

Primary Biliary Cirrhosis

National Digestive Diseases Information Clearinghouse



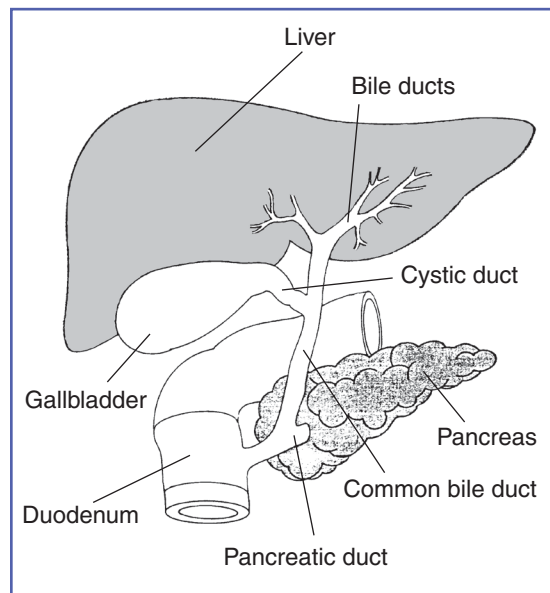
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What is primary biliary cirrhosis?

Primary biliary cirrhosis is a chronic disease that causes the bile ducts in the liver to become inflamed and damaged and, ultimately, disappear. Bile is a liquid produced in the liver that travels through the bile ducts to the gallbladder and then the small intestine, where it helps digest fats and fat-soluble vitamins A, D, E, and K. When the bile ducts become damaged from chronic inflammation, bile builds up in the liver, injuring liver tissue.



Normal liver and biliary system.

Injured liver tissue from chronic inflammation and the buildup of bile leads to cirrhosis, a condition in which the liver slowly deteriorates and malfunctions. Scar tissue replaces healthy liver tissue, partially blocking the flow of blood through the liver. Scarring also impairs the liver's ability to

- control infections
- remove bacteria and toxins from the blood
- process nutrients, hormones, and drugs
- make proteins that regulate blood clotting
- produce bile to help absorb fats—including cholesterol—and fat-soluble vitamins
- effectively replace its own cells when they become damaged

Primary biliary cirrhosis develops over time and may ultimately cause the liver to stop working completely. Most people are diagnosed early, before the disease progresses. Early treatment delays—but does not stop—the eventual onset of cirrhosis and liver failure. When a person has end-stage liver disease, a liver transplant is necessary for survival.

Primary biliary cirrhosis usually occurs between the ages of 40 and 60 and affects women more often than men.

What causes primary biliary cirrhosis?

The cause of primary biliary cirrhosis is unknown. Most research suggests the disease is an autoimmune condition. The immune system usually protects the body from harmful substances such as bacteria and viruses by attacking and destroying them. In autoimmune diseases, the immune system instead attacks the body's own tissues. In primary biliary cirrhosis, the immune system attacks the bile ducts.

Genetic factors may make a person prone to develop primary biliary cirrhosis. Primary biliary cirrhosis is more common in people who have a parent or sibling—particularly an identical twin—with the disease.

Genetic factors may also make some people prone to develop other autoimmune diseases. People with primary biliary cirrhosis may have other autoimmune conditions such as rheumatoid arthritis or autoimmune thyroiditis.

A person who has genetic factors for primary biliary cirrhosis may be more likely to develop the disease after exposure to chemicals or infections, such as urinary tract infections.

What are the symptoms of primary biliary cirrhosis?

Most people with primary biliary cirrhosis are diagnosed before symptoms begin. The first and most common symptoms people with this condition experience are

- a general feeling of tiredness, or fatigue
- pruritus—itchy skin—and darkened skin in itchy areas due to scratching

Other symptoms may develop, including

- dry eyes and mouth
- jaundice—darkening of the urine and yellowing of the skin and whites of the eyes—which occurs when the diseased liver does not remove enough bilirubin from the blood. Bilirubin is the pigment that gives bile its reddish-yellow color.

How is primary biliary cirrhosis diagnosed?

The first indication of primary biliary cirrhosis may occur when results of routine blood tests to check liver function are abnormal. The doctor will then order one or more tests to confirm the disease:

- **Anti-mitochondrial antibody (AMA) blood test.** The presence of AMA is detected in 90 percent of people with primary biliary cirrhosis.
- **Alkaline phosphatase blood test.** Primary biliary cirrhosis is likely if two blood tests performed at least 6 months apart reveal alkaline phosphatase—a liver enzyme—to be abnormally high.

- **Liver biopsy.** A liver biopsy can confirm the diagnosis but is not always necessary. A biopsy may help determine the extent of liver damage. The biopsy is performed with a needle inserted between the ribs or into a vein in the neck. Precautions are taken to minimize discomfort. A tiny sample of liver tissue is examined with a microscope for scarring or other signs of cirrhosis. Sometimes a cause of liver damage other than cirrhosis is found during biopsy.

The doctor may also order the following tests:

- **Cholesterol blood test.** People with primary biliary cirrhosis may have abnormally high levels of cholesterol in the blood. However, these high cholesterol levels are usually less harmful to people with primary biliary cirrhosis than to those without the disease.
- **Abdominal ultrasound.** An ultrasound shows whether the liver and bile ducts are inflamed. A handheld device, which a technician glides over the abdomen, sends sound waves toward the abdomen. The sound waves bounce off the liver and other organs, and their echoes create a picture of the liver and biliary system on a video monitor.

What are the complications of primary biliary cirrhosis?

Some people develop one or more complications of primary biliary cirrhosis when the disease progresses to cirrhosis.

Osteoporosis. The disease may cause bones to become fragile and more likely to break. Osteoporosis can also result from steroid use as a treatment of primary biliary cirrhosis.

Maldigestion. When a person with primary biliary cirrhosis has jaundice, the small intestine cannot easily absorb fats and fat-soluble vitamins. Maldigestion may result in diarrhea and fatty stools and can lead to weight loss in the late stages of the disease.

Portal hypertension. Normally, blood from the intestines and spleen is carried to the liver through the portal vein. But primary biliary cirrhosis may cause inflammation in the portal tract, leading to increased pressure in the portal vein. This condition is called portal hypertension.

Esophageal varices and gastropathy. When portal hypertension occurs, it may cause enlarged blood vessels in the esophagus, called varices, or in the stomach, called gastropathy, or both. Enlarged blood vessels are more likely to burst due to thin walls and increased pressure. If they burst, serious bleeding can occur in the esophagus or upper stomach, requiring immediate medical attention.

Splenomegaly. When portal hypertension occurs, the spleen frequently enlarges and sequesters or holds white blood cells and platelets, reducing the numbers of these cells in the blood. A low platelet count in the blood may be the first evidence that a patient has developed cirrhosis.

Edema and ascites. When the liver damage progresses to an advanced stage, fluid collects in the legs, called edema, and in the abdomen, called ascites. Ascites can lead to bacterial peritonitis, a serious infection.

Bruising and bleeding. When the liver slows or stops producing the proteins needed for blood clotting, a person will bruise or bleed easily.

Sensitivity to medications. Cirrhosis slows the liver's ability to filter medications from the blood. When this occurs, medications act longer than expected and build up in the body. This causes a person to be more sensitive to medications and their side effects.

Hepatic encephalopathy. A failing liver cannot remove toxins from the blood, and they eventually accumulate in the brain. The buildup of toxins in the brain—called hepatic encephalopathy—can decrease mental function and cause coma. Signs of decreased mental function include confusion, personality changes, memory loss, trouble concentrating, and a change in sleep habits.

Insulin resistance and type 2 diabetes. Cirrhosis causes resistance to insulin—a hormone produced by the pancreas that enables the body to use glucose as energy. With insulin resistance, the body's muscle, fat, and liver cells do not use insulin properly. The pancreas tries to keep up with the demand for insulin by producing more, but excess glucose builds up in the bloodstream causing type 2 diabetes.

Liver cancer. Hepatocellular carcinoma is a type of liver cancer that can occur in patients with cirrhosis. Hepatocellular carcinoma has a high mortality rate, but several treatment options are available.

Other problems. Cirrhosis can cause immune system dysfunction, leading to the risk of infection. Cirrhosis can also cause kidney and lung failure, known as hepatorenal and hepatopulmonary syndromes.

How is primary biliary cirrhosis treated?

Early Treatment

Initial treatment for primary biliary cirrhosis is aimed at relieving symptoms. Vitamin replacement therapy, calcium supplements, and drugs to treat itching are usually prescribed.

A specific treatment that stops or reverses the progression of primary biliary cirrhosis has not been found. However, medication prescribed during the early stage of the disease may slow liver damage.

Ursodiol (Actigall). Ursodiol is the only drug approved by the U.S. Food and Drug Administration for the treatment of primary biliary cirrhosis. Ursodiol assists the liver in moving bile through the ducts to the gallbladder and small intestine. Studies have shown that ursodiol prescribed early in the disease improves liver function, slowing the time it takes to progress to liver failure and the need for a liver transplant.

Researchers are studying the effects of several other medications on the progression of primary biliary cirrhosis. To date, none have shown the positive effects of ursodiol.

Treatment for Cirrhosis and Its Complications

When the disease progresses to cirrhosis, the goals of treatment are to slow the progression of scar tissue in the liver and prevent or treat the complications of the disease. Hospitalization may be necessary for people who have cirrhosis with complications.

Eating a nutritious diet. Because malnutrition is common in people with cirrhosis, a healthy diet is important in all stages of the disease. Health care providers recommend a meal plan that is well balanced. If fluid overload develops, a sodium-restricted diet is recommended. A person with cirrhosis should not eat raw shellfish, which can contain a bacterium that causes serious infection. To improve nutrition, the doctor may add a liquid supplement either for drinking or administration with a nasogastric tube—a tiny tube inserted through the nose and throat that reaches into the stomach.

Avoiding alcohol and other substances. People with primary biliary cirrhosis are encouraged not to consume alcohol or illicit substances, as both will cause more liver damage. Because many vitamins and medications—prescription and over-the-counter—can affect liver function, a doctor should be consulted before taking them.

Treatment for cirrhosis also addresses specific complications. For edema and ascites, the doctor may recommend diuretics—medications that remove fluid from the body. Large amounts of ascitic fluid may be removed from the abdomen and checked for bacterial peritonitis. Oral antibiotics may be prescribed to prevent infection. Severe infection with ascites requires intravenous (IV) antibiotics.

The doctor may prescribe a beta-blocker or nitrate for portal hypertension, which can lower the pressure in the varices and reduce the risk of bleeding. Gastrointestinal bleeding requires an immediate upper endoscopy to look for esophageal varices. The doctor may perform a band-ligation using a special device to compress the varices and stop the bleeding. People who have had varices in the past may need to take medicine to prevent future episodes.

Hepatic encephalopathy is treated by cleansing the bowel with lactulose—a laxative given orally or in enemas. Antibiotics are added to the treatment if necessary. Patients may be asked to reduce dietary protein intake. The condition may improve as other complications of cirrhosis are controlled.

People with cirrhosis who develop hepatorenal syndrome must undergo regular hemodialysis treatment, which uses a machine to clean wastes from the blood. Medications are also given to improve blood flow through the kidneys.

Liver Transplantation

A liver transplant is the only treatment that will cure primary biliary cirrhosis. A liver transplant is considered when complications cannot be controlled by treatment. A liver transplant is a major operation in which the diseased liver is removed and replaced with a healthy one from an organ donor. A team of health professionals determines the risks and benefits of the procedure for each patient. Survival rates have improved over the past several years because of drugs that suppress the immune system and keep it from attacking and damaging the new liver.

The number of people who need a liver transplant far exceeds the number of available organs. A person needing a transplant must go through a complicated evaluation process before being added to a long transplant waiting list. Generally, organs are given to people with the best chance of living the longest after a transplant. Survival after a transplant requires intensive follow-up and cooperation on the part of the patient and caregiver.

Points to Remember

- Primary biliary cirrhosis is a chronic disease that causes the bile ducts in the liver to become inflamed and damaged and, ultimately, disappear.
- Injured liver tissue from chronic inflammation and the buildup of bile leads to cirrhosis, a condition in which the liver slowly deteriorates and malfunctions.
- The cause of primary biliary cirrhosis is unknown. Most research suggests the disease is an autoimmune condition.
- Primary biliary cirrhosis is more common in people who have a parent or sibling—particularly an identical twin—with the disease.
- Most people are diagnosed early, before the disease progresses. The disease is often discovered when routine blood tests to check liver function are abnormal.
- Many people with primary biliary cirrhosis do not have symptoms until after the disease is diagnosed.
- The first and most common symptoms of the disease are itching, called pruritus, and fatigue. Other symptoms include dry eyes and mouth and jaundice.
- The anti-mitochondrial antibody (AMA) blood test, the alkaline phosphatase blood test, and a liver biopsy may be necessary to confirm a diagnosis of primary biliary cirrhosis.
- Some of the complications of primary biliary cirrhosis are osteoporosis and maldigestion.
- Early treatment delays—but does not stop—the eventual onset of cirrhosis and liver failure.
- Ursodiol (Actigall) is the only drug approved by the U.S. Food and Drug Administration for the treatment of primary biliary cirrhosis.
- Liver transplantation is the only treatment that will cure primary biliary cirrhosis. A liver transplant is considered when complications cannot be controlled by treatment.

Hope through Research

The National Institute of Diabetes and Digestive and Kidney Diseases' Division of Digestive Diseases and Nutrition supports basic and clinical research into liver diseases—including primary biliary cirrhosis—and liver transplantation. Researchers are studying

- the mechanisms of liver injury and regeneration
- ways to improve outcomes of liver transplantation
- how autoimmune liver diseases develop in the body

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research. For information about current studies, visit www.ClinicalTrials.gov.

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Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This publication was reviewed by M. Eric Gershwin, M.D., University of California at Davis.

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