

## Update: An Overview of Viral Hepatitis

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In the United States, there are two principal causes of chronic viral hepatitis: hepatitis C virus (HCV) and hepatitis B virus (HBV). Hepatitis A and E viruses also infect humans but do not cause chronic liver disease. Hepatitis delta virus infects only people with HBV infection. Hepatitis G virus, or GB virus C, causes chronic infection but, despite the name, does not cause liver disease. Thus, the problem of chronic viral hepatitis largely consists of diseases caused by HBV and HCV.

In the United States, there are an estimated 4 million people with chronic HCV infection and 1 million with chronic hepatitis B. Over the years, both chronic viral illnesses may cause cirrhosis, liver failure, or liver cancer. In fact, chronic HCV infection is the leading cause of liver failure requiring transplantation in the United States, resulting in an estimated 10,000 deaths each year.

Both viruses exist in the blood and are spread when blood or blood-contaminated body fluids breach normal skin and mucosal barriers. Thus, there are high rates of HBV and HCV infection among people with multiple blood exposures, such as hemophiliacs, injection drug users, and hemodialysis patients. There are especially high concentrations of HBV in blood, semen, and saliva of some chronic carriers, explaining the more frequent

transmission of HBV by sexual, household, and perinatal exposures.

While both HCV and HBV can cause chronic infection, their natural histories differ. More than 90% of adults will recover after acute hepatitis B, while less than 20% spontaneously resolve acute HCV infection. Although HBV infection becomes chronic less often, it generally is more likely to progress to cirrhosis over a shorter period of time than HCV infection. It is estimated that 20% of people with chronic HCV infection will develop cirrhosis over 20 years.

Both HBV and HCV infections can be detected by commercially available blood tests. With HBV, chronic infection is assumed in persons with persistence of the hepatitis B surface antigen for longer than 6 months, while prior resolved infection is marked by the absence of the surface antigen and the presence of antibodies to both the surface antigen and the core antigen. High quantities of HBV are present in blood when the e antigen is detected. The absence of the hepatitis B e antigen in association with the antibody to the e antigen generally indicates recovery from infection, even when the surface antigen persists.

Chronic HCV infection is characterized by a positive HCV enzyme immunoassay and repeated detection of HCV RNA in blood. Liver enzymes, chiefly the alanine aminotransferase, are ele-

vated at some time in most individuals with HCV infection. The majority have intermittently elevated liver enzymes, and about 10% have repeatedly elevated values. About one third have repeatedly normal levels over years. Unfortunately, liver enzyme results and even patterns do not reliably predict the stage of disease, which must be ascertained by liver biopsy.

Both HCV and HBV infections can be treated. For HBV, subcutaneous injection of interferon alfa has been the standard of care. This treatment is associated with greater clearance of infection and reduction in disease progression compared to placebo. Recently, a number of nucleoside analogs have been proposed that inhibit the viral reverse transcriptase. The most data are available for lamivudine, which, when taken orally once a day for up to a year, increased the clearance of infection and reduced disease progression at least as well as would historically be expected for interferon alfa. Drug resistance and relapse after discontinuation of therapy have been reported with lamivudine.

For HCV infection, the standard of care is long term (usually 48 or more weeks) of interferon alfa taken subcutaneously three times weekly. This regimen cures 20% to 40% of treated patients (no virus in the blood and normal liver enzymes 6 months after therapy). More individuals initially appear to respond to interferon, but later relapse. The wide efficacy range reflects differences in response and relapse rates based on the HCV strain (genotypes 2 and 3 respond more favorably), the person's age and duration of disease, the pretreatment severity of disease, the duration of treatment (12 months is better for

genotype 1), and viral load. Various interferon formulations are available; most data indicate few differences in efficacy and side-effect profile, which is substantial. The combination of ribavirin with interferon alfa appears to improve the response rate.

Recently the crystal and biochemical properties of critical enzymes have been characterized for HCV, and compounds intended to interdict viral replication are being developed. For example, inhibitors of the viral helicase and protease are expected in clinical trials before 2000. Interferon alfa formulations are also being improved. Phase III studies of interferon that can be administered once weekly are under way in 1998.

In most people, the symptoms of chronic viral hepatitis are not sufficiently severe to provoke a medical investigation until the disease is too severe to be treated. In addition, treatment of the end stages of disease, liver failure or cancer, is difficult and expensive. Thus, from many perspectives, chronic hepatitis C and hepatitis B are illnesses that warrant screening. The cost effectiveness of screening and treatment at most disease stages appear to be similar to other diseases where screening is routinely employed. Increased appreciation for the medical and economic benefits of HCV treatment and screening is necessary for these practices to become widespread.

There are safe, effective vaccinations to prevent HBV infection. Their use is recommended in all children born in the United States and in adults at risk of exposure to blood. There is no commercially available vaccine to prevent HCV infection.