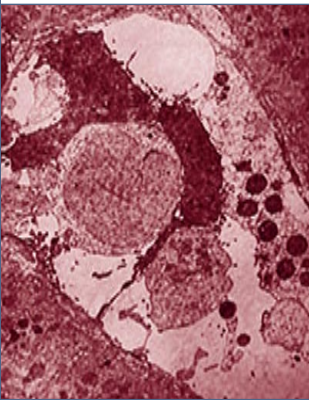


# Hepatitis C Overview

## ABOUT THE VIRUS

Hepatitis C virus (HCV) is a member of the Flaviviridae family. It is a single-stranded, positive-sense RNA virus, which is spherical and lipid-enveloped. HCV was discovered in the late 1980s, and is considered to be one of the leading causes of liver disease in the United States. Six major genotypes have been identified to date, 1-6, and more than 50 subtypes. Genotype 1 is the most common strain in the United States, accounting for approximately 75% of all infections. This is unfortunate, as genotype 1 is the least likely to respond to treatment. The genotypes differ by 31-34% in their nucleotide sequences; subtypes differ by 20-23% based on their full-length genomic sequence comparisons. This extensive genetic heterogeneity, as well as the propensity for mutation, has hindered vaccine development.



A liver cell killed by infection with the hepatitis C virus.

Courtesy of Dartmouth Medical School.

## CLINICAL MANIFESTATIONS

HCV is considered to be responsible for most cases of hepatitis since the hepatitis B (HBV) vaccine came into widespread use. The most common risk factors for HCV infection include a blood transfusion before 1992, when testing methods had not yet been developed to screen out HCV-tainted blood, IV drug abuse or contact with contaminated blood, such as tattoos or needlestick injuries. To a lesser extent, infants born to an infected mother and sex with an infected partner are also risk factors. However, an estimated 20% of patients infected with HCV do not have identifiable risk factors.

According to the CDC website, as of late 2006, approximately 170 million people worldwide are infected with HCV; 4.1 million are Americans. About 3.4 million new infections occur worldwide each year.

HCV infection is generally asymptomatic during the acute phase, making diagnosis of the infection during the acute phase very unusual. In rare cases, acute hepatitis is accompanied by jaundice, malaise, weakness, and anorexia. More rarely, fulminant hepatitis may develop in the acute phase. It is estimated that 74-86% of individuals develop persistent viremia,

which subsequently leads to chronic infection and possible cirrhosis or hepatocellular carcinoma. The development of persistent infection in most individuals is probably due to a poor T-lymphocyte response and the high propensity of the virus to mutate.

The time interval between infection and development of chronic liver disease can range from 20 to over 30 years. Once a chronic infection is established, its clinical progression can be accelerated by such things as alcohol consumption, coinfection with HIV-1 (human immunodeficiency virus) or HBV, being of the male sex, African American, or of an older age at the time of infection. A typical presentation of chronic HCV infection involves a relapsing remitting infection with recurrent bouts of hepatitis, marked by fluctuation in serum AST/ALTs. Specific symptoms are related to liver dysfunction, and involve jaundice, ascites, or GI bleeding. These are typically seen only in patients with disease that is far advanced. Depending on the patient, AST/ALT levels may even be normal during periods of remission, so the absence of ALT abnormalities does not automatically preclude the presence of HCV infection.

End stage liver disease caused by chronic HCV infection has become a primary cause of liver transplantations in Western countries. Epidemiological studies have shown the association between chronic HCV infections and hepatocellular carcinoma, which is known to result in death in approximately 33% of patients with HCV cirrhosis.

## LABORATORY DIAGNOSIS

Most individuals with HCV are diagnosed after a routine physical examination shows elevated liver enzymes. HCV is then diagnosed by two antibody tests. First, an ELISA is performed, if positive, it is often confirmed by a RIBA test. A positive antibody test means the patient has been exposed to HCV and has a 70% chance of developing chronic hepatitis C. Since HCV cannot be grown in the clinical laboratory, molecular testing is needed to confirm the presence of the virus. Tests for HCV infection have typically included both serologic assays to determine serostatus and molecular tests to monitor the viral burden (viral load) in individuals. Any patient undergoing treatment for HCV infection will have their viral load monitored regularly by quantitative real-time PCR testing. Real-time PCR testing is highly sensitive and specific, making it the ideal assay to monitor a patient's response to antiviral therapies. The ViraCor HCV quantitative real-time PCR assay has an unusually wide assay range, with a 5 IU/ml lower limit of detection, which makes it particularly helpful to the physician in ascertaining viral clearance.

## TREATMENT

Therapy with pegylated interferon and ribavirin has become the standard of care, although not all individuals will clear the virus, particularly those infected with HCV genotype 1. If the patient does not show at least a 2- $\log_{10}$  drop in viral load 12 weeks after initiating therapy, the likelihood of a sustained response is quite low and therapy should be discontinued.

Liver transplantation is the only available treatment option for individuals who have developed decompensated HCV-related cirrhosis. Liver transplantation is also indicated for some patients who have early stage hepatocellular carcinoma. Despite the fact that recurrence of HCV is almost inevitable in these individuals, their 1 and 5 year survival rates are similar to those of patients with other common indications for liver transplantation.

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