

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

## *HCV Diagnostic Tools:*

# *HCV Viral Load Tests*

Liz Highleyman  
Alan Franciscus, Editor-in-Chief

*Viral load tests are blood tests that measure HCV ribonucleic acid (RNA, or genetic material) 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 exposure to HCV based on an antibody test. A blood sample is taken and the amount 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 terms of International Units per milliliter (IU/mL).*

### *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 viral RNA is detected, a positive result is reported; if viral RNA is not detected, the test result is negative.

**Quantitative viral load tests** — These tests measure the amount of virus in one milliliter of blood. In the past the level of the viral load was correlated with the chances of responding to HCV treatment. The addition of HCV protease inhibitors to pegylated interferon plus ribavirin therapy have mostly overcome the negative affects of having a higher viral load.

**There are currently three tests commonly used for HCV viral load testing:**

**Polymerase chain reaction (PCR)** — PCR tests detect HCV RNA in the blood, which indicates current active infection. This type of quantitative PCR test is very sensitive, and can measure as few as 5-10 IU/mL.

**Branched-chain DNA (bDNA)** — The bDNA method quantitative viral load testing is easier (and cheaper) to use for 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 be detected by the test. However, the test will detect higher viral load ranges so it is useful when beginning HCV therapy.

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

### *Interpreting Viral Load Test Results*

HCV viral load is often reported as low or high.

Expressed as copies/mL:

- Low: less than 2 million copies
- High: more than 2 million copies

Expressed as International Units (IU/mL):

- Low: less than 800,000 IU/mL
- High: more than 800,000 IU/mL

Some 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. Larger prospective studies are needed to confirm these observations.

If no HCV RNA is found by a test, a person's viral load is said to be undetectable. Note that whether viral load is undetectable depends on which test is used. PCR and TMA tests can measure viral loads much lower than a bDNA test can detect. Importantly, the blood of an individual with a very

low viral load may still contain HCV even though the current tests cannot measure it; that is, the virus may not have been truly eradicated from the body.

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 laboratory each time, so that results are more comparable.

Changes in viral load are sometimes expressed in terms of logs. A log change is a 10-fold increase or decrease.

**Note:** A log drop in viral load is measured by decreasing the number by one zero. For instance, a one log drop in a viral load of 1,000,000 International Units is 100,000 International Units; a two log drop in a viral load of 1,000,000 International Units is 10,000 International Units.

**Converting copies per milliliter to International Units**

There is no standard conversion formula for converting the amount of HCV RNA reported in copies per milliliter to the amount reported in International Units. The conversion factor ranges from about one to about five HCV RNA copies per IU. Usually the lab report will list the conversion from IU/mL to copies/mL. See **Table 1** for a conversion of common viral load tests from IUs to copies.

**Table 1: Common viral load measurements converted from International Units to copies/mL.**

<b>Assay</b>	<b>Conversion Factor</b>
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
Cx HCV RNA Quantitative Assay.....	1 IU/mL = 3.8 copies/mL
SuperQuant.....	1 IU/mL = 3.4 copies/mL

**Uses of Viral Load Test Results**

Viral load test results have many uses, such as confirming active HCV infection, and measuring HCV treatment response before, during, and after therapy. Viral load has not been correlated with the risk of sexual transmission. One study

found that a higher viral load may increase the risk of HCV transmission from mother to child, but this needs to be confirmed in larger studies. *Furthermore, a correlation between HCV viral load and disease progression has not been shown.*

**Confirming active HCV infection** — After a person has tested positive for HCV antibodies, an HCV viral load test is usually performed to confirm active HCV infection. This test is necessary because in 25–45% of people exposed to HCV, the virus can be cleared on its own.

**Before treatment** — A viral load test will be performed to establish a baseline measurement.

**During treatment** — Viral load measurements are taken during treatment at 4 weeks (rapid virological response (RVR)), 12 weeks (early virological response (EVR)) and at regular time points during therapy to gauge whether the medications are working, to determine treatment duration and if a person should stop therapy because treatment would most likely be unsuccessful.

**After treatment** — Viral load measurements can be used after cessation of therapy to monitor for relapse — that is, to see if the virus becomes detectable again after being undetectable when treatment was completed.

**For more information about hepatitis C, hepatitis B and HCV coinfections, please visit [www.hcvadvocate.org](http://www.hcvadvocate.org).**

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<p><b>Executive Director</b> <b>Editor-in-Chief, HCSP Publications</b> Alan Franciscus</p> <p><b>Design</b> Paula Fener</p> <p><b>Production</b> C.D. Mazoff, PhD</p> <p><b>Contact information:</b> Hepatitis C Support Project PO Box 427037 San Francisco, CA 94142-7037 <a href="mailto:alanfranciscus@hcvadvocate.org">alanfranciscus@hcvadvocate.org</a></p>	<p>The information in this fact sheet 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.</p> <p>This information is provided by the Hepatitis C Support Project • a nonprofit organization for HCV education, support and advocacy • ©2011 Hepatitis C Support Project • Reprint permission is granted and encouraged with credit to the Hepatitis C Support Project.</p>
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