Gallstones and Cholecystitis

Gallstones may cause no symptoms and are occasionally discovered as an incidental finding when abdominal imaging is carried out for some other reason.

Epidemiology\(^\text{[1]}\)

1-4% of asymptomatic patients in the adult Western world develop symptoms annually. The most common presentations are biliary colic (56%) and acute cholecystitis (36%)\(^\text{[1]}\). Other presentations and complications can occur (see below).

10-15% of people in the adult Western world develop gallstones. UK Hospital Episode Statistics' data for the years 2003-2005 showed that 25,743 patients were admitted as an emergency with acute gallbladder (GB) disease during that period\(^\text{[2]}\).

The adage 'fair, fat, fertile, female and forty' is only part of the story. Other risk factors include:

- Increasing age.
- Positive family history.
- Sudden weight loss - eg, after obesity surgery.
- Loss of bile salts - eg, ileal resection, terminal ileitis.
- Diabetes - as part of the metabolic syndrome.
- Oral contraception - particularly in young women\(^\text{[3]}\).

Interesting information came from a 10-year study of necropsy findings in South East England. Female gallstone subjects had a higher BMI than controls but males did not. Gallstones were twice as common in those with diabetes. There was no association with heart disease. A third of elderly patients of both sexes had gallstones but most had not had surgery and gallstones were seldom a cause of death\(^\text{[4]}\).

Common bile duct (CBD) stones may occur in 3-14.7% of all patients for whom cholecystectomy is performed\(^\text{[5]}\).

Types of stone

- Bile contains cholesterol, bile pigments (from broken-down haemoglobin) and phospholipids. If the concentrations of these vary, different kinds of stones may be formed.
- Cholesterol stones (80% of all GB stones in the UK) are large, often solitary and radiolucent.
- Black pigment stones are small, friable, irregular and radiolucent:
  - Risk factors include haemolysis (eg, sickle cell anaemia, hereditary spherocytosis, thalassaemia) and cirrhosis.
- Mixed stones are faceted and are comprised of calcium salts, pigment and cholesterol, 10% are radiopaque.
- Brown pigment stones (<5% in the UK) form as a result of stasis and infection within the biliary system, usually in the presence of Escherichia coli and Klebsiella spp.

Presentation in primary care

- Up to 70% of patients with gallstones are asymptomatic at the time of diagnosis. The number of patients with progression of asymptomatic to symptomatic disease is relatively low, ranging from 10-25%\(^\text{[6]}\).
- Gallstones may cause acute or chronic cholecystitis, biliary colic, pancreatitis or obstructive jaundice.
- Biliary colic is the most common presentation, caused by a gallstone impacting in the cystic duct or the ampulla of Vater.
- The second most common presentation is acute cholecystitis, caused by distension of the GB with subsequent necrosis and ischaemia of the mucosal wall.

Biliary colic

- The pain starts suddenly in the epigastrium or right upper quadrant (RUQ) and may radiate around to the back in the interscapular region.
- Contrary to its name, it often does not fluctuate but persists from 15 minutes up to 24 hours, subsiding spontaneously or with analgesics.
- Nausea or vomiting often accompanies the pain, which is visceral in origin and occurs as a result of distension of the gallbladder due to an obstruction or to the passage of a stone through the cystic duct.

Differential diagnosis

Vague abdominal discomfort, distension, nausea, flatulence and intolerance of fats may also be caused by reflux, peptic ulcers, irritable bowel syndrome, relapsing pancreatitis and tumours - eg, stomach, pancreas, colon or gallbladder. Two or more of these conditions may overlap, so the diagnosis may not be easy.
Investigations

- Urinalysis, CXR and ECG may help exclude other diseases.
- Ultrasound is the best way to demonstrate stones, being 90-95% sensitive[7]:
  - Sometimes stones are not mobile, in which case they are not easy to differentiate from unimportant polyps and very small ones may be missed or fail to throw a helpful acoustic shadow.
  - Ultrasonography can also allow measurement of the diameter of the CBD and show the liver and hepatic bile ducts but it can only identify with certainty about half of any stones in the CBD.
  - If the ultrasound scan findings are negative but there is a high level of suspicion, such as in a patient with upper abdominal pain and abnormal LFTs, it is worth repeating the investigation after an interval. This may pick up stones which were previously missed.

- Fuller evaluation is needed if abnormal LFTs or jaundice persist, in patients with acute pancreatitis and when the CBD is noticeably dilated.
- Endoscopic retrograde cholangiopancreatography (ERCP) may be used for the diagnosis of CBD stones and has also evolved from a diagnostic to a therapeutic procedure for the removal of CBD stones[8].
- Computerised tomography (CT) may be useful when filling the bile duct is unsuccessful in ERCP or when the procedure cannot be used for other reasons.
- Intraoperative laparoscopic ultrasonography has replaced cholangiography as the method of choice for detecting CBD stones[7].

Cholecystitis[9]

Risk factors

- Gallstones or biliary sludge (95% of patients).
- Hospitalisation for trauma or acute biliary illness (this represents the other 5%, without gallstones).
- Female gender.
- Increasing age.
- Obesity.
- Rapid weight loss.
- Pregnancy.
- Crohn’s disease.
- Hyperlipidaemia.

Presentation

This follows impaction of a stone in the cystic duct, which may cause continuous epigastric or RUQ pain, vomiting, fever, local peritonism, or a GB mass.

- The main difference from biliary colic is the inflammatory component (local peritonism, fever, raised white cell count (WCC)).
- If the stone moves to the CBD, jaundice may occur.
- Murphy's sign: lay two fingers over the RUQ. Ask the patient to breathe in. This causes pain and arrest of inspiration as the inflamed GB impinges on your fingers. The sign is only positive if a similar manoeuvre in the left upper quadrant does not cause pain.
- Repeated attacks of acute cholecystitis lead to chronic cholecystitis, in which the walls of the GB become thickened and scarred and the GB becomes shrivelled.

Investigations

- FBC - the WCC is likely to be raised.
- Liver enzymes are often mildly abnormal.
- Ultrasound findings for cholecystitis:
  - Include a thickened GB wall (greater than 3 mm) and may also include pericholecystic fluid or air in the GB or the GB wall.
  - If the GB wall is thickened but there are no gallstones present then the diagnosis could still be acalculous cholecystitis.
  - Hydroxyiminodiacetic acid (HIDA) cholescintigraphy may be used to reveal a blocked cystic duct.

This occurs when an obstructed CBD becomes contaminated with bacteria. In severe cases, symptoms can include pain in the RUQ, jaundice and high swinging fevers with rigors and chills (Charcot's triad).

Obstructive jaundice

See the separate Jaundice article.

Other presentations

Cholangitis

See the separate Cholangitis article.
Pancreatitis
See the separate Acute Pancreatitis and Chronic Pancreatitis articles.

Passage of the gallstone into the bowel causes a temporary blockage of the biliopancreatic duct, leading to a premature release of pancreatic enzymes. Symptoms include persistent epigastric pain radiating to the back which is relieved by leaning forwards and profuse vomiting. One study found that a serum total bilirubin level of or greater than 68.4 μmol/L on hospital Day 2 predicted persisting CBD stones with enough specificity to serve as a practical guideline for ERCP while minimising unnecessary procedures.[10]

Empyema
The obstructed GB fills with pus. The patient may become quite toxic and there is a marked fever and leukocytosis.

Gallstone ileus
Gallstone ileus is caused by occlusion of the intestinal lumen as a result of one or more gallstones. It is a rare complication of gallstones that occurs in 1-4% of all cases of bowel obstruction. The mortality is 12-27%.[11]

The management of gallstones, biliary colic and cholecystitis[1, 9]

Many patients can be managed initially at home. Factors to be taken into account include the age of the patient, social support and the severity of symptoms.

Non-surgical
- **Biliary colic and acute cholecystitis** - these are conditions which will usually respond to an opioid such as morphine or pethidine given parenterally and/or diclofenac by suppository. These routes will overcome difficulties in absorption caused by vomiting. Pain continuing for over 24 hours or accompanied by fever usually necessitates hospital admission.
- It is generally considered that patients who require antibiotics should have them intravenously in hospital. There is no evidence base to support the use of oral antibiotics at home, except where the patient has been discharged from hospital after a course of intravenous antibiotics but without having had surgical removal of the stones. One study also supported current guidelines that antibiotics before elective cholecystectomy were unnecessary.[12]
- Chronic cholecystitis - the same principles apply to acute attacks of pain in patients with chronic cholecystitis.

Surgical
- **Early cholecystectomy** for acute GB disease is not widely practised by surgeons in England. Open cholecystectomy is more commonly used in the emergency than in the elective setting.[2]
- **Laparoscopic cholecystectomy** is the preferred procedure. A Cochrane review found that there was no difference in mortality, postoperative complications, or operative time compared with open cholecystectomy. However, hospital stay was shorter and recovery time was quicker.[13] An American study subsequently found that open cholecystectomy is associated with a higher mortality burden.[14]
- **Day case surgery** has been shown by studies to be as safe and as acceptable to patients as ‘overnight stay’ surgery and is more cost-effective.[15]
- **Early surgery** (within seven days of the onset of symptoms) appears to be safe and shortens hospital stay.[16]. One study found that it could be delivered in UK hospitals, providing emergency theatre services were efficiently managed.[17]
- **Percutaneous cholecystotomy** (surgical drainage of the GB) is useful for patients who are unfit for cholecystectomy.
- **Natural orifice transluminal endoscopic surgery** is being developed. The peritoneal cavity is accessed via a natural orifice such as the mouth, rectum or vagina. A successful cholecystectomy has been carried out on a porcine model.[18] A human vaginal cholecystectomy has also been reported.[19]. This approach may well revolutionise the management of gallstones (for women) in the future.

Risks of surgery
- **Postoperative complications** are rare but do occur. The most significant is injury to the bile duct which occurs at a rate of 0.2% in both open and laparoscopic surgery.
- Fat intolerance may develop in a small proportion of patients - and a low-fat diet is recommended. However, evidence to support the usefulness of this diet is weak.[20]
- **Post-cholecystectomy syndrome**: this refers to to heterogeneous group of symptoms and findings in patients who have undergone cholecystectomy. It’s a rare situation; these patients can present with abdominal pain, jaundice or dyspeptic symptoms.[21]

The management of silent stones[1]
Patients should be managed on a case-by-case basis. 1-4% of asymptomatic patients develop problems related to gallstones annually, so the odds are in favour of a ‘watch and wait’ policy. Younger patients tend to develop complications more frequently because they have a longer time for the gallstones to cause problems and smaller stones cause more problems than larger ones, as they are more likely to become dislodged.

The management of bile duct stones[22]
Consensus guidelines were commissioned by the British Society of Gastroenterology in 2008.

These suggest:
• Cholecystectomy and exploration of the CBD if the GB is present, preferably through a laparoscope.
• Bilary sphincterotomy and endoscopic stone extraction if the GB has been previously removed.
• Consider a biliary stent if stones are irretrievable (may be definitive treatment if the patient is unfit for surgery).
• Consider advanced endoscopic percutaneous techniques (eg, mechanical lithotripsy or extracorporeal shock-wave lithotripsy.

The preferred method is endoscopic sphincterotomy followed by laparoscopic cholecystectomy, either at the same time or at a later stage[23].

A Cochrane review found that open bile duct surgery seems superior to ERCP in clearing CBD stones. There was no significant difference in the mortality and morbidity between laparoscopic bile duct clearance and the endoscopic options. There was no significant reduction in the number of retained stones and failure rates in the laparoscopy groups compared with the pre-operative and intra-operative ERCP groups[24].

The management of other gallstone problems
• Cholangitis: medical treatment includes broad-spectrum intravenous antibiotics and correction of fluid/electrolyte disturbance. Surgical decompression of the GB may be required. Endoscopic drainage has replaced emergency surgical common duct exploration and T-tube drainage in patients with severe cholangitis. Percutaneous transhepatic biliary drainage (PTBD) is another option.
• Empyema: intravenous antibiotics are combined with urgent decompression and removal of the GB. Decompression may be carried out via a laparoscope under radiological guidance prior to GB resection, as this makes the GB easier to handle. The conversion to open cholecystectomy is 40-80% but complications are no higher with laparoscopic removal than with open surgery. One study suggested that conversion rates are proportional to the experience of the surgeon[23].
• Gallstone ileus: treatment is traditionally by laparotomy and ‘milking’ the obstructing stone into the colon or by enterotomy and extraction. Recently, laparoscopic techniques have been used.

Prevention
• Ursodeoxycholic acid is useful in preventing high-risk patients (eg, morbidly obese patients undergoing rapid weight loss following bariatric surgery) from developing gallstones[1]. However, studies suggest that ursodeoxycholic acid has no effect on the reduction of biliary symptoms, once the stones have formed[1].
• It is suggested that a healthy lifestyle, regular physical activity and the maintenance of an ideal body weight might prevent cholesterol stones and symptomatic stone-related symptoms - but the evidence here is weak[26].

Further reading & references
• Gallstone disease; NICE Clinical Guideline (October 2014)
• Single incision laparoscopic cholecystectomy; NICE Interventional Procedure Guidance, December 2014
• Gallstone disease; NICE Quality standard, December 2015

9. Cholecystitis - acute; NICE CKS, July 2013 (UK access only)
20. Gurusamy KS, Davidson BC; Gallstones. BMJ. 2014 Apr 22;348:g2669. doi: 10.1136/bmj.g2669.
22. Guidelines on the management of common bile duct stones; British Society of Gastroenterology (July 2008)
26. EASL Clinical Practice Guidelines on the prevention, diagnosis and treatment of gallstones; European Association for the Study of the Liver (2016)

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