

# Bile on the rocks a guide to gallstones

The majority of gallstones are silent, but they can result in biliary pain, cholecystitis, pancreatitis and cholangitis. Unless a patient's individual risk of gallbladder cancer is increased, asymptomatic patients should be observed and managed expectantly.

**Cholecystectomy is the definitive treatment for symptomatic gallstones.**

**ROBERT NGUYEN**  
MB BS

**CHRISTOPHER S.  
POKORNY**  
MB BS, FRACP

Dr Nguyen is Gastroenterology Registrar, Liverpool and Bankstown-Lidcombe Hospitals, Sydney; Dr Pokorny is a Visiting Medical Officer, Liverpool and Sydney Hospitals, and a Consultant Gastroenterologist in private practice in Sydney, NSW.

Gallstones are present in 10 to 15% of adults and are a major cause of morbidity worldwide. The symptoms that result are the most common abdominal reason for hospital admissions in developed countries. Gallstones also account for some cases of dyspepsia (a symptom for which approximately 25% of patients in Western countries consult their GP annually); however, asymptomatic gallstones often coexist in dyspeptic patients, and inappropriate cholecystectomy in these cases will result in persisting symptoms after surgery. Therefore, it is important to distinguish true biliary pain from nonspecific dyspepsia.

Up to 90% of gallstones are composed of either cholesterol or cholesterol mixed with pigment (the latter form when bile is supersaturated with cholesterol). The remaining stones are pigmented

(being less than 20% cholesterol) and tend to be small, multiple and black – they develop when bilirubin levels are elevated (as in haemolytic anaemia) or when the solubility of bilirubin is altered. Stasis and infection of the biliary tree, usually from *Escherichia coli* or *Klebsiella* species, may also result in the conversion of soluble conjugated bilirubin into insoluble unconjugated bilirubin and thus increase the lithogenicity of bile.

The major risk factors for gallstones are listed in the Table. Whether diabetes mellitus is a risk factor for gallstones is controversial.

## Clinical presentation

Although the majority of gallstones remain silent, up to one-third of patients will develop symptoms. Biliary pain is the main feature.

## IN SUMMARY

- Most patients with asymptomatic gallstones should be followed and managed expectantly. However, cholecystectomy is recommended in the subgroup of patients who are at increased risk of gallbladder cancer.
- Once biliary pain has developed, the risk of recurrence is high. Cholecystectomy should be considered unless the operative risk is too great.
- Laparoscopic cholecystectomy is the procedure of choice for acute cholecystitis, uncomplicated biliary pain and resolved gallstone pancreatitis.
- Endoscopic retrograde cholangiopancreatography (ERCP), sphincterotomy and biliary decompression should be performed early for gallstone pancreatitis and choledocholithiasis with persisting biliary obstruction (jaundice, cholangitis, dilated intrahepatic ducts).
- CT intravenous cholangiogram and magnetic resonance cholangiopancreatography (MRCP) have replaced ERCP as the diagnostic investigation of choice for suspected choledocholithiasis. Ultrasonography is still the best initial diagnostic imaging test for gallstone disease but has lower sensitivity for choledocholithiasis.

### Table. Major risk factors for gallstones

- Advancing age
- Female gender
- Genetics
- Pregnancy
- Physical inactivity or obesity
- Rapid weight loss
- Haemolytic anaemias
- Hypertriglyceridaemia
- Medications – for example, oestrogen and oral contraceptives, clofibrate, ceftriaxone, cyclosporin
- Terminal ileal resection or disease (especially Crohn's disease)
- Gallbladder stasis

### Biliary pain

Biliary pain is thought to arise from mechanical distension of the gallbladder when the cystic duct is obstructed. It is characterised by sudden onset, a rapid increase in intensity over about 15 minutes and a duration of up to 24 hours. The pain is typically located in the epigastrium or, less frequently, in the right upper quadrant; it may radiate to the interscapular region or the right shoulder and is typically associated with nausea and often vomiting.

Although it is described as 'biliary colic', the pain generally does not fluctuate. Large meals may precipitate the pain, although no single dietary component has been implicated, and fat intolerance is not a feature.

Fever accompanied by pain continuing for more than 24 hours is unusual and may indicate the development of acute cholecystitis necessitating hospital admission. There are often no haematological or biochemical changes in uncomplicated biliary pain.

### Acute cholecystitis

Prolonged or recurrent obstruction of the cystic duct may result in acute inflammation of the gallbladder with parietal pain. Acute cholecystitis is associated with cholelithiasis in approximately 90% of cases.

Patients with acute cholecystitis typically

### Management of gallstone disease

This image is unavailable due to copyright restrictions

Endoscopic retrograde cholangiopancreatography (ERCP) now has an established role as a therapeutic tool in managing acute cholangitis, severe gallstone pancreatitis, common bile duct stones and complications of biliary surgery. The sensitivity and specificity of the procedure for detecting choledocholithiasis is 95%, and stones can be extracted with a balloon or basket after sphincterotomy.

© JACKIE HEDA MEDICAL ILLUSTRATION, 1996

complain of persisting pain located in the right upper quadrant or epigastrium, often lasting more than four to six hours, associated with fevers, nausea and leucocytosis. On physical examination, they commonly experience an inspiratory arrest on palpation over the gallbladder fossa beneath the liver edge (Murphy's sign). In elderly patients, the sensitivity of this sign may be diminished and fever can be absent. In up to 30% of cases, the inflamed gallbladder may be adherent to the adjacent omentum, resulting in a palpable mass.

Liver function tests are usually normal in uncomplicated acute cholecystitis. The presence of jaundice (noted in up to 15% of patients) should signal the possibility of complicating conditions such as choledocholithiasis (stones in the

continued

common bile duct), cholangitis (inflammation of the biliary tree) or the Mirizzi syndrome (stone impacted in the cystic duct causing extrinsic compression of the common hepatic duct or common bile duct).

If the diagnosis or treatment of acute cholecystitis is delayed, gallbladder gangrene may develop. This complication is seen in as many as 20% of cases, with subsequent perforation occurring in 2%.

Repeated attacks of acute cholecystitis may result in chronic cholecystitis, which is characterised by a thickened and fibrotic gallbladder. These patients may have only minimal symptoms referable to the gallbladder, but are at the same risk of developing pancreatitis, choledocholithiasis and cholangitis.

Acute cholecystitis can develop in the absence of gallstones in up to 10% of cases. The clinical presentation is variable and depends on the underlying cause. Morbidity and mortality are higher in acalculous than in calculous cholecystitis

– the former is almost exclusively seen in intensive care units in patients who have critical illness, extensive burns, major trauma or sepsis or who are receiving total parenteral nutrition, are immunosuppressed or have recently undergone surgery. As such, these patients are generally not seen in community settings.

### Choledocholithiasis

Between 15 and 20% of patients with gallstones develop choledocholithiasis. The prevalence increases with age, with most stones arising from the gallbladder, but choledocholithiasis may occur after cholecystectomy.

The clinical features of choledocholithiasis vary from biliary pain to acute suppurative cholangitis secondary to infection of stagnant bile. The usual Charcot's triad (pain, jaundice and fever) occurs in 70% of cases of cholangitis; the organisms that are commonly implicated are *E. coli*, *Klebsiella* species, *Pseudomonas* species and enterococci.

### Acute pancreatitis

About 5% of patients with gallstones develop acute pancreatitis. The risk is greater in those with multiple small stones (less than 5 mm in diameter) that can pass down the common bile duct and through the ampulla. Transient obstruction or oedema at the ampulla caused by passage of a stone may occlude the pancreatic duct or allow reflux of duodenal fluid or bile into the pancreatic duct, resulting in acute pancreatitis.

The diagnosis should be considered in those with a prior history of biliary pain in association with an alanine aminotransferase (ALT) elevated to more than three times the normal level – this has a positive predictive value of 95% for diagnosing gallstone pancreatitis. Elevated aspartate aminotransferase (AST) levels are not nearly as reliable, and serum bilirubin and alkaline phosphatase (ALP) are not specific for gallstone pancreatitis. The serum amylase and lipase levels do not correlate with the clinical severity or predict the course.

### Investigations

#### Ultrasonography

Ultrasonography is the best initial imaging test for the hepatobiliary system in patients with right upper quadrant pain. The sensitivity and specificity of this investigation for diagnosing gallstones over 2 mm in diameter in the gallbladder are more than 95% (Figure 1). In addition, thickening of the gallbladder wall by more than 4 mm, the presence of pericholecystic fluid and localised tenderness over the gallbladder can be detected, each of which suggest acute cholecystitis. The sensitivity of ultrasonography for detecting choledocholithiasis is less, although dilatation of the common bile duct and intrahepatic ducts as a result of obstruction may be evident.

Plain abdominal x-rays are rarely useful in detecting gallstones because the vast majority of these stones are not radio-opaque.

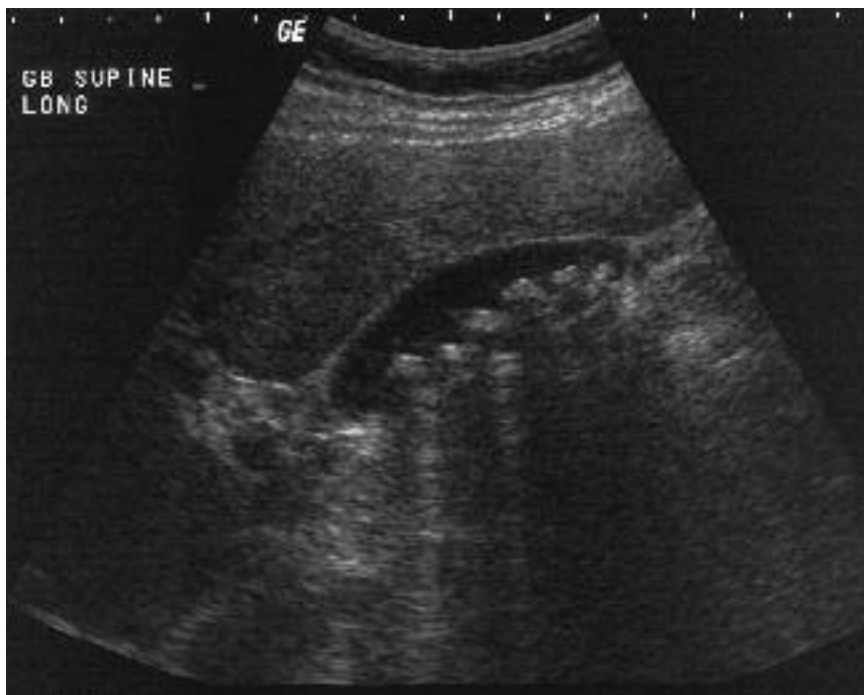


Figure 1. An upper abdominal ultrasound revealing multiple stones in the gallbladder. Characteristic acoustic shadowing is evident.

### CT, CT intravenous cholangiography and magnetic resonance cholangiopancreatography

Abdominal CT has a similar sensitivity to ultrasonography for detecting choledocholithiasis but is inferior for picking up stones in the gallbladder. CT scans have an important role in acute pancreatitis and are also useful in excluding distal common bile duct obstruction by tumours. In acute pancreatitis, a contrast enhanced CT of the abdomen may demonstrate not only choledocholithiasis, but also the presence and extent of pancreatic necrosis, which has prognostic implications.

CT intravenous cholangiography and magnetic resonance cholangiopancreatography (MRCP) have now replaced endoscopic retrograde cholangiopancreatography (ERCP) as the diagnostic investigation of choice for suspected choledocholithiasis. CT cholangiography is an effective method of analysing the biliary tree using computer generated image reconstructions, and is able to detect stones as small as 3 mm in diameter. Its major limitation is inability to adequately opacify the bile ducts when serum bilirubin levels are greater than 50 µmol/L.

MRCP is a very sensitive, specific and noninvasive modality for detecting

choledocholithiasis. It has a sensitivity of up to 95% for stones larger than 4 mm in diameter, which is similar to ERCP, but does not allow therapeutic biliary decompression in cholangitis. MRCP is currently not as sensitive as ERCP for smaller stones, small ampullary lesions, biliary strictures and primary sclerosing cholangitis. In addition, image artefacts from metallic clips or metal biliary stents may preclude an MRCP study.

### Endoscopic retrograde cholangiopancreatography

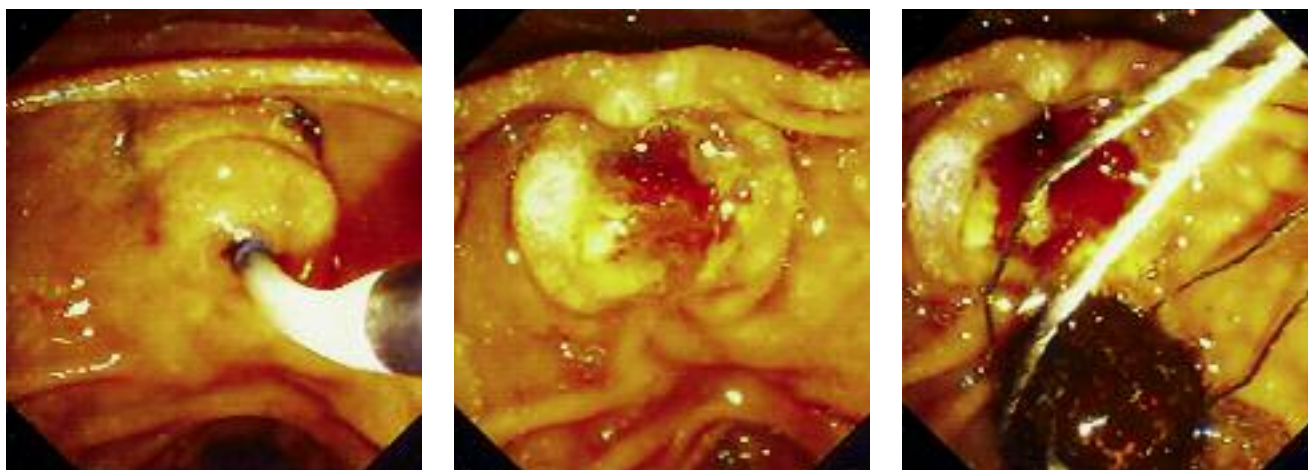
The advent of ERCP in the late 1970s has had an impact on the therapy of stones in the common bile duct (Figure 2). ERCP now has an established role as a therapeutic tool in managing acute cholangitis, severe gallstone pancreatitis, retained common bile duct stones (Figures 3a to c), and complications of biliary surgery. The sensitivity and specificity for detecting choledocholithiasis is 95%, and stones can be extracted with a balloon or basket after sphincterotomy – that is, severing the deep muscle layers of the sphincter of Oddi to allow free passage of stones down the common bile duct (Figures 4 and 5). The risks of ERCP are not insignificant, with a reported mortality of up to 2% and a complication rate of 3 to 7%.



Figure 2. Cholangiogram taken at ERCP demonstrating multiple stones in a dilated common bile duct.

### Radioisotope scanning

Hepatobiliary scintigraphy is sensitive and specific in diagnosing acute cholecystitis with an occluded cystic duct. It is also used to identify patients with gallbladder dysmotility who may have symptomatic improvement after cholecystectomy, but it is less reliable for



Figures 3a to c. Endoscopic retrograde cholangiopancreatography. a (left). Cannulation of the common bile duct. b (centre). Appearance of the ampulla after sphincterotomy. c (right). Stone after being extracted from the common bile duct with a Dormia basket.

continued

detecting chronic cholecystitis. The radioactive agents are taken up rapidly from the blood and excreted into the bile ducts, even in the presence of moderate hyperbilirubinaemia (diagnostic limitation occurs with serum bilirubin over 100  $\mu\text{mol/L}$ ). Cystic duct obstruction is suggested by failure to image the gallbladder in the presence of common bile duct and small bowel visualisation.

### Management

#### Asymptomatic gallstones

Up to two-thirds of gallstones are asymptomatic, with the risk of biliary pain estimated to be between 1 and 4% per year. Asymptomatic patients should generally be observed and managed expectantly – the exceptions are those at high risk of gallbladder cancer, such as patients with a calcified gallbladder, gallbladder polyps over 10 mm in diameter or gallstones greater than 2.5 cm in diameter. Prophylactic cholecystectomy should be recommended in this group.

#### Symptomatic gallstones

After an episode of 'biliary colic', the risk of recurrent biliary pain is of the order of 38 to 50% per year. There is also a higher likelihood of biliary complications (20%) over a five-year period in

those with symptomatic gallstones. Elective cholecystectomy should be considered in this group unless the operative risk is high.

Laparoscopic cholecystectomy is preferred over the open procedure because of the lower mortality (0.1% *v.* 0.5%) and shorter recovery time due to the smaller incisions. The main disadvantages of the laparoscopic approach are the higher incidences of bile duct injury, bile leaks, and bowel and vascular injuries. Conversion to an open cholecystectomy is necessary in up to 5% of patients who undergo the laparoscopic procedure and is more common with emergency operations.

If possible, a single stage procedure of laparoscopic cholecystectomy and intraoperative cholangiogram with laparoscopic exploration of the common bile duct should be performed because 15 to 20% of patients with stones in the gallbladder will have choledocholithiasis. This single stage procedure can be performed in institutions with the necessary expertise; however, it is not commonly practised because selective preoperative biliary imaging and preoperative ERCP followed by laparoscopic cholecystectomy is an equally appropriate management plan in patients with choledocholithiasis.

An increase in stool frequency is not

uncommon following cholecystectomy. However, this is clinically important in less than 5% of patients and often responds well to antidiarrhoeal therapy.

#### Acute cholecystitis

If acute cholecystitis is confirmed, antibiotics should be commenced and laparoscopic cholecystectomy performed within 24 to 48 hours. The alternative option (antibiotic therapy followed by elective surgery) has the disadvantage of failing in 15% of patients – they will require emergency open surgery, which carries greater morbidity and mortality.

#### Choledocholithiasis

The presence of cholangitis or jaundice with dilated intrahepatic ducts detected on ultrasonography is an indication for early ERCP and sphincterotomy to retrieve stones and decompress the biliary tree. Early elective cholecystectomy should be planned.

#### Pancreatitis

In patients with severe gallstone pancreatitis or mild pancreatitis with evidence of persistent or progressive biliary obstruction (jaundice, cholangitis, dilated intrahepatic ducts), early ERCP with sphincterotomy and stone extraction should be performed. Early use of prophylactic antibiotics may reduce sepsis in those with pancreatic necrosis and severe pancreatitis.

Patients who have recovered from an episode of mild to moderate gallstone pancreatitis without evidence of persisting obstruction should undergo elective laparoscopic cholecystectomy during that hospital admission because the risk of recurrent pancreatitis is 20% at four months. Routine preoperative ERCP is not justified in this group because most patients have passed the stones before surgery. Those with severe or complicated pancreatitis should have an interval laparoscopic cholecystectomy after recovering from the acute episode.



Figure 4. Stones and sludge being removed from the common bile duct with a balloon.

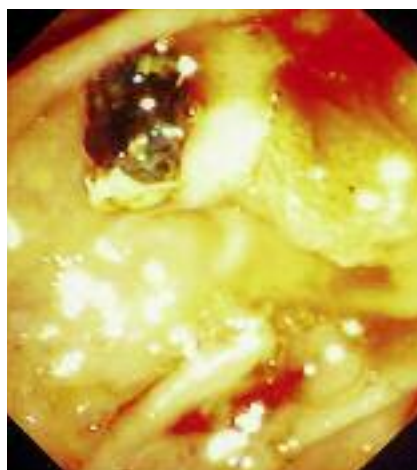


Figure 5. A stone protruding through the ampulla after sphincterotomy.

### Oral bile acid dissolution therapy and extracorporeal shockwave lithotripsy

Oral bile acid dissolution therapy and extracorporeal shockwave lithotripsy should be reserved for a very small selected subgroup of patients with uncomplicated symptomatic gallstones who are reluctant to undergo definitive cholecystectomy or are high risk surgical candidates. In clinical practice, less than 1% of patients have this form of treatment for gallstone disease. It is successful only in cholesterol gallstones – stones that are pigmented or mixed with a significant composition of pigment relative to cholesterol are rendered insoluble. The effectiveness of dissolution therapy using bile acids and extracorporeal shockwave lithotripsy is very slow and variable with higher costs and recurrence rates. Therefore, these modalities are not widely practised.

### Conclusion

Although most gallstones remain asymptomatic, those that result in biliary pain will often lead to biliary complications requiring therapy. Laparoscopic cholecystectomy with intraoperative exploration of the common bile duct is preferred in institutions with the necessary expertise. Alternatively, preoperative biliary imaging and ERCP for choledocholithiasis followed by elective cholecystectomy is an appropriate management plan, and is more commonly practised in Australia. In experienced hands the operative mortality and morbidity of laparoscopic cholecystectomy is very low.

ERCP now has a defined role in treating gallstone pancreatitis, acute cholangitis and failed laparoscopic common bile duct exploration and in managing complications of biliary surgery, particularly bile duct injuries. Given the potential morbidity and mortality of this procedure, imaging modalities such as CT intravenous cholangiogram and MRCP

have now replaced ERCP as the diagnostic tool for suspected choledocholithiasis. **MT**

### Acknowledgements

The authors thank Dr David Abi-Hanna and Dr Paul Edwards for the loan of the endoscopic photographs.

### Bibliography

1. Feldman M, Friedman SL, Sleisenger MH, Scharschmidt BF. Sleisenger and Fordtran's Gastrointestinal and liver disease. 7th ed. Philadelphia: WB Saunders, 2002.
2. Yamada T, Alpers DH, Laine L, Owyang C, Powell DW, eds. Textbook of gastroenterology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.
3. Fletcher DR. Gallstones: modern management. *Aust Fam Physician* 2001; 30: 441-445.
4. Fletcher DR, Hobbs MS, Tan P, et al. Complications of cholecystectomy: risks of the laparoscopic approach and protective effects of operative cholangiography: a population-based study. *Ann Surg* 1999; 229: 449-457.
5. Baillie J. Treatment of acute biliary pancreatitis. *N Engl J Med* 1997; 336: 286-287.
6. Barish MA, Yucel EK, Ferrucci JT. Magnetic resonance cholangiopancreatography. *N Engl J Med* 1999; 341: 258-264.
7. Agrawal S, Jonnalagadda S. Gallstones, from gallbladder to gut. Management options for diverse complications. *Postgrad Med* 2000; 108: 149-153.
8. Johnson CD. ABC of the upper gastrointestinal tract. Upper abdominal pain: gall bladder. *BMJ* 2001; 323: 1170-1173.
9. Breen DJ, Nicholson AA. The clinical utility of spiral CT cholangiography. *Clin Radiol* 2000; 55: 733-739.