## Gallstones



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## Gallstone definition and facts

- Gallstones are "stones" that form in the gallbladder or bile ducts. The common types of gallstones are cholesterol, black pigment, and brown pigment.
- The most common symptoms of gallstones are biliary colic and cholecystitis; however, usually gallstones cause no symptoms.
- The pain from biliary colic is a very specific type that comes on suddenly or rapidly and builds to a peak over a few minutes; however, the pain may vary in severity. Movement does not make the pain worse.
- Other signs and symptoms of biliary colic include:
  - o Nausea
  - $_{\circ}$   $\,$  Pain commonly felt in the upper abdomen  $\,$
  - Rarely, pain may be felt under the sternum, and is mistaken for a heart attack or angina (chest pain).

- Biliary colic usually has a pattern that varies from person to person.
- Gallstones do not cause intolerance to fatty foods, belching, abdominal distention, or gas.
- Complications of gallstones include cholangitis, gangrene of the gallbladder, jaundice, pancreatitis, sepsis, fistula, and ileus.
- Gallbladder sludge is associated with symptoms and complications of gallstones; however, like gallstones, sludge usually does not cause problems.
- The best single test for diagnosing gallstones is transabdominal ultrasonography. Other tests include endoscopic ultrasonography, magnetic resonance cholangiopancreatography (MRCP), cholescintigraphy (HIDA scan), endoscopic retrograde cholangio-pancreatography (ERCP), liver and pancreatic blood tests, duodenal drainage, oral cholecystogram (OCG), and intravenous cholangiogram (IVC).
- Gallstones are managed primarily with observation (no treatment) or removal of the gallbladder (cholecystectomy). Less commonly used treatments include sphincterotomy and extraction of gallstones, dissolution with oral medications, and extra-corporeal shock-wave lithotripsy (ESWL). Prevention of cholesterol gallstones also is possible with oral medications.
- Symptoms of gallstones should stop following cholecystectomy. If they do not, it is likely that gallstones were left in the ducts, there is a second problem within the bile ducts, or the symptoms are caused by another problem.
- Many dietary recommendations have been made for the prevention or treatment of gallstones and to prevent their symptoms, but none of them have been shown to be effective.
- Many home remedies have been suggested for eliminating gallstones, but none have been shown to be effective
- Continuing research is directed at uncovering the genes that are responsible for the formation of gallstones.

Gallbladder Attack Symptoms

Symptoms of a gallbladder attack include:

- pain in the upper right side or middle of the abdomen;
- the pain may be dull, sharp, or cramping;
- the pain typically starts suddenly;

• the pain is steady and may spread to the back or the area below the right shoulder blade.



Source: MedicineNet / Getty Images

## What are gallstones? How do they form?

Gallstones (often misspelled as gall stones) are stones that form in the gall (bile) within the gallbladder. (The gallbladder is a pear-shaped organ just below the liver that stores bile secreted by the liver.) Gallstones reach a size of between a sixteenth of an inch and several inches.

- Bile is a watery liquid made by the cells of the liver that is important for digesting food in the intestine, particularly fat, and eliminating toxic substances from the body.
- Liver cells secrete the bile into small canals within the liver referred to as canaliculi.

- The bile flows through the canaliculi and into larger collecting ducts within the liver referred to as intrahepatic bile ducts.
- The bile then flows through merged intrahepatic bile ducts out of the liver as extrahepatic (outside the liver) bile ducts, (first into the two hepatic bile ducts, then into the single common hepatic duct, and finally, after the common hepatic duct is joined by the cystic duct coming from the gallbladder, into the common bile duct.

From the bile duct, bile can flow from two different directions.

- The first direction is through the common bile duct and directly into the intestine where the bile mixes with food and promotes <u>digestion</u> of food. At the same time, toxic substances that are removed by the liver from the blood are eliminated into the intestine.
- The second direction is into an offshoot of the common bile duct, the cystic duct, and from there into the gallbladder.

Once in the gallbladder, bile is concentrated by the removal (absorption) of water. During a meal, the muscle that makes up the wall of the gallbladder contracts and squeezes the concentrated bile in the gallbladder back through the cystic duct into the common bile duct and then into the intestine. (Concentrated bile is much more effective for digestion than the un-concentrated bile that goes from the liver straight into the intestine.) The timing of gallbladder contraction - during a meal - allows the concentrated bile from the gallbladder to mix with food.

Gallstones usually form in the gallbladder; however, they also may form anywhere there is bile - in the intrahepatic, hepatic, common bile, and cystic ducts.

Gallstones also may move about in the bile, for example, from the gallbladder into the cystic or the common duct.

# What are the signs and symptoms of gallstones? Do they cause pain?

The majority of people with gallstones have no signs or symptoms and are unaware of their gallstones. (The gallstones are "silent.") These gallstones often are found as a result of tests (for example, <u>ultrasound</u>, or <u>X-rays</u> of the abdomen) performed while evaluating medical conditions other than gallstones. Symptoms can appear later in life, however, after many years without symptoms. Thus, over a period of five years, approximately 10% of people with silent gallstones will develop symptoms. Once symptoms develop, they are likely to continue and often will worsen.

When signs and symptoms of gallstones occur, they virtually always occur because the gallstones obstruct the bile ducts.

The most common symptom of gallstones is biliary colic. Biliary colic is a very specific type of pain, occurring as the primary or only symptom in 80% of people with gallstones who develop symptoms. Biliary colic occurs when the bile ducts (cystic, hepatic ducts or common bile duct) are suddenly blocked by a gallstone. Slowly progressing obstruction, as from a <u>tumor</u>, does not cause biliary colic. Behind the obstruction, fluid accumulates and distends the ducts and gallbladder. In the case of hepatic duct or common bile duct obstruction, this is due to continued secretion of bile by the liver. In the case of cystic duct obstruction, the wall of the gallbladder secretes fluid into the gallbladder. The distention of the ducts or gallbladder causes biliary colic.

Characteristically, biliary colic comes on suddenly or builds rapidly to a peak over a few minutes.

- It is a constant pain; it does not come and go, though it may vary in intensity while it is present. IT is not cramp-like.
- It lasts for 15 minutes to 4-5 hours. If the pain lasts more than 4-5 hours, it means that a complication usually cholecystitis has developed.
- The pain usually is severe, but movement does not make the pain worse. In fact, patients experiencing biliary colic often walk about or writhe (twist the body in different positions) in bed trying to find a comfortable position.
- Biliary colic often is accompanied by <u>nausea</u>.
- Most commonly, biliary colic is felt in the middle of the upper abdomen just below the sternum.
- The second most common location for pain is the right upper abdomen just below the margin of the ribs.
- Occasionally, the pain also may be felt in the back at the lower tip of the scapula on the right side.
- On rare occasions, the pain may be felt beneath the sternum and is mistaken for angina or a <u>heart</u> attack.
- An episode of biliary colic subsides gradually once the gallstone shifts within the duct so that it is no longer causing obstruction.

Biliary colic is a recurring symptom. Once the first episode occurs, there are likely to be other episodes. Moreover, there is a pattern of recurrence for each individual, that is, in some individuals the episodes tend to remain frequent while in others they are infrequent. The majority of people who develop biliary colic do not go on to develop cholecystitis or other complications. There is a misconception that contraction of the gallbladder is what causes the obstruction of the ducts and biliary colic. Eating, even fatty foods, does not cause biliary colic; most episodes of biliary colic occur during the night, long after the gallbladder has emptied.

Gallstones are blamed for many symptoms they do not cause. Among the symptoms gallstones do not cause are:

- dyspepsia (including abdominal bloating and discomfort after eating),
- intolerance to fatty foods,
- belching, and
- flatulence (passing gas or farting).

## What causes gallstones?

Gallstones are common; they occur in approximately 20% of women in the US, Canada and Europe, but there is a large variation in the prevalence among different ethnic groups. For example, gallstones occur 1 ½ to 2 times more commonly in Scandinavians and Mexican-Americans. Among American Indians, gallstone prevalence is more than 80%. These differences probably are accounted for by genetic (hereditary) factors. First-degree relatives (parents, siblings, and children) of individuals with gallstones are 1 ½ times more likely to have gallstones than if they do not have a first-degree relative with gallstones. Further support for a genetic predisposition comes from twin studies. Thus, among non-identical pairs of twins (who share 50% of their genes with one another), both individuals in a pair have gallstones 8% of the time. Among identical pairs of twins (who share 100% of their genes with one another), both individuals have gallstones 23% of the time.

Several conditions are associated with the formation of gallstones, and the way in which they cause gallstones can vary. (See risks of gallstones.)

## Who is at risk of gallstones?

## Risk for cholesterol gallstones

There is no relationship between cholesterol in the blood and cholesterol gallstones. Individuals with elevated blood cholesterol do not have an increased prevalence of cholesterol gallstones. A common misconception is that <u>diet</u> is responsible for the development of cholesterol gallstones, however, it isn't. The risk factors for developing cholesterol gallstones include:

- 1. Gender. Gallstones occur more commonly in women than men.
- 2. Age. Gallstone prevalence increases with age.
- 3. <u>Obesity</u>. <u>Obese</u> individuals are more likely to form gallstones than thin individuals.
- 4. <u>Pregnancy</u>. Pregnancy increases the risk for cholesterol gallstones because during pregnancy, bile contains more cholesterol, and the gallbladder does not contract normally. This change in composition of bile during pregnancy is due to the hormonal changes that occur during pregnancy. Gallstones that form during pregnancy may remain following the pregnancy or may dissolve once the composition of bile has returned to the nonpregnant state.
- 5. <u>Birth control pills</u> and <u>hormone therapy</u> Increased levels of hormones caused by either treatment mimics pregnancy.
- 6. Rapid <u>weight loss</u>. Rapid <u>weight loss</u> by whatever means, whether it is a very low calorie <u>diet</u> or obesity surgery, causes cholesterol gallstones in up to 50% of individuals. Many of the gallstones will disappear after the weight is lost, but many do not. Moreover, until they are gone, they may cause problems.
- 7. Crohn's disease. Individuals with Crohn's disease of the ileum are more likely to develop gallstones. Gallstones form because patients with Crohn's disease lack enough bile acids to solubilize the cholesterol in bile. Normally, bile acids that enter the small intestine from the liver and gallbladder are absorbed back into

the body and are secreted again by the liver into bile. In other words, the bile acids recycle. In Crohn's disease, the ileum is diseased. Bile acids are not absorbed normally, the body becomes depleted of bile acids, and less bile acids are secreted in bile. As a result, there are not enough detergent bile acids to keep cholesterol dissolved in bile, resulting in gallstone formation.

 Increased blood <u>triglycerides</u>. Gallstones occur more frequently in individuals with elevated blood <u>triglyceride levels</u>. The reason for this is unclear.

## What is the treatment for gallstones?

Most gallstones are silent, and do not need treatment.

- If silent gallstones are discovered in an individual at age 65 (or older), the chance of developing symptoms from the gallstones is only 20% (or less) assuming a life span of 75 years. In this instance, it is reasonable not to treat the individual.
- In younger individuals, no treatment also may be appropriate if the individuals have serious, life-threatening diseases, for example, serious <u>heart disease</u>, that are likely to shorten their life span.
- On the other hand, in healthy young individuals, treatment should be considered even for silent gallstones because the individuals' chances of developing symptoms from the gallstones over a lifetime will be higher. Once symptoms begin, treatment should be recommended since further symptoms are likely and more serious complications can be prevented.

## Cholecystectomy

Cholecystectomy (removal of the gallbladder surgically) is the standard treatment for gallstones in the gallbladder. Surgery may be done through a large abdominal incision, laparoscopically or robotically through small punctures in the abdominal wall.

Laparoscopic surgery results in less pain and a faster recovery. Robot-assisted laparoscopic surgery has 3D visualization. Cholecystectomy has a low rate of complications, but serious complications such as damage to the bile ducts and leakage of bile occasionally occur. There also is risk associated with the general anesthesia that is necessary for either type of surgery. Problems following removal of the gallbladder are few. Digestion of food is not affected, and no change in diet is necessary. Nevertheless, chronic <u>diarrhea</u> occurs in approximately 10% of patients.

#### Sphincterotomy and extraction of gallstones

Sometimes a gallstone may be stuck in the hepatic or common bile ducts. In such situations, there usually are gallstones in the gallbladder as well, and cholecystectomy is necessary. It may be possible to remove the gallstone stuck in the duct at the time of surgery, but this may not always be possible. An alternative means for removing gallstones in the duct before or after cholecystectomy is with sphincterotomy followed by extraction of the gallstone.

Sphincterotomy involves cutting the muscle of the common bile duct (sphincter of Oddi) at the junction of the common bile duct and the duodenum in order to allow easier access to the common bile duct. The cutting is done with an electrosurgical instrument passed through the same type of endoscope that is used for ERCP. After the sphincter is cut, instruments may be passed through the endoscope and into the hepatic and common bile ducts to grab and pull out the gallstone or to crush the gallstone. It also is possible to pass a lithotripsy instrument that uses high frequency sound waves to break up the gallstone. Complications of sphincterotomy and extraction of gallstones include risks associated with general anesthesia, perforation of the bile ducts or duodenum, bleeding, and pancreatitis.

## Oral dissolution therapy

It is possible to dissolve some cholesterol gallstones with medication taken orally. The medication is a naturally occurring bile acid called ursodeoxycholic acid or <u>ursodiol</u> (Actigall, Urso). Bile acids are one of the detergents that the liver secretes into bile to dissolve cholesterol. Although one might expect therapy with ursodiol to work by increasing the amount of bile acids in bile and thereby cause the cholesterol in gallstones to dissolve, the mechanism of ursodiol's action actually is different. Ursodiol reduces the amount of cholesterol secreted in bile. The bile then has less cholesterol and becomes capable of dissolving the cholesterol in the gallstones.

There are important limitations to the use of ursodiol:

- It is only effective for cholesterol gallstones and not pigment gallstones.
- It works only for small gallstones, less than 1-1.5 cm in diameter.
- It takes one to two years for the gallstones to dissolve, and many of the gallstones reform following cessation of treatment.

Due to these limitations, ursodiol generally is used only in individuals with smaller gallstones that are likely to have a very <u>high cholesterol</u> content and who are at high risk for surgery because of ill health. It also is reasonable to use ursodiol in individuals whose gallstones were perhaps formed because of a transient event, for example, rapid loss of weight, since the gallstones would not be expected to recur following successful dissolution. Another use of ursodiol is to prevent the formation of gallstones in patients who will <u>lose weight</u> rapidly.

## Extracorporeal shock-wave lithotripsy

Extracorporeal shock-wave lithotripsy (ESWL) is an infrequently used method for treating gallstones, particularly those lodged in bile ducts. ESWL generators produce shock waves outside of the body that are then focused on the gallstone. The shock waves shatter the gallstone, and the resulting pieces of the gallstone either drain into the intestine on their own or are extracted endoscopically. Shock waves also can be used to break up gallstones via special catheters passed through an endoscope at the time of ERCP.

## What are the complications of gallstones?

Biliary colic is the most common symptom of gallstones, but, fortunately, it is usually a self-limited symptom. There are, however, more serious complications of gallstones.

## Cholecystitis

Cholecystitis means inflammation of the gallbladder. Like biliary colic, it too is caused by sudden obstruction of the ducts, usually the cystic duct by a gallstone. In fact, cholecystitis may begin with an episode of biliary colic. Obstruction of the cystic duct causes the wall of the gallbladder to begin secreting fluid, but for unclear reasons, inflammation sets in. At first the inflammation is sterile, that is, there is no infection with bacteria; however, over time the bile and gallbladder become infected with bacteria that travel through the bile ducts from the intestine.

With cholecystitis, there is constant pain in the right upper abdomen. Inflammation extends through the wall of the gallbladder, and the right upper abdomen becomes particularly tender when it is pressed or even tapped. Unlike with biliary colic, however, it is painful to move around. Individuals with cholecystitis usually lie still. There is <u>fever</u>, and the white blood cell count is elevated, both signs of inflammation. Cholecystitis usually is treated with antibiotics, and most episodes will resolve over several days. Even

without antibiotics, cholecystitis often resolves. As with biliary colic, movement of the gallstone out of the cystic duct and back into the gallbladder relieves the obstruction and allows the inflammation to resolve.

## Cholangitis

Cholangitis is a condition in which bile in the common, hepatic, and intrahepatic ducts becomes infected. Like cholecystitis, the infection spreads through the ducts from the intestine after the ducts become obstructed by a gallstone. Patients with cholangitis are very sick with high <u>fever</u> and elevated white blood cell counts. Cholangitis may result in an <u>abscess</u> within the liver or sepsis. (See discussion of sepsis that follows.)

#### Gangrene

Gangrene of the gallbladder is a condition in which the inflammation of cholecystitis <u>cuts</u> off the supply of blood to the gallbladder. Without blood, the tissues forming the wall of the gallbladder die, and this makes the wall very weak. The <u>weakness</u> combined with infection often leads to rupture of the gallbladder. The infection then may spread throughout the abdomen, though often the rupture is confined to a small area around the gallbladder (a confined perforation).

## Jaundice

<u>Jaundice</u> is a condition in which bilirubin accumulates in the body. Bilirubin is brownishblack in color but is yellow when it is not too concentrated. A build-up of bilirubin in the body turns the skin and whites of the eye (sclera) yellow. Jaundice occurs when there is prolonged obstruction of the bile ducts. The obstruction may be due to gallstones, but it also may be due to many other causes, for example, tumors of the bile ducts or surrounding tissues. (Other causes of jaundice are a rapid destruction of red blood cells that overwhelms the ability of the liver to remove bilirubin from the blood or a damaged liver that cannot remove bilirubin from the blood normally.) Jaundice, by itself, generally does not cause problems.

#### Pancreatitis

Pancreatitis means inflammation of the pancreas. The two most common causes of pancreatitis are <u>alcoholism</u> and gallstones. The pancreas surrounds the common bile duct as it enters the intestine. The pancreatic duct that drains the digestive juices from the pancreas joins the common bile duct just before it empties into the intestine. If a gallstone obstructs the common bile duct just after the pancreatic duct joins it, the flow of pancreatic juice from the pancreas is blocked. This results in inflammation within the pancreas. Pancreatitis due to gallstones usually is mild, but it may cause serious illness and even death. Fortunately, severe pancreatitis due to gallstones is rare.

#### Sepsis

Sepsis is a condition in which bacteria from any source within the body, including the gallbladder or bile ducts, enter into the blood stream and spread throughout the body. Although the bacteria usually remain within the blood, they also may spread to distant tissues and lead to the formation of abscesses (localized areas of infection with formation of pus). Sepsis is a feared complication of any infection. The signs of sepsis include high fever, high white blood cell count, and, less frequently, rigors (shaking chills) or a drop in <u>blood pressure</u>.

## Fistula

A fistula is an abnormal tract through which fluid can flow between two hollow organs or between an abscess and a hollow organ or skin. Gallstones cause fistulas when the hard gallstone erodes through the soft wall of the gallbladder or bile ducts. Most commonly, the gallstone erodes into the small intestine, stomach, or common bile duct. This can leave a tract that allows bile to flow from the gallbladder to the small intestine, stomach, or the common bile duct. If the fistula enters the distal part of the small intestine, the concentrated bile can lead to problems such as <u>diarrhea</u>. Rarely, the gallstone erodes into the abdominal <u>cavity</u>. The bile then leaks into the abdominal <u>cavity</u> and causes inflammation of the lining of the abdomen (peritoneum), a condition called bile <u>peritonitis</u>.

#### Ileus

Ileus is a condition in which there is an obstruction to the flow of food, gas, and liquid within the intestine. It may be due to a mechanical obstruction, for example, a tumor within the intestine, or a functional obstruction, for example, inflammation of the intestine or surrounding tissues that prevents the muscles of the intestine from working normally and propelling intestinal contents. If a large gallstone erodes through the wall of the gallbladder and into the stomach or small intestine, it will be propelled through the small intestine. The narrowest part of the small intestine is the ileo-cecal valve, which is located at the site where the small intestine joins the colon. If the gallstone is too large to pass through the valve, it can obstruct the small intestine and cause an ileus. Gallstones also may cause ileus if there are other abnormal narrowings in the intestine such as a tumor or scarring.

#### Cancer

<u>Cancer of the gallbladder</u> usually is associated with gallstones, but it is not clear which comes first, that is, whether the gallstones precede the <u>cancer</u> and, therefore, could potentially be the cause of the <u>cancer</u> or the gallstones form because <u>cancer</u> is present. Cancer of the gallbladder arises in less than 1% of individuals with gallstones. Therefore, concern about future development of cancer is by itself not a good reason for removing the gallbladder when gallstones are present.