

HEPATITIS C UPDATE

BACK IN 2000, when we last revisited hepatitis C virus (HCV), the best thing since sliced bread was combined therapy for HCV using interferon and ribavirin. Well, HCV has since become even more treatable, and this issue of the *CD Summary* describes new approaches to management of HCV, and Oregon's expanded surveillance program.

HCV EPIDEMIOLOGY 101

According to the National Health and Nutrition Examination Survey of 1988–94, 1.8% of the US population have antibody to HCV.¹ Following exposure, only one-third of patients develop any symptoms which may be clinically indistinguishable from acute infection with hepatitis A or B.² Since acute HCV infections are rarely symptomatic, it is difficult to monitor the rate of new infections, but the CDC estimates that about 35,000 new cases occur annually in the US, down from 180,000 a year in the late 1980s.³ Genotype 1 accounts for 70%–75% of HCV infections in the US.

The majority (75%–85%) of HCV infections will go on to become chronic.³ Younger age, female sex, and certain histocompatibility complex genes are associated with spontaneous viral clearance. African American men are least likely to clear the virus. Of those chronically infected, as many as 50% may develop persistently elevated serum alanine aminotransferase (ALT) levels, and 10%–15% will develop cirrhosis.⁴ Estimates of the proportion of chronically infected persons who develop cirrhosis 20 years after infection vary widely—from 2%–4% in children and young women, to as high as 20%–30% in middle-aged transfused subjects. Risk factors for cirrhosis include older age at time of infection, male sex, immunodeficiency, concurrent hepatitis B infection,

obesity and alcohol use. Alcohol intake as low as 30 g/day in men (roughly equivalent to two beers, 2 glasses of wine or 2 mixed drinks) and 20 g/day in women have been shown to increase the risk of cirrhosis.³

WHO SHOULD BE SCREENED?

HCV transmission occurs primarily through exposure to infected blood. This exposure can occur through injection drug use, blood transfusion before 1992, solid organ or tissue transplantation from infected donors, unsafe medical exposures, occupational exposure to infected blood, and birth to an infected mother. Sexual transmission is rare. For a person with chronic HCV infection, the estimated risk of sexual transmission to an uninfected partner is 0% to 0.6% per year for those in monogamous relationships, and 0.4% to 1.8% per year for uninfected persons with multiple sexual partners. The presence of other STDs or sexual practices that traumatize the mucosa (e.g., receptive anal sex) increase risk. CDC recommends testing the groups of people in the Table.⁴

The usual approach is to test initially for antibodies to HCV, then to use HCV ribonucleic acid (RNA) to confirm viremia.³ Because most persons with ongoing HCV infection have HCV RNA levels in the range of the quantitative assays and because the quantity of HCV RNA is useful to know before beginning treatment, many practitioners routinely check only quantitative RNA. However, qualitative tests are more sensitive and

are recommended for confirming viremia in patients who are negative by a quantitative assay. The recombinant immunoblot (RIBA) assay is less often used in clinical practice. A negative RIBA in a patient with a positive HCV antibody test indicates a false positive result on the initial antibody test. A positive RIBA followed by two or more negative HCV RNA tests (using a sensitive qualitative assay) suggests that the infection has resolved, and no further testing is indicated.

WHAT DO I TELL PATIENTS WHO TEST POSITIVE?

All HCV-infected persons should be informed that transmission to others can occur through contact with their blood. They should be counseled to avoid sharing toothbrushes and shaving equipment and be cautioned to cover any bleeding wound. HCV is not transmitted by hugging or the sharing of eating utensils. There is no need to curtail any normal household activities, and household contacts of HCV-infected persons do not need to be tested. There are no daycare, school, or workplace restrictions for HCV.³

Most infections occur as a result of injection drug use, making interventions to reduce illicit drug use or to promote safer injection practices of prime importance in preventing further spread. Active injection drug users should be encouraged to stop injecting and referred for substance

CDC HCV SCREENING GUIDELINES

CDC recommends screening for people who

- have ever injected illegal drugs, even if only one time many years ago;
- were notified that they received blood from a donor who later tested positive for hepatitis C;
- received a blood transfusion or solid organ transplant before July 1992;
- received clotting factor(s) made before 1987;
- have ever been on long-term kidney dialysis; or
- have evidence of liver disease (e.g., persistently abnormal ALT levels).



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abuse treatment. Those who are unwilling to stop should be counseled to avoid reuse or sharing of syringes, needles, water, and cotton or other paraphernalia; to clean the skin with a new alcohol swab before injecting; and to dispose safely of the syringe and needle after one use.

HCV-infected persons may be counseled that the risk of sexual transmission is low and that the infection itself is not a reason to change sexual practices for those in long-term relationships. In these situations, CDC does not routinely recommend testing sexual partners. Those persons engaging in high-risk sexual activities should always be counseled to use condoms. All patients with chronic HCV should be vaccinated against hepatitis A, and persons with risk factors for hepatitis B should also receive hepatitis B vaccine.

LATEST THERAPY FOR HCV

First, a few definitions. A negative PCR during therapy is known as an early virologic response (EVR). Absence of circulating virus 6 months after finishing therapy is termed a sustained virologic response (SVR) and is very good news—these patients often demonstrate improved histology and an improved quality of life, and relapse is rare. Randomized, controlled trials have demonstrated that pegylated interferon (produced by binding polyethylene glycol to the interferon molecule) plus ribavirin is more effective than standard interferon plus ribavirin or pegylated interferon alone. In recent trials in which all patients received 48 weeks of treatment, the SVR for pa-

tients with genotype 1 was 42%–46% and for genotypes 2 or 3 the SVR was 76%–82%.⁵ Other factors associated with an improved response rate were lower baseline viral levels, less fibrosis or inflammation on liver biopsy, and lower body weight or body surface area. Patients with genotype 2 or 3 require only 6 months of therapy, and patients with genotype 1 typically undergo 12 months of therapy.

Major side effects of combination therapy include influenza-like symptoms, hematologic abnormalities, and neuropsychiatric symptoms. Side effects resulted in discontinuation of treatment in 10%–14% of patients.³ Education about side effects and their management is an integral aspect of treatment. Frequent monitoring of neuropsychiatric side effects, cytopenia and adherence to therapy is necessary.

WHO SHOULD BE TREATED?

All patients with chronic HCV are potential candidates for antiviral therapy. Treatment is recommended for patients with an increased risk of developing cirrhosis—viz., those with detectable HCV RNA levels higher than 50 IU/mL, a liver biopsy with portal or bridging fibrosis, and at least moderate inflammation and necrosis. Most patients with these biopsy findings will have elevated ALT values.

Experts vary on whether patients with normal ALTs should be treated (or even biopsied). About 1%–10% of patients with normal ALTs have bridging fibrosis and cirrhosis, and more have at least portal fibrosis. Treatment despite normal ALT should be considered in the face of

comorbidities (e.g., HIV infection) that are likely to accelerate the progression of hepatic disease; or factors that make response to treatment more likely (e.g., infection by HCV genotype 2 or 3, younger age, or normal body weight). On the other hand, factors that portend either a higher incidence of adverse events (medical or psychiatric comorbidities) or a lower response rate (older age or overweight) suggest that treatment might best be eschewed.

WHAT'S NEW IN OREGON

In collaboration with a variety of stakeholders, we recently developed a state HCV plan that provides guidance on topics such as education, outreach and surveillance. The planning group recommended that positive tests for HCV be made reportable by labs in Oregon. Although clinicians are required only to report *acute* cases of hepatitis C, you may be contacted by DHS or your local health department for more information on *any* patient who has tested positive for HCV, as we attempt to improve our understanding of the HCV epidemic in Oregon.

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