

a series of articles
written by medical
professionals about
the management
and treatment of
hepatitis C

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Cirrhosis in Chronic Hepatitis C Infection

Diagnosing cirrhosis

Cirrhosis is the presence of large amounts of scar tissue in the liver as a result of many years of liver inflammation and injury. Cirrhosis is usually diagnosed by doing a liver biopsy. The normal liver has no evidence of scar tissue (figure 1). When bands of scar tissue develop and surround groups of liver cells (also known as regenerative nodules), the diagnosis of cirrhosis is established (figure 2). The liver biopsy may miss the diagnosis of cirrhosis if the sample obtained is too small or it is fragmented.

In some cases, a liver biopsy is not performed and the presence of cirrhosis is presumed based on laboratory test results and physical exam findings that suggest advanced liver disease. In cases of advanced cirrhosis, a liver biopsy may be contraindicated as the likelihood of complications is increased.

There are many causes of cirrhosis. Virtually any liver disease that persists for years may eventually lead to the formation of cirrhosis. Chronic hepatitis C is a common cause of cirrhosis.

Cirrhosis in hepatitis C infection

Only the minority of patients with hepatitis C infection progress to cirrhosis. Studies have shown that 20% to 25% of people with hepatitis C will develop cirrhosis (1). There are some individuals that are more likely to progress to cirrhosis than others (2). The current or past use of significant amounts of alcohol is the single most important factor in accelerating progression to cirrhosis (3). For this reason, we recommend that all patients with chronic hepatitis C abstain totally from alcohol.

Other factors that may increase the likelihood of progression to cirrhosis include co-infection

with HIV (human immunodeficiency virus) and/or hepatitis B virus. Recent research suggests that excessive iron in the liver may also accelerate progression to cirrhosis (4). In some patients, progression to cirrhosis occurs despite none of these factors being present. Virus-specific factors or the type of immune response to the infection may be responsible for the progression to cirrhosis in these individuals.

More recently it has been observed that progression to fibrosis (scar tissue) and cirrhosis appears to accelerate after age 45. The reasons for this are not clear, but it is suspected that changes in the immune response to the hepatitis C infection may cause increased fibrosis after age 45 (5). This is another reason why we are becoming more aggressive in treating hepatitis C in young people, even if fibrosis has not yet developed.

Factors that are associated with a lower likelihood of progression to cirrhosis include young age at time of infection, female gender, no history of alcohol use and past treatment with interferon. It should be noted that the genotype of the virus and the viral load have no relationship whatsoever to the development of cirrhosis.

What are the symptoms of cirrhosis?

In early cases of cirrhosis, there are no specific symptoms

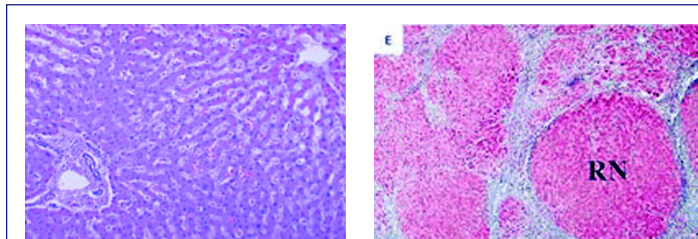


Figure 1.
Normal Liver. No significant scar tissue is present.

Figure 2.
Cirrhosis. Bands of scar tissue (shown in blue) surround groups of liver cells (shown in pink). RN = regenerative nodule

that would make the physician suspect cirrhosis. At an early stage, even laboratory tests may not show evidence of cirrhosis. Currently we do not have an accurate way of diagnosing cirrhosis by doing a blood test. Even though there is a commercially available blood test for detecting advanced fibrosis in the liver, the accuracy of this test in patients with hepatitis C is still unknown, and currently it is unable to differentiate cirrhosis from less-advanced stages of fibrosis.

As the cirrhosis becomes more advanced, symptoms from the complications of cirrhosis may develop. By this time, laboratory test abnormalities suggestive of decreased liver function (abnormal levels of bilirubin and albumin; and abnormal coagulation parameters) also develop. Complications from cirrhosis include ascites, variceal bleeding, encephalopathy and liver cancer.

The severity of the cirrhosis is determined based on laboratory test results and findings on physical exam. The liver biopsy plays no role in determining the severity of the cirrhosis. Factors that are taken into account to determine the severity of cirrhosis include the serum albumin (albumin is a protein produced by the liver), the PT or INR (measures the ability of the blood to clot) and the level of

serum bilirubin (bilirubin is a substance excreted by the liver, which, when it accumulates, causes jaundice). In addition, the presence or absence of ascites (fluid accumulation in the abdomen) and encephalopathy (confusion caused by toxins not filtered by the liver) are also used to grade the severity of cirrhosis.

A point system known as the Child's-Pugh-Turcotte score (CPT score) has been devised to determine the severity of the cirrhosis. Depending on the total score, a patient is classified as Class A (early cirrhosis) through Class C (advanced cirrhosis).

Prognosis of cirrhosis

Patients with early cirrhosis (CPT Class A) from hepatitis C infection who have no complications from cirrhosis have an excellent prognosis. Even without treating the hepatitis C infection, 10 years after diagnosing cirrhosis the majority (>75%) continue to do well with no liver-related complications (6). It is believed that treatment of the hepatitis C with interferon will provide an even better prognosis.

The diagnosis of early cirrhosis should not be considered a fatal diagnosis. Most patients will continue to do well for decades. There is no reason to refer a person with cirrhosis to a liver transplant center unless the cirrhosis is

advanced (CPT class C) or complications from cirrhosis have developed.

Medical Care of the Patient With Cirrhosis from Hepatitis C

The medical care of the hepatitis C patient with well compensated (CPT class A & B) is designed to keep them healthy as long as possible and to monitor for possible complications of cirrhosis and intervene early when they develop. The treatment of the hepatitis C infection should also be addressed. Patient education, preventive medicine and routine monitoring every 6 months by a gastroenterologist or hepatologist are the main components of the care of these patients.

Patient Education

Alcohol use: All patients with cirrhosis should totally abstain from alcohol use. It is not known if there is a safe level of alcohol intake for patients with liver disease. Alcohol is a well known toxin to the liver and total abstinence for patients with liver disease is mandatory.

Acetaminophen use: Contrary to popular belief, acetaminophen (the active ingredient in Tylenol®) is perfectly safe for patients with cirrhosis as long as it is used cautiously. Any person who drinks alcohol regularly should not consume any acetaminophen. For patients with early cirrhosis (CPT class A or B), the use of acetaminophen is safe as long as the recommended dose is not exceeded (1,000 mg per dose, repeated no more often than every 6 hours). Patients with more advanced cirrhosis should take only 1/2 of the recommended dose. In fact, for patients with cirrhosis, acetaminophen, when used as described, is the preferred medication for the treatment of pain.

Vibrio vulnificus Infection: *Vibrio vulnificus* is an organism that lives in salt-water, particularly

in the Southeast Atlantic and the waters of the Gulf of Mexico. However, infections have been reported from all coastal areas in the United States. This infection can be acquired by eating raw or poorly cooked seafood (raw oysters, sushi) or by going in sea water with open skin sores. In patients with cirrhosis this infection can be lethal. Patients with cirrhosis should not eat raw seafood and should abstain from going in the ocean if open sores are present.

Multivitamin use: Many patients with cirrhosis take multivitamins in an attempt to feel better. While there is no evidence that multivitamins make people with cirrhosis feel any better, taking too many vitamins may worsen the liver disease. Vitamin A is toxic to the liver, patients with cirrhosis should not take more than 5,000 Units per day. Vitamin A as beta-carotene is not toxic to the liver and can be taken in any amount. Vitamin E, if taken in doses over 1,200 IU per day could cause bleeding. Iron promotes the formation of scar tissue in the liver. Persons with cirrhosis who are not iron deficient should not take multivitamins with iron.

Preventive Care

Keeping patients with cirrhosis healthy is important and can often be achieved if we take measures to prevent other diseases that can affect the liver or threaten the health of patients with cirrhosis. Often, the medical care of these patients is centered on the liver disease and doctors may forget to screen for preventable diseases that affect other organs.

Immunizations: Patients with hepatitis C infection should be immunized against hepatitis A and hepatitis B infections unless blood tests show that they are already immune. Influenza vaccine (flu shot) should be administered once a year. Pneumococcal vaccination (prevents the most common type

Child-Pugh-Turcotte Criteria

	1 Point	2 Points	3 Points
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Bilirubin (mg/dL)	<2	2-3	>3
Ascites	None	Minimal	Moderate
Encephalopathy	None	Grade 1-2	Grade 3-4
PT (sec prolonged)	<4	4-6	>6
INR	<1.7	1.7-2.3	>2.3

Class A: 5-6 points; Class B: 7-9 points; Class C: 10-15 points

of bacterial pneumonia) should be given once every 5 years. It has been shown that patients with cirrhosis who develop influenza or pneumococcal pneumonia are much more likely to die than otherwise healthy people who develop these diseases.

Dental examination: Gingivitis or infection of the gums can seed bacteria into the blood stream. In healthy individuals this is of minor consequence, but in cirrhotics, it can cause severe infections. Moreover, if a patient with cirrhosis needs a liver transplant, the presence of gingivitis will prevent him or her from receiving a liver. We recommend our patients with cirrhosis to visit a dentist once a year. As the liver disease becomes more advanced (CPT Class B or C) we recommend dental exams every 6 months.

Prevention of Bleeding: As the cirrhosis progresses, blood is unable to pass through the liver on its way to the heart. As a result, the blood finds other ways of getting to the heart. One of these paths could be through veins in the esophagus and stomach. As a result these veins become engorged and may rupture, leading to severe internal bleeding, a complication that can cause death. These large vessels are called varices. People with early cirrhosis have a 5% to 45% chance of having varices, the risk increases to over 60% in people with advanced cirrhosis. Varices can be detected by doing upper endoscopy, a test that examines the inside of the esophagus and stomach. If varices are found, medications or endoscopic treatment can reduce the chances of bleeding (7).

Detection of liver cancer: Cirrhosis predisposes to liver cancer. Liver cancer, when diagnosed early, can be treated or resected, or liver transplantation can be offered (8). Early liver cancer produces no symptoms. For this reason we recommend a liver

ultrasound examination and a blood test measuring levels of alfa-fetoprotein every 6 months. Elevated levels of alfa-fetoprotein or more advanced liver disease may require an abdominal CT scan (computerized tomography) or MRI (Magnetic Resonance Imaging) study to detect small liver cancers.

General Health Maintenance: When patients with liver disease see their physicians, their medical care is centered on the liver disease. Often, other preventive care issues are neglected. Patients with liver disease should see their primary care physician on a regular basis to be sure these items are taken care of. Screening for breast, uterine, prostate and colon cancer in appropriate individuals should be regularly scheduled. Patients with hepatitis C and cirrhosis have a higher incidence of diabetes. Monitoring and treating diabetes is important to maintain good health.

Treatment of the hepatitis C infection

The presence of cirrhosis is not a contraindication to treating the hepatitis C infection. Most patients with early cirrhosis can be safely treated with interferon and ribavirin. Eradication of the virus results in improvement in liver function and is associated with a decreased risk of liver cancer and liver failure. Even if the virus is not eradicated with treatment, there is evidence that taking interferon and ribavirin reverses the liver disease and delays the onset of liver failure and liver cancer. For patients who were not able to clear the virus with treatment, long-term treatment with reduced dose interferon may be beneficial in delaying the onset of complications of cirrhosis and is generally well tolerated.

Once advanced cirrhosis is present, treatment with interferon and ribavirin may not be possible. Patients with anemia, low platelet or white cell counts or complications from cirrhosis such as ascites

and encephalopathy may not be able to tolerate treatment. In those cases, evaluation for liver transplantation instead of treatment with interferon and ribavirin may be advised.

Summary

Only a minority of patients with hepatitis C infection progress to cirrhosis. Cirrhosis is usually diagnosed by performing a liver biopsy. Early cirrhosis is not associated with any specific symptoms or laboratory test abnormalities. Once cirrhosis develops, patients usually live for decades without complications. Successful treatment of the hepatitis C infection will decrease the chance of developing complications from cirrhosis. Patients with cirrhosis should take steps to maintain good health, receive adequate immunizations and regular medical care. Close monitoring by their primary care physician as well as a gastroenterologist or hepatologist is important for the early detection of possible complications.


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