WHAT IS CIRRHOSIS?

Cirrhosis is an often irreversible scarring of the liver. This is usually the result of various problems that damage liver cells over time. Eventually, damage becomes so severe that the normal structure of the liver is changed and it stops functioning correctly.

The disease process often takes the following path:

Scarring. The main damage in cirrhosis is triggered by scarring (fibrosis) that occurs from injuries due to alcohol, viruses, fatty liver disease (NASH) or other problems. Eventually, the liver is taken over by scar tissue and becomes a series of nodules which do not allow chemicals to flow through and the liver stops functioning. The scar tissue and nodules act like small dams and alter the flow of blood and bile in and out of the liver.

Altered Blood and Bile Flow. The changes in blood and bile flow have significant consequences, with both the liver and other organs responding to the altered flow:

- Blood flow coming from the intestine into the liver is slowed by the narrow blood vessels. It backs up through the portal vein (a major vein near the intestines) and seeks other routes.
  - New, abnormally twisted and swollen veins called varices can form in the stomach and lower part of the esophagus in order to compensate for the backup blood.
  - Extra blood can flow through the spleen which will soon be overloaded, and platelets begin to be “chopped up”.
- Bile also builds up in the bloodstream, resulting in high levels of bilirubin, which causes a yellowish cast in the skin called jaundice.
- Fluid buildup also occurs in the abdomen (called ascites) and swelling in the arms and legs is common. This is do to the liver basically “sweating” off extra fluid from the high pressures.

Changes in Liver Size. The liver enlarges in the first phases of the disease. In advanced stages, the liver sometimes shrinks, this is cirrhosis.

WHAT ARE THE SYMPTOMS OF CIRRHOSIS?

Early cirrhosis often has NO symptoms.

However, symptoms can include the following:

- Fatigue and loss of energy.
- Loss of appetite and nausea.

Patients in later stages may develop the following symptoms:

- Jaundice. This is a yellowish cast to the skin and eyes, which occurs because the liver cannot process bilirubin for elimination from the body.
- The palms of the hands may be reddish and blotchy (palmar erythema).
- Loss of body hair.
Abnormalities in hormone-affected organs. In men with alcoholic cirrhosis, the testicles may shrink and their breasts may become swollen, sometimes painfully.

Ascites. A swollen belly is a sign of ascites, the most common major complication of cirrhosis, which occurs when fluid accumulates in the abdomen. Fever, abdominal pain, and tenderness when the belly is pressed indicate that the fluid is infected, but infection can occur without any symptoms.

Fluid buildup and swelling (edema) in legs.

Confusion or changes in sleep-wake cycle (awake during night, sleepy during the day).

The Liver
The liver is the largest organ in the body. In the healthy adult, it weighs about three pounds. The liver is wedge shaped, with the top part wider than the bottom. It is located immediately below the diaphragm and occupies the entire upper right quadrant of the abdomen under the right sided rib cage.

Vital Functions
The liver performs over 500 vital functions.

Processing Healthful Nutrients. It processes all of the nutrients the body requires, including proteins, glucose, vitamins, and fats.

Bile Production. The liver produces bile, a green-colored fluid that is formed in the liver and helps the body absorb fats and fat-soluble vitamin. Bile is formed from bilirubin, a yellow-green pigment produced from the breakdown of hemoglobin, the oxygen-carrying component in red blood cells. Bile contains bile salts, fatty acids, cholesterol and other substances. Bile travels from the liver to the gallbladder, where it is stored until after a meal. It is then secreted into the intestines where it helps digest fat.

Eliminating Toxins. One of the liver’s major contributions to life is to render harmless potentially toxic substances, including alcohol, ammonia, nicotine, drugs, and harmful by-products of digestion.

Recycling Blood. The liver and spleen removes old red blood cells from the blood. The iron contained in them is recycled in the bone marrow to make new red blood cells.

The Liver’s Blood Supply
The liver is rich in blood. It holds about a pint, or 13% of the body’s supply. It is furnished with blood from two large vessels, the hepatic artery and the portal vein, and is drained of blood by the hepatic vein. (The word “hepatic” derives from the Latin word for liver.)

The hepatic artery. This artery supplies blood to the liver directly from the heart, and it is this blood that nourishes the liver.

The portal vein. The portal vein carries blood into the liver that has been circulating through the stomach, spleen, and intestine. This is the blood that the liver processes. The liver extracts nutrients and toxins from this blood.
The hepatic vein. This vein carries blood from the liver and connects to the inferior vena cava, a large vein that conducts blood back to the heart.

**HOW SERIOUS IS CIRRHOSIS?**
Cirrhosis is the seventh leading cause of death by disease in the US, killing more than 25,000 people each year. A damaged liver affects almost every bodily process, including the functions of the digestive, hormonal, and circulatory systems. The most serious complications are those associated with so-called decompensation, which means that the liver can not keep up with the body’s demands. 90% of the liver must be non-functioning for this to occur. Therefore, patients can live for years, sometime decades with few symptoms or problems related to cirrhosis.

Sign of “decompensation” include the following:

- **Bleeding** from the GI tract
  - From Esophageal (swallowing tube) or gastric (stomach) varices
  - From Portal Hypertensive Gastropathy (swelling of the stomach lining)
- **Fluid buildup** in the belly (ascites)
  - Infection of the fluid can be life-threatening
  - Fluid can leak into lungs and cause shortness of breath
- **Medical confusion** (encephalopathy). Impaired brain function occurs when the liver cannot detoxify harmful substances
  - Can lead to coma
- **Liver Cancer**

Cirrhosis is often irreversible, but the rate of progression can be very slow, depending on its cause and other factors. Five-year survival rates are about 85% and can be lower or higher depending on severity.

- For example, for alcoholics with cirrhosis who stop drinking, a survival rate of five years or more can be as high as 85%. For those who continue drinking, the chance for living beyond five years is no higher than 60%.
- In patients with hepatitis B or C, the five-year survival rate after a diagnosis of cirrhosis ranges between 71% to 85%.
- About two-thirds of patients with primary biliary cirrhosis never develop symptoms and can have a normal life span. Once symptoms of liver damage, such as jaundice, occur, however, the average survival time declines. In one study of women diagnosed with primary biliary cirrhosis, about 36% developed symptoms over an 11-year period, and 11% either died or required liver transplantation.

Unfortunately, physicians are usually unable to determine when cirrhosis first occurred, which makes it difficult to determine prognosis.

**How Does Cirrhosis Shorten Your Life?**

1. **Variceal bleeding** or Stomach/esophagus bleeding which can occur without warning
2. **Ascites** or Fluid Build-up on your belly which can become infected

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3. **Encephalopathy** or Medical Confusion which can result in a coma

4. **Liver Cancers** and Tumors

In cirrhosis, liver cell damage slows down blood flow. This causes a backup of blood through the portal vein, a condition called portal hypertension. The effects of portal hypertension can be widespread and serious, including fluid buildup and bleeding.

**Variceal Bleeding.**

One of the most serious symptoms of portal hypertension is the development of varices, which are **blood vessels that enlarge** to provide an alternative pathway for blood diverted from the liver. In about two-thirds of patients they form in esophagus (the “food pipe”). They pose a high risk for rupture and bleeding because of the following characteristics:

- They are thin-walled.
- They are often twisted.
- They are subject to high pressure.
- Internal bleeding from these varices (variceal bleeding) occurs in 20% to 30% of cirrhosis patients. The risk of death from a single episode can reach 70%.

It is important for patients to be screened for esophageal varices with a scoping procedure. A blood pressure medication called a **beta blocker** (Nadolol, propranolol) may decrease the chance of these vessels bleeding.

**Ascites and Fluid Buildup.**

Ascites is fluid buildup in the abdomen. It is uncomfortable and can reduce breathing function and urination. Ascites is usually caused by portal hypertension, but it can result from other conditions. Swelling can also occur in the arms and legs and in the spleen. Although ascites itself is not fatal, it is a marker for severe progression. Infection of this fluid, called peritonitis, can be deadly. Once ascites occurs, only half of patients survive after two years. Some physicians even believe that ascites signals the need for liver transplantation, particularly in alcoholic cirrhosis.

Nearly all patients with ascites can benefit from the following measures:

- Restricting salt. (Nearly **Everything** a person eats has salt in it! Start reading labels and calculating <2000 mg of sodium a day.)
- Abstaining from alcohol. (Sometimes abstaining from alcohol is enough to reverse this complication.)
- Taking diuretics, usually spironolactone (Aldactone) and furosemide (Lasix). Previously, spironolactone was usually given alone, but experts now use it by itself only in patients with minimal fluid buildup. Patients should be monitored carefully for dehydration and high or low potassium levels, kidney failure, or encephalopathy. Weight loss from diuretics usually should not exceed 1 or 2 pounds per day, but there is no limit for patients with massive swelling.

**Mental Impairment and Encephalopathy**

Mental impairment is a common event in advanced cirrhosis. In severe cases, the disease causes encephalopathy (damage to the brain), with mental symptoms that range from confusion to coma and death. A combination of conditions associated with cirrhosis causes this serious complication:
Buildup in the blood of harmful intestinal toxins, particularly ammonia.

An imbalance of amino acids that effect the central nervous system.

Encephalopathy is often triggered by certain conditions, including the following:

- Gastrointestinal bleeding.
- Constipation.
- Infection.
- Surgery.
- Dehydration.
- Narcotic and Sedative Drugs.

Symptoms of Encephalopathy. Early symptoms of hepatic encephalopathy include sleep-wake reversal (wanting to sleep all day and stay up all night), forgetfulness, unresponsiveness, and trouble concentrating. Sudden changes in the patient’s mental state, including agitation or confusion, may indicate an emergency condition. Other symptoms include bad fruity-smelling breath and tremor. Late stage symptoms of encephalopathy are stupor and eventually coma.

The first step in managing encephalopathy (damage to the brain) is to treat any precipitating cause, if known, such as:

- High ammonia levels.
- Bleeding.
- Low oxygen.
- Dehydration.
- Infection.
- Use of sedatives.

Ammonia is the leading toxin in causing encephalopathy related to cirrhosis. Mild encephalopathy is managed by directing therapy toward eliminating ammonia in the intestine:

- Lactulose (Cephulac, Chronulac, Constulose, Duphalac, Enulose) and lactitol, known as disaccharides, help lower blood ammonia levels by binding the toxins and allowing the bowels to flush the bound toxins out of the body. Simply having 2-3 bowel movements a day will not BIND to the toxins. Lactulose must be titrated up or down for 2-3 bowel movements in 24 hours. Too many bowel movements will cause dehydration and risk confusion and kidney failure.
- Antibiotics, such as metronidazole, rifamycin, Xifaxin or neomycin, are effective in reducing levels of ammonia-producing bacteria in the intestine, although long-term use of these drugs can cause toxic side effects.
- Adding non-ammonia producing bacteria to the intestine, including L. acidophilus and E. faecium, is showing promise as a safe and effective treatment.

Liver Cancer

Cirrhosis greatly increases the risk for liver cancer, regardless of the cause of cirrhosis. About 4% of patients with cirrhosis caused by hepatitis C develop liver cancer some time in their life. In Asia about 15% of people who have chronic hepatitis B develop liver cancer.
Lab Tests
Certain blood tests are used to determine liver function. They include the following:

- **Serum albumin** concentration. Albumin is a protein the liver normally makes. Low levels show decreased liver function.
- **Prothrombin time (PT)/INR**. The PT/INR test measures in seconds the time it takes for blood clots to form. The liver makes blood clotting factors. Higher INR means thinner blood and worse liver function.
- **Bilirubin**. Indicative of liver damage, bilirubin, a red-yellow pigment is normally metabolized in the liver and then excreted in the urine. In patients with hepatitis, the liver cannot process bilirubin, and blood levels of this substance rise, sometimes causing jaundice.

The results of these tests along with the presence of specific complications (ascites and encephalopathy) are used for calculating the severity of cirrhosis.

The MELD score to determine where a patient is on the transplant list uses the INR, Total Bilirubin and Creatinine (a measure of kidney function).

Other Tests Used to Detect Complications of Cirrhosis
*Paracentesis*. If ascites is present, paracentesis is performed to determine its cause. This procedure involves using a thin needle to withdraw fluid from the abdomen. The fluid is tested for different factors to determine the cause of ascites:

- Bacteria cultures and white blood cell counts. (These are used to determine the presence of infection.)
- Protein levels. Low levels of protein in the fluid plus a low white blood cell count suggest that cirrhosis is the cause of the ascites.

*Screening for Liver Cancer*. Patients with cirrhosis are usually screened for liver cancer using ultrasound and tests for a substance called alpha-fetoproetin (AFP). Screening is not necessary in patients without cirrhosis.

WHAT LIFESTYLE FACTORS CAN HELP MANAGE CIRRHOSIS?
A healthy lifestyle is particularly important for people with cirrhosis.

Dietary Factors

**If Ascites is present**: **Salt restriction is the most important lifestyle change.**

*Sodium/Salt* Less than 2000mg per day. Salt is in EVERYTHING. From soda to soup. Tips to avoid extra sodium- NEVER use the salt shaker or a salt substitute. NEVER eat canned vegetables, canned soups, crackers, chips, sausage, bacon, sandwich meat, processed cheeses, frozen meals. Read ALL labels.

   - *Do NOT use salt substitutes!*!! These contain potassium chloride instead of sodium chloride and may make a person’s potassium to high and put them at risk for sudden cardiac death!
Healthy Foods. Because important antioxidant vitamins are depleted in the cirrhotic liver, cirrhosis patients should maintain a diet rich in fresh fruits, vegetables, and whole grains.

Antioxidant Supplements. There is some preliminary laboratory evidence that various antioxidant supplements including vitamin E, selenium, and S-adenosylmethionine (SAMe) may help protect against liver damage and cirrhosis. Supplements, however, are not recommended for people with liver disease except with the advice of a physician. A multi-vitamin without iron is usually recommended (Centrum Silver type). Some vitamins, such as vitamins D and A, are metabolized in the liver and can be toxic.

Iron Restrictions. Elevated iron levels have been associated with cirrhosis from many causes. Patients should avoid iron-rich foods, such as red meats, liver, spinach and iron-fortified cereals and should avoid cooking with iron-coated cookware and utensils.

Supplemental Nutritional Products. Supplemental nutritional beverages may be helpful, particularly for patients with both alcoholism and cirrhosis. In one study, patients with both alcoholism and cirrhosis drank Ensure every day as a supplement to their regular diet. After six months they showed significant improvement in many signs of overall health compared to those who didn’t consume the beverage.

Pain Medicine
- It is okay to use Tylenol (acetaminophen) as long as a person is not drinking. However, you must be very careful not to use more than 2 grams in 24 hours (regular strength 325mg = 1 tablet every 4 hours or extra strength 500mg= a total of 4 tablets in 24 hours).
- Do not use ibuprophen/advil/aleve/naprsyn/nuprin or anything with similar ingredients as this may cause stomach bleeding, worse ascites (fluid on the belly) and kidney problems.
- Avoid narcotics as much as possible as they may cause confusion. If they must be use, use smallest dose as far apart as possible, because a cirrhotic liver will not “use up” the drugs as fast as a normal liver.

Limiting Fluids
Fluid restriction is not usually necessary, but patients with severe ascites should discuss limiting fluid with their physicians.

Vaccinations
- Get annual Flu shots
- Ask your physician about vaccinations against hepatitis A & B

Warnings on Alternative and So-Called Natural Remedies
It should be strongly noted that alternative or natural remedies are not regulated and their quality is not publicly controlled. In addition, any substance that can affect the body’s chemistry can, like any drug, produce side effects that may be harmful. Even if studies report positive benefits from herbal remedies, the compounds used in such studies are, in most cases, not what are being marketed to the public.
There have been a number of reported cases of serious and even lethal side effects from herbal products. In addition, some so-called natural remedies were found to contain standard prescription medication.

The following warnings are of particular importance for people with liver disease:

- Kava kava (an herb used for anxiety and tension) can be toxic to the liver and cause severe hepatitis and even liver failure if taken excessively.
- Black licorice (not red) can increase blood pressure and may be harmful in people with hypertension.

The following website is building a database of natural remedy brands that it tests and rates. Not all are available yet. http://www.ConsumerLab.com

The Food and Drug Administration has a program called MEDWATCH for people to report adverse reactions to untested substances, such as herbal remedies and vitamins (call 800-332-1088).

**Liver Transplantation**

Liver transplantation may be indicated in the following patients:

- Those who have developed life-threatening cirrhosis and who have a life expectancy of more than 12 years.
- Patients with liver cancer that has not spread beyond the liver may also be candidates.

Survival rates after transplantation are similar among those who have hepatitis B, hepatitis C, or alcoholic liver disease. Current five-year survival rates after liver transplantation are between 60% and 80%. Patients also report improved quality of life and mental functioning after liver transplantation. Patients should seek medical centers that perform more than 50 transplants per year and produce better-than-average results.

At the time of this report, more than 17,000 patients were waiting for a liver transplant.

Liver Transplantation in Patients with Hepatitis. One of the primary problems with many hepatitis patients is recurrence of the virus after transplantation.

- One study of patients with hepatitis C reported five-year risks of 80% for viral recurrence and 10% for cirrhosis.
- Viral recurrence is also high in hepatitis B patients. Recurrence in hepatitis B has been significantly reduced with the use of monthly infusions of hepatitis B immune globulin (HBIG), with or without lamivudine. Life-long administration may be necessary. Lamivudine or other hepatitis B drugs may also be helpful in preventing recurrence of hepatitis B after liver transplantation in children as well as adults.

**Liver Transplantation in Autoimmune Liver Diseases**

Patients who require transplantation for primary biliary cirrhosis are those who develop major complications of portal hypertension and liver failure or who have poor quality of life and short survival without the procedure. Patients with primary biliary cirrhosis may be at higher risk for early rejection of the transplanted organ than patients with other forms of cirrhosis.

Rejection is also high after transplantation for autoimmune hepatitis. In one study three-quarters of the patients experienced organ rejection, and half required retransplantation within a year in one study. Autoimmune hepatitis recurred in 25% of patients studied.
Liver Transplantation in Alcoholism. There is considerable controversy over whether liver transplantation should be performed in alcoholics with cirrhosis who are unlikely to abstain. One French study reported no differences in survival, transplant rejection, and other indicators of success and failure after transplantation between alcoholics and non-alcoholics and between alcoholics who abstained and those who relapsed after the procedure.

Where Else Can Help for Cirrhosis Be Found?
American Association for the Study of Liver Diseases. Call (202) 429-5179.
American Liver Foundation: www.liverfoundation.org. Call (800) GO-LIVER.
Centers for Disease Control and Prevention, Hepatitis Branch: www.cdc.gov/ncidod/diseases/hepatitis. Call (888) 4HEPCDC.
Hepatitis Foundation International: www.hepfi.org. Call (800) 891-0707 or (973) 239-1035.

Information on Primary Biliary Cirrhosis
Primary Biliary Cirrhosis Organization: pbcers.org.

Other Web Sites
The journal Hepatology: www.hepatology.org.