Hepatitis C Infection and Injection Drug Use: The Role of Hepatologists in Evolving Treatment Efforts

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Treatment regimens for both substance abuse and hepatitis C infection are complex and evolving. New pharmacotherapy for opioid addiction allows for office-based treatment and, thus, an opportunity for expanded treatment in the context of hepatitis C infection. The current article addresses the newly evolving, complex issues in the medical management of hepatitis C and injection drug use. (HEPATOLOGY 2004;40:516–519.)

The majority of incident infections with the hepatitis C virus (HCV) are acquired through injection drug use practices. For most injection drug users, drug use occurred in the past. However, drug addiction is a chronic disease with a continuing possibility of former drug users' relapsing back to drug use. Injection drug users, both current and reformed, are at risk for HCV and other infectious diseases, and they commonly display comorbidities associated with drug use, such as psychiatric illnesses. Accordingly, drug users can undergo successful medical management through a team approach that addresses not only the medical consequences of drug use but also the frequently accompanying mental health, infectious disease, and behavioral and social problems. Thus, HCV infection in these individuals is a complex and challenging medical issue. HIV coinfection frequently co-occurs in HCV-infected drug users. Recent recommendations of an international panel of experts suggest that treatment of persons coinfected with HCV and HIV should be undertaken not only by hepatologists or gastroenterologists expert in dealing with HCV infection but also by infectious disease specialists in a step-by-step approach as part of the patient's global care and treatment.1

HCV treatment of active drug users was recommended by the 2002 National Institutes of Health Consensus Conference panel on a case-by-case basis, but the NIH did not provide guidance and support for the hepatologists or gastroenterologists generally involved in administering such treatment. This article addresses the basis for HCV care and treatment and the manner in which they can be successfully administered to this challenging patient population. These recommendations include the need for hepatologists to: (1) become knowledgeable regarding substance use and abuse; (2) be comfortable and comprehensive in addressing the issue of substance use and abuse with patients, including risk reduction, relapse, and HCV reinfection; (3) become certified in treating opioid addiction with buprenorphine; and (4) participate in caring for HCV-infected injection drug users as part of a global care and treatment team, realizing the importance of managing the addiction problem in conjunction with treatment of the accompanying infectious disease or diseases.

Understanding the Patient Injecting Drugs

The 2002 National Survey on Drug Use and Health2 reports that 3.7 million Americans above the age of 12 years have experimented with heroin use. Patterns of drug use can be categorized as experimental, as part of normal curiosity; recreational, based on peer support or acceptance; facilitation, to enhance skills or performance; abuse as a consequence of pleasure seeking; and compulsive use to avoid abstinence effects.3 Treatment of compulsive or addictive drug use may result in complete recovery or a relapsing scenario in which the use of drugs is intermingled with periods of long remissions.4 Indeed, vulnerability to relapse can last years or a lifetime. Recent neurological imaging studies5,6 have shown that addiction results in profound metabolic changes in the brain. The national drug control strategy has characterized injection drug use as a disease with a need for treatment and support services from effective programs that include faith- and community-based organizations.7 A recent study8 has shown that for individuals who use tobacco and alcohol,
there is a greater exposure opportunity and hence likelihood for use of illegal drugs, such as cocaine or heroin. Indeed, many drug users regard the use of illegal drugs as a personal choice, similar to tobacco and alcohol use.

Injection drug users do not fully utilize health care services, are disenfranchised from the medical care system, and frequently require inducement and support to access and engage in medical care and treatment. Individuals who do enter substance abuse programs often have associated comorbidities, such as physical injuries and mental health disorders. Relapse to drug use and HCV reinfection remain medical issues of concern for drug users in treatment. HCV screening studies have shown that for both adolescents and adults entering the criminal justice system, nearly one in five individuals are infected with HCV. Thus, community mental health clinics and psychiatric hospitals, community based walk-in clinics, prison-related health systems, HIV clinics, and methadone clinics are common locations for these individuals either at high risk for new HCV infection or with already existing HCV infection. Accordingly, these are venues in which hepatologists and others with HCV treatment expertise could participate in providing health care services to individuals infected with HCV.

HCV Care and Treatment and Injection Drug Use

An evolving body of data indicates that either current injection drug use or substance abuse are not necessarily barriers to care and treatment. Indeed, injection drug users respond to HCV treatment in a fashion similar to those without a history of substance abuse. Interim data from a recent study suggest that treatment of HCV-infected individuals utilizing methadone maintenance for the control of opioid addiction is as effective as treatment for non-drug users with HCV infection, although general management issues are more difficult to handle. Currently, treatment recommendations for individuals on methadone maintenance therapy, endorsed by the American Association for the Study of Liver Disease and the Infectious Diseases Society of America, state that the use of methadone does not preclude medical management of hepatitis C. However, it must be noted that patients on methadone maintenance therapy may have difficulty in completing interferon-based therapy regimens.

An increasing number of cohort studies report that combination therapy for hepatitis C can be effective even for active drug users. However, active drug users with HCV often have substantial comorbidities that challenge their medical management. Two essential aspects of management are that an interactive and trusting patient-provider relationship must be established and that patients must be deemed treatment-ready, much as is the case for patients with HIV infection who are brought to treatment readiness prior to the initiation of antiretroviral therapy. Similarly, care programs focused on bringing active drug users to HCV treatment readiness, with or without modification of their drug use, would maximize HCV treatment outcomes for this hard-to-reach and hard-to-treat population. This approach of careful monitoring of drug-related issues together with aggressive intervention, as needed, would increase the likelihood that injection drug users and substance abusers who are HCV-infected and have associated psychiatric illness would complete their HCV treatment. In this context, clinicians must be prepared to address psychiatric conditions and drug use, including relapse to drug use, and to integrate early interventions for these conditions into their HCV treatment algorithm. Unfortunately, few programs or treatment models are designed to systematically manage substance use and comorbidities of patients with HCV prior to and during interferon-based therapy.

Medical Management of HCV for Injection Drug Users

The basic principles of medical ethics, including the Kantian principle of respect for person, principle of beneficence, and principle of distributive justice, mandate healthcare services for injection drug users. These principles relate that drug-using individuals are neither inferior to other patients nor less deserving of care and treatment, as well as that health care providers should act to best advance the medical interests of their patients. However, medical management of HCV in active drug users is more difficult and more time consuming than is HCV treatment of non–drug users. There are also concerns regarding medication noncompliance without an adherence intervention and the possibility of HCV reinfection with relapse to drug use. Although HCV reinfection has been demonstrated both in chimpanzees and humans, the evidence is based largely on serologic markers rather than on clinical manifestations. Thus, active injection drug users should not be automatically denied treatment on the basis of continued drug use. When treatment decisions are considered, it is imperative for the provider to discuss the various care and treatment options with appropriate informed consent, detailing the risks versus the benefits of medical options. The hoped-for benefit, of course, is the eradication of the HCV infection, thus reducing the likelihood of life-threatening liver disease. Unfortunately, factors associated with a poor response, such as infection with HCV genotype 1 and coinfection with HIV, are commonly represented among drug users. Also, there is a relatively high rate of adverse
effects of the treatment in addition to the risk for relapse to drug use. Clearly, treatment of HCV infection in injection drug users represents a major challenge requiring a comprehensive approach by multiple health care providers that address all conditions that may coexist and the utilization of novel approaches for care and treatment.

Models of care range from referral and consultative services to integrated care and “one-stop shopping” for health care. Subspecialty consultation can occur within community-based outreach programs, through partnerships with community-based organizations that provide coordinated psychiatric care, counseling, and case management, in risk-reduction programs, within HIV clinics, or in newly evolving HIV/HCV coinfection clinics. Fully integrating HCV care and treatment can occur in an HIV setting or a substance abuse treatment program, such as that of methadone maintenance. In the latter settings, support services are provided by non-hepatologists who would greatly benefit from the participation of those experienced in treating liver disease. As HCV infection becomes accepted as a primary care issue in the context of HIV and substance-abuse management, hepatologists can support the process of integrative management by becoming more knowledgeable about opioid addiction and the use of buprenorphine treatment. This pharmacotherapeutic approach will permit office-based management of opioid addiction within the setting of general internal medicine. A waiver to the Drug Addiction Treatment Act of 2000 is obtained through physician training events for the practice of opioid addiction therapy using buprenorphine (see http://buprenorphine.samhsa.gov/training.html).

Liver disease remains a serious medical issue for injection drug users with HCV infection. For persons with HIV/HCV coinfection, liver disease is now the leading cause of morbidity and mortality. A recent multicenter epidemiological study indicated that 46% of coinfected patients had severe liver disease. Without HCV care, management of their addiction and associated comorbidities, and treatment for their liver disease, these individuals are at high risk of progression to end-stage liver disease. Thus, it is critical that hepatologists and others with the necessary expertise become full-fledged participants in the care and treatment of injection drug users with HCV infection (Table 1).

A final issue that needs to be addressed: How might a hepatologist obtain support/reimbursement for forming new collaborations and providing needed health services to drug users? Noting that private and federal health insurance programs may not fully support addiction treatment services, new collaborations and models of care for HCV care and treatment can be supported as demonstration projects through Health Services Resources Administration (www/hrsa.gov) or Substance Abuse and Mental Health Services Administration (www.samsha.gov). In addition, both the National Institute on Drug Abuse (www.nida.nih.gov) and the National Institute on Alcoholism and Alcohol Abuse (www.niaaa.gov) support health services research programs that can fund treatment and health care services research projects, as do certain foundations and pharmaceutical companies. Currently, long-term funding sources for these services remain elusive and need to be addressed.

In Europe, the use of buprenorphine and the expansion of opioid addiction treatment into an office-based and primary care setting has gained wide acceptance. In addition, legal access to syringes and equipment are available in selected countries to reduce the transmission of both hepatitis C and HIV. In both the Netherlands and Canada, safe injection facilities are available to reduce the spread of bloodborne diseases. Thus, health services research and support by federal and international agencies, such as the World Health Organization, encompass both safe injection strategies and treatment issues.

### References
