

Managing Chronic Hepatitis C Virus Infection

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It was discovered in the 1970s that most cases of post-transfusion viral hepatitis were caused by neither of the then known hepatitis viruses: termed type A and type B.^{1,2} In these cases, in which a patient had obvious signs of viral hepatitis, but the type A and type B hepatitis viruses were not found, the patient's illness was designated non-A, non-B hepatitis. In 1989, the hepatitis C virus (HCV) was identified by molecular cloning as the primary causal agent of non-A, non-B hepatitis.^{3,4} Today, it is estimated that more than 3 million Americans are infected with HCV.^{5,6} This article examines the epidemiology, clinical features, diagnosis, and treatment of chronic HCV infection.

EPIDEMIOLOGY

Screening for HCV infection is performed by testing for the presence of antibodies to HCV within a patient. According to a recently published nationwide survey conducted by the Centers for Disease Control and Prevention (CDC), the prevalence rate of HCV-antibody (anti-HCV) positivity in the general population is 1.8%, with 74% also positive for HCV RNA.⁷ (The presence of detectable HCV RNA is a sign of chronic HCV infection.) In that survey, 65% of patients with HCV infection were 30 to 49 years of age. For African Americans, the prevalence of seropositivity is 3.2%, compared with 1.5% for non-Hispanic whites.⁵ For current abusers of intravenous drugs, the prevalence rate of HCV infection has been estimated to be 79%.¹

One of the most efficient means by which the virus is transmitted is through an individual receiving infected blood or blood products by way of transfusion (Table 1). In the 1960s, the rate at which viral hepatitis was acquired by patients who had undergone transfusion therapy was, in some reports, estimated to be 20% or more.^{1,8} The risk remained substantial even after elimination of commercial donors and the introduction of surrogate markers such as elevated alanine aminotransferase (ALT) levels and hepatitis B antibodies. However, since 1992, when the second-generation antibody test for HCV became available, all blood for transfusion has been routinely screened for the virus. As a result of this, the risk of infection with HCV via blood transfusion has been reduced to an estimated 0.001% per unit of blood

transfused.⁹ Also, viral inactivation procedures have been implemented since 1992, and because of this and the rigorous screening procedures, patients with hemophilia have been better protected from receiving infected coagulation factors. Moreover since 1994, all commercially available immunoglobulin products produced in the United States must be negative for HCV or must undergo viral inactivation.¹

However, patients who underwent blood transfusions before 1992 have a substantial risk of having received infected blood, as do patients who received organ transplants during this time. Moreover, up to 90% of patients with hemophilia who were treated with factor VIII before 1985 or factor IX before 1987 are reported to have been infected with HCV.^{6,10}

Another very efficient means by which the virus is transmitted is through the use and sharing of contaminated needles or other equipment for the intravenous administration of illegal drugs. One study has suggested that HCV may be transmitted during cocaine inhalation, through the use of contaminated straws,¹¹ though the significance of intranasal cocaine use as a risk factor has been questioned. From the author's experiences, a history of intranasal cocaine use has been the *only* reported risk factor in a substantial number of patients.

Nosocomial transmission of HCV has generally been rare in the United States, but all health care personnel should be aware of the risks when proper infection control and decontamination procedures are not practiced. It is because of rigorous implementation of such procedures that the rate of HCV infection among health care workers is no higher than that found in the general population, approximately 1% to 2%.¹ The risk of seroconversion after a single incident of being accidentally stuck with a contaminated needle in the health care setting has averaged 1.8%¹ but has been reported to be as high as 10% in some foreign health

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care centers.¹² The risk of transmission from infected health care workers to patients appears to be very low, with only isolated reports recorded.¹

The one hospital setting where the rate of HCV transmission is particularly high is in the hemodialysis unit. The prevalence of HCV infection among chronic hemodialysis patients is approximately 10%, with some centers reporting rates as high as 60%.¹³ This alarmingly high rate of infection has been attributed to infection control measures not being practiced (eg, hospital personnel using a single medication vial for different patients).¹ The risk of HCV infection increases with the number of years the patient has been receiving hemodialysis treatment.¹

Although the hepatitis B virus (HBV) is commonly transmitted sexually, HCV appears to be less readily transmitted by this means. Studies of spouses of patients with chronic HCV infection reveal a low rate of viral transmission, ranging from 0% to 4.4% (average 1.5%).¹ However, about 15% of the patients with acute HCV infection documented by the CDC's surveillance system have a history of sexual contact, either with an infected individual or with multiple sexual partners, with no other risk factors for transmission.^{1,14} As with the transmission of other blood-borne viruses, HCV transmission from men to women and among homosexual men appears to be more efficient than transmission from women to men, but is still much less common than for HBV and HIV. The CDC has concluded that sexual transmission of HCV does occur, albeit generally inefficiently and at a relatively low rate.¹

Vertical transmission of HCV, from the HCV-positive mother to her child, during the perinatal period, has been reported.¹ Also, a mother having an HIV infection appears to increase the risk for vertical transmission.¹ For HIV-negative women who are infected with HCV, the risk of vertical transmission is approximately 5%. For women positive for both HCV and HIV, the rate of HCV transmission rises to 14% or more.¹

Another puzzling aspect of HCV transmission involves the role of nonsexual household contact. For an undetermined but presumably small percentage of individuals, such household contact with an HCV-positive person represents the only means of transmission.¹ In studies conducted overseas, the prevalence of HCV transmission through nonsexual household contact was reported to be 4%,¹⁵ but most clinicians in the United States have the impression that the risk of transmission through household contact is substantially lower. Theoretically, such transmission could take place through sharing razor blades, toothbrushes, and other household items potentially contaminated with infected

Table 1. Risk Factors for Hepatitis C Virus (HCV) Infection

Receipt of blood or blood products (especially before 1992)*
Intravenous drug use
Intranasal cocaine use
Chronic hemodialysis
HCV-positive mother (especially with HIV coinfection)
Needlestick in health care setting
Sexual contact with an HCV-positive person (low)
History of tattooing and/or body-piercing†

*Since 1992, the risk of infection via blood transfusion has significantly declined.

†These have not been established as significant risk factors in the United States.

blood. Patients with HCV infection are therefore advised to avoid sharing such items with family members.

Procedures such as tattooing, body piercing, barbering, and folk medicine practices have been associated with HCV transmission in other countries, but case studies in the United States have failed to discover a corresponding association with such procedures and practices.¹ Although HCV transmission via tattooing or body piercing with improperly sterilized instruments is certainly possible, it has so far not been established as a significant risk factor in this country. Finally, some 10% of recorded cases of HCV infection in the United States are not associated with any risk factors for virus transmission.¹

CLINICAL FEATURES

Symptoms of acute HCV infection may include malaise, anorexia, and abdominal pain,¹ and a minority of persons may become jaundiced. However, acute HCV infection causes overt illness in only a minority of individuals. Most of the patients with acute infection are asymptomatic or have only mild symptoms and do not seek medical care, being unaware of their illness. Viewed from a different perspective, the vast majority of patients found to have chronic HCV infection cannot recall any suggestive illness in past years (ie, when they were in the acute stage of infection). For patients who have acute HCV infection and who are overtly ill, the diagnosis of the infection is complicated by the fact that some of those individuals may present symptoms before seroconversion. The reason for this is that the average time from exposure to the onset of symptoms is 6 to 7 weeks, whereas the average time to anti-HCV seroconversion is

Table 2. Risk Factors for Rapid Progression to Cirrhosis in Hepatitis C Virus–Positive Patients

Consumption of 50 g or more of alcohol daily
Acquisition of infection after age 40
Male sex
Coinfection with HIV*

Data from Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups. *Lancet* 1997;349:825–32.

*Benhamou Y, Bochet M, Di Martino V, et al. Liver fibrosis progression in human immunodeficiency and hepatitis C virus coinfecting patients. The Multivirc Group. *Hepatology* 1999;30:1054–8.

8 to 9 weeks.^{16,17} Thus, a negative anti-HCV test result does not rule out the possibility of acute HCV infection. In patients with suspected acute viral hepatitis, a polymerase chain reaction (PCR) assay testing for HCV RNA should be performed to rule out acute HCV infection.

Seventy-five percent to 85% of patients initially exposed to HCV eventually develop chronic infections,¹ a considerably higher percentage than those who remain chronically infected after exposure to HBV. It is for this reason that chronic infection with HCV poses the greatest concern for health care practitioners. Recent evidence suggests that the spontaneous clearance rate is higher in those infected during infancy or early childhood.¹⁸

Although some patients complain of chronic fatigue or abdominal discomfort, individuals with chronic HCV infection are typically unaware of their condition, and they may remain asymptomatic for many years or decades. Chronic infection with HCV is usually discovered as a result of elevated ALT levels reported as part of a routine medical examination or from a blood test performed as a part of blood donor screening. Laboratory findings in patients with chronic HCV infection are markedly variable, however. Approximately 60% to 70% of patients with chronic HCV infection will have persistent elevations in ALT levels. The remainder may have intermittently or persistently normal ALT readings, even though the viral levels in patients with normal ALT levels are indistinguishable from those with high ALT levels. Moreover, patients with persistently normal ALT levels often have abnormal liver biopsy specimens, although the histologic findings on average tend to be milder.¹ Thus, a single normal reading or even repeatedly normal ALT readings do not exclude chronic liver disease caused by HCV. Similarly, it would be an error for a physician to ignore elevated ALT levels

simply because of the perception that the elevation is “too mild to be important.”

Follow-up studies have reported that approximately 20% of patients with chronic HCV infection develop cirrhosis of the liver within 20 years after infection, and that 1% to 4% of patients with cirrhosis develop hepatocellular carcinoma annually.⁵ A French study of over 2,000 patients with chronic HCV infection has reported a median estimated time of 30 years to cirrhosis.¹⁹ Risk factors for rapid progression to cirrhosis included initial infection after age 40, male sex, and consumption of 50 g or more of alcohol daily (**Table 2**). Men who were initially infected after age 40 years had a median time of 13 years to cirrhosis.¹⁹ In contrast, in a large cohort of Irish women infected by HCV from contaminated anti-D immune globulin in the late 1970s, the prevalence of cirrhosis after 17 years was only 2%; even here, however, an additional 18% of patients had bridging fibrosis, considered to be a harbinger of future cirrhosis.²⁰ It has recently become apparent that coinfection with HIV is associated with a greater likelihood for fibrosis and more rapid progression of liver disease.²¹

Patients with chronic HCV infection and liver disease are also at risk for acquiring fulminant hepatitis A virus (HAV) infection. In one study, 17 of 432 patients (3.9%) with chronic HCV infection contracted HAV infection over a follow-up period of 7.5 years. Seven of these patients (41%) went on to develop fulminant hepatitis,²² underscoring the need to vaccinate HAV-seronegative patients with hepatitis A vaccine. (Immunization against HBV is also recommended in HBV-seronegative patients.)

DIAGNOSIS

Diagnosis of HCV infection is most commonly made by identification of antibodies to the virus in the blood. Antibody tests include the enzyme immunoassay (EIA) for routine testing and the recombinant immunoblot assay (RIBA) for confirmatory testing. False-positive EIA test results may occur in patients with autoimmune liver disease or in volunteer blood donors with no risk factors and normal liver tests, making confirmatory testing necessary in certain populations.

The RIBA test was the first confirmatory test to become available, but many hepatologists now proceed directly to an HCV RNA test, in particular, a PCR assay, which may be qualitative (only revealing whether HCV RNA is present or not) or quantitative (which is slightly less sensitive in one of the most commonly used assays but still detects HCV RNA in the overwhelming preponderance of infected patients).

Another type of quantitative RNA assay, the branched DNA test, is highly reproducible but has the limitation of requiring more than 200,000 viral copies/mL to be present in serum, compared with reported thresholds as low as 1000 copies/mL, or even less, for some quantitative PCR assays and 100 copies/mL for qualitative PCR tests. There is currently a trend toward reporting quantitative PCR results by a newly standardized system of international units (IU/mL).

An additional test ordered by most hepatologists for determining HCV infection in patients is an assay that analyzes HCV genotype, reflecting disparities in genetic sequences among different viral populations. Of 6 major genotypes, designated via numerals 1 through 6, HCV genotypes 1, 2, and 3 are found in most US patients, with about 70% having genotype 1. HCV infection associated with genotype 1 has the lowest response rate to antiviral therapy and appears to require a longer duration of therapy (from 6 to 12 months), factors that enter into discussion with patients.

Patients who should be tested for antibody to HCV include those with documented exposure to HCV, such as health care workers who have been stuck with contaminated needles or who have had other exposures to HCV-infected blood and children born to HCV-positive women.¹ In addition, patients with other known risk factors for HCV infection should be tested. This includes anyone who has ever injected illicit drugs with needles that have been used by others, patients who have received clotting factor concentrates before 1987, and those who have received blood transfusions or organ transplants before July 1992, as well as all patients who have received long-term hemodialysis treatment or who have unexplained elevations in ALT or aspartate aminotransferase (AST) levels.

Individuals for whom HCV testing is not presently recommended include health care workers who do not have a history of exposure to HCV, individuals who have had only nonsexual household contact with people infected with HCV, and the general population, including pregnant women without risk factors for HCV infection.¹ In the absence of specific risk factors, the prevalence of positive HCV test results in these populations is generally expected to be low. The usefulness of routine HCV screening in several groups of patients remains uncertain. These groups include people who have received tissue (but not blood or organ) transplants, people who inhale cocaine through straws used by others but who have never used intravenous drugs, those with a history of tattooing or body piercing, people with long-term sex partners who are positive for HCV, and those with a history of multiple sex

partners or of sexually transmitted diseases.¹ However, many hepatologists do routinely screen the long-term sexual partners of HCV-infected individuals.

TREATMENT

Interferon Monotherapy

Until June of 1998, the only products approved by the US Food and Drug Administration for treatment of chronic HCV infection were various forms of interferon- α . These include Intron A (interferon α -2b recombinant), Roferon-A (interferon α -2a, recombinant), and Infergen (interferon α -1). Initially, the recommended duration of therapy was 6 months, but in the mid-1990s it was recognized that 12 months of therapy reduced the risk of relapse in those who attained negative results on PCR testing and/or had normal ALT levels during the first 6 months. Still, only 10% to 20% of patients with chronic infection have a sustained response to treatment with interferon monotherapy.⁵ Factors associated with a particularly low likelihood of response to this form of therapy include having HCV genotype 1, a high pretreatment viral load, and cirrhosis.

Interferon monotherapy is currently limited to patients who cannot be expected to tolerate ribavirin (used in the newer combination therapy), such as patients with coronary artery disease or baseline anemia from chronic renal failure or a hemoglobinopathy. Interferon *is not* approved for patients younger than 18 years. Women who are pregnant should not be treated with interferon. Patients with decompensated cirrhosis are generally not considered candidates for antiviral therapy (monotherapy or combination therapy).

Adverse effects of interferons include headache, fatigue, myalgia, and fever. Depression and suicidal behavior may also occur in patients taking interferons, and warrant extreme caution in patients with a history of preexisting psychiatric disorders. Adverse effects of interferons are discussed in further detail in the following section.

Combination Therapy

In June 1998, the FDA approved Rebetron, a combination therapy that includes interferon α -2b and the antiviral drug, ribavirin, for the treatment of chronic HCV infection in patients who had relapsed following a successful course of interferon monotherapy. In December 1998, this combination therapy was approved for patients who had not previously been treated with interferon.

In patients who had previously responded to therapy with interferon but then relapsed, 49% of those who were given combination therapy for 6 months had a

Table 3. Predictors of Response to Antiviral Therapy for Chronic Hepatitis C Virus (HCV) Infection

HCV genotype non-1
 Low pretreatment viral load
 Absence of cirrhosis
 Younger age
 Female sex

Data from McHutchison JG, Gordon SC, Schiff ER, et al. Interferon alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. Hepatitis Interventional Therapy Group. *N Engl J Med* 1998;339:1485–92 and Poynard T, Marcellin P, Lee SS, et al. Randomised trial of interferon alpha2b plus ribavirin for 48 weeks or for 24 weeks versus interferon alpha2b plus placebo for 48 weeks for treatment of chronic infection with hepatitis C virus. *Interventional Therapy Group. Lancet* 1998;352:1426–32.

sustained virologic response, compared with 5% of those who were given interferon alfa-2b plus placebo. Combination therapy was associated with significant improvement in liver histology and normalization of serum ALT levels.²³

In pooled data from 2 large multicenter studies in therapy-naïve patients with chronic HCV infection, 40% of patients receiving combination therapy had undetectable HCV RNA levels 6 months after a 48-week course of treatment, compared with 15% of those who received 48 weeks of interferon alfa-2b monotherapy.^{24,25}

For the many patients who have failed to respond to interferon monotherapy in the past, their response to combination therapy has been studied in a large number of centers.²⁶ Sustained response rates have occurred in 10% to 32%. Although, combination therapy is not officially approved for use in prior nonresponders to interferon alone, it is considered an important option by many clinicians for these patients, particularly those with more advanced fibrosis.

In the trials of combination therapy, viral genotype has emerged as the most important predictor of virologic response to treatment.^{24,25} Infection with HCV genotype 1 is associated with lower response rates, but response to combination therapy still greatly exceeds that seen with interferon monotherapy in treatment-naïve patients. In one study, 64% of treatment-naïve patients with infections associated with genotypes 2 or 3 had a sustained response at a 6-month follow-up, as opposed to 31% of those with genotype 1.^{24,25} Increasing the length of treatment from 24 weeks to 48 weeks improved the sustained response rate in patients with genotype 1, particularly with high viral loads. No such difference in efficacy between 6 and

12 months was reported in patients infected with HCV of genotypes 2 or 3.²⁵ Other predictors of response to treatment are listed in **Table 3**. A very high prevalence of genotype 1, and possibly other, as yet undescribed factors, may explain lower response rates in African Americans.²⁷

Prime candidates for treatment with combination therapy include patients with detectable HCV RNA, elevated ALT levels, and liver biopsy findings of portal or bridging fibrosis or at least moderate inflammation or necrosis. Patients with minimal inflammation and no fibrosis may also be offered treatment, but if such patients have long-standing infection and wish to defer therapy, this is a reasonable option provided they are followed regularly. Because of poor results, interferon monotherapy was considered optional in patients with compensated cirrhosis. With the improved results of combination therapy, most hepatologists consider therapy to be strongly indicated in these patients. For patients with persistently normal ALT levels, the 1997 National Institutes of Health Consensus Conference concluded that interferon therapy should be restricted to clinical trials.⁵ This recommendation is being re-evaluated in trials with combination therapy. Preliminary observations suggest response rates comparable to those in patients with elevated ALT.

A controversial application of antiviral therapy is maintenance treatment for nonresponders, which some clinicians have adopted in light of data suggesting anti-inflammatory and antifibrotic effects for interferon.²⁸ Further studies of maintenance therapy are needed before it can be recommended for widespread use. Two large US multicenter studies evaluating peginterferon (discussed later) as maintenance therapy have been initiated.

Contraindications. Significant teratogenic and embryocidal effects from ribavirin have been reported in animal studies. Therefore, combination therapy must not be used by women who are or may become pregnant during therapy or during the 6 months after stopping therapy, or by their male partners. The need for strict adherence to contraceptive measures must be emphasized. Pregnancy testing should be performed at monthly intervals in women of childbearing age who are receiving ribavirin.

Dosage and administration. Rebetron is at present the only combination treatment approved for chronic HCV infection. Combination therapy with Rebetron is as follows: Patients with body weights of 75 kg or less should receive two 200 mg capsules of ribavirin in the morning and 3 capsules in the evening. Those with body weights greater than 75 kg should take three

200 mg capsules in the morning, followed by 3 in the evening. The dosage for interferon alfa-2b is 3 million IU, 3 times per week, by subcutaneous injection. Virologic response should be evaluated at 24 weeks. Discontinuation of therapy should be considered in patients who still have detectable levels of HCV RNA at that time. Treatment may be continued for an additional 24 weeks in all other patients, depending on baseline disease characteristics, clinical and virologic response, and tolerability. Patients with infection involving genotype 1 who are responding at the 6 month point should be treated for a year to minimize the risk of relapse, while patients with genotypes 2 and 3 may stop treatment after 6 months. However, in patients with advanced fibrosis, or cirrhosis, many clinicians would extend treatment to a year even if the patient is infected with a "more favorable" genotype.

Adverse effects. Hemolytic anemia frequently occurs in patients treated with ribavirin. The mean decrease in hemoglobin is 2.5 g/dL, but may exceed 3 g/dL or even 4 g/dL, thus requiring dosage reduction or discontinuation. Complete blood cell counts should be obtained at baseline and at weeks 1, 2, and 4 of therapy, then monthly or more frequently, if clinically indicated. In light of rare reports of myocardial ischemia associated with hemolysis, ribavirin should be used very cautiously, if at all, in patients who have a history of coronary disease. When there is doubt, stress testing and consultation with a cardiologist are strongly advised before treatment.

The most common adverse events associated with combination therapy are flu-like symptoms such as headache, fatigue, myalgia, and fever, which traditionally have been associated with interferon. These appear to decrease in severity as treatment is continued, although fatigue often persists throughout the treatment course.

Severe adverse psychiatric events have been reported in patients treated with interferons. Depression and suicidal behavior, including suicidal ideation, suicide attempts, and completed suicide may occur. For these reasons, therapy should be used with extreme caution in patients with a history of severe depression or other major psychiatric disorders. Physicians should monitor all patients for evidence of depression, and in severe cases, treatment should be stopped and psychiatric intervention sought. These warnings apply to all interferon products used to treat HCV infection.

A noteworthy adverse effect of interferon is thyroid dysfunction, which occurs in about 5% of patients and may lead to hypothyroidism requiring long-term thyroid replacement therapy or less commonly, hyper-

thyroidism requiring ablative therapy. Thyroid tests, including thyroid-stimulating hormone (TSH), should be evaluated every 3 months during either combination therapy or interferon monotherapy.

Side effects of combination therapy that occur more frequently than with interferon alone, and appear attributable to ribavirin itself, include nausea, dry cough, dyspnea, chest pain, rash, dry skin, and pruritus. The dyspnea may occasionally be disproportionate to the degree of anemia produced by the drug.

The ultimate effect of combination therapies on the risk for developing cirrhosis and liver cancer will require long-term follow-up over a period of years. However, in light of the marked improvement in hepatic inflammation, as well as favorable effects on fibrosis, there is no reasonable doubt that viral eradication profoundly affects the long-term course of the liver disease. Sustained virologic response in cirrotics has already been shown to decrease the risk of liver cancer.

Special Considerations in Antiviral Therapy

Special populations in which antiviral therapy must be strongly considered include patients coinfecting with HIV, who are at risk of more rapidly progressive liver disease. Patients on renal dialysis are often referred by nephrologists for treatment to attempt HCV eradication prior to kidney transplantation. A course of interferon monotherapy may be considered, but ribavirin is contraindicated because of anemia. Patients with essential mixed cryoglobulinemia (EMC), a known extrahepatic complication of HCV, may have a remission in their EMC-associated symptoms if they have a virologic response.

Future Treatments

Much interest currently centers on the potential efficacy of pegylated (PEG) interferon, which requires administration only once per week because of delayed clearance. It is formed by the linkage of a molecule of polyethylene glycol to a molecule of interferon. Two products already subjected to clinical trials are peginterferon alfa-2b (using a linear 12 kd PEG molecule) and peginterferon alfa-2a (which uses a branched 40 kd PEG molecule). Both of these pegylated products have been shown to double the sustained response rate of their corresponding standard interferons when given as monotherapy.^{29,30} Moreover, a very recent trial that studied peginterferon alfa-2b, 1.5 µg/kg body weight, once weekly combined with ribavirin, 800 mg daily, demonstrated a sustained response rate of 54% compared with 47% for standard combination therapy. Patients with HCV genotype 1 had sustained response rates of 42% with peginterferon alfa-2b and 33% with

standard interferon alfa-2b.³¹ The results of studies evaluating peginterferon alfa-2a and ribavirin are anticipated. Pegylated interferon may well replace standard interferon in the next 1 to 2 years.

It is hoped that novel antiviral agents, such as protease, helicase and viral RNA inhibitors, will be developed in the next few years that have activity against HCV. A class of drugs called ribozymes, which are nucleic acids that cleave target RNA sequences by acting as "molecular scissors," are eliciting considerable interest. Finally, agents like interleukin-10 are attracting interest for their potential anti-inflammatory and/or anti-fibrotic properties even though they do not suppress HCV replication.

PRIMARY PREVENTION

At present, there is no vaccine for HCV infection. Guidelines for the primary prevention of HCV infection include screening all blood, plasma, tissue, organs, and semen donations for the presence of anti-HCV.¹ Before testing, donors with known risk factors for HCV should be excluded. Plasma products, including clotting factor concentrates and immunoglobulin products, are required to undergo a process of viral deactivation.

Other primary prevention practices include counseling users of illicit drugs, with the goal of enrolling them in drug treatment programs; if they continue to use injectable drugs, they should be educated regarding the dangers of sharing needles and other equipment. Similarly, patients with a history of sexually transmitted diseases or high-risk sexual practices should be counseled regarding the risk for HCV and other bloodborne infections.¹

In the hospital and other healthcare settings, it is essential that standard barrier precautions for the handling of blood and the disposal of needles be strictly observed. All staff should be thoroughly familiar with such precautions, which include the use of gloves when touching blood, body fluids, secretions, excretions, and contaminated equipment. More stringent precautions are required in the hemodialysis unit, as there is a higher risk of infection. Staff should be required to use gloves whenever they touch patients or equipment, and instruments and medications should not be shared among patients.¹

SUMMARY

HCV infection is today the most common chronic blood-borne viral infection in the United States.^{5,6} Because the virus is now routinely screened for and because of increased awareness of the risks of infection

on the part of the public, the number of new cases of infection per year since the 1980s has dropped significantly. During the 1980s, an estimated 230,000 new HCV infections occurred each year.¹ In 1996, approximately 36,000 new infections were estimated to have occurred.¹ However, this is still a high number, and currently, HCV infection is responsible for 8,000 to 10,000 deaths per year from resultant chronic liver disease.¹⁴ Compounding the problem is the fact that the majority of people infected with HCV are unaware that they have been exposed to the virus, and the majority of individuals acutely infected with HCV go on to develop chronic infection, with the potential for developing cirrhosis over subsequent decades.

Because physicians working in the hospital environment treat a large number of patients with a variety of risk factors for HCV, familiarity with the disease, as well as with its treatment and prevention, is essential. Antiviral therapy can help prevent continuing liver damage and forestall the development of cirrhosis. This is accomplished by reducing the viral load to less than detectable levels and normalizing ALT levels. Not all patients benefit from such treatment, however. The combination of interferon alfa-2b and ribavirin has demonstrated a sustained virologic response in up to 40% or more of patients and now constitutes first-line therapy for chronic HCV infection. Pegylated interferon is on the horizon and novel therapeutic strategies can be expected in the future. **HP**

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