

Gallstones and Gallbladder Disease

What Are Gallstones And Gallbladder Disease?

Gallstones are formed from bile, a fluid composed mostly of water, bile salts, lecithin, and cholesterol. Bile is first produced by the liver and then secreted through tiny channels within the liver into a duct. From there, bile passes through a larger tube called the common duct, which leads to the small intestine. Then, except for a small amount that drains directly into the small intestine, bile flows into the gall bladder through the cystic duct. The gallbladder is a four-inch sac with a muscular wall that is located under the liver. Here, most of the fluid (about two to five cups a day) is removed, leaving a few tablespoons of concentrated bile. The gallbladder serves as a reservoir until bile is needed in the small intestine for digestion of fat. When food enters the small intestine, a hormone called cholecystokinin is released, signaling the gallbladder to contract. The force of the contraction propels the bile back through the common bile duct and then into the small intestine, where it emulsifies fatty molecules so that fat and the fat-absorbable vitamins A, D, E, and K can enter the blood stream through the intestinal lining.

About three-quarters of the gallstones found in the US population are formed from cholesterol. Cholesterol makes up only five percent of bile; it is not very soluble, however, so in order to remain suspended in fluid, it must be properly balanced with bile salts. If the liver secretes too much cholesterol into the bile, if the bile becomes stagnant and forms sludge because of a defect in the mechanisms that cause the gallbladder to empty, or if other factors are present, supersaturation can occur. Cholesterol may then precipitate out of the bile solution to form gallstones, a condition known as cholelithiasis. The process is very slow and most often painless. Gallstones can range from a few millimeters to several centimeters in diameter.

About 15% of gallstones are known as pigment stones. They are composed of calcium bilirubinate, or calcified bilirubin, the substance formed by the breakdown of hemoglobin in the blood. Pigment stones can be black or brown and often form in the gallbladders of people with hemolytic anemia or cirrhosis.



Patients may also have a mixture of pigment and cholesterol gallstones. At any point, stones may obstruct the cystic duct, which leads from the gallbladder to the common bile duct, and cause pain (biliary colic), infection and inflammation (cholecystitis), or all of these. About 15% of people with stones in the gallbladder also have stones in the common bile duct (choledocholithiasis), which sometimes pass into

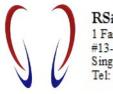
the small intestine but also may lodge in the duct and cause distention, infection, or pancreatitis.

What Are The Symptoms Of Gallstones And Gallbladder Disease?

About 80% of people with gallstones never experience any symptoms. Most others remain asymptomatic (without symptoms) for at least two years after stone formation begins. If symptoms do occur, the chance of developing pain is about 2% per year for the first ten years after stone formation, after which the chance for developing symptoms decreases. On average, symptoms take about eight years to develop. The reason for the decline in incidence after ten years is not known, although some physicians suggest that younger, smaller stones may be more likely to cause symptoms than larger ones.

Biliary Pain

The mildest and most common symptom of gallbladder disease is intermittent pain called biliary colic, which occurs either in the mid- or the upper-right portion of the upper abdomen. Large or fatty meals can precipitate the pain, but it usually occurs several hours after eating, often waking the patient during the night. Biliary colic produces a steady pain, which can be quite severe. Changes in position, over-the-counter pain relievers, and passage of gas do not relieve the symptoms. The patient may have a fever and experience nausea or vomiting. Biliary colic typically disappears after one to five hours. The chance of a recurring attack within a year is less than 50%. In one study, 30% of people who had had one or two attacks experienced no further biliary pain over the next ten years.



Symptoms of Acute Cholecystitis

Acute gallbladder inflammation (acute cholecystitis) causes symptoms that are similar to those of biliary colic but are more severe and serious. The pain begins abruptly. Severe pain and tenderness in the upper right abdomen are the most common complaints. The discomfort is intense and steady and can last for up to days. Infection is usually present, and about a third of patients have fever. Nausea and vomiting are more likely to occur with acute cholecystitis than with biliary colic. Patients with acute cholecystitis frequently complain of pain when drawing a breath. The pain can radiate from the abdomen to the back. Acute cholecystitis is usually caused by gallstones, but, in some cases, can occur without stones. Anyone who experiences an attack of acute cholecystitis should seek medical attention; it can progress to gangrene or perforation of the gallbladder if left untreated.

Symptoms of Chronic Cholecystitis

Chronic gallbladder disease (chronic cholecystitis) occurs because of the prolonged presence of gallstones and low-grade inflammation. Scarring causes the gallbladder to become stiff and thick. Symptoms of this condition tend to be vague. Complaints of gas, nausea, and abdominal discomfort after meals are common, but they occur just as often in people without gallbladder disease. Such symptoms, in fact, often remain even after treatments for gallbladder disease. Symptoms of Common Bile Duct Stones (Choledocholithiasis) and Cholangitis Stones lodged in the common bile duct (choledocholithiasis) can block the flow of bile and cause jaundice. When it causes inflammation in the bile duct the condition is known as cholangitis. It causes fever, chills, nausea and vomiting, and severe pain in the upper-right quadrant of the abdomen. Heartbeat may become rapid and the patient may experience a drop in blood pressure.

How Serious Are Gallstones And Gallbladder Disease?

Most gallstones provoke no symptoms at all. One study reported that the risk of developing symptoms was 10% at five years, 15% at ten years, and only 18% at fifteen years, with no deaths reported. Asymptomatic gallstones seldom lead to problems. Death from gallstones is very rare,



accounting for only 0.2% of annual deaths in the United States. Serious effects from gallstones are usually from stones in the bile duct or surgical complications.

Gallbladder Cancer

Gallstones are present in about 80% of people with gallbladder cancer, which is responsible for about one-third to one-half of gallstone-related deaths. Gallbladder cancer is very rare, however, even among people with gallstones. Less than 1% of people with gallstones who do not have their gallbladders removed develop this cancer. People who have symptomatic gallstones, however, have four times the risk as those without symptoms. Whether gallstones themselves cause the cancer, or whether some factor in bile is responsible for both conditions is unknown. One study demonstrated that gallbladder removal reduced the likelihood of bile duct cancer, suggesting that gallstones themselves were responsible.

Complications in the Gallbladder

Acute cholecystitis can cause severe inflammation and even necrosis (tissue death) in the gallbladder (the cause of gangrene). Perforation and gangrene or abscess formation may occur when severe symptoms persist for many days. Abscess or gangrene carries a 25% mortality rate. In between 1% and 2% of persons with acute cholecystitis, the gallbladder is perforated, which has up to a 30% mortality rate . The risk for perforation increases with a condition called emphysematous cholecystitis, in which gas forms in the gallbladder. This condition is most common in people with diabetes.

Empyema of the gallbladder, or pus in the gallbladder, occurs in 2% to 3% of patients with acute cholecystitis. Abdominal pain is usually severe and is typically present for more than seven days. The physical exam is not distinctive. Mortality approaches 25% for those with empyema; death often occurs as a result of septicemia (systemic infection). Both perforation and empyema require prompt surgery. The complications can be avoided, however, by seeing a physician as soon as gallbladder symptoms occur.



Complications in the Common Bile Duct

Gallstones occasionally lodge in the common bile duct instead of the gallbladder, a condition called choledocholithiasis. When this occurs, stones can block the flow of bile out of the liver, causing jaundice.

Cholangitis (infection of the bile ducts) is a common and serious complication of choledocholithiasis. If antibiotics are administered immediately, the infection clears up in 75% of patients. When cholangitis does not improve the condition can be life threatening, and either surgery or a procedure known as endoscopic sphincterotomy is required to open and drain the ducts. Elderly patients who develop acute cholangitis may require special care. If they develop symptoms of widespread infection (fever, rapid heart beat, fast breathing, mental confusion) or do not respond to standard treatment, immediate drainage of the biliary tract is indicated.

Pancreatitis

Gallstones are responsible for about 45% of all cases of acute pancreatitis (acute inflammation of the pancreas), a condition that can be life threatening. Pancreatitis can result from choledocholithiasis, because the pancreatic duct, which carries digestive enzymes, joins the common bile duct right after it enters the intestine and so may be blocked by common duct stones. If a gallstone passes through or lodges in the lower common bile duct, pancreatitis can result. It is sometimes difficult to differentiate between pancreatitis and acute cholecystitis, but a correct diagnosis is critical since treatment is very different. Blood tests showing high levels of pancreatic enzymes (amylase and lipase) can usually indicate the diagnosis of pancreatitis in patients who come to the emergency room with severe abdominal pain. Imaging techniques are useful in confirming a diagnosis. Ultrasound is used often. A computed tomography (CT) scan, along with a number of laboratory tests, can determine the severity of the condition. The treatment is intravenous fluids and painkillers; also, the patient is not allowed to eat or drink anything. Mild cases usually subside within a week, and cholecystectomy (removal of the gallbladder) is often then performed. About 25% of pancreatitis cases are severe, and this rate is



much higher, about 66%, in people who are obese. Urgent endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and drainage of the ducts to remove any stones may be very beneficial in these cases. [See How Is Gallstone Disease Diagnosed? Below.]

Who Gets Gallstones And Gallbladder Disease?

Age and Gender

Between 10% and 20% of all adults over 40 have gallstones; only 1% to 3% of the population, however, complain of symptoms during the course of a year. Gallstones occur in nearly 25% of women in the US by age 60 and up to 50% by age 75. About 20% of men have gallstones by the time they reach 75 years of age. Because most cases are asymptomatic, however, the rates may be underestimated in elderly men. One study of nursing home residents reported that 66% of the women and 51% of the men had gallstones. Men who have their gallbladders removed, moreover, are more likely to have severe disease and more operative complications than women. Gallstone disease is relatively rare in children. Those at risk are children with a spinal injury, a history of abdominal surgery, sickle-cell anemia, impaired immune systems, or children who receive nutrition intravenously. Gallstones in children are more likely to be pigmented. Girls do not seem to be more at risk than boys.

Women are probably at increased risk because estrogen stimulates the liver to remove more cholesterol from blood and divert it into the bile. Pregnant women with stones are more likely to have symptoms. Increased risk of gallstone formation has been observed in women who take oral contraceptives and in those taking estrogen replacement therapy after menopause. There appears to be a very low or no risk with low-dose oral contraceptive. One study suggests that oral and patch forms of estrogen replacement therapy posed equal risks for cholesterol supersaturation and therefore gallstone formation. Oral estrogen, however, has a greater effect on the liver itself and raises triglycerides, a fatty acid that increases the risk for cholesterol stones. Postmenopausal women at high risk for both gallstones and disorders related to estrogen loss may want to check with their physicians for alternatives to hormone replacement therapy. [See Estrogen Therapy.]



Ethnicity

Hispanics and Northern Europeans have a higher risk for gallstones than people of Asian and African descent. (People of Asian descent who develop gallstones are most likely to have the pigment type.) Native Americans, particularly Pima Indians, are especially prone to developing gallstones; Pima women have an 80% chance of developing gallstones during their lives.

Obesity and Weight Changes

Researchers report that gallstones are more likely to develop in men and women who are overweight or obese and who consume a diet high in saturated fats and refined sugars. Experiments using rats showed that obesity resulted in lower levels of bile salts relative to cholesterol in the bile, causing a higher risk for cholesterol supersaturation and the formation of stones. The risk for gallstones is also increased, however, with rapid weight loss. One study reported new gallstones in 28% of obese subjects consuming ultra-low-calorie liquid diets. Weight cycling (dieting and then putting back weight) also increases the risk for gallstones. One 16-year study found that the risk for gallstone surgery was 68% higher for women who lost and then regained more than 20 lb at least once than in women whose weight remained stable.

Cholesterol and Cholesterol-Lowering Drugs

Gallstone formation does not correlate with overall cholesterol levels, but persons with low HDL cholesterol (the so-called good cholesterol) levels or high triglyceride levels are at increased risk. The cholesterol-lowering drugs gemfibrozil (Lopid) and clofibrate (Atromid-S) reduce blood cholesterol levels by increasing the amount secreted into the bile, thus increasing the risk for gallstones. These drugs, in any case, have potentially serious side effects and are not used for lowering cholesterol if other drugs can be tolerated, including niacin and the statins, which do not contribute to the formation of gallstones. [see Cholesterol.]

Other Risk Factors

Conditions that decrease the flow of bile and therefore increase the risk of gallstone formation include fasting, pregnancy, and intravenous feeding. Cirrhosis poses a major risk for gallstones,



particularly pigment gallstones. Gallbladder disease may progress more rapidly in patients with diabetes, who tend to suffer worse infections. In addition to the cholesterol-lowering drugs mentioned above, the diuretic thiazide may slightly increase the risk for gallstones. Chronic hemolytic anemia, including sickle cell anemia, increases the risk for pigment gallstones.

How Can Gallstones And Gallbladder Disease Be Prevented?

Dietary Considerations

Maintaining a normal weight and avoiding fasts are the keys to reducing the risk of gallstones. For people who are overweight who attempt ultra-low-calorie diets, one study has shown that gallstones may be prevented by taking ursodiol or ursodeoxycholic acid (Actigall), which is ordinarily used to dissolve existing gallstones. [See Non-Surgical Therapy for Gallstones under What Are the Treatments for Gallstones? below.] It should be noted that this medication is very expensive.

A less costly and easier solution for some people has been reported in studies that have found an association between a lower risk for gallstones in people who consumed foods rich in monounsaturated fats (found in olive and canola oils) and fiber.

Alcohol in small amounts (one ounce per day) has been found to reduce the risk in women by 20%, although it should be stressed that alcohol is easily abused, and higher amounts may increase the risk of many diseases, including breast cancer in women . Some studies indicate that vitamin C may be protective. In one study, the men who drank two or more cups of regular coffee daily (instant, filtered, espresso) had a 40% lower risk of developing the disease over ten years than did the men who did not drink coffee regularly. Those who drank more than four cups had the lowest risk. The benefits and risks of caffeine consumption vary depending on the individual's health, so high consumption of coffee to prevent gallstones is not recommended as a general preventive measure.,



Exercise

Exercising regularly and vigorously may reduce the risk of gallstones and gall bladder disease. One study indicated that men who performed endurance-type exercise (such as jogging and running, racquet sports, and brisk walking) for thirty minutes five times per week reduced their risk for gallbladder disease by up to 34%. The benefit depended more on the intensity of activity than the type of exercise. Some researchers guess that in addition to controlling weight, exercise helps normalize blood sugar levels and insulin levels, which, if abnormal, may contribute to gallstones.

Nonsteroidal Anti-Inflammatory Drugs

Some data had indicated that taking nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin or ibuprofen, protects against the development of gallstones. A recent study of more than 400 chronic arthritis sufferers who took NSAIDs regularly, however, reported no significant protection.

How Are Gallstones And Gallbladder Disease Diagnosed?

The diagnostic challenge posed by gallstones is to be sure that abdominal pain is caused by stones and not by some other condition. Ultrasound or other imaging techniques easily find gallstones. Nevertheless, because gallstones are common and most cause no symptoms, simply finding stones does not necessarily explain a patient's pain, which may be caused by numerous other conditions.

Ruling out Other Disorders

In patients with abdominal pain, causes other than gallstones are usually responsible if the pain lasts less than 15 minutes, frequently comes and goes, or is not severe enough to limit activities. Irritable bowel syndrome (IBS) has some of the same symptoms as gallbladder disease, including difficulty digesting fatty foods. In IBS, however, pain usually occurs in the lower abdomen. Acute appendicitis, inflammatory bowel disease (Crohn's disease or ulcerative colitis), pneumonia, stomach ulcers, hiatal hernia, pancreatitis, hepatitis, kidney stones, urinary tract



infections, diverticulosis or diverticulitis, pregnancy complications, and even a heart attack may mimic a gallbladder attack.

Physical examination

A physical exam often reveals tenderness in the right upper area of the abdomen in acute cholecystitis and sometimes in biliary colic. There is usually no tenderness in chronic cholecystitis.

Laboratory tests

Laboratory tests are usually normal in people with simple biliary pain or chronic cholecystitis. In acute cholecystitis, and especially choledocholithiasis (stones in the bile duct), however, blood tests of the liver show elevations of the enzyme alkaline phosphatase and bilirubin. Bilirubin is the orange-yellow pigment found in bile; high levels cause jaundice, which gives the skin a yellowish tone. Physicians will also check blood levels of liver enzymes known as aspartate (AST) and alanine (ALT) aminotransferases, which are elevated when common bile duct stones are present. A high white blood cell count (leukocytosis) is a common finding but does not occur in a significant minority of patients with cholecystitis.

Imaging Techniques for Gallstones and Cholecystitis

Ultrasound. Ultrasound, the diagnostic method most frequently used to detect gallstones, is a simple, rapid, and noninvasive imaging technique. Ultrasound detects gallstones as small as two millimeters in diameter with an accuracy of 90% to 95%. The patient must not eat for six or more hours before the test, which takes only about 15 minutes. During the same procedure, the physician can check the liver, bile ducts, and pancreas and quickly scan the gallbladder wall for thickening (characteristic of cholecystitis).

Cholescintigraphy. Cholescintigraphy, another nuclear imaging technique, is noninvasive and useful if ultrasound does not reveal cholecystitis but the condition is still suspected because of biliary pain. In this procedure, a tiny amount of a radioactive tracer is injected intravenously.



This material is excreted into bile. A camera detects the tracer as the liver passes it into the gallbladder. In acute cholecystitis, the dye enters the common bile duct instead of the gallbladder, indicating that a gallstone is obstructing the cystic duct. Cholescintigraphy can take one to two hours and even longer. The scan detects total gallbladder obstruction but cannot identify individual gallstones. It cannot detect chronic cholecystitis. Occasionally, the scan gives false positive results, particularly in alcoholic patients with liver disease or patients who are fasting or receiving all nutrients intravenously.

Oral Cholecystography.

Cholecystography is an abdominal x-ray that can detect stones that have a ring of calcium around them, which is opaque on an x-ray. Unfortunately, only 10% to 30% of stones have these so-called radiopaque qualities. In this procedure, a tablet containing an iodine compound that appears on an x-ray is taken one day before the test. It is absorbed by the intestine, excreted by the liver, and concentrated in the gallbladder, where it will be seen on an x-ray taken the following day. Radiopaque stones are outlined by the dye. A diseased gallbladder, however, will not usually be seen because its outlet is blocked and so will not absorb the dye. Rarely, the gallbladder walls are calcified as a result of chronic inflammation, and the gallbladder appears on a plain abdominal x-ray as a so-called porcelain gallbladder.

Diagnostics Tests for Common Bile Duct Stones (Choledocholithiasis)

If there is evidence for common bile duct stones, such as dark urine, jaundice, pancreatitis, or elevated liver function tests, then more extensive tests may be used.

Invasive Diagnostic Procedures. Accurate diagnosis must often rely on *endoscopic retrograde cholangiopancreatography (ERCP)*. This procedure involves the use of an endoscope (a flexible telescope containing a miniature camera and other instruments), which is passed through the mouth, the stomach, and into the upper small intestine, where the bile duct emerges. This is a difficult procedure and patients should be sure their physician is experienced in performing it. This procedure has the added advantage of being useful for stone removal in the common duct.

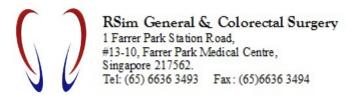


[For more details of this procedures, see Treatment for Common Duct Stones (Choledocholithiasis) under What Are the Treatments for Gallstones? below.]

An invasive x-ray technique, *percutaneous transhepatic cholangiography*, uses a long, thin needle inserted through the skin and into the liver to inject a contrast dye into the bile duct. Cholangiography is also sometimes used during surgery to guide the surgeon in removing stones from the bile duct.

Both of these techniques are expensive, invasive, and have rare but serious risks; they should be used only when disease is considered likely. These invasive procedures are not necessary if preoperative ultrasound and blood tests are normal and there is no history of jaundice or pancreatitis. [See Treatment for Common Bile Duct Stones (Choledocholithiasis) under What Are the Treatments for Gallstones? below.]

Imaging Techniques for Choledocholithiasis. Although ultrasound is useful for the diagnosis of gallstones, it is not as sensitive for identifying common bile ducts stone. A new procedure called *endoscopic ultrasound (EUS)*, however, may prove to be accurate for this purpose and even eventually serve as an alternative to ERCP. One study also indicated that in patients under 70 years old ultrasound images along with blood tests for gamma-glutamyl transferase (a liver enzyme) may be very useful for predicting the presence of common bile duct stones. Studies are reporting that magnetic resonance imaging (MRI) techniques are almost as accurate as invasive procedures in identifying normal and abnormal ducts. The procedure, however, may not detect very small stones. A technique known as helical, or spiral, CT scanning is showing promise. With this process, the patient lies on a table that moves while the x-ray tube is rotating, shortening the time that a standard CT scan takes and obtaining clearer images. None of these techniques allows removal of the stones, as ERCP does. They may be useful, however, for ruling out cases in which the probability of duct stones is low and so avoid the invasive procedure.



What Are The Treatments For Gallstones And Gallbladder Disease?

Acute pain for gallstones and gallbladder disease is usually treated in the hospital, where diagnostic procedures are performed to rule out other conditions and complications. On an ongoing basis, there are three approaches to gallstone treatment: expectant management, nonsurgical removal of the stones, or surgical removal of the gallbladder.

Expectant Management

Guidelines from the American College of Physicians state that when a person has no symptoms, the risks of both surgical and nonsurgical treatment for gallstones outweigh the benefits. Experts suggest a wait-and-see approach for such patients, which they have termed expectant management. Exceptions to this policy are people at risk for gallbladder cancer, subgroups at high risk for complications of gallstones (including Pima Native Americans), those with stones larger than three centimeters, and people who have polyps on the gallbladder. One study reported that very small gallstones increase the risk for acute pancreatitis, a serious condition; some experts therefore believe that gallstones smaller than five millimeters warrant immediate surgery.

There are some minor risks with expectant management. Gallstones almost never spontaneously disappear, except sometimes when they are formed under special circumstances, such as pregnancy or sudden weight loss. At some point, then, the stones may cause pain, complications, or both, and require treatment. For 30-year olds with asymptomatic gallstones, the probability of eventually needing an operation is about 30%, for 50-year olds it is 20%, and for 70-year olds it is 15%. In addition, the slight risk of developing gallbladder cancer might encourage younger people who are asymptomatic to have their gallbladders removed.

In-Hospital Treatment for Biliary Pain

Patients who come to the hospital for acute biliary pain are given fluids and pain killers. Drugs known as antispasmodics and anticholinergics, usually dicyclomine (Bentyl), is the first choice for relief of gallbladder pain because they reduce muscles spasm. Meperidine (Demerol) is often



used if dicyclomine is not effective. (Some physicians believe morphine should be avoided for gallbladder disease.) Drugs to stop vomiting may also be administered. Patients with evidence of infection, including fever or an elevated white blood cell count, will be put on antibiotics. If a patient has been admitted to the hospital with acute cholecystitis, surgery is often warranted but is usually performed at least 48 hours after admission when inflammation has subsided. Some patients can wait longer. If biliary duct stones are suspected, the patient may require ERCP for diagnosis and treatment [see below]. If the patient has no fever or underlying serious medical problems and shows no signs of severe pain or complications and if laboratory tests are normal, then he or she may be discharged with oral antibiotics and pain relievers.

Surgical Removal of the Gallbladder (Cholecystectomy)

General Considerations for Gallbladder Removal. Every year, about 500,000 people have their gallbladders removed. The gallbladder is not an essential organ, and even today, only surgical removal of the gallbladder (cholecystectomy) guarantees that the patient will not suffer a recurrence of gallstones. Candidates for surgery are patients who have experienced one very severe or several less severe gallstone attacks, or who have cholecystitis or pancreatitis. Cholecystectomy may be performed within several days of hospitalization for an acute attack. Some patients can be safely discharged after an attack of acute cholecystitis and undergo elective surgery several months later. This is one of the most common surgical procedures performed on women and can even be performed on pregnant women with low risk to the baby and mother. The primary advantages of surgical removal of the gallbladder over nonsurgical treatment are not only the elimination of gallstones, but also the prevention of gallbladder cancer. As with any major operation, of course, there is complication. When cholecystectomy is performed as elective surgery, the mortality rates are very low. (Even in the elderly, mortality rates are only between 0.7% to 2%). Emergency cholecystectomy carries a much higher mortality rate (as high 19% in ill elderly patients).

Although removal of the gallbladder has not been known to cause any long-term adverse effects aside from occasional diarrhea, some researchers have been concerned about its effects on the



body's cholesterol levels. One study found that within three days of the operation, levels of total cholesterol and LDL returned to their preoperative levels. After three years, however, some types of cholesterol not ordinarily associated with coronary artery disease had risen significantly. These results did not necessarily indicate any increased risk for coronary artery disease, but they did show that the metabolism of cholesterol by the liver had been altered. People who have had their gallbladders removed should have their cholesterol levels checked periodically, as should every adult. Short-term treatment with cholesterol-lowering drugs containing HMG-CoA reductase inhibitors, commonly known as statins, such as pravastatin (Pravachol), appears to lower cholesterol levels in surgical patients.

Laparoscopic Cholecystectomy

Until the early 1990s, open cholecystectomy (the removal of the gallbladder through an abdominal incision) was the standard treatment. Now, laparoscopic cholecystectomy (commonly called lap choly), which uses small incisions, is the most commonly used surgical approach. First performed in 1987, laparoscopy is now used in nearly 90% of all cholecystectomies in the United States. Laparoscopy is usually performed on patients who have electively chosen to have their gallbladders removed. It is even proving to be safe for pregnant women who require cholecystectomy. Studies are indicating that it may be a good option as emergency surgery for elderly patients who at risk for complications from anesthesia because of other underlying medical conditions. It is not usually the procedure of choice for people with acute cholecystitis in whom gangrene has developed.

With laparoscopy, removal of the gallbladder is guided by a laparoscope, which is a bit like a periscope. General anesthesia is required. The surgeon first creates space in the abdomen by filling it with carbon dioxide, which flows out of a needle inserted through the navel. Four small incisions in the abdomen enable the surgeon to insert instruments and a laparoscope, a thin telescope that can relay an image of the area to a video monitor. The surgeon separates the gallbladder from the liver and other areas and removes it through one of the incisions. Laparoscopic cholecystectomy requires general anesthesia, but patients can still leave the



hospital earlier than with open surgery, the incision is small, and there is less post-operative pain and disability than with the open procedure. The procedure is now commonly done as outpatient surgery.

The procedure is very difficult and long, however, and patients should never be shy about inquiring into the number of laparoscopies the surgeon has performed; it should not be fewer than 30. In about 5% to 10% of laparoscopies, conversion to open cholecystectomy is required during the procedure. Patients at higher risk for conversion to open surgery are those with thick-walled and contracted gall bladders, those whose gallbladder can be felt as a palpable lump before the operation, and patients who have undergone multiple abdominal operations. The most serious complication of laparoscopy is injury to the bile duct, which can cause serious liver damage. In about 6% of procedures, the surgeon misses gallstones or they are spilled and remain in the abdominal cavity. In a small percentage, they may cause obstruction or abscesses that require open surgery. As with all surgeries, there is a risk for infection, but it is very low. Preventive antibiotics are not necessary and confer no benefit. There may be an increased rise for gastroesophageal reflux disorder (heartburn and other symptoms) after laparoscopy.

Because of the appeal of laparoscopy, gallstone operations have increased by as much 40% in some parts of the country. Of concern is a significant increase in its use by patients who have inflammation in the gallbladder but no gallstones and even in those who have no symptoms. Experts report that although laparoscopy has reduced hospital stays, overall medical costs have increased because more operations are being performed. Some experts argue that open cholecystectomy may even be better than laparoscopy as initial surgery in certain situations. They argue that even as experience increases, studies are reporting a higher complication rate, particularly in injuries to the bile duct, for laparoscopy than with open cholecystectomy.

Open Cholecystectomy

Before laparoscopy, the standard surgical treatment for gallstones was open cholecystectomy (surgical removal of the gallbladder), which requires a wide incision and leaves an unsightly



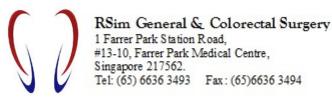
surgical scar. The patient usually needs to stay in the hospital for five to seven days and may not return to work for a month. Some experts believe, however, that it has a number of advantages compared to laparoscopy. It is faster to perform, less expensive, and may have fewer complications. The riskiness of this procedure increases with other factors, such as the age of the patient or if common bile duct exploration for duct stones is necessary at the same time as the cholecystectomy. As in laparoscopic cholecystectomy, bile duct injury is a possible complication, which requires additional and difficult operations. This occurs, however, in only 0.1% to 0.2% of procedures.

Minilaparotomy

Minilaparotomy is another variant of open cholecystectomy and uses a much smaller incision. This results in a faster recovery time; patients can return to work in ten days to three weeks. Wider experience will be required, however, before it is known with certainty whether minilaparotomy with its greatly diminished ability to see abdominal structures is as safe as standard approaches. In some studies comparing minilaparotomy with laparoscopy, the complication rate was similar for both procedures and minilaparotomy was less expensive, although patients usually have less postoperative pain with laparoscopy. Minilaparotomy has some drawbacks; it is not appropriate for obese patients, and it does not give the surgeon a view of the abdominal cavity (which laparoscopy does) to detect other problems.

Minimally Invasive Open Cholecystectomy.

This variant of open cholecystectomy may offer a safe, less costly, and aesthetically comparable alternative to laparoscopic cholecystectomy. In this procedure, as with minilaparotomy, the incision is much smaller than with open cholecystectomy, but the technique for actually removing the gallbladder is quite different. The operation has all the advantages of laparoscopy, including a short hospital stay, a quick recuperation, and a very small incision, and the operation time is shorter. Injury to the biliary tract, the incidence of serious complications, and the need for reoperations are very rare. Surgeons must be specifically trained to perform this special surgical technique, however, and not all patients are candidates.



Non-Surgical Therapy for Gallstones

Medical therapy for gallstones is available for some patients who are unwilling to undergo surgery or who have serious medical problems that increase the risks of surgery. Nonsurgical treatment, however, usually cannot be used for patients who have acute gallbladder inflammation or common bile duct stones since delaying or avoiding surgery could be hazardous in these cases. The introduction of laparoscopic cholecystectomy has greatly reduced the use of non-surgical therapies.

Oral Dissolution Therapy

Oral dissolution therapy uses bile acids in pill form to dissolve gallstones and may be used in conjunction with lithotripsy. [See Extracorporeal Shock Wave Lithotripsy below.] Ursodiol or ursodeoxycholic acid (Actigall) and chenodiol (Chenix) are the standard oral bile acid drugs used for dissolution. Most physicians prefer Actigall. Patients with small stones of high cholesterol content are most likely to benefit from this treatment, although a recurrence rate of 10% per year for the first five years has been reported in patients on this therapy. Actigall is considered to be among the safest of common drugs and does not seem to have significant side effects. Long-term treatment appears to notably reduce the risk of biliary pain and acute cholecystitis.

The technique is moderately effective, however, since gallstones recur in the majority of patients. In addition, this therapy works only on cholesterol-based stones that are less than 1.5 cm in diameter. Gallstones that are calcified or composed of bile pigments are not amenable to oral dissolution therapy. It is less effective in obese patients. Only about 30% of patients are candidates for oral dissolution therapy, and the number may be much lower if obesity and noncompliance with therapeutic regimens are taken into account. Ursodiol is very expensive; the treatment can take up to two years and can cost thousands of dollars per year.

Contact Dissolution Therapy

Contact dissolution therapy requires the injection of the organic solvent methyl tert-butyl ether (MTBE) into the gallbladder to dissolve gallstones. This is a somewhat technically difficult and



hazardous procedure and should be performed only by experienced physicians in hospitals where research on this treatment is being done. Preliminary studies indicate that MTBE rapidly dissolves stones. The ether remains liquid at body temperature and dissolves gallstones within five to twelve hours. Serious side effects include severe burning pain.

Extracorporeal Shock Wave Lithotripsy

Gallstone fragmentation by this technique may be an appropriate therapy for some patients who cannot undergo surgery for gallstones. The treatment works best on solitary stones of less than two centimeters. Less than 15% of patients are good candidates for lithotripsy. High-energy, ultrasound shock waves are directed through the abdominal wall toward the stones as the patient sits in a tub of water. The shock waves travel through the soft tissues of the body and break up the stones. The stone fragments are then usually small enough to be passed through the bile duct and into the intestines. Lithotripsy is generally combined with bile acid treatment to help dissolve the fragmented pieces of the original gallstone. The use of lasers for lithotripsy is under investigation.

Although mortality rate for lithotripsy is essentially zero, complications include pain in the gallbladder area and pancreatitis, usually occurring within a month of treatment. In addition, not all of the fragments may clear the bile duct. Adding erythromycin to the treatment regimen may help remove these fragments. About 35% of patients who are left with fragments are at risk for further problems, some severe. The chance of recurrence is high with this procedure.

Treatment for Common Bile Duct Stones (Choledocholithiasis)

Endoscopic Retrograde Cholangiopancreatography (ERCP) with Endoscopic Sphincterotomy. Common bile duct stones are present in 10% to 15% of patients having cholecystectomy. In such cases, the most frequent choice of physicians in equipped institutions is endoscopic retrograde cholangiopancreatography (ERCP) with endoscopic sphincterotomy, also called papillotomy, to remove common bile duct stones prior to laparoscopy. The procedure clears stones in up to 85% of cases. It has been effective for cholangitis caused by common bile duct stones and in cases of



acute pancreatitis caused by gallstones, although its use in this latter condition is controversial. ERCP can be done successfully even in critically ill patients on mechanical ventilators. In this procedure, the endoscope is passed through the mouth and stomach and into the duodenum (top part of the small intestine) to the common bile duct. After injection of contrast material into the duct orifice, ERCP allows visualization by x-ray of the biliary tree and any contained stones. In endoscopic sphincterotomy, tiny incisions are made through the scope to widen the ampulla of Vater (the junction between the common bile duct, pancreas, and intestine). The catheter passes into the common bile duct and the stones are captured, usually in a microbasket, and pulled back into the intestine. Endoscopic sphincterotomy is the procedure of choice when stones remain after gallbladder surgery.

Complications of ERCP and endoscopy sphincterotomy occur in up to 9.8% of cases and can be serious. Of major concern is inflammation of the pancreas (pancreatitis); younger adults are at higher risk for pancreatitis than the elderly. Pancreatitis is caused by certain enzymes that are produced in increased levels if the pancreas is irritated during the procedure. In such cases, obstruction can occur and the condition can become life threatening. The use of a drug called gabexate may lower the risk for this problem. The next most common complications are bleeding and infection. Antibiotics may be given before the operation to prevent infection, although one study reported that they had little benefit. All of these complications are the same whether the procedure is used for diagnosis or treatment. Long-term complications include stone recurrence (nearly always bilirubinate) or new gallstones, acute cholecystitis (only in patients with gallstones), liver cancer, and abscesses. ERCP and endoscopic sphincterotomy are difficult procedures and patients must be certain their physician is experienced with them; ideally he or she should have performed at least 180 ERCPs.

Elderly patients with acute cholangitis, particularly if they are critically ill, should receive endoscopic biliary drainage in which the tube is passed down through the nasal passages. They should not be given endoscopic sphincterotomy. Treatment of bile duct stones using endoscopic sphincterotomy or surgery should be deferred until acute cholangitis resolves or drainage fails.



Alternatives to Endoscopic Sphincterotomy for Stone Removal. Other methods are being used for removal of common bile duct stones once ERCP has been performed. Endoscopic balloon dilation has shown success rates similar to endoscopic sphincterotomy with a lower occurrence of complications. Using this procedure, a deflated balloon at the end of the endoscope is moved up the bile duct beyond the stone; the balloon is then inflated and pulled back, pushing the stone out the small intestine as it moves. Endoscopic balloon dilation causes less trauma to the biliary sphincter. Occasionally, however, it is not wholly effective and follow-up procedures, such as lithotripsy, must be performed. This procedure is only appropriate when common bile duct stones measure less than eight to ten millimeters in diameter.

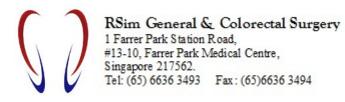
Endoscopy with a technique called mechanical lithotripsy is also sometimes used for common bile duct stones. In this procedure, a tiny steel crushing basket is inserted through the endoscope into the bile duct; the basket expands to trap and then crush the stone. It is capable of crushing and removing very large stones. Laser and electric probes are also being used which send shock waves against the stone to crush it.

Where Else Can Help For Gallstones And Gallbladder Disease Be Obtained?

National Digestive Diseases Information Clearinghouse, Two Information Way, Bethesda, MD 20892-3570. Call (301-654-3810) or on the Internet (<u>http://www.niddk.nih.gov/</u>)

American Gastroenterological Association, American Digestive Health Foundation, 7910 Woodmont Avenue, 7th Floor, Bethesda, MD 20814. Call (301 654-2055) or on the Internet (http://www.gastro.org)

American Society for Gastrointestinal Endoscopy, 13 Elm Street, Manchester, MA 01944 (http://www.asge.org/)



Society for Surgery of the Alimentary Tract, Inc., 6900 Grove Road, Thorofare, NJ 08086-9447. Call (609-251-0558) or on the Internet (<u>http://www.ssat.com/</u>)

American Liver Foundation, 75 Maiden Lane, Suite 603, New York, NY 10038. Call (800-GO LIVER) or (800-465-4837) or on the Internet (<u>http://www.liverfoundation.org/</u>)

National voluntary organization dedicated to preventing, treating, and curing gallbladder diseases through research and education. Provides patient brochures, video and audio tapes.

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