

Gallstone

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A **gallstone** is a stone formed within the gallbladder out of bile components.^[1] The term **cholelithiasis** may refer to the presence of stones in the gallbladder or to the diseases caused by gallstones.^[2] Most people with gallstones (about 80%) never have symptoms.^{[1][3]} In 1–4% of those with gallstones, a crampy pain in the right upper part of the abdomen, known as biliary colic, occurs each year.^[4] Complications of gallstones include inflammation of the gallbladder, inflammation of the pancreas, and liver inflammation.^{[1][4]} Symptoms of these complications may include pain of more than five hours duration, fever, yellowish skin, vomiting, or tea-color urine.^[1]

Risk factors for gallstones include birth control pills, pregnancy, a family history of gallstones, obesity, diabetes, liver disease, or rapid weight loss. Gallstones are formed in the gallbladder, typically from either cholesterol or bilirubin.^[1] Gallstones may be suspected based on symptoms.^[4] Diagnosis is then typically confirmed by ultrasound. Complications may be detected on blood tests.^[1]

Prevention is by maintaining a healthy weight and eating a proper diet. If there are no symptoms, treatment is usually not needed. In those who are having gallbladder attacks surgery to remove the gallbladder is typically recommended. This can be either done through several small incisions or through a single larger incision. Surgery is typically done under general anesthesia. In those who are unable to have surgery, medication to try to dissolve the stones or shock wave lithotripsy may be tried.^[1]

In the developed world, 10–15% of adults have gallstones.^[4] Rates in many parts of Africa, however, are as low as 3%.^[5] Gallbladder and biliary related diseases occurred in about 104 million people (1.6%) in 2013 and they resulted in 106,000 deaths.^{[6][7]} Women more commonly have stones than men and they occur more commonly after the age of 40. Certain ethnic groups have gallstones more often than others. For example, 48% of American Indians have gallstones. Once the gallbladder is removed, outcomes are generally good.^[1]

Gallstone

Synonyms cholelith



Numerous small gallstones made up largely of cholesterol

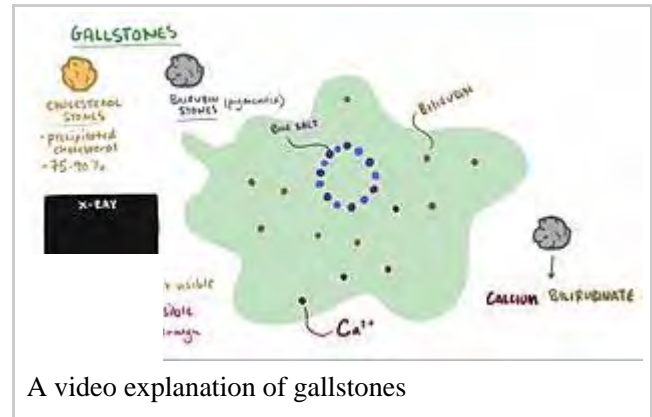
Pronunciation cholelith /ˈkɒləlɪθ/, cholelithiasis /ˌkɒləlɪˈθaɪəsis/

Classification and external resources

Specialty	General surgery
ICD-10	K80 (http://apps.who.int/classifications/icd10/browse/2016/en#/K80)
ICD-9-CM	574 (http://www.icd9data.com/getICD9Code.aspx?icd9=574)
OMIM	600803 (https://omim.org/entry/600803)
DiseasesDB	2533 (http://www.diseasesdatabase.com/ddb2533.htm)
MedlinePlus	000273 (https://medlineplus.gov/ency/article/000273.htm)
eMedicine	emerg/97 (http://www.emedicine.com/emerg/topic97.htm)
MeSH	D042882 (https://www.nlm.nih.gov/cgi/mesh/2017/MB_cgi?field=uid&term=D042882)

Contents

- 1 Definitions
- 2 Signs and symptoms
 - 2.1 Other complications
- 3 Risk factors
- 4 Pathophysiology
 - 4.1 Composition
- 5 Diagnosis
- 6 Treatment
 - 6.1 Surgical
 - 6.2 Medical
- 7 Other animals
- 8 See also
- 9 References
- 10 External links



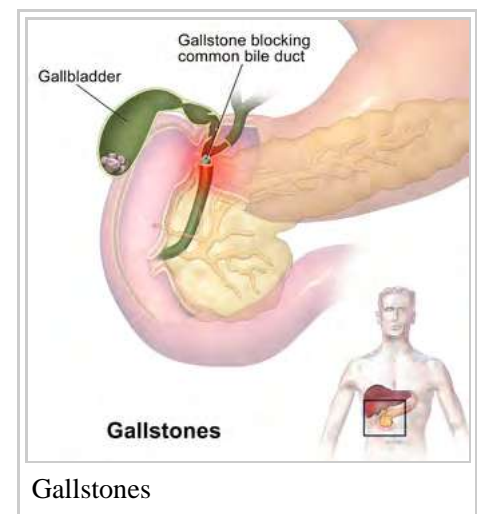
Definitions

Gallstone disease refers to the condition where gallstones are either in the gallbladder or common bile duct.^[2] The presence of stones in the gallbladder is referred to as cholelithiasis, from the Greek *chol-* (bile) + *lith-* (stone) + *iasis-* (process). If gallstones migrate into the ducts of the biliary tract, the condition is referred to as choledocholithiasis, from the Greek *chol-* (bile) + *docho-* (duct) + *lith-* (stone) + *iasis-* (process). Choledocholithiasis is frequently associated with obstruction of the biliary tree, which in turn can lead to acute ascending cholangitis, from the Greek: *chol-* (bile) + *ang-* (vessel) + *itis-* (inflammation), a serious infection of the bile ducts. Gallstones within the ampulla of Vater can obstruct the exocrine system of the pancreas, which in turn can result in pancreatitis.

Signs and symptoms

Gallstones may be asymptomatic, even for years. These gallstones are called "silent stones" and do not require treatment.^{[8][9]} The size and number of gallstones present does not appear to influence whether or not people are symptomatic or asymptomatic.^[10] A characteristic symptom of gallstones is a gallstone attack, in which a person may experience colicky pain in the upper-right side of the abdomen, often accompanied by nausea and vomiting, that steadily increases for approximately 30 minutes to several hours. A person may also experience referred pain between the shoulder blades or below the right shoulder. These symptoms may resemble those of a "kidney stone attack". Often, attacks occur after a particularly fatty meal and almost always happen at night, and after drinking.

In addition to pain, nausea, and vomiting, a person may experience a fever. If the stones block the duct and cause bilirubin to leak into the



bloodstream and surrounding tissue, there may also be jaundice and itching. This can also lead to confusion. If this is the case, the liver enzymes are likely to be raised.^[11]

Other complications

Rarely, in cases of severe inflammation, gallstones may erode through the gallbladder into adherent bowel potentially causing an obstruction termed gallstone ileus.^[12]

Other complications include ascending cholangitis if there is a bacterial infection which can cause purulent inflammation in the biliary tree and liver, and acute pancreatitis as blockage of the bile ducts can prevent active enzymes being secreted into the bowel, instead damaging the pancreas.^[11]

Risk factors

Gallstone risk increases for females (especially before menopause) and for people near or above 40 years;^[13] the condition is more prevalent among both North and South Americans and among those of European descent than among other ethnicities. A lack of melatonin could significantly contribute to gallbladder stones, as melatonin inhibits cholesterol secretion from the gallbladder, enhances the conversion of cholesterol to bile, and is an antioxidant, which is able to reduce oxidative stress to the gallbladder.^[14] Researchers believe that gallstones may be caused by a combination of factors, including inherited body chemistry, body weight, gallbladder motility (movement), and low calorie diet. The absence of such risk factors does not, however, preclude the formation of gallstones.

A clear relationship has been proven between diet and gallstone formation. According to a study limited to 80 patients in Nepal, non-vegetarians have 9 times the incidence of gallstones compared to vegetarians.^[15] The methodology of the study has been disputed.^[16] Nutritional factors that may increase risk of gallstones include constipation; eating fewer meals per day; low intake of the nutrients folate, magnesium, calcium, and vitamin C;^[17] and, at least for men, a high intake of carbohydrate, a high glycemic load, and high glycemic index diet.^[18] Wine and whole-grained bread may decrease the risk of gallstones.^[19]

Rapid weight loss increases risk of gallstones.^[20] Patients taking orlistat, a weight loss drug, may already be at increased risk for the formation of gall stones. Weight loss with orlistat can increase the risk of gall stones.^[21] On the contrary, ursodeoxycholic acid (UCDA), a bile acid, also a drug marketed as Ursodiol, appears to prevent formation of gallstones during weight loss.^[22] A high fat diet during weight loss also appears to prevent gallstones.^[22]

Pigment gallstones are most commonly seen in the developing world. Risk factors for pigment stones include hemolytic anemias (such as from sickle-cell disease and hereditary spherocytosis), cirrhosis, and biliary tract infections.^[23] People with erythropoietic protoporphyria (EPP) are at increased risk to develop gallstones.^{[24][25]} Additionally, prolonged use of proton pump inhibitors has been shown to decrease gallbladder function, potentially leading to gallstone formation.^[26]

Pathophysiology

Cholesterol gallstones develop when bile contains too much cholesterol and not enough bile salts. Besides a high concentration of cholesterol, two other factors are important in causing gallstones. The first is how often

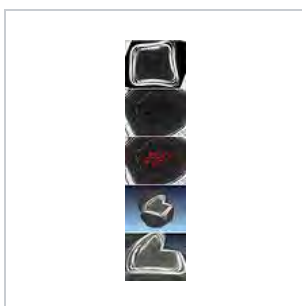
and how well the gallbladder contracts; incomplete and infrequent emptying of the gallbladder may cause the bile to become overconcentrated and contribute to gallstone formation. This can be caused by high resistance to the flow of bile out of the gallbladder due to the complicated internal geometry of the cystic duct.^[27] The second factor is the presence of proteins in the liver and bile that either promote or inhibit cholesterol crystallization into gallstones. In addition, increased levels of the hormone estrogen, as a result of pregnancy or hormone therapy, or the use of combined (estrogen-containing) forms of hormonal contraception, may increase cholesterol levels in bile and also decrease gallbladder movement, resulting in gallstone formation.

Composition

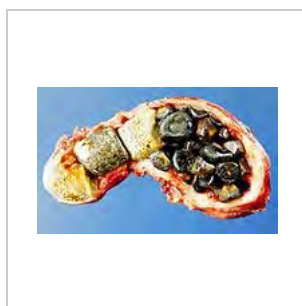
Gallstones can vary in size and shape from as small as a grain of sand to as large as a golf ball.^[28] The gallbladder may contain a single large stone or many smaller ones. Pseudoliths, sometimes referred to as sludge, are thick secretions that may be present within the gallbladder, either alone or in conjunction with fully formed gallstones. The clinical presentation is similar to that of cholelithiasis. The composition of gallstones is affected by age, diet and ethnicity.^[29] On the basis of their composition, gallstones can be divided into the following types:



Gallbladder opened to show small cholesterol gallstones



μCT of a gallstone



The large, yellow stone is largely cholesterol, while the green-to-brown stones is mostly bile pigments



Images of a CT of gallstones



Large gallstone

Cholesterol stones

Cholesterol stones vary from light yellow to dark green or brown or chalk white and are oval, usually solitary, between 2 and 3 cm long, each often having a tiny, dark, central spot. To be classified as such, they must be at least 80% cholesterol by weight (or 70%, according to the Japanese- classification system).^[30] Between 35%

and 90% of stones are cholesterol stones.^[3]

Bilirubin stones

Bilirubin ("pigment", "black pigment") stones are small, dark (often appearing black), and usually numerous. They are composed primarily of bilirubin (insoluble bilirubin pigment polymer) and calcium (calcium phosphate) salts that are found in bile. They contain less than 20% of cholesterol (or 30%, according to the Japanese-classification system).^[30] Between 2% and 30% of stones are bilirubin stones.^[3]

Mixed stones

Mixed ("Brown Pigment") stones typically contain 20–80% cholesterol (or 30–70%, according to the Japanese-classification system).^[30] Other common constituents are calcium carbonate, palmitate phosphate, bilirubin and other bile pigments (calcium bilirubinate, calcium palmitate and calcium stearate). Because of their calcium content, they are often radiographically visible. They typically arise secondary to infection of the biliary tract which results in the release of β -glucuronidase (by injured hepatocytes and bacteria) which hydrolyzes bilirubin glucuronides and increases the amount of unconjugated bilirubin in bile. Between 4% and 20% of stones are mixed.^[3]

Diagnosis

Diagnosis is than typically confirmed by ultrasound. Complications may be detected on blood tests.^[1]

A positive Murphy's sign is a common finding on physical examination during a gallbladder attack.

Treatment

Surgical

Cholecystectomy (gallbladder removal) has a 99% chance of eliminating the recurrence of cholelithiasis. Surgery is only indicated in symptomatic patients. The lack of a gallbladder may have no negative consequences in many people. However, there is a portion of the population—between 10 and 15%—who develop a condition called postcholecystectomy syndrome^[31] which may cause gastrointestinal distress and persistent pain in the upper-right abdomen, as well as a 10% risk of developing chronic diarrhea.^[32]

There are two surgical options for cholecystectomy:

- Open cholecystectomy is performed via an abdominal incision (laparotomy) below the lower right ribs. Recovery typically requires 3–5 days of hospitalization, with a return to normal diet a week after release and to normal activity several weeks after release.^[8]
- Laparoscopic cholecystectomy, introduced in the 1980s,^[33] is performed via three to four small puncture holes for a camera and instruments. Post-operative care typically includes a same-day release or a one

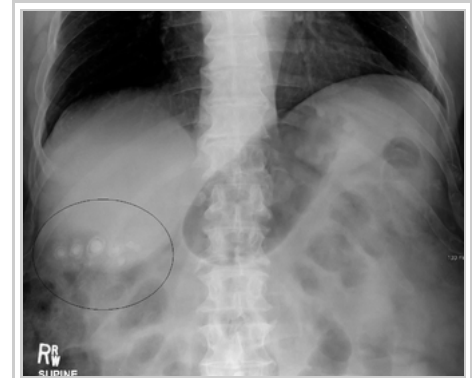


A 1.9 cm gallstone impacted in the neck of the gallbladder and leading to cholecystitis as seen on ultrasound. There is 4 mm gall bladder wall thickening.

night hospital stay, followed by a few days of home rest and pain medication.^[8] Laparoscopic cholecystectomy patients can, in general, resume normal diet and light activity a week after release, with some decreased energy level and minor residual pain continuing for a month or two. Studies have shown that this procedure is as effective as the more invasive open cholecystectomy, provided the stones are accurately located by cholangiogram prior to the procedure so that they can all be removed.

Medical

Cholesterol gallstones can sometimes be dissolved with ursodeoxycholic acid taken by mouth, but it may be necessary for the person to take this medication for years.^[34] Gallstones may recur, however, once the drug is stopped. Obstruction of the common bile duct with gallstones can sometimes be relieved by endoscopic retrograde sphincterotomy (ERS) following endoscopic retrograde cholangiopancreatography (ERCP). Gallstones can be broken up using a procedure called extracorporeal shock wave lithotripsy (often simply called "lithotripsy"),^[34] which is a method of concentrating ultrasonic shock waves onto the stones to break them into tiny pieces. They are then passed safely in the feces. However, this form of treatment is suitable only when there is a small number of gallstones.



Gallstones as seen on plain X-ray



Large gallstone as seen on CT

Other animals

Gallstones are a valuable by-product of animals butchered for meat because their use as a purported antipyretic and antidote in the folk remedies of some cultures, in particular, in China. The finest gallstones tend to be sourced from old dairy cows, which are called *niuhuang* (yellow thing of cattle) in Chinese. Much as in the manner of diamond mines, slaughterhouses carefully scrutinize workers for gallstone theft.^[35]

See also

- Porcelain gallbladder

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External links

- MedlinePlus Encyclopedia *Gallbladder removal* (https://medlineplus.gov/ency/article/100021_1.htm)
- 5-Minute Clinical Consult *Cholelithiasis* (<http://www.unboundmedicine.com/5minute/ub/view/5-Minute-Clinical-Consult/116129/all/Cholelithiasis>)
- cholelithiasis US (http://rad.usuhs.edu/medpix/cow_image.html?imageid=29001) Classic gallstone with shadow and cholecystitis
- Gallstones In-Depth Report (<http://www.nytimes.com/health/guides/disease/acute-cholecystitis-gallstones/print.html>) from nytimes.com.



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