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

HCSP FACT SHEET

HCV ADVOCATE

•HCV DISEASE PROGRESSION•

Overview of HCV Disease Progression

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Foreword

If acute hepatitis C infection (HCV) becomes a chronic infection it can eventually progress to a more serious disease. Over time it can produce fibrosis (light, moderate and severe scarring), cirrhosis (extensive scarring), decompensated cirrhosis (potentially life-threatening scarring), liver cancer, the need for a new liver (liver transplant) and for some it could lead to death. This fact sheet will discuss the various stages of hepatitis C disease progression.

Acute Hepatitis C

According to the CDC, there are approximately 18,000 acute infections of hepatitis C annually in the United States. People exposed to the hepatitis C virus usually develop detectable HCV antibodies within one to two months after exposure. In the first two weeks of the acute phase HCV RNA (viral load) quickly rises (5 to 10 million IU/ml [international units]), just before the ALT levels starts to peak and symptoms begin to appear. The ALT levels will begin to rise as high as 1000 IU/mL, indicating liver inflammation. If any symptoms do appear, they can last from 3 to 12 weeks after exposure.

Only about one-third of people initially infected with hepatitis C develop symptoms. These may include flu-like symptoms, jaundice, fever, and nausea.

The people who develop symptoms are more likely to clear the virus spontaneously. The reasons that some people spontaneously clear HCV is not completely understood, but some studies have shown that a broad-based immune response by CD4 and CD8 T-cells to the hepatitis C virus helps to eliminate the virus.

There is also some evidence that other factors influence spontaneous clearing; women are more than twice as likely as men to clear the virus spontaneously. White men are also twice as likely to clear acute infection compared to Black men. Age and immune status also affect the rate of spontaneous resolution. The older

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you are, and if the immune system is compromised, the less likely a person will spontaneously clear an acute infection.

It is hard to identify people with acute infection due to the lack of symptoms and viral markers. When acute infection can be detected and treated, the cure rate can be as high as 90%.

Fibrosis

Liver fibrosis refers to the accumulation of tough, fibrous scar tissue in the liver. Formation of scar tissue is a normal bodily response to injury, but with fibrosis this healing process goes wrong. When hepatocytes (functional liver cells) are injured due to infection with the hepatitis C virus, the immune system is activated to repair the damage. In a healthy person, the damage is repaired by the immune system. In someone infected with hepatitis C, the damage occurs faster than the body can fix it, and fibrosis develops.

Fibrosis Risk Factors

Liver fibrosis does not occur at the same rate in all individuals, and in some people with chronic hepatitis C or B fibrosis remains stable or may even regress over time. Several factors influence fibrosis progression. Fibrosis occurs more rapidly in men than in women and also in older people – particularly those over age 50. Progression does not seem to be linear—that is the process appears to accelerate as more damage occurs. Immune system compromise, for example due to coinfection with HIV or use of immunosuppressive drugs after a liver transplant, also has been shown to accelerate fibrosis. Heavy alcohol consumption is strongly associated with worsening fibrosis and cirrhosis. Finally, studies indicate that steatosis (fatty liver) and insulin resistance are associated with more rapid and severe fibrosis. In contrast, HCV viral load does not appear to have much effect on fibrosis progression. HCV genotype 3 also is associated with the formation of steatosis, but the exact mechanism of action is not completely understood.

Genotype 3 has also been found to increase the rate of fibrosis, cirrhosis, and liver cancer compared to HCV genotype 1.

Measuring Fibrosis

There are many tests to measure fibrosis and cirrhosis. The most common tests are the percutaneous liver biopsy. The liver biopsy is an outpatient procedure that involves inserting a biopsy needle through the ribcage into the liver. The liver tissue sample is removed and examined by a pathologist who will issue a report on the health of the liver.

In 2013 the Food and Drug Administration (FDA) approved the Fibroscan. The Fibroscan is a machine that sends vibration waves through the liver to estimate the amount of scarring. There are various blood tests that are also used to indicate the level of damage to the liver. The Fibroscan and blood tests are used together to help diagnose the health of the liver.

Effects of Fibrosis

In the early stages of fibrosis, the liver functions relatively well, and few people experience symptoms. However, as the inflammation and liver injury continue, scar tissue builds up and connects with existing scar tissue, which can eventually disrupt the metabolic functions of the liver. If the disease progresses, it can lead to cirrhosis, a condition in which the liver is severely scarred, its blood flow is restricted, and its ability to function is impaired.

HCV Genotype

In general people infected with HCV genotype 3 have a faster disease progression to cirrhosis and liver cancer than HCV genotype 1.

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Cirrhosis is divided into two categories – *compensated and decompensated.*

Compensated Cirrhosis

Compensated cirrhosis means that the liver is heavily scarred but can still perform many vital bodily functions. Many people with compensated cirrhosis may experience few or no symptoms. It is critical for people to take the necessary steps to make sure that they are receiving the appropriate medical care, which includes HCV therapy to help slow down or stop the disease progression process. The current interferon-free HCV medications can cure most people with compensated cirrhosis.

Decompensated Cirrhosis

Decompensated cirrhosis means that the liver is extensively scarred and unable to function properly. People with decompensated cirrhosis eventually develop many symptoms and complications that can be life-threatening. The current interferon-free medications can cure people of HCV even those with decompensated cirrhosis, but careful monitoring is critical.

Symptoms and Complications of Decompensated Cirrhosis

Patients with decompensated cirrhosis can develop a variety of symptoms such as fatigue, exhaustion, loss of appetite, nausea, jaundice, weight loss, stomach pain, impotence, bruising and bleeding, and other potentially life-threatening symptoms.

Many complications can develop because the liver is unable to perform many of its vital functions.

Complications of cirrhosis can include:

- Portal hypertension—severe scarring can prevent blood from entering or leaving the liver, which can lead to spontaneous bacterial peritonitis (infection), varices (weakened blood vessel in the stomach, esophagus and rectum become stretched and dilated which can result in internal bleeding) and other potentially life-threatening complications. Portal hypertension causes many of the complications below.
- Ascites—accumulation of fluid in the abdominal cavity
- Edema—swelling in the extremities especially in the feet and legs
- Bleeding problems because the liver can not make clotting factors
- Menstrual irregularities and gynecomastia (breast enlargement in men) because the liver is not able to regulate female and male hormones
- Encephalopathy—personality changes, changes in sleep patterns, violent behavior, sluggish movements, drowsiness, confusion, stupor, and coma due to ammonia and toxins that build up in the brain.
- Pruritus—itching can develop that can be debilitating.
- Kidney—function deteriorates to cause various kidney disorders.
- Liver cancer can develop.
- Muscle wasting

When the liver completely breaks down, and it is unable to perform its job, it is called end-stage liver disease. The goal at this stage is to try to manage complications due to a deteriorating liver.

Liver Cancer

Hepatitis C is the leading cause of liver cancer in the United States. Other causes include long-term alcohol consumption, tobacco use, obesity, diabetes anabolic steroids (male hormones) arsenic (from drinking water), toxins, industrial waste, aflatoxins (produced by fungus found in peanuts, corn, grains and nuts).

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Overview of HCV Disease Progression

There are usually no symptoms of liver cancer, but if there are symptoms they may include:

- Pain or discomfort in the upper right side of the stomach
- Pain in the back or right shoulder
- Appetite loss or feeling full after a small meal
- Unexplained weight loss
- Bloated or swollen belly
- Unexplained fatigue or weakness
- Fever
- Bruising, bleeding
- Nausea or vomiting
- Jaundice (yellow skin and eye)
- Dark, tea-colored urine
- Pale, clay - colored stools
- Tremors, confusion, disorientation

Risk Factors / Screening

There are many factors that are taken into consideration when screening for liver cancer. Those at risk for liver cancer are those who have a history of liver cancer, people with cirrhosis, Blacks, Asians, and Pacific Islanders, and people with hepatitis B or C.

People with hepatitis C will be screened every 6 months for liver cancer if they develop advanced fibrosis. There are various screening tests and imaging tests to detect liver cancer.

Treatment

The treatments depend on many factors including the type of cancer, the size of the tumor and how much it has spread within the liver.

Liver Transplantation

There have been many advances and improvements in liver transplantation in the last couple of decades. Now, the overall five-year survival rate is approximately 5%. Unfortunately, people with hepatitis C, do not do as well fare as well as others who receive a liver transplant.

Unfortunately, the number of livers needed far outweigh the demands for liver, and most people are wait-listed for a liver transplant. In the U.S., livers are allocated on a regional basis by the United Network for Organ Sharing (UNOS).

Liver Transplant Procedures

The most common transplant procedure is orthotropic liver transplantation (OLT)—that is the damaged liver is removed, replaced with a new one (usually from a recently deceased donor). The major blood vessels and bile ducts are connected to the new organ.

The MELD (Model for End-Stage Liver Disease) was adopted in 2008 that uses three lab tests–bilirubin, creatinine, and prothrombin time (a measure of blood clotting)–to predict how likely patients are to die. The system is intended to give priority to people who need new livers most urgently, but are still well enough to benefit, rather than those who have been waiting longest.

To address the shortage of deceased donor livers, alternative methods have been developed to increase the liver supply:

- **Split Liver Transplant:** Because of the liver's ability to regenerate itself, a deceased donor liver can be split into two pieces and transplanted into two recipients, with each piece growing into a fully functioning organ.
- **Living Donor Transplant:** A living donor transplant uses a liver segment from a live person, usually a relative, but not always.
- **Lower Quality Livers:** Under some

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circumstances—a poorer quality allograft is preferable to no new liver at all. In particular, a liver from a donor with hepatitis B or C may be given to a recipient who already has the same infection(s).

There have been studies on treating HCV infection pre- and post-transplant that have resulted in medium to high cure rates that lead to good results. Now that we are treating people earlier in the course of their disease the need for liver transplantation as a result of hepatitis C should start to dramatically decrease in the next 5 to 10 years.

Post-Transplant Complications

Liver transplant recipients may experience a number of complications following surgery, including graft rejection, increased risk for infection, and blood vessel or bile duct leakage. Rejection, infection, and recurrence of the original disease–for example, hepatitis C or liver cancer–are the leading causes of post-transplant mortality.

Liver graft rejection may occur either as an acute episode soon after transplantation (usually within the first two weeks) or gradual worsening over a longer period. Signs and symptoms of graft rejection may resemble those of viral hepatitis, including fever, fatigue, weakness, abdominal pain, jaundice, and elevated liver enzymes. Sometimes chronic rejection does not cause symptoms initially but can damage the new liver over time.

Transplant recipients take immunosuppressive drugs to prevent the immune system from attacking the foreign organ. These agents work by altering T-cell activity and cytokine production.

These and other drugs are used in combination regimens, and the mix may change over time. Acute rejection is usually managed with a high dose of steroids. Studies have shown that many patients can safely reduce and eventually stop steroids after the first few months without significantly increasing their risk of organ rejection.

Because the immune function is suppressed, transplant recipients are at increased risk for infection. During the first weeks or months after surgery, when the strongest immunosuppressive regimens are used, patients are prone to develop bacterial infections, viral, and fungal infections.

Transplant patients are susceptible to some of the same opportunistic illnesses affecting people with AIDS, including cytomegalovirus (a virus in the herpes family), pneumocystis pneumonia, toxoplasmosis, and persistent yeast infections. Immune suppression also increases the risk of developing certain cancers.

Some of these infections can be prevented by using prophylactic drugs, and most can be successfully treated. In addition to using antibiotics and other specific medications, doses of immunosuppressive drugs may need to be reduced.

Transplant recipients who do not experience overt organ rejection or develop opportunistic infections may still experience detrimental effects over the long term.

Self-Help Tips:

There are many steps that people can take to stay healthy with hepatitis C:

- Get treated as soon as possible to stop HCV disease progression
- Become your own best advocate

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Overview of HCV Disease Progression

- Eat a healthy diet based on the www.choosemyplate.gov
- Get regular exercise – talk to your medical provider about an exercise program
- Avoid alcohol or at the very least, limit how much you drink
- Don't eat raw or under cooked shellfish
- Get vaccinated against hepatitis A and hepatitis B if you are not already immune
- Be careful when mixing over-the-counter drugs, prescription drugs, herbal supplements and street drugs
- Reduce stress
- Rest when you are tired

Portions of the text were taken from:

Liver Transplantation – an HCSP Fact Sheet, by Liz Highleyman

"HealthWise—Hepatitis C & Liver Cancer (HCC)," by Lucinda Porter, RN

Related publications:

- **An Overview of HCV Diagnostic Tests**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/diagnostic.pdf
- **An Overview of Extrahepatic Manifestations of Hepatitis C**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/Extrahepatic.pdf
- **CAM: Complementary and Alternative Medicine (Overview)**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/CAM_Complementary_and_Alternative_Medicine_Overview.pdf

For more information

- **Americans with Disabilities Act**
  www.ada.gov
- **Centers for Disease Control and Prevention**
  www.cdc.gov
- **National Cancer Institute:**
  www.cancer.gov
- **Mayo Clinic**
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