Screening for Hepatitis C Virus Infection

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G&H What are the official recommendations for hepatitis C virus screening?

PYK The recommendations for hepatitis C virus (HCV) screening vary, but they all have a common underlying theme: Individuals should be screened for HCV if they have risk factors that increase their chances of having been exposed to infected blood. For instance, intravenous drug users are the largest cohort of at-risk individuals in the United States. Other individuals who should be screened for HCV infection include people who have intimate contact with HCV-infected individuals, those who had blood transfusions before the mid-1980s, people with a history of tattoos or piercings, individuals who have engaged in high-risk behaviors, those with elevated alanine aminotransferase (ALT) levels or other abnormal liver test results, those with HIV infection or hemophilia, those on hemodialysis, and sexual partners of those with HCV infection.

G&H How frequently are the official HCV screening recommendations updated?

PYK The current HCV screening guidelines from the Centers for Disease Control and Prevention (CDC) were last updated in 2009. The guidelines from the American Association for the Study of Liver Diseases were also recently amended strictly to reflect the new antiviral therapies that were approved in May 2011.

G&H Do you feel that current HCV screening recommendations are adequate?

PYK In an ideal setting, the existing guidelines would capture the majority of people who are at risk for HCV infection. While the current screening guidelines do capture the appropriate risk groups, the biggest problem is connecting with people who should be screened in order to implement these guidelines. Many people have risk factors for HCV infection but do not seek care from a physician, or they may not recognize that their behavior could have exposed them to HCV. For instance, an individual may have taken part in some high-risk behavior 30 years ago, but he may not remember it or may not realize this behavior increased his risk for HCV infection. In addition, the perception remains that HCV infection cannot be successfully treated; thus, some people may suspect that they were exposed to the virus, but they may not wish to be screened because of their perception that current therapies are not effective.

G&H In your opinion, which specific groups should be screened for HCV infection?

PYK The people who should always be screened for HCV are those with a history of intravenous drug use; individuals with chronically elevated liver enzyme levels; individuals who partook in any kind of high-risk behavior—such as intranasal cocaine use, tattooing, or extensive piercing—particularly in the 1960s, 1970s, and 1980s; those who had blood transfusions before 1986; individuals receiving care in hemodialysis units; and those who live with HCV-infected individuals. The reason we need to screen these particular individuals is because the majority of people who are infected with HCV are asymptomatic; they do not have signs or symptoms of hepatitis, so they do not suspect that they are infected.
**G&H** Which of your patients do you screen for HCV?

**PYK** I work in a liver clinic, so many of my patients have already been diagnosed with HCV before they are referred. If patients have not already been diagnosed, then I ask about all appropriate risk factors. If a patient has any risk factors for HCV, he or she then undergoes appropriate HCV antibody testing, even if his or her ALT level is normal. Also, I recommend HCV screening for anyone with an elevated ALT level.

**G&H** What are the potential consequences of screening too many individuals?

**PYK** Cost-effectiveness will be a huge part of healthcare economics in the coming years, so we need to ensure that screening remains cost-effective. As with any such program, screening more people for HCV increases the costs associated with testing. On the other hand, screening and diagnosing individuals with HCV may allow clinicians to prevent the consequences or sequelae of HCV infection—such as cirrhosis, decompensated liver disease, and liver cancer—which are often treated with expensive therapies (including liver transplantation). Moreover, if patients do not receive successful therapy, it is also very expensive to die from liver disease. Therefore, effectively screening individuals who are at risk of HCV infection is to everyone’s advantage, as the availability of effective therapies allows clinicians to prevent these individuals from progressing to complications.

From the point of view of healthcare economics, it is very important for us to find individuals with HCV because this disease can be cured, even in patients who have progressed to cirrhosis. Finding these individuals is particularly important now, as patients with HCV infection are becoming elderly, meaning that they are going to develop additional comorbidities beyond those associated with HCV infection. An estimated 3–4 million individuals in the United States are infected with HCV, so effectively treating this condition could significantly reduce healthcare costs in the United States.

**G&H** Why is cost-effectiveness an important consideration when trying to determine a screening strategy?

**PYK** Clinicians want to be able to screen the appropriate populations in a cost-effective manner by targeting the appropriate populations, as screening allows them to identify the individuals who require evaluation and possible therapy, thereby arresting the natural history of the disease. Given that healthcare costs account for such a large part of the current financial situation in the United States, the costs of improving quality of life for patients with different conditions are going to be carefully monitored and scrutinized over the next several decades, so it will be essential that HCV screening and therapies remain cost-effective. The previous standard of care—peginterferon and ribavirin therapy—was shown to be cost-effective for the treatment of HCV infection, and newer therapies have also been shown to be cost-effective.

While new drugs add expense, they also increase efficacy. Already, 70–75% of all HCV-infected individuals who can tolerate therapy can now be successfully treated. The future will bring an increase in cure rates with a decrease in the duration of therapy and, importantly, an improvement in tolerability with non–interferon-based therapies, thus allowing many more HCV-infected individuals to be treated.

The development of these new HCV therapies represents a unique opportunity to treat a blood-borne disease that has substantial morbidity and mortality. Currently, HCV infection accounts for the highest number of liver transplantation procedures in the United States, and the number of people with advanced fibrosis is only going to increase. Thus, HCV infection is an important public health issue that clinicians need to face. By way of comparison, 3–4 million individuals are infected with HCV, and 1 million people are infected with HIV. The infectious disease community has been very effective in their response to the HIV epidemic, with the introduction of screening programs as well as the development of effective therapies that have made HIV a treatable, chronic disease. HCV infection does not have a chronic phase, making screening and therapy even more important. Patients who are infected with HCV can undergo a finite duration of therapy, after which their only concern is sequelae related to scarring of the liver, and sequelae related to fibrosis have been demonstrated to improve following successful therapy in many patients with HCV infection.

**G&H** Currently, do you feel that clinicians are screening too much or not enough?

**PYK** I believe we are underscreening for HCV, which is why the recent *Annals of Internal Medicine* paper was so important. The authors of this paper proposed screening the entire cohort of people born between 1945 and 1965, which is the age group that has the highest prevalence of HCV infection. As individuals in this group get older, they will likely see a primary care physician, which is an opportunity for clinicians to diagnose these individuals. Again, making the initial diagnosis is important, but the key component of this strategy will be linkage to care: Screening should occur in the context of a public information campaign so individuals know that testing for HCV can lead not only to a diagnosis but also to effective therapy. In order to encourage people to seek screening, discussion of testing needs to be linked very firmly to the idea that HCV
is currently treatable—I prefer to use the word curable—and new therapies are on the horizon that will allow HCV therapy to also be well tolerated. With these new therapies, I believe many people will be able to undergo HCV therapy without experiencing substantial side effects.

**G&H** Do you support the idea of birth-cohort screening for HCV?

**PYK** Yes. Birth-cohort screening for HCV could be very beneficial. Data from the CDC and surveillance studies have shown that the cohort of individuals who have the highest rate of HCV infection is comprised of those individuals born between 1945 and 1965, and we now have the opportunity to offer effective therapy to these individuals. Therefore, birth-cohort screening for HCV infection could be an extremely effective strategy if it is linked with appropriate referral for evaluation of the disease and therapy, when warranted. [Editor’s note: Following this interview, the CDC endorsed HCV screening for individuals born between 1945 and 1965.]

**G&H** How has the addition of protease inhibitors to HCV therapy changed clinicians’ thinking about HCV screening?

**PYK** The addition of protease inhibitors to HCV therapy for genotype 1–infected individuals has improved sustained virologic response (SVR) rates to over 70%, which is an incremental improvement of approximately 30%. This improvement has offered a great degree of hope to the majority of people who are infected with this virus. Also, about half of individuals can now be successfully treated with just 24–28 weeks of therapy. In addition, newer generations of therapies are currently being tested, and they hold the promise of even higher SVR rates and better tolerability. However, additional side effects are associated with the first generation of protease inhibitors, and they do add to the expense of therapy.

**G&H** What are some of the factors that limit testing among patients who are known to be at risk of HCV infection?

**PYK** One factor that limits testing is that some individuals do not routinely visit a primary care physician and/or seek out HCV testing. Also, many individuals lack access to care; for instance, there is a high prevalence of HCV infection among homeless individuals and in prison populations. Overall, a conservative estimate is that around one quarter to one half of all HCV-infected individuals have been diagnosed, meaning that at least half of all HCV-infected individuals remain undiagnosed. This is an extremely large number of individuals with a chronic disease that, if left untreated, can progress to end-stage liver disease, cirrhosis, and liver cancer. Again, the cost of treating people once they progress to end-stage liver disease is very high, so earlier diagnosis and treatment are paramount.

**G&H** What are some strategies to help address these barriers?

**PYK** Public awareness campaigns are important to let people know that they should be screened if they have certain risk factors. The most important step is then to link screening to care: Once the diagnosis is made, HCV-infected individuals need to be referred to an appropriate clinician for evaluation in order to determine whether or not they require therapy.

**G&H** Overall, how can screening for HCV be improved?

**PYK** The major way that screening could be improved is to adopt a policy of widespread mass screening. Again, the strategy that was recently proposed in the *Annals of Internal Medicine* was to screen the entire cohort of individuals born between 1945 and 1965. To be truly effective, such screening would need to be linked to appropriate evaluation and therapy. Also, the introduction of protease inhibitors has been a particularly substantial advance in HCV therapy. If left untreated, HCV can cause chronic disease and substantial morbidity and mortality. However, we now have therapies that can cure the disease with a finite course of therapy, which is truly remarkable.

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