
a series of fact sheets written
by experts in the field of liver
disease

Disease Progression: Symptoms and Complications of Cirrhosis

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After many years of infection with hepatitis C the liver can become severely scarred. The process starts with inflammation which can lead to light scarring—fibrosis. Over time (usually many years) the liver can become extensively scarred—this is called cirrhosis. Cirrhosis is classified into two types—compensated and decompensated.

Compensated cirrhosis is defined as a liver that is heavily scarred but can still perform most of the important chemical functions that keep the body running smoothly. In fact, people may not even know that the liver is damaged because many people will have only a few or non-specific symptoms. For this reason, it is important for everyone with hepatitis C to be monitored on a regular basis. The need for constant monitoring is even more important once someone develops cirrhosis since HCV disease progression and complications of cirrhosis speed up or accelerate.

Many people mistakenly believe that once someone develops cirrhosis it is an automatic death sentence.

This is not necessarily the case. People with compensated cirrhosis can live for a long time, and it is the ideal time to make healthy lifestyle changes and seek treatment with HCV medications that will hopefully stop, slow down or even reverse some of the damage that hepatitis C has caused.

Decompensated cirrhosis means that the liver is severely scarred and damaged. At this stage HCV treatment is not usually recommended because treatment with interferon can quicken or accelerate the disease progression process—sometimes very quickly. Having said this, people with decompensated cirrhosis are the most in need of immediate HCV medical treatment. Treatment with HCV medications in people with decompensated cirrhosis is most successful when it is conducted in a liver transplant center where patients can be regularly monitored to watch out for and prevent accelerated HCV disease progression. Although the studies have only included a small number of patients, several have yielded surprisingly successful outcomes.

The symptoms of decompensated cirrhosis can be serious and have life-threatening consequences, but many of them can be successfully managed. The most common conditions and symptoms include (in alphabetical order):

Ascites & Edema

A complication of portal hypertension is the accumulation of fluid in the abdominal cavity, called ascites. Albumin is the substance that is made by the liver that helps to maintain blood volume. The formation of ascites is a two-pronged breakdown—first, the liver does not produce enough albumin; second, blood is not able to pass through the liver because of the scarring and the body tries to compensate by equalizing the pressure by reducing the volume of blood. During this process plasma leaks out of vessel walls into the abdominal cavity. Another complication is when there is excess fluid in tissue – called edema. This usually affects the lower extremities.

Ascites is treated by reducing the amount of sodium (salt) in the body through diet and medications called diuretics (spironolactone and furosemide). If sodium reduction and the use of diuretics doesn't work, a large-volume paracentesis (LVP) is performed that removes the fluid from the abdominal cavity through a catheter inserted into the abdominal cavity. At the same time albumin is given intravenously to help normalize blood volume and to help stop the 'leakage' of fluid into the abdominal cavity. In addition, a procedure called TIPS (see bleeding Varices) is used to increase the flow of blood through the liver which will help to maintain normal blood volume.

A potential complication of ascites is spontaneous bacterial peritonitis (SBP). This can occur when the ascitic fluid becomes infected with bacteria. Because SBP can be severe and life-threatening it is treated with antibiotics. If a person is deemed to be at risk for SBP, drugs are given before infection occurs—prophylactically.

Bleeding Varices

Another complication of portal hypertension is that the blood that normally flows through the liver is forced into smaller veins (especially those veins in the esophagus and stomach). The veins will become stretched and, due to the increased pressure produced by portal hypertension, these veins can rupture causing hemorrhage. Since the liver is not producing enough proteins to help blood clot, people can have massive bleeding episodes.

Treatment of bleeding varices consists of using beta-blockers (propranolol or nadolol), esophageal variceal band ligation (banding the veins that will or have ruptured) along with various medications that will prevent infection and decrease the blood flow in the portal vein. A combination approach using band ligation and beta-blockers has been shown to work better than using just one type

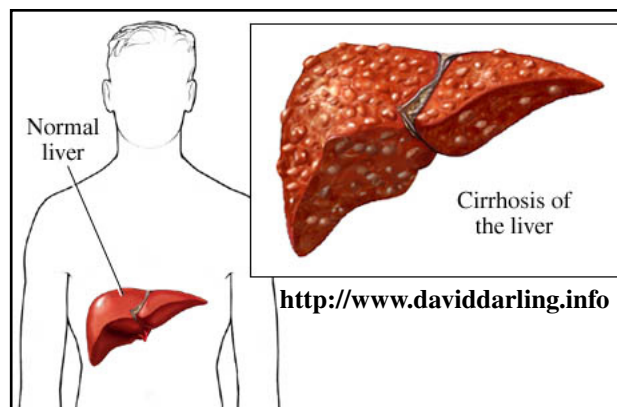
of treatment. Another procedure uses transjugular intrahepatic portosystemic shunts, or TIPS, which are placed between the portal vein and the hepatic vein in the liver to increase the flow of blood through the liver to reduce the degree of complications caused by portal hypertension.

Bruising and Bleeding

The liver manufactures proteins that help blood to clot. When the production of these proteins is reduced or stopped easy bruising and bleeding can occur. One example would be frequent nose bleeds. There are currently no medications approved to help produce the proteins that help the blood to clot, but there are some drugs in development that look promising.

Gynecomastia

Another possible complication of liver disease is enlarged breasts in men, also called gynecomastia. In addition to liver disease causing gynecomastia certain medications, alcohol, street drugs, other health conditions, malnutrition and certain herbal products can also cause it. It occurs in people with cirrhosis because the liver is unable to effectively regulate testosterone (male hormone) and estrogen (female hormone). A common misconception is that only males produce testosterone and females produce estrogen, but both males and females produce both hormones. The job of the liver is to regulate the hormones based on a person's gender. Gynecomastia is sometimes confused with fatty breast tissue (false gynecomastia), but is not the same condition. The symptoms of gynecomastia include swollen or enlarged breast tissue and tenderness. Men may also lose chest hair and testicles may shrink.



Hepatic Encephalopathy

One of the most important functions of the liver is to filter out or remove toxins such as ammonia. If the

liver is badly damaged these toxins accumulate in the blood stream and travel to the brain, which can lead to encephalopathy. The symptoms of encephalopathy include changes in sleep patterns (reversal of sleep cycle—insomnia at night and daytime sleepiness), difficulty concentrating and loss of memory. A person may become confused and disorientated. Severe symptoms include changes in personality, coma, swelling of the brain and possibly death.

Treatment of encephalopathy consists of the use of disaccharides such as lactulose, and antibiotics such as neomycin and rifaximin to flush out the ammonia from the body. Rifaximin recently entered into phase III studies for the treatment of hepatic encephalopathy. In people with minimal hepatic encephalopathy yogurt that contains live bacteria has also been found to help.

Infections

When cirrhosis develops the liver's ability to produce immune factors is impaired. At this point a person should be monitored very carefully, and medications should be used to help prevent common infections from getting severe.

Itching (Pruritis)

When the skin itches it is called pruritus. It can be caused by many factors including medications, allergies, dry skin, etc. Excessive itching in someone with decompensated cirrhosis may indicate that bile excretion from the liver is blocked and that bile salts are being deposited in the skin.

Jaundice

In the late stages of decompensated cirrhosis the liver is unable to process the by-product of old red blood cells, called bilirubin. Instead of the bilirubin being excreted into the bile and eliminated from the body via feces, it will accumulate in the blood. The symptoms of jaundice include yellowing of the skin, whites of the eyes, pale stools and brownish urine.

Kidneys

When the liver is damaged it can also affect other

organs like the kidneys. The term used for this is hepatorenal syndrome or HRS. HRS is a life-threatening condition caused when a failing liver affects the flow of blood into the kidneys. Treatment of HRS is usually a combination of intravenous albumin (stabilizes blood volume) and drugs to stabilize pressure within arteries and veins.

Liver cancer

Liver cancer, or hepatocellular carcinoma, can develop in someone with severe fibrosis or cirrhosis. Treatment of liver cancer can involve chemotherapy, resection (to remove the tumor) and, if the cancer hasn't spread beyond the liver, liver transplant.

Malnutrition

When nutrient rich blood from the intestines is blocked from entering the liver malnutrition can occur. Symptoms of malnutrition include fatigue, dizziness, weight loss and impaired immune response. Treatment of malnutrition typically involves the replacement of the missing nutrients and treatment of the symptoms as required.

Menstrual Irregularities

Women may experience changes in their menstrual cycles because the liver isn't able to regulate the balance between testosterone and estrogen hormones.

Nail changes

The appearance of nails (finger, toe) may change—the nails may be more curved and the appearance may be more white than pink.

Portal hypertension

Portal hypertension occurs when the liver is so scarred and damaged that blood which normally flows into and out of the liver is restricted. The blood is blocked from entering the liver and it can back up causing a form of high blood pressure in one of the main veins of the liver called the portal vein. Portal hypertension can lead to a variety of complications many of which are listed in this article.

Please see bleeding varices for a description of the various treatment approaches that also pertain to the treatment of portal hypertension.

Spider angioma (Nevi)

Spider nevi are commonly found on the face, neck, upper trunk and arms. The majority of cases are seen in people with liver disease, but they can also occur in women who are taking hormones. In people with liver disease, spider nevi are caused by the inability of the liver to process or detoxify estrogen, which leads to high levels of estrogen in the blood. Spider nevi appear as a red dot with veins radiating from the central spot (like a spider).

Sepsis

Sepsis refers to a bacterial infection in the blood or body tissues that can be caused by the inability of the liver to fight off a severe bacterial infection. Severe sepsis is life-threatening.

Signs and Warnings of Decompensated Cirrhosis

If you have loved ones or clients that have some of these symptoms they should seek medical care as soon as possible.

- Jaundice—yellowing of the skin and whites of the eyes
- Easy bruising or excessive bleeding episodes (especially frequent nose bleeds)
- Ascites – you can actually hear the ascetic fluid if a person moves from side to side. Legs and feet will also be swollen from edema
- Mental problems—inability to concentrate, loss of intelligence, sleepiness, changes in behavior, violent episodes
- Flapping—when hands are bent at the wrist, the hands will flap
- Severe itching (pruritis)
- Severe weight loss

Be Sure to Check Out the Other Factsheets in This Series:

HCV Disease Progression

- *Acute Hepatitis C*
- *Cirrhosis*
- *Fibrosis*
- *Steatosis*
- *Liver Transplantation*

For more information about hepatitis C, hepatitis B and HCV coinfections, please visit www.hcvadvocate.org.

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