

# Hepatitis C: Who Should Be Treated?

by Julie R. Smith and Jorge L. Herrera

Nearly 4 million people in the United States test positive for hepatitis C, many of whom are unaware of their infection. It is usually discovered inadvertently when an individual undergoes a physical exam for insurance purposes, donates blood or asks to be tested because of a known risk factor (Table 1). Rarely do patients present with overt symptoms of acute hepatitis, because the initial infection is asymptomatic in over 80% of exposures. Fortunately, the majority of those chronically infected will develop mild liver disease and never progress to end-stage disease; however, a certain percentage will develop cirrhosis and may suffer with significant health problems secondary to hepatitis.

## EVALUATION

Confirmation of the infection is an important early step usually performed by the patient's gastroenterologist, hepatologist or primary care physician, if their intent is to evaluate and treat. Patients who test positive for HCV antibody or RIBA should be tested for HCV-RNA by PCR (Hepatitis C viral RNA by polymerase chain reaction), to confirm viremia. Viral quantitation becomes

important when antiviral treatment begins in order to evaluate effectiveness, but has no relation to the severity of the disease. Patients with high viral load are less likely to respond to antiviral therapy.

Genotype is the most important determinant of response to antiviral therapy. Six genotypes with multiple subtypes vary geographically, with the most prevalent in the U.S. being genotype 1, accounting for approximately 70% of infections. Genotypes 2 and 3 account for most of the remaining 30% of infections. Genotype 1 is the most resistant strain of the virus with only 40% to 45% of patients treated with pegylated interferon and ribavirin achieving a sustained viral response. In contrast, genotype 2 patients have sustained response rates approaching 85%. Genotype, however, has no relationship to severity of disease.

Establishing the severity of the disease helps in counseling patients whether or not treatment is necessary. Unfortunately, there are no non-invasive diagnostic tests that can reliably determine the presence of fibrosis or cirrhosis. Currently, liver biopsy remains the single most accurate test to assess severity of liver disease. The liver biopsy provides information that can be used to determine a patient's prognosis and aids in the decision making process as to whether or not to be

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aggressive with antiviral therapy. While a liver biopsy is not mandatory prior to initiating antiviral therapy, it provides information that is invaluable when managing these patients during therapy.

## TREATMENT

When first discovered in 1989, little was known about the hepatitis C virus, diagnostic tests were not very accurate, and treatment was not very efficacious. Interferon, an immune modulator, was the first medication approved for the treatment of hepatitis C. It was used as a subcutaneous injection three times per week with only about 10% of patients achieving a sustained response. In 1996 came the next improvement, with the addition of ribavirin, a nucleoside analog whose mechanism of action is unknown. With the combination, response rates increased to 30% to 60%, depending on the viral genotype. Most recently, the development of pegylated interferon allows the injection to be given only once per week and, when used in combination with ribavirin, a greater number of patients are able to clear the virus. The sustained response rates have been shown to be 45%–50% for genotype 1 and as high as 85% in patients with genotype 2. Primary treatment goal is usually sustained viral response, but in patients with fibrosis or cirrhosis an important secondary goal is to slow progression of the disease and allow improvement in fibrosis of the liver.

Currently, the treatment regimen is 12 months in duration using combination therapy of pegylated interferon and ribavirin. Side effects of this treatment can be significant, including anemia, depression, leukopenia, flu-like symptoms, and other side effects, all of which will decrease the patient's quality of life during therapy and have potential to cause morbidity and mortality. The medications are also teratogenic and birth control practiced by both male and females undergoing therapy is absolutely required for the duration of treatment and for 6 months after. To make matters more difficult, the medications are very expensive and not all insurance carriers cover the cost of treatment. For these reasons, the decision to place a patient on treatment should be individualized, taking into account the patient's age, genotype, degree of liver injury, duration of disease, commitment to therapy, psychiatric history, and financial status, as well as the presence of any relative or absolute

contraindications to this therapy. Common contraindications include decompensated liver disease, anemia, leukopenia or thrombocytopenia, untreated psychiatric disorders, renal insufficiency, seizure disorders, severe cardiac disease, pregnancy, severe asthma, uncontrolled diabetes or autoimmune diseases. Patients who are using illicit intravenous drugs and/or drinking alcohol are not considered candidates for therapy.

For patients who have no obvious contraindications, the need for treatment should be individualized. Because the disease may not cause cirrhosis in all, a patient who has had the infection for more than 20–30 years and has no or only minimal fibrosis on biopsy (Stage 0–1) is less likely to progress to cirrhosis in the near future. Therefore, if there are unfavorable factors present, such as genotype 1, high viral load, other illnesses, or the patient is >60 years of age, treatment may be postponed or never undertaken at all. Whereas, a patient with bridging fibrosis (Stage 2 or 3) on biopsy, who is young (<45) and has no contraindications, should be treated aggressively, because the chances of progression are much higher.

Patients who already have cirrhosis, but who are well compensated, can benefit from treatment in an effort to slow or stop progression, realizing that the chances of viral eradication are lower than in those without cirrhosis. If there are already signs of hepatic decompensation treatment is usually not indicated or should be monitored very carefully, as the risk of causing the liver disease to worsen exists.

The following are some examples of patients who should definitely consider aggressive treatment:

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**Table 1**  
**Risk factors for hepatitis C infection**

- Transfusion of blood or blood products prior to 1992
- Intravenous illicit drug use, past or present (even if only once)
- History of hemodialysis
- Tattoos or body piercing with shared tools
- Needle stick injury
- Multiple sexual partners
- History of sexually transmitted disease
- Incarceration

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1. A 30 year old female with mild fibrosis on liver biopsy, with genotype 2 infection for 10 years. This individual has an excellent chance of a sustained virologic response and, if left untreated, may progress simply because of her young age.

2. A 50 year old man with bridging fibrosis and genotype 1. If left untreated, this man is at significant risk of developing cirrhosis within the next 5-10 years. His chances of viral eradication are approximately 50%, but the benefits of treatment also include slowing of progression of fibrosis. Aggressive treatment should be started and side effects managed aggressively to promote adherence, providing him the best chances for a sustained response.

Here are some examples of patients who should not undergo treatment:

1. A 68 year old woman with no fibrosis, who had a blood transfusion at age 30, and suffers with severe diabetes, coronary artery disease and hypertension. This patient is more likely to suffer complications from her other illnesses rather than chronic hepatitis C. The treatment is not likely to improve her quality of life or prolong survival.

2. A 40 year old man with poorly controlled manic-depressive disorder who has attempted suicide in the past. Interferon causes depression and can severely aggravate this patient's condition. The decision to treat an individual such as this must be carefully thought out with the aid of a psychiatrist, regardless of the severity of the underlying liver disease.

The third category of patients includes those who have time to wait and can reasonably choose to postpone treatment for a few years.

1. A 28 year old female, with genotype 1 and no fibrosis, who wishes to start a family. She can safely wait for a few years to undergo treatment. The chance of transmission to an infant is very low and should not be a deterrent to pregnancy.

2. A 45 year old male with no fibrosis on biopsy, genotype 1, high viral load and probable duration of infection of 25 years. This patient can safely postpone treatment. However, it is recommended that he undergo a repeat liver biopsy in 4-5 years to assess for progression.

The treatment of hepatitis C involves a detailed evaluation of the patient's history and clinical parameters in order to make an individualized decision. The decision

to treat should be viewed as a team effort among the patient, his or her family, and the physician. Patient education and reassurance are key factors in allowing the patient to make reasonable decisions regarding her/his chronic hepatitis C infection. Mid level providers such as physician assistants and nurse practitioners can play an important role in patient education and adherence to treatment. Patients are much more likely to tolerate the treatment and complete therapy if they have actively participated in the decision to initiate therapy. ■

#### Additional Reading and Resources

1. Herrera JL, Roveda KP. Hepatitis C: What recent advances in therapy mean for your patients. *Consultant*, 1999; 32:436-447.
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4. Herrine SK. Approach To The Patient With Chronic Hepatitis C Infection. *Ann Intern Med*, 2002;136:747-757.

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Dr. Herrera is a member of the HCV Advocate Medical Writers' Circle, a publication of the Hepatitis C Support Project (HCSP) / HCV Advocate web site. Members of the HCV Advocate Medical Writers' Circle are experts in the field of liver disease who partner with HCSP to help educate and support medical providers and the HCV community.

The Hepatitis C Support Project (HCSP) is registered non-profit advocacy organization. The mission of HCSP is to offer support to those who are affected by the hepatitis C Virus (HCV), hepatitis B virus (HBV) including hepatitis coinfections. Support is provided broadly, through information and education as well as access to support groups. The (Project) seeks to serve the hepatitis community as well as the general public.

Visit the HCV Advocate web site at [www.hcvadvocate.com](http://www.hcvadvocate.com) for regularly updated information on HCV, HBV, and hepatitis coinfections.

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