

HCSP TRAINING MANUAL

SECTION V: DIAGNOSING HCV

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The information in this guide is designed to help you understand and manage HCV and is not intended as medical advice. All persons with HCV should consult a medical practitioner for diagnosis and treatment of HCV.

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DIAGNOSING HCV

Objectives:

- *Be able to discuss the various types of tests used to diagnose HCV*
- *Be able to describe antibody tests and how they are used*
- *Be able to discuss HCV viral load and how viral load tests are used*
- *Be able to discuss the different types of viral load tests*
- *Be able to describe the hepatitis C virus and its lifecycle*
- *Be able to define HCV genotypes and quasi-species*
- *Be able to describe HCV genotype tests and how they are used*
- *Be able to list the various biochemical/ liver function tests*
- *Be able to explain the significance of ALT levels*
- *Be able to describe liver biopsies and how they are used*
- *Be able to describe the four histological stages of liver damage*

Diagnosing HCV: Key Points

- *ELISA test detects HCV antibodies in the blood.*
- *Viral load tests indicate whether HCV is actively replicating.*
- *Genotype tests reveal what type of HCV a person has.*
- *Several different lab values are measured to help determine liver health.*
- *The most common liver enzyme/function test measures ALT levels.*
- *Other liver function tests include AST, AP, GGT, albumin, bilirubin, platelet count, and prothrombin time.*
- *Liver biopsies and non-invasive markers are used to gauge the extent of liver damage.*
- *Viral load tests, genotype tests, liver enzyme/function tests, and liver biopsies can help doctors manage HCV disease progression and decide whether HCV treatment is necessary, whether it is likely to be successful, and whether or not the drugs are working.*

Diagnosing HCV:

General Information

A variety of different tests are used to diagnose hepatitis C and to gauge disease progression. These include tests to determine whether a person has ever been infected with HCV (*antibody tests*), whether they have active HCV infection (*viral load tests*), and what type of HCV they have (*genotype tests*). HCV is a single-stranded RNA virus that was identified in 1989. HCV has six major genetic variants known as genotypes; genotypes 1a and 1b are most common in the United States. Several tests are done in HCV-positive people to measure the health of the liver. These tests are commonly called liver or enzyme/function tests, and they measure the levels of enzymes and other chemicals in the blood. The most common liver enzyme/function test measures alanine aminotransferase (ALT) levels. A *liver biopsy* is used to determine the extent of liver damage; in a biopsy, a small sample of liver tissue is removed with a needle and examined under a microscope. *Imaging tests* such as ultrasound and CT scans can show the general size and structure of the liver. Viral load tests, genotype tests, liver enzyme/function tests, and liver biopsies are all used to help guide HCV management and treatment. Because normal value ranges and test results can vary from lab to lab, it is recommended that the same laboratory be used consistently so that results can be compared over time.

HCV Antibody Tests:

When the body is exposed to HCV, the immune system produces antibodies against the virus. *Antibodies* are proteins that attach to foreign invaders, marking them for destruction by the immune system. These antibodies can be detected by HCV screening tests. Two antibody tests are typically used to detect HCV antibodies. HCV ELISA (enzyme-linked immunosorbent assay) is a simple and sensitive blood test. RIBA (recombinant immunoblot assay) is a second test that is usually done in people without known risk factors after a positive HCV ELISA to confirm the presence of HCV antibodies. It usually takes a few weeks – but may take as long as six months – before the immune system produces enough antibodies to be detected by a screening test. This interval of 2-26 weeks is known as the “*window period*.” If a person is HCV antibody positive, they have likely been infected with HCV; otherwise, they are said to be HCV antibody negative. Most people who completely clear HCV from their bodies will retain anti-HCV antibodies for life.

Sometimes a person will test positive for HCV antibodies when they have never been infected with HCV; this is known as a false-positive result. Conversely, people may

test negative for HCV antibodies when they have in fact been infected with HCV; this is called a false-negative result. Some people test negative and then positive, or vice versa; when this happens, the test results are said to be indeterminate. In some cases, if a person tests negative for HCV antibodies but has symptoms of HCV, or if there is reason to believe they may have been exposed to the virus, a viral load test (described below) may be performed to look for HCV genetic material in the blood.

The signal-to-cut-off (s/co) ratio is a complicated method for determining (with reasonable certainty) that a positive EIA (enzyme immunoassay) result is in fact a true HCV antibody result. The same blood sample that is used for the EIA test is re-tested three times and if it is found that the strength or signal reaches a certain point that there is a 95% chance that the positive EIA test is a true HCV antibody response. This process is used in situations where there may be barriers for someone to having an HCV RNA or viral load test performed to confirm active infection, i.e., lack of money or insurance coverage to pay for the HCV RNA test.

HCV antibody tests are not routinely done, so people who believe they may have been exposed to HCV should ask their healthcare provider for a test. The Home Access® Hepatitis C Test, in which the user pricks their finger to draw a sample of blood with a spring-loaded lancet and sends it to a laboratory for analysis, is also available. Because anonymous HCV testing is not widely available, home tests can be valuable for people who wish to keep their HCV status confidential.

Orasure Quick HCV Rapid Antibody test for whole blood and fingerprick has been approved by the Food and Drug Administration (FDA). Orasure has submitted an application for a CLIA (Clinical Laboratory Improvement Amendments Act of 1988) waiver in order that organizations can conduct field testing. The oral swab application from Orasure is currently being reviewed by the FDA and approval is expected in early 2012 and a CLIA waiver will be approved later the same year. The oral swab technology is similar to the HIV oral rapid test which uses fluid collected from the top and lower gums to detect HIV antibodies.

HCV Viral Load Tests:

HCV Viral Load Tests: Key Points

- *HCV viral load tests measure the presence of HCV in the blood.*
- *HCV viral load may be used to confirm active infection.*
- *HCV viral load tests are used to predict response to treatment and to determine how well HCV medications are working.*

- *The three HCV viral load tests are the PCR assay, the bDNA assay, and the TMA assay.*
- *Correlation of HCV viral load and disease progression has not been shown.*

HCV Viral Load Tests:

General Information

Viral load tests are blood tests that measure HCV ribonucleic acid (RNA) in the blood. The presence of viral RNA indicates that the virus is actively replicating (reproducing and infecting new cells). A viral load test is usually first done after a person has tested positive for HCV with an antibody test. A blood sample is taken and the amount or presence of HCV RNA in a milliliter of blood is measured. Viral load tests confirm whether an individual is actively infected with HCV. Viral load test results were previously measured in number of copies, but are now reported in International Units (IUs) per milliliter.

Types of HCV Viral Load Tests

There are two categories of HCV viral load tests:

Qualitative viral load tests – these tests determine the presence of HCV RNA in the blood. This type of test is usually used to confirm chronic infection with HCV. If the virus is detected, a positive result is reported; if the virus is not detected, the test result is negative.

Quantitative viral load tests – these tests measure the amount of virus in one milliliter of blood. They are used to assess if treatment with interferon or interferon/ribavirin is likely to be successful and, later, whether treatment is working.

There are currently three commonly used HCV viral load tests:

Polymerase chain reaction (PCR) – PCR tests detect HCV RNA in the blood, which indicates current active infection. Quantitative PCR tests are very sensitive and can measure as few as 5 to 10 IU/mL (Cobas Amplicor HCV).

Branched-chain DNA (bDNA) – The bDNA method is easier (and cheaper) to apply to a large number of samples, but only measures viral loads greater than 615 IU/mL. This means that if a person has a viral load below 615 IU/mL, HCV could be present in the blood but not detected by the test.

Transcription-mediated amplification (TMA) – The TMA technology allows for the amplification and detection of nucleic acids (components of genetic material) in blood serum. This test can measure as few as 5 to 10 IU/mL. This test appears easier and cheaper to use, streamlining test processing and producing consistent, reliable, and speedier results.

Interpreting Viral Load Test Results

HCV viral load can span from between 0-50 million, but it is usually expressed as low or high viral load.

Expressed as copies/mL:

Low: Under 2,000,000

High: Over 2,000,000

Expressed as International Units (IU/mL):

Low: Under 800,000

High: Over 800,000

Some recent studies have suggested that the cut-off between low and high viral load may be set too high. These studies have shown that people with a viral load under 400,000 IU/mL respond better to current medications compared to those who have a viral load above 400,000 IU/mL. More data is needed to confirm these observations.

If no HCV RNA is found on a test, the viral load is said to be undetectable. **Note:** *whether viral load is undetectable depends on which test is used. PCR and TMA tests can measure viral loads much lower than those a bDNA test can detect.*

There is no standard conversion formula for converting the amount of HCV RNA reported in copies per milliliter to the amount reported in IUs. The conversion factor ranges from two to five HCV RNA copies per IU. Some experts use a factor of three to convert from RNA copies to IUs. In other words, multiply the IUs/mL by three to arrive at an approximate RNA copy/mL number. Usually the lab test results will list the conversion of IU/mL to copies/mL in the lab report. Another method for expressing the number of copies is in exponential form. For example, 2.2×10^6 translates to 2,200,000 copies. Changes in viral load are sometimes expressed in terms of logs. A log change is a 10-fold increase or decrease. For example, a change from 1,000,000 copies to 10,000 copies is a 2-log decrease. Viral load test results can vary depending on how a blood sample is handled and

stored. Furthermore, results may vary from lab to lab. For this reason, most experts recommend that people should get their viral load testing done by the same lab each time, so that results are more comparable.

Uses of Viral Load Test Results

The immediate value of a quantitative viral load test is questionable, since the amount of virus detected does not appear to correlate with disease progression. However, such tests do have significant value when measuring the amount of virus before, during, and after treatment with interferon or interferon plus ribavirin. Before treatment, viral load measurement can help predict how well treatment will work. A low viral load prior to treatment is a positive predictor of treatment response. During treatment, a decrease in viral load indicates that treatment is working. A treatment is said to produce a complete viral response if it reduces viral load to an undetectable level. After treatment, viral load measurements can be used to monitor for relapse (that is, the virus becomes detectable again after the end of treatment in which the virus was eradicated). See **Section VIII: Medical Treatments for HCV** for more on treatment and viral load.

International Units

The FDA now requires that all approved viral load tests be reported in International Units per milliliter (IU/ml) as defined by the World Health Organization (WHO) International Standard for HCV RNA for Nucleic Acid Amplification Technology (NAT) Assays. This will result in consistency when comparing results from different tests or from one lab to another. In addition, it will be easier to compare the results from different clinical trials when viral load measurements are standardized.

Conversion Chart:

Assay	Conversion Factor
Amplicor HCV Monitor v2.0 (manual procedure)	1 IU/mL = 0.9 copies/mL
Cobas Amplicor HCV Monitor v2.0 (semi-automated procedure)	1 IU/mL = 2.7 copies/mL
Versant HCV RNA 3.0 Quantitative Assay	1 IU/mL = 5.2 copies/mL
LCx HCV RNA Quantitative Assay	1 IU/mL = 3.8 copies/mL
SuperQuant	1 IU/mL = 3.4 copies/mL

HCV and Its Lifecycle:

HCV and Its Lifecycle: Key Points

- *HCV is a single-stranded RNA virus.*
- *HCV consists of a core, which contains genetic material, and an envelope.*
- *HCV replication in liver cells can lead to liver damage and cancer.*

HCV and Its Lifecycle:

General Information

The hepatitis C virus (HCV) is a positive-sense single-stranded ribonucleic acid (RNA) virus. It is a flavivirus. Some other flaviviruses are West Nile, Yellow Fever, Dengue Fever and Japanese Encephalitis. HCV is spherical in shape and 40-60 nanometers in diameter. The virus consists of an inner core, which contains the virus' RNA (genetic material), and an outer lipid (fat) envelope. The HCV genome (genetic blueprint) encodes at least ten different gene products, or proteins, which make up the virus' core, envelope, and enzymes needed for replication.

HCV Replication

The lifecycle of HCV is poorly understood, in part because the virus is difficult to grow and study in laboratory cell and tissue cultures. A useful HCV cell culture model was only recently developed, but much of the replication process is still a mystery. HCV enters hepatocytes, or liver cells, by binding to receptors on the cell's surface and fusing with the cell membrane. Once inside the cell, the virus core releases its genetic material and replicates (reproduces). Using the host cell's ribosomes – which can be thought of as tiny factories – the RNA copies, or transcribes, itself using nucleotides (genetic building blocks) taken from the host cell. Then, the RNA directs the production of the various viral proteins, which are assembled to form new virions (virus particles). Finally, the new viruses "bud" through the host cell membrane and go on to infect other cells. The presence of HCV RNA in the blood (measured by viral load tests) indicates that the virus is actively replicating. Various viral enzymes – including RNA-dependent RNA polymerase, helicase, and protease – are needed for HCV replication. Drugs that target these enzymes can inhibit viral replication and stop infection of new cells. Viral replication within a liver cell typically results in cell death, but may also stimulate abnormal cell reproduction.

HCV Genotypes and Quasispecies:

HCV Genotype and Quasispecies: Key Points

- *A genotype is one of the variant types of HCV.*

- *Quasispecies are different types of HCV within a genotype.*
- *Quasispecies are the result of the constant mutation of HCV.*
- *The variability of HCV makes it hard for the immune system to clear the virus, and also makes it difficult to develop effective treatments and a vaccine.*
- *An individual's HCV genotype can be determined by a blood test.*
- *Genotype information is valuable for predicting HCV treatment response.*
- *Genotypes 1a and 1b are most common in the U.S.*
- *Genotype information does not appear to predict disease progression.*

HCV Genotype and Quasispecies:

General Information

The hepatitis C virus has several strains called genotypes. Different strains of HCV are very similar, but they have enough genetic differences to classify them into six major genotypes: 1, 2, 3, 4, 5 and 6. Some experts have proposed additional genotypes 7-11. Within genotypes are further divisions called subtypes (for example 1a and 1b) and quasispecies.

HCV constantly changes and mutates as it replicates. Scientists believe there are literally millions of different HCV quasispecies. A single individual with HCV may have a large number of different quasispecies. The variability of HCV and its rapid mutation rate make it hard for the immune system to clear the virus, which is why so many people develop chronic disease. This variability also makes it difficult to find medications that are effective against all types of HCV and hard to develop a vaccine that will protect against all HCV strains.

Distribution of HCV Genotypes

HCV genotypes and subtypes are distributed differently in different parts of the world, and certain genotypes predominate in certain areas. Genotypes 1-3 are widely distributed throughout the world. Subtype 1a is prevalent in North and South America, Europe, and Australia. Subtype 1b is common in North America and Europe, and is also found in parts of Asia. Genotype 2 is present in most developed countries, but is much less common than genotype 1. Subtype 3a appears to be prevalent among injection drug users.

HCV Genotype	Distribution
1, 2, 3	Worldwide
4	Middle East, Africa
5	South Africa
6	Southeast Asia

Genotype Tests and HCV Progression

Genotypes can be determined by a blood test. The majority of people with HCV in the United States (approximately 70-75%) are infected with genotypes 1a and 1b. Two other genotypes are less common in this country: genotype 2 (15%) and genotype 3 (6-15%). Genotypes 4, 5, and 6 are seen in the U.S. but are much less common.

A genotype test is usually only performed once since the genotype will remain the same throughout the course of HCV infection and disease progression. However, reinfection with a different or multiple genotypes can occur if someone has multiple exposures and becomes re-infected with HCV. See **Section VIII: Medical Treatments for HCV** for more information on genotypes and treatment.

There have been studies to try to determine whether the rate of disease progression differs based on genotype. Most data do not show a correlation between disease progression and genotype, but this needs to be studied in greater detail. Recent data is consistently confirming that there is a strong correlation between steatosis (fat in the liver) and genotype 3.

Liver Enzyme/Function Tests:

Key Points

- *Liver enzyme/function tests help measure how well the liver is working.*
- *Liver enzyme/function tests measure levels of liver enzymes, proteins, and other substances in the blood.*
- *The most common liver enzyme/function test measures alanine aminotransferase (ALT) levels.*
- *ALT levels are often – but not always – elevated in people with HCV.*
- *ALT levels are used to guide decisions about HCV treatment and gauge how well treatment is working.*
- *Other liver enzyme/function tests include the aspartate aminotransferase (AST),*

alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGT), albumin, bilirubin, platelet count, and prothrombin time tests.

- *Liver enzyme/function test results can vary from lab to lab.*

Liver Enzyme/Function Tests:

General Information

Liver enzyme/function tests, also known as a hepatic panel, are laboratory tests that help measure how well the liver is working. The liver carries out many vital bodily functions (see **Section II: The Liver**). When it is not functioning properly, levels of various enzymes, proteins, and other substances may rise or fall; these abnormal levels can be detected using blood tests.

ALT Levels

When liver cells are damaged, enzymes called aminotransferases (also known as transaminases) may leak into the blood. Measuring alanine aminotransferase (ALT, formerly known as SGPT) is the most useful liver function test in people with HCV. A normal ALT level for adult men ranges from 0-48 IUs per liter (IU/L). Many people with acute or chronic HCV infection have elevated ALT levels – which may be the first sign of liver disease – but others (20-30%) maintain normal levels. In general, patterns of changes in ALT levels over time are more informative than any single measurement. People with persistently normal ALT levels typically have mild disease and less severe liver damage. However, ALT levels are not a fool-proof indicator of the extent of liver damage. Some people, especially women and people of African descent, may have normal ALT levels even when they have serious liver disease. Exceptions may also occur during advanced stages of liver disease. Some experts believe that the hormone estrogen is responsible for lower ALT levels in women. Experts increasingly recommend that HCV-positive people with persistently elevated ALT levels should undergo a biopsy to check for liver damage.

ALT levels may also be used to help guide HCV treatment decisions. Many experts recommend that HCV-positive people with normal ALT levels should not receive treatment, but should instead have their ALT levels measured regularly to monitor changes or have a liver biopsy performed to get a better picture of the true health of the liver. The most recent NIH Consensus Statement (June 2002) stated that patients with normal ALT levels should not be denied treatment for HCV; however, this issue remains controversial and more studies are needed to understand further

disease progression in HCV patients with normal ALT levels. ALT levels may also be monitored in people receiving treatment. If the drugs are working well, ALT usually falls to normal levels even though this is not always the case. Sometimes liver enzyme levels increase, often in a spiking fashion, in people undergoing treatment (especially with pegylated interferon). After treatment ends, ALT levels can provide an indication of possible relapse in the absence of an HCV RNA test.

Other Liver Enzyme/Function Tests

Other laboratory measurements that may indicate liver damage include aspartate aminotransferase (AST, formerly known as SGOT), alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGT), albumin, and bilirubin levels. AST is a liver enzyme similar to ALT; a normal level is 0-42 IU/L. AST may also be elevated in people with muscle damage, so it is not as specific as ALT as an indicator of liver damage. High levels of AP and GGT, two other liver enzymes, may indicate obstructed bile flow; a normal AP level is 35-125 IU/L and a normal GGT level is 30-60 IU/L. Low levels of serum albumin (hypoalbuminemia), a protein produced by the liver that plays a role in maintaining normal blood volume, is associated with cirrhosis; a normal level is 3.2-5.0 g. Bilirubin is a pigment that is often present in the blood of people with liver inflammation; it is produced when the hemoglobin in red blood cells is broken down; a normal bilirubin level is 0-1.3 mg. High bilirubin levels in the blood (hyperbilirubinemia) may lead to jaundice (a yellowing of the skin and whites of the eyes), dark urine, and pale-colored feces. Elevated bilirubin levels are typically associated with worsening liver disease or with obstructed bile flow.

Platelet count and prothrombin time (also called protime, or PT) are measures of blood clotting ability. Platelets (thrombocytes) are blood cell fragments that form blood clots; a normal platelet count is 130,000-400,000 per micro liter (mcL). People with liver disease may develop an enlarged spleen (splenomegaly) that traps and destroys more platelets than usual. Blood clotting may also be adversely affected in people with liver damage if the liver cannot synthesize sufficient clotting proteins. Prothrombin time is an indication of blood clotting speed; prolonged prothrombin time may indicate liver dysfunction. Because many factors can affect blood clotting, laboratories determine normal PT each day; blood samples are then compared to this daily norm. A normal PT is about 10-12 seconds. Test results are reported as a multiple of the daily norm; for example, a PT of 22 seconds would be two times a control norm of 11 seconds. PT is generally considered prolonged if it is 1.2 times normal or higher.

Sample Value Ranges for Liver Enzyme/Function Tests*

Alanine aminotransferase (ALT)	0-48 IU/L
Aspartate aminotransferase (AST)	0-42 IU/L
Albumin	3.2-5.0 g
Alkaline phosphatase (AP)	35-125 IU/L
Gamma-glutamyl transpeptidase (GGT)	30-60 IU/L
Bilirubin	0-1.3 mg
Platelet count	130,000-400,000/mcl
Prothrombin time (PT)	10-12 seconds

*Value ranges may differ from one lab to another.

Liver Biopsies:

Liver Biopsies: Key Points

- *Liver biopsies can help determine the extent of liver damage.*
- *Biopsy results can help guide decisions about HCV treatment.*
- *A long, thin needle is inserted into the liver to extract a tissue sample.*
- *Complications from liver biopsy are rare.*
- *There are four histological stages of liver damage.*
- *There are many non-invasive tests to measure the extent of liver fibrosis.*

Liver Biopsies:

General Information

Liver biopsies measure the severity of liver damage, including the degree of inflammation, the extent of fibrosis (fibrous tissue) or cirrhosis (scarring), and the general health of the liver. Biopsies can help assist a doctor in determining if HCV medicines are needed. HCV Treatment works best when liver damage is less extensive. Most experts recommend no treatment if liver biopsy results show little or no damage. However, this viewpoint is being challenged since people with minimal liver damage are more likely to respond to current HCV medicines. Biopsy results can also help gauge how well HCV treatment is working; in many cases successful treatment can slow or reverse the progression of liver damage. Traditionally, biopsies have not been recommended for people with normal ALT

levels. However, research indicates that some people may have liver damage even when their liver function tests are normal. Some experts now believe that liver biopsies are useful for determining the extent of liver damage even in people with persistently normal ALT levels. In most cases, a biopsy is done only once; however, sometimes a doctor may recommend subsequent biopsies to gauge how well HCV treatment is working or whether liver disease is progressing.

Biopsy Procedures

In the most common liver biopsy procedure, called a percutaneous (through the skin) biopsy, a doctor typically uses a local anesthetic to numb the skin and muscles of the abdomen. Then, a long, slender needle is inserted through the abdominal wall and into the liver. Many doctors use ultrasound to determine the best biopsy site and to help avoid other abdominal organs. A small specimen of liver tissue is drawn out through the needle. The liver cells are examined under a microscope for signs of damage. Other liver biopsy procedures include transjugular biopsy (in which a sample is taken through the jugular vein in the neck), laparoscopic biopsy (in which a lighted instrument is inserted through a small incision in the abdomen), and fine-needle aspiration biopsy (in which a thinner needle is used).

The percutaneous biopsy procedure is very brief, typically a few seconds. About half of people experience no pain during or after a liver biopsy, while others may experience localized pain or pain that spreads to the right shoulder. If necessary, people can ask their doctors for a mild tranquilizer before a biopsy and for pain medication afterwards. The procedure is usually done on an outpatient basis, and most people are able to return home within 3-6 hours. Complications from liver biopsies are rare, occurring in 1-3% of cases; bleeding, pain, and low blood pressure are the most common complications. Biopsies are not recommended for people who have low hemoglobin or platelet levels, prolonged PT, or have taken aspirin or ibuprofen for several days preceding the biopsy. The most common reason for a liver biopsy is to help the provider and patient decide on whether or not to be treated; however, now that the treatment response rates are up to about 80%, many medical providers and patients may decide to be treated without having a liver biopsy.

HCV Staging

Liver biopsy results are reported in terms of histological stages (histology refers to the examination of tissue). The most common grading and staging tool is the Metavir scoring system which was developed specifically for patients with hepatitis C.

- *Stage I* is liver inflammation without fibrosis.
- *Stage II* is inflammation plus fibrosis in one area (portal) of the liver.
- *Stage III* indicates that fibrosis has developed over adjacent areas of the liver.
- *Stage IV* is cirrhosis and loss of normal liver architecture.

People progress through these stages at different rates. Often people have early (Stage I) or moderate (Stage II or III) liver damage for many years without developing cirrhosis (Stage IV). However, once an individual has shown progression to stage II or III, time of progression to the next stage is shorter than in individuals who have not progressed (stage 0 or I).

Stage of Disease*	Terminology
Early stage, mild activity (I)	Chronic persistent hepatitis C or mild chronic active hepatitis C
Intermediate stage (II or III)	Chronic active hepatitis C with fibrosis
Advanced stage (IV)	Cirrhosis

** Within each stage disease severity can vary widely; for example, Stage IV cirrhosis is classified into two different types: compensated cirrhosis and decompensated cirrhosis.*

Non-invasive Markers of Liver Fibrosis

There are tests that have been developed that will hopefully eliminate the need for a liver biopsy. These types of tests include measuring various combinations of serum markers and a test that scans the liver to measure liver stiffness. Results from clinical trials on these non-invasive markers have shown that some of them are accurate in predicting little/no fibrosis or extensive fibrosis/cirrhosis, but are not very accurate for grading or staging fibrosis in between these scores.

Other Diagnostic Tools:

General Information

Several other tests may be done in people with HCV to detect various conditions associated with HCV. These will vary depending on a person's symptoms and stage of disease.

Imaging Tests

Imaging tests are used to visualize the general size, structure, and texture of the liver. The most common are ultrasound tests, which use sound waves, and com-

puted tomography (CT or CAT) scans. Such tests can also show damage to the major blood vessels that serve the liver and can help identify tumors that may indicate liver cancer.

Blood Tests

Alpha-fetoprotein (AFP) is a substance often found in the blood of people with hepatocellular carcinoma (HCC) a type of liver cancer associated with advanced hepatitis C. AFP is elevated in more than half of people with HCC, and may act as a biological tumor marker. A steady increase in AFP levels or a level above 200 mg/ml is a warning sign for liver cancer. However, people with small liver tumors often have normal AFP levels, and marginally elevated levels may occur in people experiencing a hepatitis “flare-up” even if they do not have liver cancer. In addition, AFP may be present in people with certain other types of cancer, so it is not a sure indication of HCC. An ultrasound test is used in combination with AFP test to monitor for HCC.

A complete blood count (CBC) is an inventory of all the different cellular components of the blood, including red blood cells, white blood cells, and platelets. People with chronic HCV sometimes have blood cell deficiencies, or low blood cell counts, including anemia (reduced ability of red blood cells to carry oxygen), neutropenia (low levels of a type of white blood cell), and thrombocytopenia (a low level of platelets). When a person has portal hypertension (high blood pressure in the veins serving the liver), blood can back up into an organ called the spleen. Because the spleen is responsible for removing old blood cells from circulation, a backup of blood can lead to the removal of an excessive number of blood cells. A CBC may be done in people with chronic HCV to see if they have any of these conditions. A hematocrit is another test for anemia.

Endoscopy

Endoscopy is a procedure in which a lighted tube is inserted into the body to allow a doctor to view internal organs. Endoscopy of the esophagus and stomach may be done to look for varices, or enlarged blood vessels resulting from portal hypertension.

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The information in this guide is designed to help you understand and manage HCV and is not intended as medical advice. All persons with HCV should consult a medical practitioner for diagnosis and treatment of HCV.

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