

Medical Writers' Circle

a series of articles

written by medical
professionals about
the management
and treatment of
Hepatitis C

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Hepatitis C – Who Should Be Treated?

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). 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 (an alternate test for hepatitis C infection) should be tested for HCV-RNA by PCR (Hepatitis C viral RNA by polymerase chain reaction), a blood test that confirms the presence of the virus in the blood. The majority of people with a positive HCV antibody test, elevated liver enzymes (transaminases: AST and ALT) and known risk factors for infection will have detectable virus in the blood by PCR test. Viral load, or quantitation of the amount of virus present, will become important when antiviral treatment begins in order to evaluate effectiveness, but has no relation to the severity of the disease.

Genotype is another important test that should be performed early, before antiviral treatment is started. 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. It is

very important that both patient and provider understand that genotype has no relationship to severity of disease. This test is used only to predict the likelihood of response to treatment. Studies show that genotype 1 patients have a 40% to 45% chance of achieving a sustained response after therapy with pegylated interferon and ribavirin. In contrast, genotype 2 patients have sustained response rates approaching 85%.

The next step in the patient's evaluation involves determining the extent of liver damage. Hepatitis C causes inflammation that can lead to development of scar tissue in the liver, eventually progressing to cirrhosis. It usually takes decades for hepatitis C infection to progress to cirrhosis, and in many, cirrhosis will never develop. Unfortunately, there are no blood tests, scans or X-rays that can reliably show the degree of liver damage. Currently, liver biopsy remains the single most accurate test to assess severity of liver disease. The liver biopsy is an outpatient procedure with low

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**

risk of complications and, if adequate, the specimen will show the degree of inflammation and fibrosis which is present. This information is necessary in determining a patient's prognosis and aids in the decision making process as to whether or not to be aggressive with antiviral 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 (the virus remains undetectable in the blood for more than 6 months after therapy is completed). 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 or "long-acting" 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 goals are usually viral eradication or "cure" (sustained viral response). An important secondary goal is to slow progression, allowing the liver to heal and adding years of health. This secondary goal is important primarily for those people who have a

pre-treatment liver biopsy that shows 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 (can cause birth defects) 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

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be individualized, taking into account the patient's age, genotype, degree of liver injury, duration of disease, psychological history, and financial status, as well as the presence of any relative or absolute contraindications to this therapy. Common contraindications include untreated psychiatric disease, kidney disease, 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 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 (have not developed complications from

cirrhosis), 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 decompensation, such as complications of cirrhosis, treatment is usually not indicated or should be monitored very carefully, as the risk of causing total decompensation exists.

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

1. A 30 year-old female with mild fibrosis upon liver biopsy, who has been infected for 10 years and has genotype 2. This individual has an excellent chance of a cure 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 less than 50%, but the benefits of treatment also include slowing of progression of fibrosis. Aggressive treatment should be started and side effects managed properly so that he can maintain the highest recommended dose of medication, allowing him the most benefit from therapy.

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

1. A 68 year-old women with early bridging 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 would probably do her more harm than good.

2. A 40 year-old man with severe psychiatric 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 liver biopsy.

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 minimal fibrosis on biopsy, genotype 1, 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. 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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3. Lauer GM, Walker BD. *Hepatitis C infection.* NEJM 2001; 345:41-52
4. www.niddk.nih.gov/health/digest/pubs/chrnhepc/chrnhepc.htm
5. www.hepatitisneighborhood.com
6. <http://hepatitis-central.com/hcv/maintoc.html>
7. www.LiverFoundation.org

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The Mission of the Hepatitis C Support Project is to offer support to those who are affected by the hepatitis C Virus (HCV) and HIV/HCV coinfection.

Support is provided broadly, through information and education, as well as access to support groups. The (Project) seeks to serve the HCV community as well as the general public.

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