

Testing for Hepatitis C Virus Infection Should Be Routine for Persons at Increased Risk for Infection

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In the United States, chronic hepatitis C virus (HCV) infection affects an estimated 3 million persons, most younger than 50 years of age. It is one of the leading causes of chronic liver disease morbidity and mortality and the most common indication for liver transplantation. Effective treatment can eradicate the virus and eliminate or reduce liver inflammation and fibrosis, and counseling and immunization can modify or prevent the adverse effect of cofactors (for example, alcohol consumption or co-infections) on disease progression. However, controversy surrounds the need to routinely identify asymptomatic HCV-infected persons. Because no data currently demonstrate that treatment or other interventions will reduce future cases of HCV-related chronic disease and deaths, the U.S. Preventive Services Task Force found insufficient evidence to recommend for or against routine screening for HCV infection in adults at high risk. Chronic hepatitis C would require

many years of follow-up to determine the incidence of complication after treatment of or other interventions in asymptomatic persons. It seems inappropriate to wait several decades to measure the impact of early identification of this viral infection when current data support a positive therapeutic effect that points to long-term benefits. In addition, treatment and other interventions must be provided before cirrhosis or liver failure occurs. Therefore, medical and public health professionals should continue the practice of screening persons for risk factors; offering testing to those at increased risk for HCV infection; and providing infected persons with appropriate counseling, medical evaluation, and treatment.

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In 1998, the Centers for Disease Control and Prevention recommended that testing be routinely offered to persons most likely to be infected with hepatitis C virus (HCV) (Table) (1). This recommendation was part of a national strategy to identify HCV-infected persons and prevent the consequences of their infection, including transmission to others and further liver injury to themselves. Routine testing of the general population was not recommended.

These testing recommendations were made only after sufficient progress in characterizing HCV-related disease burden, epidemiology, and natural history, as well as in developing diagnostics and therapeutics to fulfill the public health criteria for screening. These included 1) recognition that many persons in the United States (2.7 million) had chronic HCV infection, 2) identification of specific groups at increased risk for infection, 3) reliable tests for diagnosis and medical management, 4) improved antiviral therapies, 5) consensus guidelines on management and treatment of hepatitis C (3, 4), 6) natural history data on the risk for HCV-related cirrhosis and other complications, and 7) identification of factors associated with increased morbidity or mortality (for example, alcohol consumption or co-infections) that could be modified or prevented through counseling and immunization.

Using different criteria, the U.S. Preventive Services Task Force, a nonfederal group of health experts that reviews published research and makes recommendations about preventive health care, published its statement on screening for HCV infection in adults in 2004 (5). Although the Task Force stated that the complications from chronic HCV infection present an enormous health burden that is expected to increase 2- to 4-fold over the next few decades, that screening can accurately detect chronic HCV infection, and that antiviral treatment can success-

fully eradicate viremia (6), it found insufficient evidence to recommend for or against routine screening for HCV infection in high-risk asymptomatic adults. The Task Force made its recommendation because it found no studies proving that screening for HCV infection leads to better long-term clinical outcomes, specifically fewer cases of HCV-related chronic disease and fewer deaths due to actions taken as a result of screening (for example, counseling and treatment). Also, it found insufficient evidence to determine the balance of benefits and harms.

We agree that currently no conclusive data from population-based studies indicate that antiviral therapy or modification of alcohol intake among HCV-infected persons decreases morbidity or mortality from cirrhosis or primary liver cancer. However, chronic hepatitis C is a protracted disease that requires prolonged follow-up (>20 to 30 years) to prove that treatment or other interventions increase life expectancy or quality. In the meantime, we have current data on which to base conclusions about such long-term benefits. Virus elimination (sustained virologic response) in 40% to 50% of treated persons infected with genotype 1 and 75% to 85% of those infected with genotypes 2 and 3, coupled with normalization of serum alanine aminotransferase (ALT) levels and improved liver histology, provides compelling evidence of a positive therapeutic effect (7, 8). The U.S. Food and Drug Administration licensed treatment for chronic hepatitis C on the basis of these intermediate therapeutic effects and concluded that treatment benefits outweighed potential harms. Subsequent studies have demonstrated that these effects are maintained for at least 10 years, which further supports the expectation that current benefits will translate into long-term ones (9).

Independent of the benefits of treatment, there is com-

Table. Recommendations for Hepatitis C Virus Testing*

Routine testing for HCV infection recommended because of high risk for infection or need for postexposure management

- Persons who ever injected illegal drugs
- Persons who received clotting factors made before 1987
- Persons who received blood or organs before July 1992
- Persons who ever received long-term hemodialysis
- Persons with unexplained abnormal ALT levels
- Health care, emergency medical, and public safety workers after needlestick or mucosal exposures to HCV-positive blood
- Children born to HCV-positive women

May benefit from HCV testing but low risk for infection

- Long-term monogamous sex partners of HCV-positive persons (counseling and testing of partners may provide reassurance)

* Information obtained from references 1 and 2. ALT = alanine aminotransferase; HCV = hepatitis C virus.

elling evidence for providing counseling, immunization, and other appropriate services to prevent or modify the combined adverse effects of cofactors and HCV infection on rapidity and severity of disease progression and on mortality. Hepatitis C virus infection and alcohol use are the leading causes of chronic liver disease–related morbidity and mortality in the United States (10, 11), and HCV-infected persons with cirrhosis are 2 to 16 times more likely to have a history of high alcohol intake than those with less severe liver disease (12, 13). Persons infected with HCV are also at increased risk for fulminant hepatitis if infected with hepatitis A virus and for more rapid progression of cirrhosis and liver failure if co-infected with HIV (14, 15). Finally, chronic hepatitis C is the most common indication for liver transplantation (16).

Thus, there are many good reasons for testing persons at increased risk. Persons with HCV infection identified through targeted testing can seek medical evaluation to determine the severity of their disease, to consider treatment, and to make lifestyle changes that could reduce the likelihood of disease progression. In addition, people who know their HCV infection status can avoid infecting others.

There are also potential harms associated with screening. The harms cited by the Task Force were related to false-positive test results (for example, anxiety), knowledge of HCV status (for example, discrimination), medical evaluation (for example, complications of liver biopsy), and treatment (for example, side effects) (5, 6). Most of these potential harms can be prevented or substantially reduced. For example, there is no reason for a patient to receive a false-positive result on a screening test. All positive results on HCV screening tests should be confirmed with additional, more specific testing (1, 2, 17, 18), which is routinely available to clinicians. This recommendation, which is consistent with testing practices for hepatitis B surface antigen and HIV antibody, minimizes unnecessary medical visits and psychological harm for persons with false-positive results on screening assays. In addition, it ensures that counseling, medical referral, and evaluation are targeted to

patients confirmed as having been infected with HCV. Cost-efficient methods for routine confirmatory HCV testing have been developed (17).

As the Task Force indicated, severe complications of liver biopsy are rare, with an incidence of 0.3% (6). However, even rare adverse events can be minimized by performing liver biopsy only when the results will influence treatment recommendations (2). In addition, the side effects of treatment are usually self-limited and can be minimized by recommending treatment only for patients most likely to benefit, that is, those with an increased risk for cirrhosis (2, 4, 18). These patients are characterized by detectable HCV RNA, a liver biopsy specimen with portal or bridging fibrosis, and at least moderate inflammation and necrosis. Most also have persistently elevated ALT levels. In some patient populations, the risks and benefits of therapy are less clear and treatment decisions should be individualized according to severity of liver disease, potential for serious side effects, likelihood of treatment response, and presence of comorbid conditions (2, 4, 18).

The potential harm of learning that one is HCV-positive is more difficult to define. It could involve disclosure of test results, which might result in disrupted personal relationships and possible discriminatory action, such as loss of employment, insurance, and educational opportunities. To minimize possible adverse consequences, the Centers for Disease Control and Prevention recommends that testing be preceded by appropriate counseling (1), which allows the individual patient to make an informed decision about testing. Furthermore, when routine testing is limited to those most likely to be infected, a high proportion of persons with positive results can be identified by testing a small proportion of the population (19).

The Task Force did recommend that physicians test patients with signs or symptoms of liver disease for HCV infection. However, most persons with chronic hepatitis C are asymptomatic despite the presence of active disease. The most frequent symptom of chronic hepatitis is fatigue, which is typically mild and intermittent and is often difficult to attribute to liver disease. Symptoms do not reliably develop in chronic hepatitis until cirrhosis is present (20); at that point, it is too late for therapy to have a major impact on survival. Most patients with HCV infection are identified when they donate blood or when abnormal ALT levels are detected during a routine medical examination or evaluation for an unrelated problem. An abnormal ALT value is a laboratory abnormality, not a symptom or sign of liver disease. The Centers for Disease Control and Prevention and the National Institutes of Health's Consensus Development Conference Panel recommend testing persons with abnormal ALT levels for HCV infection; this is widely accepted as the standard of care (1, 2, 4, 18).

We clearly need further research on the long-term effectiveness of antiviral therapy and counseling to reduce hepatitis C–related liver damage. There is also a need to expand approaches to managing persons with chronic hep-

atitis C in the general population, many of whom have confounding medical or other conditions (21). However, the sheer number of relatively young persons with chronic HCV infection who may develop complications as they age emphasizes the need to identify them as part of current clinical and public health prevention activities. It seems inappropriate to interrupt current HCV testing practices and wait several decades to prove beyond doubt that rates of HCV-related chronic disease will decrease with early identification. It is imperative that medical and public health professionals use the available evidence and the collective judgment of experts to continue the best practice of screening persons for risk factors; offering testing to those at increased risk; and providing infected persons with appropriate counseling, medical evaluation, and treatment.

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