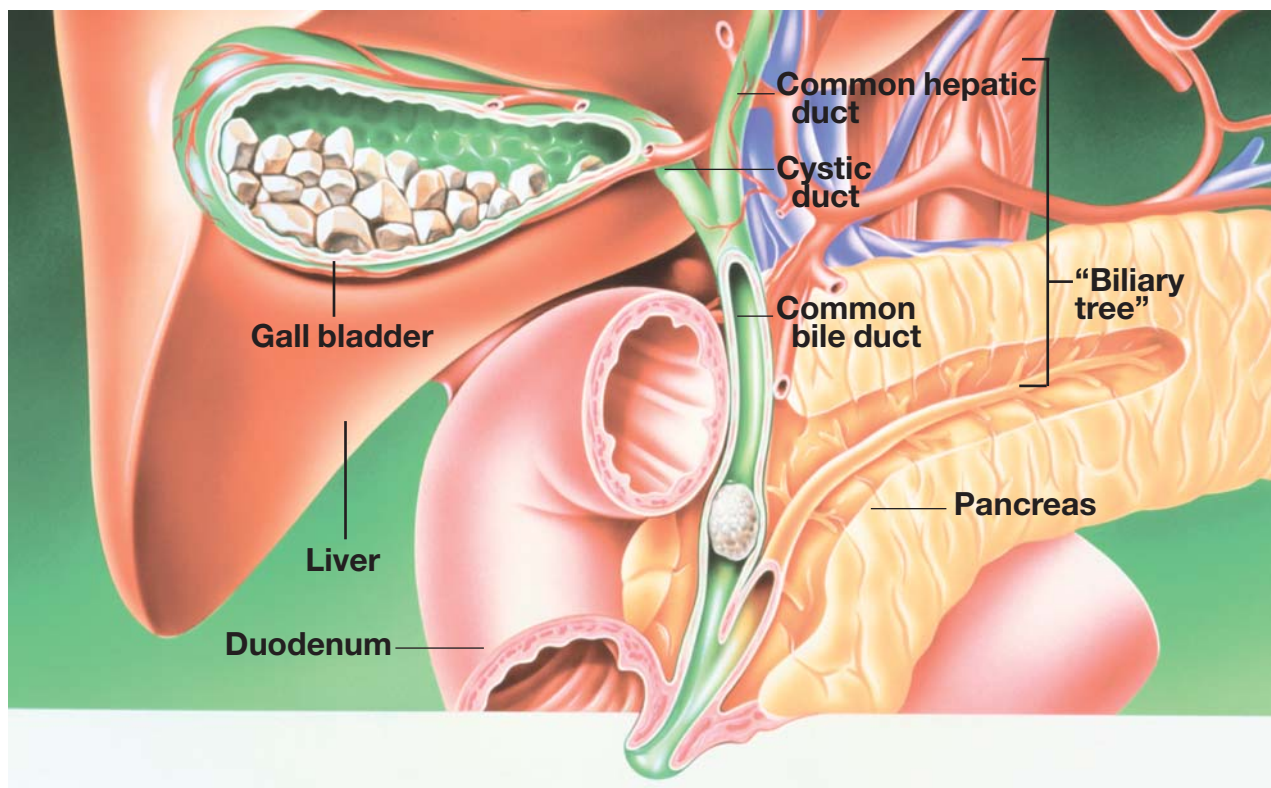
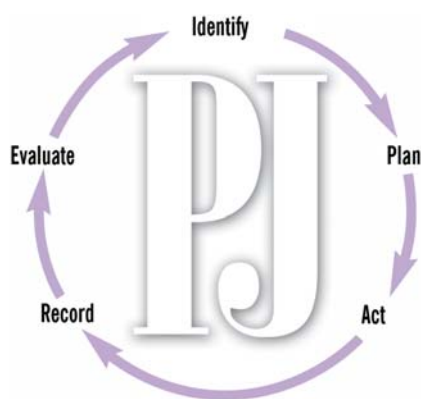


Management of gallstone disease

Gallstones are a major cause of health care expenditure and affect an estimated 5.5 million people in the UK. They are found in 12 per cent of men and 24 per cent of women. In this article, **Quentin Nunes** and **Ian Beckingham** give an overview of the presentation and diagnosis of gallstones and look at current treatment options



Cross section of the abdomen



Identify knowledge gaps

1. How are gallstones formed?
2. List three common symptoms of gallstone disease.
3. What are the treatment options?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "common disease states" (see appendix 4 of "Plan and record").

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Gallstones are small hard masses of cholesterol, calcium bilirubinate, calcium carbonate or calcium bicarbonate (or a mixture of these), formed in the gall bladder or bile duct. They can vary between less than a millimetre to a few centimetres in diameter. Most gallstones form when there is supersaturation of bile with cholesterol — cholesterol and cholesterol-dominant stones account for 80 per cent of all stones in the UK. Stone formation is further aided by decreased gall bladder motility. Decreased motility is seen in pregnancy and diabetes and can be caused by hormone replacement therapy or other drugs (eg, loperamide and ondansetron).

"Pigment stones" are less common. Black pigment stones are more common in patients with haemolytic diseases (eg, sickle cell anaemia, hereditary spherocytosis, thalassaemia) and cirrhosis. Brown pigment stones are uncommon in the UK (<5 per cent of stones). They form as a result of stasis and infection within the biliary system, usually in the presence of *Escherichia coli* and *Klebsiella* spp which produce β -glucuronidase that converts soluble conjugated bilirubin back to the insoluble unconjugated state, leading to the formation of soft, earthy, brown stones. See Panel 1 (p124) for the function of the gall bladder.

Risk factors associated with cholesterol gallstones include:

- Being female
- Being over 40 years old
- Obesity
- Hyperlipidaemia
- Pregnancy
- Taking hormone replacement therapy

Clinical presentations

Although many people have gallstones, only 10 per cent have symptoms and require treatment. Clinical presentations can vary, but the most common are biliary colic, acute cholecystitis and jaundice.

Biliary colic The most common presentation of gall stone disease is biliary colic (chronic cholecystitis). Pain, which is visceral in origin, starts in the central or right upper abdomen and can radiate to the back. It is possible for people to confuse this symptom with other conditions, such as a heart attack or a gastric ulcer. Often, the pain does not fluctuate and can last for anything between 15 minutes and 24 hours. Nausea or vomiting often accompany the pain.

Most episodes of biliary colic can be managed at home. Pain persisting for more than 24 hours or accompanied by fever suggests acute cholecystitis and usually necessitates hospital admission.

Fatty meals can stimulate gall bladder contraction and so pain can occur a few hours after eating a large fatty meal.

Acute cholecystitis The cystic duct connects the gall bladder to the bile duct and gallstones can block this. When obstruction of the cystic duct persists, an acute inflammatory response can occur. Leucocyte concentration increases and a fever can develop. Irritation of the adjacent peritoneum causes localised tenderness in the right upper abdomen, just below the rib cage. The severity of pain is variable.

Jaundice Jaundice due to gallstones usually occurs when a stone migrates from the gall bladder into the common bile duct. Symptoms include yellow skin and eyes, itchy skin, pale stools and dark urine.

Less commonly, jaundice can be due to chronic cholecystitis associated with fibrosis of the gall bladder and impaction of a stone in Hartman's pouch compressing the common hepatic duct.

Acute cholangitis When the common bile duct is obstructed and becomes contaminated with bacteria (usually from the duodenum), the bile duct can become inflamed (cholangitis). When severe, cholangitis presents as a triad (Charcot's triad) of right upper abdominal pain, jaundice and a high swinging fever with rigors and chills. This requires urgent treatment.

Acute pancreatitis Gallstones can pass down the common bile duct, resulting in temporary obstruction of the pancreatic duct.



Gallstones can vary between less than a millimetre to a few centimetres in diameter

Acute pancreatitis develops in 5 per cent of all patients with symptomatic gallstones.

Gallstone ileus Acute cholecystitis can cause the gall bladder to stick to adjacent jejunum or duodenum. Subsequent inflammation can result in a fistula between these structures and the passage of a gallstone into the bowel. Large stones can become impacted, resulting in small bowel obstruction.

Investigations

A physical examination in a person with acute cholecystitis or biliary colic will usually reveal abdominal tenderness, but this is inconclusive.

Radiological Ultrasound is the initial investigation of choice in gall stone disease. Diagnostic features include the presence of gallstones, a distended thick-walled gall bladder, fluid retention around the gall bladder and Murphy's sign (tenderness and rigidity under the right ribs, that worsens with inspiration).

Around 10 per cent of patients with gallstones will also have common bile duct stones (see below). However, ultrasound is often not sensitive enough to detect stones at this site and these stones can be demonstrated by a dilated common bile duct though computed tomography, the diagnostic modality of choice. Endoscopic retrograde cholangiopancreatography (ERCP) using an endoscope to obtain images of the pancreas and biliary tree) has the advantage of being both diagnostic and therapeutic (see below).

Biochemical Biochemical investigations include a full blood count and liver function tests. A mild derangement of liver enzymes and a raised white cell count is often present in acute cholecystitis. Liver function tests show a cholestatic pattern when there is accompanying jaundice and elevated conjugated bilirubin and alkaline phosphatase with normal or mildly elevated transaminases.

Treatment of gallstone disease

It should be noted that finding stones does not necessarily explain pain — as most patients with gallstones are asymptomatic,

Panel 1: Gall bladder

The gall bladder is a small pear-shaped organ situated on the underside of the liver. Its role is to store and concentrate bile secreted by the liver. When a person has a fatty meal and this enters the duodenum, cholecystikinin is released. This forces the gall bladder to contract, delivering bile into the intestine via the common bile duct and the cystic duct (see Figure 1). Enzymes from the pancreas are also released in response to food.

Bile aids the digestion and absorption of fats. Bile contains bile salts (eg, cholic and chenodeoxycholic acids), which emulsify fats, phospholipids, cholesterol, proteins and bilirubin.

Biliary colic is the most common presentation of gall stone disease

other conditions (eg, gastric ulcer etc) must be discounted.

Medical treatment Most episodes of biliary colic can be managed at home with analgesics and anti-emetics. Acute cholecystitis usually requires admission to hospital, where initially a non steroidal anti-inflammatory drug (intramuscularly or rectally) or an opioid analgesic is given. Treatment progress is monitored by resolution of tachycardia, temperature and tenderness. In addition, patients should be given a broad spectrum parenteral antibiotic (eg, a second generation cephalosporins) because secondary bacterial infections are common.

Acute cholangitis requires urgent treatment with broad spectrum antibiotics and early decompression of the biliary system by endoscopic or radiological stenting, or surgical drainage if stenting is not available. Delay can rapidly result in septicaemia or the development of liver abscesses with a significant mortality.

The main treatment for gallstones is surgical removal of the stone(s) and gall bladder.

Cholecystectomy Cholecystectomy (removal of the gall bladder) is the optimal treatment of gallstone disease and laparoscopic cholecystectomy is now the gold standard. Over 50,000 cholecystectomies are performed every year in the UK. The only specific contraindications to laparoscopic cholecystectomy are coagulopathy and the later stages of pregnancy.

Laparoscopic cholecystectomy has a lower mortality than the standard open procedure (0.1 versus 0.5 per cent for the open procedure) mainly due to a lower incidence of post-operative cardiac and respiratory complications. Smaller incisions that cause less pain and the subsequent reduction in opiate analgesic requirements have resulted in the procedure being performed with a single overnight stay in most centres and as a day case in selected patients. Most patients can return to sedentary work after seven to 10 days.

Post-operative recovery Patients are allowed oral fluids on return to the ward and are managed with oral analgesics (predominantly paracetamol and non-steroidal anti-inflammatory drugs). They can eat within a few hours and, increasingly, many patients are discharged the same day. There are no dietary restrictions. There may be occasional bruising around the entry ports. Wounds can gape slightly and discharge a small amount of serous fluid. Dressing changes and observation are adequate. Increasing redness spreading away from the wound edges and associated with increasing wound pain or purulent discharge should be swabbed and the patient given a broad spectrum antibiotic (eg, co-amoxiclav 375 mg *tds* for three days). It may be helpful to open the wound to allow improved drainage.

After removal of the gall bladder the bile produced by the liver passes through the bile

Removal of the gall bladder is the optimal treatment of gallstone disease

Gallstones are hard deposits of cholesterol and bile salts

duct as before, but rather than being stored, it leaks into the duodenum. Most patients can do without a gall bladder, especially one that is "diseased", but about 10 per cent of patients experience a change in bowel habit (typically looser or more frequent stools, or both) as a result of a change in bile salt concentration within the bowel. This often settles within a few weeks of surgery. Standard anti-diarrhoeals (eg, loperamide 2mg per stool) usually work well when necessary.

About 1 per cent develop "troublesome" diarrhoea as a result of the almost continuous flow of bile into the duodenum.

Alternative therapies There are several alternatives to cholecystectomy. These include oral dissolution therapy (using bile acids such as ursodeoxycholic acid), contact dissolution (direct instillation — either percutaneously or endoscopically — of methyl-tetra-butyl ether or mono-octanoin) and lithotripsy (using sound energy to shatter the stones).

Success rates vary widely but around 50 per cent of appropriately selected patients achieve stone clearance using these alternative methods. However, less than 10 per cent of all patients are suitable for these treatments. Patients must have:

- Cholesterol stones less than 20mm in diameter
- A functioning gall bladder and patent cystic duct (ie, mild symptoms)

It should be noted that if the gall bladder is not removed, life-long bile acid therapy may be necessary to prevent recurrent stone formation (see Panel 2) and this can be expensive. Therefore, there is currently little place for these therapies, which are reserved for patients who refuse surgery.

Common bile duct stones Common bile duct stones can be primary or secondary (to gallstones). Patients with abnormal liver func-

Science Photo Library

Panel 2: Ursodeoxycholic acid

Ursodeoxycholic acid is a bile acid that will dissolve cholesterol stones. However this can take a long time. The dose is 8–12mg/kg daily, with or after food, as a single dose at bedtime or in two divided doses. Treatment is continued for three or four months after the stones have dissolved (determined by ultrasound).

Side effects include nausea, vomiting, diarrhoea and pruritis. Gallstones can also calcify — another problem with non-surgical treatment. In addition, as the stones shrink and become more mobile, the risk of biliary colic can increase.

According to the British National Formulary, treatment can be given for up to two years. However, most surgeons using Ursofalk recommend life-long treatment because recurrence of stones is still likely after this time.

tion test results or in whom an ultrasound scan shows a dilated common bile duct should have imaging of the bile ducts with magnetic resonance cholangiopancreatography or endoscopic ultrasound before surgery.

The optimal treatment for stones in the common bile duct is removal of both the stones and the gallbladder. This can be performed in two stages: by pre-operative ERCP followed by laparoscopic cholecystectomy, or as a single stage cholecystectomy with exploration of the common bile duct either by laparoscopic or open surgery. The morbidity and mortality (2 per cent) of open surgery is higher than that of the other two options. In elderly or frail patients ERCP with division of the sphincter of Oddi (sphincterotomy) and stone extraction alone may be an appropriate alternative because the risk of developing further symptoms is only 10 per cent in this population. When common bile duct stones are suspected in patients who have had previous cholecystectomy, ERCP is both diagnostic and therapeutic.

Dietary recommendations

We do not advise a specific diet for prevention of gallstones but because a low fat diet in patients with gallstones helps prevent attacks of biliary colic in some patients, it is worth trying. Saturated fats and refined sugars have

A low fat diet in patients with gallstones may help prevent attacks of biliary colic

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Do you have any patients taking Ursosalk? Speak to them about their condition.
2. Review the advice you would give for lowering cholesterol.
3. Review your knowledge of other kinds of stones (eg, kidney stones).

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities.

Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

been proved to be associated with gallstone disease and a study last year showed that formation of gallstones increases with an increase in daily calorie intake.

Taking cholesterol-lowering drugs has been linked with cholesterol stones. Lowering blood cholesterol increases bile cholesterol and this, in turn, can promote stone formation.

CPD diary: independent pharmacist gears up for everything

Ramesh Patel is an independent community pharmacist in Hounslow, Middlesex, and has been on the Register for 29 years. Mr Patel works a busy six-day week (9am to 7pm) and has three children, one of whom is also a pharmacist.

An example of CPD that I have done recently is to go to an update on the new contract, organised by Hounslow PCT. These meetings are held every two or three months in a room at a local college and run from 7 to 9pm. We are usually given at least a month's notice, so it is easy to plan to get away from the pharmacy on time. The meetings are always well attended and you get to catch up with other local pharmacists.

My pharmacy is taking part in a repeat dispensing pilot and at the last PCT meeting I found out how other participants were doing and what kind of responses they had been getting. The meetings are interesting — you get to know what is happening within the trust and what the people who run the PCT are thinking. So it is useful for tendering for new services. We plan to gear up for everything on offer and already supply emergency hormonal contraception on a patient group directive. It is worth finding time to attend because it makes me better informed and, therefore, a better pharmacist. It also makes us better remunerated.

I have not yet got round to recording using the Society's "Plan and record" system but have been keeping notes of the CPD I have done. I know I have to start using it now. I do not think I will use the website however, because I am not so comfortable with typing.

If you would like to share an example of your CPD contact Lin-Nam Wang (tel: 020 7572 2413 or email: Lin-Nam.Wang@pharmj.org.uk).



When I first qualified there were no formal CPD or continuing education options — no training materials or courses and no recording as such. In those days, we did not even put the names of drugs on labels and hardly anyone asked about side effects or how a drug worked. But now people expect much more from pharmacists and responsibility has shifted. One of my daughters, Anita, is also a pharmacist. For her, the CPD cycle comes easily but for me it is not so natural. However, I know that now it is the only way to stay in the profession. Anita inspires me. For example, recently we went to a Centre for Pharmacy Postgraduate Education workshop together. Pharmacists my age should not be frightened of CPD but take the bull by the horns.