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CIRRHOSIS

Overview

Cirrhosis is a condition that causes irreversible scarring of the liver. As scar tissue replaces normal tissue, blood flow through your liver is affected, making it increasingly difficult for your liver to carry out functions that are essential for life and health. Among other major tasks, the liver detoxifies harmful substances, purifies your blood and manufactures vital nutrients.

Cirrhosis rarely causes signs and symptoms in its early stages. But as liver function deteriorates, you may experience fatigue, exhaustion, nausea, unintended weight loss and swelling in your legs and abdomen. In time, jaundice — a yellowing of your skin and the whites of your eyes — and intense itching can develop.

In the United States, alcoholism and chronic infection with the hepatitis C virus are the leading causes of cirrhosis. But other factors, including damaged bile ducts, immune system problems and prolonged exposure to certain environmental toxins can cause liver scarring.

Although liver damage from cirrhosis is irreversible, the disease usually progresses slowly and symptoms are often controllable. Specific treatment for cirrhosis depends on the underlying cause, but anyone with cirrhosis must avoid alcohol and other substances that harm the liver. When damage is so severe that liver function is seriously impaired, a liver transplant may be the only option.

Signs and symptoms

You may not have signs and symptoms of cirrhosis in the early stages of the disease. But as more scar tissue replaces healthy tissue and liver function declines, you may experience some of the following:

- Lack of appetite
- Weight loss
- Nausea
- Small, red spider veins under your skin or easy bruising
- Weakness
- Fatigue

- Yellowing of your skin and eyes and dark, cola-colored urine
- Bleeding from engorged veins in your esophagus or intestines
- Loss of interest in sex
- Fluid in your abdominal cavity (ascites)
- Itching on your hands and feet and eventually on your entire body
- Swelling of your legs and feet from retained fluid (edema)
- Mental confusion, such as forgetfulness or trouble concentrating (encephalopathy)

Causes

Weighing between 3 and 4 pounds, your liver is the largest internal organ in your body. It's located on the right side of your abdomen, just beneath your lower ribs. A healthy liver performs hundreds of vital functions, including processing most of the nutrients absorbed from your intestine, removing drugs, alcohol and other harmful substances from your bloodstream, and manufacturing bile — the greenish fluid stored in your gallbladder that helps digest fats. It also produces cholesterol, blood-clotting factors and certain other proteins.

Because of the complexity of the liver and its exposure to so many potentially toxic substances, it would seem especially vulnerable to disease. But the liver has an amazing capacity for regeneration — it can heal itself by replacing or repairing injured cells. In cirrhosis, however, the healing process seems to go slightly awry. In response to chronic injury, cells called stellate cells increase dramatically in size and number. This leads to the formation of excess scar tissue that interferes with the liver's ability to function. And although groups of cells may continue to regenerate, the pattern of regeneration isn't normal.

What damages the liver?

Many people associate cirrhosis with alcohol abuse, and in fact, chronic alcoholism is the primary cause of cirrhosis in the United States. Alcoholic cirrhosis usually occurs after a decade or more of heavy drinking, although the amount of alcohol that can injure the liver varies from person to person. The liver is particularly vulnerable because it breaks down alcohol into highly toxic chemicals. Some of these chemicals trigger inflammation that eventually destroys liver cells. In time, web-like scars and small knots of abnormal tissue replace healthy liver tissue. In the initial stages of cirrhosis, the liver swells, but it later shrinks as larger areas of scar tissue form.

Other causes of cirrhosis include:

Chronic hepatitis B and C. The serious liver infection hepatitis C ranks second only to alcoholism as a cause of cirrhosis. Nearly a quarter of people with chronic hepatitis C develop cirrhosis — often as long as two decades or more after infection — and many with cirrhosis eventually progress to end-stage liver disease or to liver cancer. Infection with another hepatitis strain, hepatitis B, also can lead to cirrhosis.

Autoimmune hepatitis. In this disorder, the body's immune system attacks liver cells, causing inflammation similar to the inflammation that occurs in viral hepatitis. Normally, your immune system protects you from viruses, bacteria and other disease-causing organisms. It's not clear why the body sometimes attacks its own cells, but researchers believe a virus or bacteria might trigger this response in people with a genetic predisposition to develop an autoimmune disorder. Many people with autoimmune hepatitis also have other autoimmune problems such as thyroiditis, Graves' disease or ulcerative colitis. Autoimmune hepatitis can affect people of any age, although it's more common in women than in men. Because the inflammation is usually severe and chronic, it may lead to cirrhosis and eventually to liver failure.

Nonalcoholic fatty liver disease (nonalcoholic steatohepatitis). In this disorder, fat accumulates in the liver, leading to inflammation and occasionally to scar tissue. Although the exact cause isn't known, nonalcoholic fatty liver disease seems to be associated with diabetes, obesity and elevated lipid levels.

Inherited diseases. These include disorders that cause high levels of certain minerals such as copper (**Wilson's disease**) or iron (**hereditary hemochromatosis**) to accumulate in the liver. Other inherited conditions that may cause cirrhosis include **cystic fibrosis** and **alpha-1-antitrypsin deficiency** — a disorder in which abnormal protein damages liver cells.

Blocked or inflamed bile ducts. Bile is a fluid that aids in the digestion of fats. It's produced in your liver and travels to your gallbladder and small intestine (duodenum) through thin tubes called bile ducts. Diseases such as primary biliary cirrhosis or primary sclerosing cholangitis can cause the ducts to become inflamed, scarred or blocked. This forces bile back into the liver, where it damages tissue and eventually may lead to cirrhosis. Complications from surgery on the liver, bile ducts or gallbladder (secondary biliary cirrhosis) also can lead to blocked bile ducts. Babies sometimes develop cirrhosis as a result of biliary atresia — a condition in which the bile ducts are closed or missing at birth.

Prolonged exposure to toxic materials. Your liver is the primary clearinghouse for alcohol, drugs and other toxins. Prolonged exposure to environmental toxins such as arsenic and severe reactions to some drugs — including prescription drugs — can sometimes cause severe liver disease.

Risk factors

In the United States, excessive alcohol consumption is the single greatest risk factor for cirrhosis. The type of alcohol is less important than the amount consumed over a period of years. What's more, even small amounts of alcohol can be damaging if you're infected with the hepatitis B or C virus.

Other risk factors include:

Chronic infection with hepatitis C or B. Most people with hepatitis C became infected through blood transfusions received before 1992, the year improved blood-screening tests became available. You can also contract the virus from contaminated needles associated with intravenous (IV) drug use or, less commonly, from needles used in tattooing or body piercing. Long-term infection with hepatitis C slowly damages the liver, and about one in five people go on to develop cirrhosis, usually decades after the initial infection. The older you are when you're infected with the hepatitis C virus, the more likely you are to develop cirrhosis. In the United States, hepatitis B is usually transmitted sexually or through contaminated needles.

Your sex. More men than women develop cirrhosis, possibly because men tend to drink more heavily than women do.

Certain inherited diseases. These include diseases that cause excess copper or iron to be deposited in the liver as well as alpha-1 antitrypsin deficiency — a disorder in which the liver produces an abnormal protein that can cause lung damage and cirrhosis in children and adults — and glycogen-storage diseases, which prevent glycogen, the stored form of glucose, from being formed or released when it's needed by the body.

Drug reactions and exposure to environmental toxins. In rare cases, cirrhosis may result from a severe reaction to methotrexate, an immune-suppressing drug, or to amiodarone, which is used to treat heart arrhythmias. Long-term exposure to environmental toxins such as arsenic also can cause cirrhosis.

When to seek medical advice

If you're experiencing any of the signs and symptoms of cirrhosis — weight loss, fatigue, jaundice and swelling in your legs or abdomen, especially if you drink alcohol or have had hepatitis — see your doctor. A physical exam and certain tests can help diagnose cirrhosis and rule out other reasons for your signs and symptoms.

Screening and diagnosis

Because cirrhosis seldom causes signs and symptoms in the early stages, your doctor may discover the disease during a routine medical examination. By gently pressing your abdomen, your doctor can often tell whether your liver is enlarged and firm, a sign of liver disease. As cirrhosis progresses, however, your liver often shrinks, leading to a backflow of blood and an enlarged spleen, which also may be detected in a physical exam.

If your doctor suspects cirrhosis, you're likely to have certain tests, including:

Liver blood tests. A damaged liver releases certain enzymes. Measuring these enzymes may help determine whether you have liver damage.

Bilirubin test. Bilirubin, a red-yellow pigment that results from the normal breakdown of red blood cells, is metabolized in your liver and excreted in your urine. But in advanced cirrhosis, your liver can't process bilirubin, leading to high blood levels of the pigment.

Ultrasound (ultrasonography). This noninvasive test uses sound waves to produce a picture of internal organs, including the liver. Ultrasound is painless and usually takes less than 30 minutes. While you lie on a bed or examining table, a wand-shaped device (transducer) is placed on your body. It emits sound waves that are reflected from your liver and transformed into a computer image.

Computerized tomography (CT) scan. This test uses X-rays to produce cross-sectional images of your body. It can provide an accurate look at internal organs, but it generates more radiation than conventional X-rays do.

Magnetic resonance imaging (MRI). Instead of X-rays, MRI creates images using a magnetic field and radio waves. Sometimes a contrast dye also may be used. The test can take from 15 minutes to an hour.

Liver biopsy. Although other tests can provide a great deal of information about the extent and type of liver damage, a biopsy is the only way to definitively diagnose cirrhosis. In this procedure, a small sample of tissue is removed from your liver and examined under a microscope. Your doctor is likely to use a thin cutting needle to obtain the sample. Needle biopsies are relatively simple procedures requiring only local anesthesia, but your doctor may choose not to do one if you have bleeding problems or severe abdominal swelling (ascites). Risks include bruising, bleeding and infection.

Complications

Because cirrhosis disrupts the normal function of your liver, it can cause a number of serious complications:

Increased pressure in the portal vein. Blood from your intestine, spleen and pancreas enters your liver through a large blood vessel called the portal vein. If scar tissue blocks normal circulation through the liver, this blood backs up, leading to increased pressure within the vein (portal hypertension).

Enlarged veins (varices). When circulation through the portal vein is blocked, blood may back up into other blood vessels — mainly those in your stomach and esophagus. Sometimes veins also form around your navel and at the rectum. The blood vessels are thin-walled, and because they're filled with more blood than they're meant to carry, are likely to bleed. Massive bleeding in the upper stomach or esophagus from these blood vessels is a life-threatening emergency that requires immediate medical care.

Fluid retention. Liver disease can cause large amounts of fluid to accumulate in your legs (edema) and abdominal cavity (**ascites**). Edema is especially common in alcoholic cirrhosis. Several factors play a role, including portal hypertension and changes in the hormones and chemicals that regulate fluids in your body. Ascites can be

uncomfortable and may interfere with breathing. In addition, abdominal fluid may become infected (spontaneous bacterial peritonitis) and require treatment with antibiotics. Although not life-threatening in itself, ascites is usually a sign of advanced cirrhosis.

Bruising and bleeding. Cirrhosis interferes with the production of proteins that help your blood clot and with the absorption of vitamin K, which plays a role in synthesizing these proteins. As a result you may bruise and bleed more easily than normal. Bleeding in the gastrointestinal tract is particularly common.

Jaundice. This occurs when your liver isn't able to remove bilirubin — the residue of old red blood cells — from your blood. Eventually, bilirubin builds up and is deposited in your skin and the whites of your eyes, causing a yellow color. Excreted bilirubin may turn your urine dark brown and your stools a pale clay color.

Itching. Bile salts deposited in your skin can cause intense itching.

Hepatic encephalopathy. A liver damaged by cirrhosis has trouble removing toxins from your body — normally one of the liver's key tasks. The buildup of toxins such as ammonia — a byproduct of protein digestion — can damage your brain, leading to changes in your mental state, behavior and personality (hepatic encephalopathy). Symptoms of hepatic encephalopathy include forgetfulness, confusion and mood changes, and in advanced cases, delirium and coma.

Weak bones (osteoporosis). Cirrhosis interferes with your liver's ability to process vitamin D and calcium, both of which are essential for bone growth and health. As a result, weak, brittle bones and bone loss are a common complication of the disease. Taking calcium and vitamin D may help prevent osteoporosis.

Liver cancer. Cirrhosis can increase the risk of liver cancer, which occurs when malignant cells begin growing in the tissues of your liver.

Liver failure. This occurs when extensive damage to liver cells makes it impossible for your liver to function.

Treatment

Although liver damage from cirrhosis is irreversible, treatment can often help prevent further damage and reduce complications. The therapy used depends on the underlying cause of the cirrhosis.

Treating alcoholic cirrhosis

Abstaining from alcohol is the main treatment for alcoholic cirrhosis. Therapy is tailored to the individual and may involve a chemical dependency evaluation, a brief intervention, counseling, an outpatient treatment program or a residential inpatient stay.

Nutrition is also often a key part of therapy because people with cirrhosis, and especially alcoholic cirrhosis, are frequently malnourished. A doctor or dietitian is likely to recommend a high-calorie, nutrient-dense dietary plan to help liver cells regenerate.

Researchers are also studying certain substances that may prove useful in treating alcoholic cirrhosis. These include drugs that block factors that contribute to liver inflammation and a soybean extract that may stop the progression of liver scarring.

In addition to treating the cause of cirrhosis, your doctor will focus on preventing or improving any complications:

Portal hypertension. Your doctor may prescribe blood pressure medications such as beta blockers to help lower portal vein pressure and prevent bleeding from enlarged blood vessels.

Bleeding blood vessels. To help stop actively bleeding blood vessels, you may be given drugs such as octreotide (Sandostatin), a derivative of a natural hormone that constricts blood vessels. You may take these medications alone or in combination with certain procedures. One such procedure, endoscopic variceal band ligation, treats bleeding in the esophagus. In this procedure, latex bands are used to pinch off the blood supply to bleeding blood vessels. If this isn't successful, your doctor may use a catheter with a balloon on the end to compress the veins and stop the bleeding. When bleeding is severe or recurs often, you may need a procedure to create a bypass (shunt) between the venous system in your liver and your general venous system. Called transjugular intrahepatic portosystemic shunt, the procedure, which is performed through a vein in your neck, is a fairly low-risk alternative to more invasive surgeries.

Fluid retention. Sometimes avoiding alcohol and salt are all you need to reduce fluid buildup in your legs or abdomen. If not, your doctor may prescribe diuretics. Severe cases may require paracentesis — a procedure in which large amounts of fluid are removed through a thin tube inserted in the abdomen.

Itching. Doctors often prescribe antihistamines or other medications such as cholestyramine (Questran) and rifampin (Rifadin, Rimactane) to reduce itching caused by metabolites in the blood.

Treatments for hepatic encephalopathy. The medication lactulose (Cholac, Kristalose, Duphalac), a synthetic sugar, can help lower blood ammonia levels by changing the type of bacteria in your intestine and decreasing the absorption of ammonia. Your doctor may also prescribe an antibiotic to reduce the number of ammonia-producing bacteria in your intestine.

Liver failure. When complications can't be controlled or liver function is severely impaired, a liver transplant may be the only option for some people. Although liver transplantation is often successful, the number of people awaiting transplants far exceeds the number of donated organs. But several new developments in transplantation may make it possible for more people to receive the organ they need.

These developments include the donation of liver segments from living donors, splitting one donated liver between two recipients, new organ allocation policies and, especially, new approaches to liver transplants for people with hepatitis C. Until recently, hepatitis C-infected livers were routinely discarded. But studies show that people already infected with hepatitis C who receive livers from hepatitis C-positive donors do as well

as if they had received a liver not infected with the virus. This may mean that many more livers will become available for people with hepatitis C. Nevertheless, hepatitis C may recur in the new liver.

Prevention

Although not all cases of cirrhosis are preventable, the following measures can greatly reduce your risk:

Avoid alcohol or drink in moderation. Alcohol is a toxin that must be filtered by your liver. In the process, liver cells become damaged. Unfortunately, you may not recognize that you have a problem with alcohol before serious liver damage has occurred. Knowing and recognizing a family history of alcoholism for you or others is an important step in seeking treatment.

Protect yourself from hepatitis C. Because there's no vaccine to prevent hepatitis C, the only way to protect yourself is to avoid exposure to the virus. If you aren't absolutely certain of the health status of a sexual partner, use a new condom every time you have sex. Don't use nasal cocaine and avoid sharing needles or other drug paraphernalia. Contaminated drug paraphernalia is responsible for about half of all new cases of hepatitis C. See your doctor if you have or have had hepatitis C or think you may have been exposed to the virus.

Protect yourself from hepatitis B. Getting a vaccine for hepatitis B is the best way to protect yourself and others. However, other measures also can keep you safe. Know the health status of every sexual partner. If you don't know, use a new condom every time you have sex. And if you use needles to inject drugs, be sure they're sterile and don't share them.

Self-care

Although the damage from cirrhosis is irreversible, the disease often progresses slowly, and you can take steps to reduce further liver damage:

Avoid alcohol. This is the single most important measure you can take to help protect your liver and reduce the risk or severity of complications. Avoiding alcohol is crucial, no matter what type of cirrhosis you have.

Limit medications. Because your damaged liver isn't able to detoxify and eliminate drugs from your system, discuss all medications, including nonprescription drugs, with your doctor. In general, avoid aspirin and nonsteroidal anti-inflammatories such as ibuprofen and naproxen. The best pain reliever is acetaminophen (Tylenol, others) as long as you don't take more than 2 grams a day. Be especially careful not to combine any analgesic with alcohol, even if you take only the recommended daily amount of the drug.

Avoid people who are sick. When your liver is damaged, you can't fight off infections as easily as healthy people. Do everything that's reasonable to avoid getting sick. Get vaccinated for hepatitis A and B, influenza and pneumococcal pneumonia.

Eat a healthy diet. Because cirrhosis can cause a number of nutritional deficiencies along with weight loss, it's especially important to eat a diet high in calories and nutrients. Emphasize fresh fruits, vegetables, whole grains and small amounts of protein. These foods are high in nutrients, including vitamins A, C and E, which tend to be depleted in people with cirrhosis. Your doctor may also prescribe vitamin supplements.

Restrict salt. Because the sodium in salt causes your body to retain water, it can contribute to or increase fluid buildup in your legs and abdomen. In addition to not adding salt to your food, it's best to avoid high-sodium prepared foods, such as canned soups and cold cuts, and condiments such as soy sauce, catsup and mayonnaise. Lemon juice and herbs make good salt substitutes.

Avoid raw shellfish. Uncooked oysters, clams and other shellfish may contain the bacterium *vibrio vulnificus*, which can be extremely dangerous for people with cirrhosis. It's best to avoid shellfish altogether, but if you do eat them, be sure they're thoroughly cooked.

Complementary and alternative medicine

A number of complementary and alternative therapies — many of them herbs and nutritional supplements — are available for liver problems. Some of these therapies, such as milk thistle, have been intensively studied. Others, including the antioxidants alpha lipoic acid (thioctic acid), vitamin E, and N-acetylcysteine — an amino acid byproduct — are under investigation.

Some of the more well-known and studied alternative therapies include:

Milk thistle (*Silybum marianum*). In Europe, the herb milk thistle has been used for centuries to treat jaundice and other liver disorders. Today, scientific studies suggest that the chief constituent of milk thistle, silymarin, may aid in healing and rebuilding the liver. Silymarin seems to stimulate the production of antioxidant enzymes that help the liver neutralize toxins. It also seems to increase the production of new liver cells and may even improve the severe scarring of cirrhosis. Milk thistle is available in capsule or alcohol-free extracts at many natural food stores and some drugstores. Check with your doctor before trying this or any other herb to make sure it won't interact with other medications you're taking.

Omega-3 fatty acids. Found primarily in fish such as salmon, in fish oils, flax and flaxseed oils, and in walnuts, omega-3 fatty acids may help protect the liver.