile salts, large quantities of plasma are poured into the ascitic fluid. The onset is with excruciating, generalized, abdominal pain. Examination shows a shocked patient, with low blood pressure and persistent tachycardia. There is board-like rigidity of the diffusely tender abdomen. Paralytic ileus is a frequent complication. Bile peritonitis should always be considered in any patient with unexplained intestinal obstruction. In a matter of hours secondary infection follows and the temperature rises while abdominal pain and tenderness persist.

Laboratory findings are non-contributory. Abdominal paracentesis reveals bile, usually infected. Serum bilirubin rises and this is followed by an increase in alkaline phosphatase levels. Cholescintigraphy or cholangiography will show the leakage of bile.

Treatment

Rupture of the gallbladder is treated by cholecystectomy. Biliary leakage from the common bile duct can be treated by endoscopic stenting (with or without sphincterotomy) or nasobiliary drainage. If the leak does not seal over in 7–10 days, surgery may be necessary. Scanning-guided drainage of collections may be necessary.

Association between cholecystectomy and colorectal cancer

Both cohort studies and meta-analyses have suggested a possible increase in carcinoma of the proximal colon after cholecystectomy [168–170]. This is not seen in all populations studied, and some have suggested that some bias may be present in the studies. The data relating cholecystectomy (and cholelithiasis) to colonic adenoma are even less secure and prospective data in larger populations have been suggested. The putative mechanism for any risk relates to possible changes in faecal bile acids and cholesterol metabolites, which may promote colorectal oncogenesis. Cholecystectomy may allow greater exposure of conjugated primary bile acids to anaerobic intestinal bacteria and so increase production of carcinogens. Since cholecystectomy is done for clinical reasons this possible association is of questionable clinical relevance—particularly with the development of surveillance programmes for colonic tumour.

Common duct stones

The majority of stones in the common bile duct have passed from the gallbladder. Migration is related to the size of the stone relative to the cystic and common bile duct. Stones may pass uneventfully into the duodenum, cause acute pancreatitis, acute cholangitis, isolated abdominal pain or remain clinically silent in the duct. They may result in partial *obstruction to the common bile duct* with intermittent obstructive jaundice. Infection behind the obstruction, *cholangitis*, is common and is one cause of liver abscess.

After cholecystectomy stones may be left unintentionally in the common bile duct, or slip there from the cystic duct stump. These present in a similar way.

Stones not of gallbladder origin but forming in the duct usually follow partial biliary obstruction due to other residual calculi, traumatic stricture, sclerosing cholangitis or congenital biliary abnormalities. Infection may be the initial event. Stones are brown (see Fig. 12.10b), single or multiple, often oval and conforming to the long axis of the duct.

Effects of common bile duct stones

Bile duct obstruction is usually partial and intermittent since the calculus exerts a ball-valve effect at the lower end of the common bile duct.

Asymptomatic. Duct stones are sometimes discovered incidentally on scanning after investigation of mildly cholestatic liver function tests, or when another system is being scanned (e.g. virtual colonoscopy). It is often surprising that the patient has had no symptoms. In the

elderly, they may present simply as general malaise, or mental and physical debility [171].

Pain with abnormal liver tests. Pain occurs in about three-quarters of patients, is usually severe, colicky and intermittent and needs analgesics for its relief. Sometimes it is a constant, sharp, severe pain. The site may be right upper quadrant or epigastric. It radiates to the back and to the right scapula. It is associated with vomiting. Palpation of the epigastrium is painful. The serum has the changes of cholestasis with one or more of raised alkaline phosphatase, γ -glutamyl transpeptidase and conjugated bilirubin. In acute obstruction the transaminase levels may be briefly very high. Full blood count may show neutrophilia.

Cholangitis. The classical picture is of jaundice, abdominal pain, chills and fever (Charcot's triad). This triad also is not specific to duct stones, and can be seen occasionally in viral hepatitis.

It is important to make a judgement on the severity of cholangitis, since this has a major influence on management. Most patients have mild or moderate cholangitis, based on clinical and laboratory data and the response to antibiotic therapy [172]. In those who do not respond to antibiotic therapy, or have features of septic shock, resuscitation and urgent biliary decompression is necessary. Confusion and hypotension added to Charcot's triad has been termed Reynold's pentad, which was associated with *acute obstructive suppurative cholangitis*, and the need to perform urgent bile duct drainage [173]. Grades of severity of cholangitis have been defined recently in the Tokyo Guidelines [174] with the severe type being that with associated organ dysfunction (one only of hypotension, confusion, respiratory or renal dysfunction (creatinine $>170\mu\text{mol/L}$), or raised INR >1.5 or platelets $<100\times 10^9/\text{L}$). Mild and moderate cholangitis (by definition without organ dysfunction) separate according to the response to antibiotics. The message is clear – severe cholangitis must be recognized and managed urgently.

The bile is infected, probably from the duodenum. However the presence of bacteria alone is insufficient to give signs of systemic infection. The biliary pressure must rise due to bile duct blockage. Sepsis may be intermittent or constant. *Blood culture* should be performed during the febrile episode. *Escherichia coli* is the commonest infecting organism. Others include *Klebsiella*, *Streptococcus*, *Pseudomonas*, *Bacteroides* and *Clostridium sp.*

Acute pancreatitis is due to a stone wedging at, or passing through, the ampulla. The patient presents with an acute abdomen with or without vomiting, and systemic collapse if severe. Serum amylase is raised.

Imaging

As already discussed, where there is suspect biliary tract disease, ultrasonography is the investigation of choice. Dilated ducts and the stone may be seen, but the absence of these should not be regarded as definitive. If the symptoms are strongly suggestive of bile duct stone and there are gallbladder stones, then investigation should be taken further. MRCP is valuable (see Fig. 12.5). Alternatives are EUS or CT. The aim is to detect the duct stone before ERCP is done, usually with sphincterotomy.

Management of duct stones

This depends on the clinical situation—emergency or elective—on the age and general condition of the patient and on the facilities and clinical expertise available. Antibiotics will be given for their systemic effect to treat or prevent septicaemia, and this is probably more relevant than their entry into bile. They are only temporarily effective in controlling the septicaemia if the bile duct is completely obstructed. Decompression is needed. Other measures include control of fluid and electrolyte balance and intravenous vitamin K, if the prothrombin time is prolonged.

Common duct stones without cholangitis

These are usually treated by elective ERCP, sphincterotomy and stone removal. Antibiotics are given to cover the procedure. Stone removal without sphincterotomy is possible, in most cases after balloon dilatation of the sphincter [175]. However the risk of pancreatitis appears to be higher using this technique than sphincterotomy [176].

Patients with gallbladder *in situ*

Endoscopic sphincterotomy is definitive for residual postcholecystectomy stones with only 10% having further biliary problems [177]—a similar outcome to surgical treatment.

If the gallbladder is still *in situ* and contains stones, subsequent management depends upon the age and clinical state of the patient. In the elderly, several studies have shown that, after endoscopic sphincterotomy, 5–10% need cholecystectomy for gallbladder disease during 1–9 years' follow-up [178]. However, a randomized trial of sphincterotomy alone versus open cholecystectomy with surgical removal of duct stones found that 15% of patients treated by sphincterotomy alone subsequently required cholecystectomy during a mean follow-up of 17 months [179]. This compared with 4%

of the surgical group needing sphincterotomy after the cholecystectomy for a retained duct stone.

In an otherwise fit patient with duct and gallbladder stones, endoscopic sphincterotomy with subsequent cholecystectomy is the favoured approach unless there are medical or other factors rendering the patient unfit for surgery [172].

Acute cholangitis

The strategy is treatment with antibiotics, with appropriate fluid management followed by ERCP and sphincterotomy. The urgency of endoscopic interventional is governed by the clinical state of the patient, the response to antibiotic and the availability of ERCP with an appropriate team.

The choice of antibiotic depends upon the state of the patient and local policy. A cephalosporin usually suffices. Quinolones (e.g. ciprofloxacin) are an alternative. Cholangiography is timed according to the state of the patient and the response to antibiotics. Stones are removed after endoscopic sphincterotomy. If the stones cannot be extracted, bile drainage is provided by insertion of an endoprosthesis or nasobiliary tube.

This management is necessary independent of whether the gallbladder is *in situ* or not. Subsequent decisions on cholecystectomy have been discussed above.

Acute cholangitis is also the frequent presentation of patients with a blocking or blocked stent placed for a biliary stricture. Management is stent replacement, with antibiotics beforehand. Antibiotic choice may be more complicated if patients have received several different agents previously, and have resistant biliary microorganisms. Previous bile culture should be checked to direct the choice.

Multivariate analysis has identified seven features associated with a poor outcome in a mixed group of patients with cholangitis treated surgically and by non-surgical techniques. These were acute renal failure, cholangitis associated with liver abscess or liver cirrhosis, cholangitis secondary to high malignant biliary strictures or after percutaneous transhepatic cholangiography, female gender and age over 50 years [180].

Acute obstructive suppurative cholangitis

As described above, clinical features that identify this syndrome are fever, jaundice, pain, and, more importantly, features of single or multiple organ dysfunction. Confusion and hypotension may be followed by renal failure and thrombocytopenia, as part of a disseminated intravascular coagulopathy. This situation indicates the need for biliary decompression by the least invasive approach, as soon as the patient's state allows.

Antibiotics should cover Gram-negative colonic bacteria, and/or any organism cultured. There are several alternatives but piperacillin/ tazobactam is a good choice, with an aminoglycoside (e.g. gentamicin) and metronidazole if the clinical picture is life threatening. Aminoglycoside should only be used for as short a period as possible because of the risk of nephro- and ototoxicity. Most cases are caused by common duct stones. ERCP is done with sphincterotomy and stone removal, if coagulation and anatomy permit. If not, then a stent or nasobiliary tube is inserted.

The aim of any procedure is to *guarantee decompression of the biliary system*. The endoscopic approach is now accepted as the first choice, although there is still a mortality of around 5–10% [181,182]. If this method fails, percutaneous transhepatic external bile drainage is the second choice. Every attempt should be made not to raise the biliary pressure more than necessary by contrast injection, simply to place a drain (either by endoscopic or percutaneous approach), to avoid worsening septicaemia. A full diagnostic cholangiogram is not usually necessary. Surgical operation carries a greater mortality than non-surgical techniques, being between 16 and 40% [182].

After biliary decompression there is usually rapid resolution of septicaemia and toxemia. If not, drainage of the biliary system should be checked, or another source of sepsis sought, such as empyema of the gallbladder or liver abscess.

Acute gallstone pancreatitis

Gallstones travelling down the bile duct may produce acute pancreatitis as they pass through the ampulla. The stones are usually small and pass into the faeces. The inflammation then subsides. Sometimes the stone does not pass out of the ampulla and pancreatitis persists and may be severe. Abnormal liver function tests, particularly transaminases, and ultrasound are the most useful tests to identify the patient with pancreatitis due to gallstones [183]. Early (within 72h) ERCP and sphincterotomy to remove the stone(s) has been shown to reduce complications and cholangitis in patients with severe, but not mild, biliary pancreatitis, and in those with coincident jaundice or cholangitis [184,185]. The optimal timing and selection of patients awaits further study.

Biliary sludge may also cause attacks of acute pancreatitis [186]. Biliary microscopy or EUS may be useful to define this.

Large common duct stones

Stones greater than 15mm in diameter are sometimes difficult or impossible to remove with a standard basket

Table 12.4. Non-surgical treatment options for large common duct stones

Mechanical lithotripsy ('crushing basket')
Endoprosthesis
Extracorporeal shock-wave lithotripsy
Electrohydraulic lithotripsy
Laser lithotripsy



Fig. 12.20. Endoscopic retrograde cholangiopancreatography in a patient with acute cholangitis. The common bile duct contains a large stone which could not be removed. A stent was inserted to provide drainage.

or balloon after sphincterotomy. There are several options (Table 12.4), which will depend upon local expertise.

Mechanical lithotripsy may crush the stone but is limited by basket design and stone shape and size. However 90% success is possible [187].

Extracorporeal shock-wave lithotripsy can fragment 70–90% of large common duct stones with subsequent clearance of fragments through the sphincterotomy in the majority of patients, with less than a 1% 30-day mortality [188,189].

Endoscopic electrohydraulic and laser lithotripsy, if available, may be used for difficult stones [190].

The easiest method, particularly in the poor-risk patient, is the insertion of an *endoprosthesis* (Fig. 12.20),

which may be long term, or temporary before surgical or endoscopic duct clearance. Early complications are seen in 12%, with a mortality of 4% [191]. Biliary colic, cholangitis and cholecystitis are late complications [192]. Stones may become smaller after stenting and may then be easier to remove at later ERCP [193].

Trans T-tube tract removal of stones

Retained stones can be removed percutaneously along the T-tube tract in 77–96% of patients [194] with a complication rate of 2–4% (cholangitis, pancreatitis, tract perforation). The T-tube should have been in place for 4–5 weeks before stone removal to allow a fibrous tract to form. Because of the availability of endoscopic techniques including sphincterotomy, percutaneous removal is now infrequently used. With a T-tube in place the endoscopic approach is successful in about 75% [194].

Mirizzi syndrome

Impaction of a gallstone in the cystic duct or neck of the gallbladder can cause partial common hepatic duct obstruction [195]. Jaundice and/or recurrent cholangitis follows and the stone may erode into the common hepatic duct creating a single cavity [196].

Ultrasound shows dilated intrahepatic and common hepatic ducts, but the cause may not be seen or correctly interpreted. Cholangiography shows mid-duct obstruction (Fig. 12.21). There may be the appearances of a stone, and from the outset it may be obvious that this is in cystic rather than bile duct. However, the appearances may initially suggest a common duct stone and only when attempts have failed to remove it does it become clear that the situation is more complicated. The operator must be alert to the possibility of a cystic duct stone and Mirizzi syndrome. Endoscopic therapy is possible (stent insertion) to decompress the biliary system before surgery. Endoscopic stone retrieval is occasionally possible [197]. Surgery consists of removing the diseased gallbladder and the impacted stone.

A higher frequency of gallbladder carcinoma has been reported in Mirizzi syndrome than with long-standing gallstone disease alone [198].

Intrahepatic gallstones

Stones in the intrahepatic ducts are particularly common in certain parts of the world such as the Far East and Brazil, where they are associated with recurrent pyogenic cholangitis and parasitic infestation (see Chapter 32). Gallstones form in chronically obstructed bile ducts due to such conditions as anastomotic biliary–enteric stricture, primary sclerosing cholangitis or Caroli's disease. They are usually of brown pigment type.

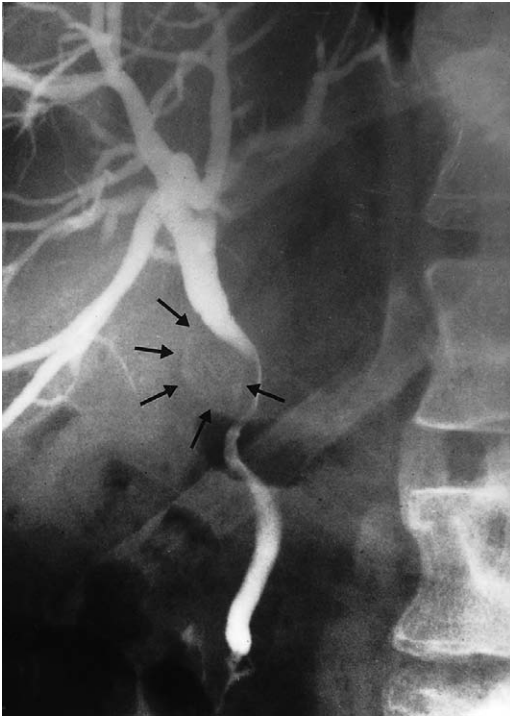


Fig. 12.21. Percutaneous cholangiography in Mirizzi syndrome shows a large gallstone impacted in the cystic duct (arrowed) which has caused obstruction to the common hepatic duct.



Fig. 12.22. Endoscopic retrograde cholangiopancreatography in haemobilia shows filling defects, representing blood clot in the bile ducts.

Secondary hepatic infection may result in multiple abscesses.

Percutaneous techniques using large-bore transhepatic catheters, combined with surgery if necessary, can clear stones in over 90% of patients, leaving the majority symptom free [199]. The percutaneous transhepatic cholangioscopic approach alone can clear intrahepatic stones in over 70%, with a major complication rate of 7.5% [200]. Removal of stones on the right side is more difficult. There is stone recurrence in 40% of patients who have duct strictures, within 5 years. Surgical resection may need to be considered.

Haemobilia [201]

Haemorrhage into the biliary tract may follow trauma including surgical and needle liver biopsy, aneurysms of the hepatic artery or one of its branches, extra- or intrahepatic tumours of the biliary tract, hepatocellular carcinoma, gallstone disease, inflammation of the liver especially helminthic or pyogenic, and rarely varicose veins related to portal hypertension. Iatrogenic disease such as liver biopsy and percutaneous transhepatic cholangiography and bile drainage now accounts for 40%.

Clinical features are pain related to the passage of clots, jaundice and haematemesis and melaena. Minor

episodes may be shown only by positive occult blood tests in faeces.

Diagnosis is suspected whenever upper gastrointestinal bleeding is associated with biliary colic, jaundice or a right upper quadrant mass or tenderness.

MRCP, ERCP or percutaneous cholangiography may show the clot in the ducts (Fig. 12.22).

Treatment

Many resolve spontaneously. If bleeding continues angiography with embolization of a bleeding vessel if seen is indicated [202]. If clot obstructs the bile duct or gives colic, ERCP and drainage or sphincterotomy may be necessary [203].

Bile duct–bowel anastomotic stricture

Choledochojejunostomies and hepaticojejunostomies may stricture. Between 10 and 30% of patients with such anastomoses will need a further procedure—surgical or radiological [124,204]. Of the recurrent strictures, two-thirds occur within 2 years and 90% by 5 years [205]. If the patient remains symptom-free for 4 years postoperatively, there is a 90% chance of complete cure. This

happy result reduces with the number of operations, but can follow many attempts at repair.

Clinical features

Restricting presents as fever, rigors and jaundice. There may be pain. Previous episodes of mild flu-like symptoms may precede the major attack. Cholangitis does not necessarily indicate restenosis, but can be due to intrahepatic strictures or stones, or improperly constructed enteric loops up to the anastomosis with reflux and increased pressure [206].

Investigations

Investigations in the acute phase show leucocytosis and abnormal liver function tests, often with a transient rise in transaminase (due to short-term acute obstruction) with later elevation of alkaline phosphatase and γ -glutamyl transpeptidase.

Radiology

A plain film of the abdomen may show air in the biliary tree and the site of the stricture. Air in the ducts does not necessarily imply a fully patent anastomosis; the alternative is intermittent obstruction. Ultrasound may show dilated ducts but often does not because of the intermittent nature of the obstruction.

Cholangiography by the percutaneous transhepatic route shows whether the anastomosis is strictured (Fig. 12.23); careful fluoroscopic observation of the rate of flow of contrast across the anastomosis is of equal importance to the fixed images examined later. If there has been prolonged partial obstruction with recurrent cholangitis, the changes of secondary sclerosing cholangitis may be seen.

Investigation of the patient with cholangitis but an apparently patent anastomosis is a challenge, since no one imaging technique can be relied upon to demonstrate the cause [206]. Scintigraphy may be useful. There may be poor drainage through the afferent loop of a Roux-en-Y anastomosis.

Treatment

Usually access to the biliary system is only possible percutaneously. A percutaneous transhepatic balloon catheter is passed across the stricture and the balloon inflated. After dilatation, an internal-external catheter with numerous side holes sitting above and below the dilated stricture is left in place. Dilatation can be repeated. Balloon dilatation is usually used without endoprosthesis insertion.

Success rates of percutaneous approaches vary considerably; balloon dilatation is effective in three-quarters

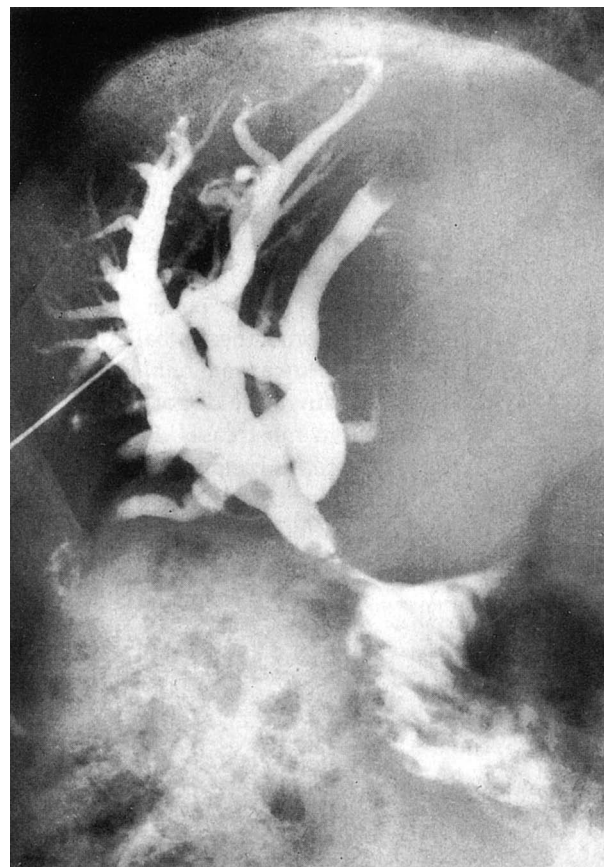


Fig. 12.23. Percutaneous transhepatic cholangiogram in a patient with hepaticojejunostomy following postcholecystectomy stricture. There is restenosis at the anastomosis with dilatation of the ducts in the right lobe.

of patients with a 30-month follow-up [207]. However, the multidisciplinary approach is essential to tailor treatment according to the individual patient in order to reduce the risk of secondary biliary cirrhosis. A retrospective comparison has shown better results with surgical repair than with percutaneous balloon dilatation at around 30 months (90 vs. 65%) [208]. However, the multidisciplinary approach (using both options as necessary) gave a successful outcome in all patients.

Chronic pancreatitis

Pancreatitis, usually of alcoholic aetiology, can cause narrowing of the intrapancreatic portion of the common bile duct. The resultant cholestasis may be transient during exacerbations of acute pancreatitis. This is presumably due to oedema of the pancreas. More persistent cholestasis follows encasement of the low bile duct in a progressively fibrotic pancreatitis. Pseudocysts of the pancreatic head can also cause biliary obstruction.

Bile duct stenosis affects about 8% of patients with chronic alcoholic pancreatitis. It should be suspected if



Fig. 12.24. Endoscopic retrograde cholangiopancreatography in a patient with alcoholic chronic pancreatitis. Note the 'rat tail' narrowing of the distal common bile duct (arrow).

the serum alkaline phosphatase is more than twice elevated for longer than 1 month. ERCP shows a smooth narrowing of the lower end of the bile duct, sometimes adopting a rat tail configuration (Fig. 12.24). The main pancreatic duct may be tortuous, irregular and dilated. Pancreatic calcification may be present.

Liver biopsy shows portal fibrosis, features of biliary obstruction and sometimes biliary cirrhosis. Features of alcoholic liver disease are unusual. Hepatic fibrosis regresses after biliary decompression [209].

Management

Early diagnosis is essential as biliary cirrhosis and acute cholangitis can develop in the absence of clinical jaundice.

If alcohol is responsible for the pancreatitis the patient must abstain completely.

The place of surgery is controversial. Clinical, laboratory and imaging data do not necessarily distinguish those patients with significant bile duct obstruction from those with alcoholic liver disease or normal liver histology. Liver biopsy is valuable in deciding whether surgical decompression of the bile duct is necessary.

Plastic stents successfully relieve bile duct obstruction due to chronic pancreatitis. Placement of multiple plastic stents, to preserve wider dilatation of the stricture, for 12 months has led to an effective outcome after 4 years' follow up, though patients with calcific do worse than those with non-calcific pancreatitis [210]. Covered meta-

llic stents may have a place but are under study [211]. Acute cholangitis, biliary cirrhosis and protracted jaundice are strong indicators for surgery [212]. Choledochoenterostomy is the usual procedure.

Primary sclerosing cholangitis and autoimmune pancreatitis (see Chapter 16)

Extra- and intrahepatic bile ducts are diffusely involved in approximately 80% of patients with primary sclerosing cholangitis. If the patient develops persistent jaundice or recurrent sepsis, investigations are necessary to show whether there is a dominant stricture, that is one which appears to be causing significant obstruction compared with the diffuse changes elsewhere. Ultrasound may show duct dilatation; MRCP or ERCP will show a dominant stricture if present. Brush cytology is necessary. Differentiation of benign stricturing from cholangiocarcinoma is difficult and often impossible.

In autoimmune pancreatitis the biliary tree may be involved with sclerosing cholangitis-like changes, with or without the characteristic pancreatic changes. Steroids typically reverse the bile duct changes, differentiating this syndrome from classic PSC [213].

Bile duct pathology following liver transplantation

See Chapter 36.

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