

Prevention and Treatment of Hepatitis C in Injection Drug Users

Brian R. Edlin

Injection drug users constitute the largest group of persons infected with the hepatitis C virus (HCV) in the United States, and most new infections occur in drug users. Controlling hepatitis C in the U.S. population, therefore, will require developing, testing, and implementing effective prevention and treatment strategies for persons who inject drugs. Fortunately, a substantial body of research and clinical experience exists on the prevention and management of chronic viral diseases among injection drug users. The need to implement interventions to stop the spread of HCV among drug users is critical. The capacity of substance-use treatment programs need to be expanded to accommodate all who want and need treatment. Physicians and pharmacists should be educated in how to provide access to sterile syringes and to teach safe injection techniques, both of which are lifesaving interventions. The treatment of hepatitis C in drug users requires an interdisciplinary approach that brings together expertise in treating hepatitis and caring for drug users. Treatment decisions should be made individually by patients with their physicians, based on a balanced assessment of risks and benefits and the patient's personal values. Physicians should carefully assess, monitor, and support adherence and mental health in all patients, regardless of whether drug use is known or suspected. Research is needed to better understand how best to prevent and treat hepatitis C in substance users. In the meantime, substantial progress can be made if existing knowledge and resources are brought to bear. (HEPATOLOGY 2002;36:S210-S219.)

Injection drug users constitute the largest group of persons infected with the hepatitis C virus (HCV) in the United States, and most new infections occur in drug users. The prevalence of antibodies to HCV in most studies of injection drug users is 80% to 90%,¹⁻³ and incidence rates generally range from 10% to 20% per year.³⁻⁷ Controlling hepatitis C in the U.S. population, therefore, will require developing, testing, and implementing effective prevention and treatment strategies for persons who inject drugs.⁸ Fortunately, a substantial body of research and clinical experience exists in the prevention and management of chronic viral diseases among drug users. This report discusses the prevention and treatment

of hepatitis C in injection drug users, with attention to the specific questions posed to the Consensus Panel.

Treatment of Hepatitis C in Drug Users

Decisions about the treatment of hepatitis C in patients who use illicit drugs, as in other patients, should be made by the patients together with their physicians based on individualized risk-benefit assessments.⁹ Risk-benefit considerations for drug users include those that apply to all patients with hepatitis C, including the limited likelihood of achieving a sustained virological response, particularly in patients with genotype 1 infection, African-American ethnicity, or both; the substantial side effects; and, if the disease is not advanced, the option of delaying therapy while better regimens are developed. Moreover, although the likelihood of achieving a sustained virological response has been well studied in various patient groups, little is known about the likelihood that patients will develop clinical endpoints—cirrhosis, liver cancer, end-stage liver disease, or death—and even less is known about how much or even whether treatment will reduce those risks. Before embarking on therapy, therefore, patients should understand that although one can estimate the likelihood that treatment will clear HCV infection (or

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus.

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Address reprint requests to: Brian R. Edlin, M.D., Associate Adjunct Professor and Director, Urban Health Study, University of California, San Francisco, 3180 18th St., Suite 302, San Francisco, CA 94110. E-mail: bredlin@itsa.ucsf.edu; fax: 415-476-3406.

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achieve a histological benefit), it is not known whether treatment will reduce their chances of becoming sick or dying from hepatitis C. Patients should have access to treatment, but they should make their own decisions, with the aid of a balanced portrayal of the known risks and benefits. For patients with advanced hepatic fibrosis, in whom clinical progression is more imminent, treatment may be more compelling, although data are still needed on the effects of treatment on clinical endpoints such as decompensated cirrhosis and mortality in such patients. Liver biopsy examination can assist in making treatment decisions by identifying patients with advanced fibrosis, in addition to providing information to all patients about their disease status and prognosis.

For patients in stable, long-term recovery, including those receiving methadone maintenance therapy, there is no reason to withhold hepatitis C treatment because of a past history of illicit drug use. For active drug users, adherence, psychologic side effects, and the possibility of reinfection may present challenges to effective treatment. Each of these issues requires attention, but none warrants categorically excluding all active or recent drug users from therapy.⁹ Rather, these issues should be considered in each individual patient on a case-by-case basis. Patients who believe they can adhere to therapy can be allowed to try. Much less is lost by treating a patient who does not adhere to therapy than by letting a patient progress to cirrhosis or death without a trial of treatment because of a prior assumption that the patient would not adhere to the regimen.

Adherence. There is abundant evidence from diseases other than hepatitis C that drug users can adhere to medical treatments.¹⁰⁻²⁸ When compared with nonusers in conventional clinical settings, drug users often, although not always, have lower levels of adherence (Table 1). But rates of adherence among drug users range from 30% to nearly 100%, a range that is similar to that in patients being treated for hypertension, diabetes, or asthma.²⁹⁻³¹ Moreover, when programs are designed specifically for drug users by groups with experience working with substance abuse, adherence rates often exceed 80%.²³⁻²⁸ In addition, numerous studies have shown that most physicians are not able to predict patient adherence accurately.³²⁻³⁸ Thus, although there are many effective strategies for improving patient adherence, attempting to screen out patients who are predicted to have poor adherence is not effective. The extensive and rapidly growing literature on adherence has been summarized in the latest revision of the treatment guidelines for human immunodeficiency virus (HIV) infection.³⁹ These guidelines recommend that readiness for treatment be assessed before

Table 1. Adherence by Injection Drug Users to Medical Treatments

Study	N	Adherence	Regimen	Adherence Less in Drug Users Than Others? (Yes or No)
Tulsky, 2000 ¹⁰	118	33%	TB PT	No
Pablos-Mendez, 1997 ¹¹	184	35%	TB Rx	Yes
Singh, 1996 ¹²	46	38%	ART	Y/N*
Ferrando, 1996 ¹³	57	47%	AZT	No
Haubrich, 1999 ¹⁴	173	51%	HAART	Y/N*
Pilote, 1996 ¹⁵	244	53% to 84%	TB appt	Y/N*
Eldred, 1998 ¹⁶	244	60%	HIV Rx	No
Moatti, 2000 ¹⁷	164	65%	HAART	Not assessed
Lucas, 2001 ¹⁸	764	66%	HAART	Y/N*
Bangsberg, 2000 ¹⁹	34	67% to 89%	HAART	Not assessed
Singh, 1999 ²⁰	123	76%	ART	No
Bamberger, 2000 ²¹	68	76%	HAART	Not assessed
Chaisson, 2001 ²²	300	79%	TB PT	Not assessed
Broers, 1994 ²³	313	81%	AZT	Y/N*
Samet, 1992 ²⁴	83	83%	AZT	Y/N*
Mezzelani, 1991 ²⁵	79	85%	HBV vaccine	Not assessed
Marco, 1998 ²⁶	62	86%	TB Rx	No
Lorvick, 1999 ²⁷	27	96%	TB PT	Not assessed
Harrison, 1995 ²⁸	71	97%	HIV vaccine	No

Abbreviations: TB PT, tuberculosis preventive therapy; TB Rx, tuberculosis therapy; ART, antiretroviral therapy; AZT, zidovudine; HAART, highly active antiretroviral therapy; HBV, hepatitis B virus.

*Yes in some analyses and no in some analyses (in some studies, e.g., lower rates of adherence were found in all illicit drug users but not in injection drug users, or in current but not former drug users, or in univariate but not multivariate analysis). Adherence measures differed among studies.

therapy in all patients and that no patient be excluded automatically from treatment.

Tolerance and Effectiveness. Few data are available on results of hepatitis C treatment in active injection drug users who are not receiving treatment for drug use. Several recent studies, however, have shown the safety and effectiveness of hepatitis C treatment in patients receiving drug use treatment, even when they were not completely abstinent from illicit drug use.⁴⁰⁻⁴³ In a study of 50 heroin injectors entering opiate detoxification in Munich, Germany, 34 patients were treated with interferon alfa monotherapy and 16 were treated with combination therapy of interferon and ribavirin for 24 to 48 weeks, depending on HCV genotype.⁴⁰ The overall sustained virological response rate was 36% (Fig. 1), a rate comparable to that in other populations treated for hepatitis C, even though 80% of patients relapsed to drug use during the study. This response rate exceeded the 10% to 20% response rate for interferon alfa monotherapy that was recommended in the 1997 Consensus Development Conference⁴⁴ and was similar to rates of response achieved with combination therapy in nonuser populations. In this study, all patients were managed by physicians who specialized in hepatology and in addiction medicine. Patients

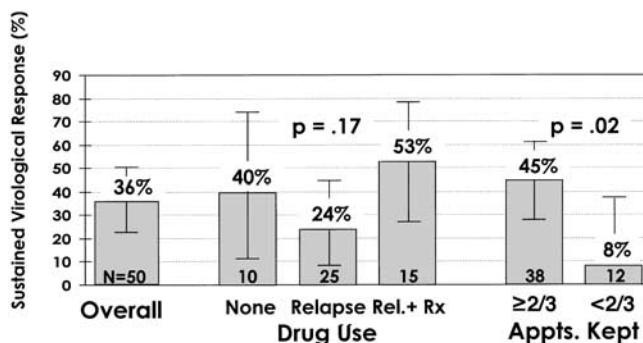


Fig. 1. Sustained virological response rates to interferon-based treatment of hepatitis C in injection drug users entering opiate detoxification (N = 50). A total of 50 heroin injectors entering opiate detoxification in Munich, Germany, were simultaneously treated for chronic hepatitis C with either interferon alfa monotherapy (n = 34) or combination therapy with interferon alfa and ribavirin for 24 to 48 weeks depending on genotype. The sustained virological response rate was 36% overall, a rate comparable with that in other populations treated for hepatitis C, even though 80% of the patients relapsed to drug use during treatment. Sizeable proportions of patients had sustained virological responses, regardless of whether they relapsed to drug use or received methadone maintenance therapy. The strongest predictor of virological response was whether patients kept their weekly clinic appointments. Error bars show 95% confidence limits. Rel. + Rx, patients who relapsed to drug use and then received methadone maintenance therapy. Data from Backmund et al.⁴⁰

who relapsed to drug use were offered methadone maintenance therapy but were allowed to continue treatment for HCV even if they continued to inject illicit drugs. Sizeable proportions of patients had a sustained virological response, regardless of whether they relapsed to drug use or received methadone maintenance therapy (Fig. 1); indeed, sustained response rates were not significantly associated with either relapse to drug use or receipt of methadone maintenance therapy. The strongest predictor of virological response was adherence to their weekly clinic appointments. Of those who kept at least two thirds of appointments, 45% had a sustained virological response, compared with only 8% of those who did not. This study showed that drug users receiving treatment for substance use can be treated successfully for hepatitis C, despite ongoing drug use. The study also showed the importance of combining expertise in hepatology and substance use and maintaining strong relationships with patients that can continue even when patients relapse to drug use.

Another ongoing study from Oakland, CA, reported a sustained virological response rate of 29% among 66 methadone maintenance patients treated with combination therapy of interferon alfa and ribavirin.⁴¹ This response rate was achieved despite the patients' relatively older age, longer duration of infection, more advanced liver disease, and predominance of genotype 1—all factors associated with reduced response rates. Treated patients were highly selected on the basis of demonstrated motivation to re-

ceive treatment for hepatitis C and attendance at weekly pretreatment educational sessions. Nevertheless, patients had substantial levels of psychiatric comorbidity and substance use: nearly two thirds of patients had a prior psychiatric diagnosis, mostly depression; more than 80% had received antidepressants by the time they completed treatment; 20% continued to drink alcohol during treatment, mostly in moderate quantities; and a third used illicit drugs during treatment. The patients discussed their medication experiences in weekly group support sessions. Careful attention was paid to managing side effects, and no serious psychologic side effects occurred. More than a third of patients required an increase in methadone dose. Response rates were not significantly associated with level of abstinence from illicit drugs before treatment, use of alcohol or illicit drugs (other than marijuana) during treatment, or pre-existing psychiatric diagnosis. Interestingly, patients who smoked marijuana were significantly more likely to respond to antiviral therapy than nonusers. This study showed that drug users receiving treatment for substance use can be treated successfully for hepatitis C despite ongoing drug use, moderate alcohol consumption, and significant psychiatric comorbidity.⁴² The study also showed the importance of distinguishing among different types of illicit drug use. Finally, it showed that with careful attention to managing side effects (including mental health assessment and monitoring, treatment of pre-existing or medication-related depression, and adjustment of methadone doses), that the psychologic side effects of interferon in drug users need not be excessive.

Reinfection. There have been few studies on the risk for reinfection in drug users treated successfully for hepatitis C. However, what data exist suggest that reinfection is rare in drug users who clear HCV with therapy even if they continue to inject drugs, as long as steps are taken to minimize the risk. Substance abuse is a chronic, relapsing condition. Acknowledging this fact, the investigators in the Munich study instructed all patients in safe injection practice so that they could avoid acquiring and transmitting blood-borne diseases in the event that they relapsed to drug use.⁴⁰ Of the patients in the study who achieved an end-of-treatment response, 12 injected drugs during the 24 weeks after treatment, but only 2 redeveloped HCV RNA during the follow-up period. This viral relapse rate was no higher than would be expected in patients not using drugs. Both patients who became HCV-RNA positive had HCV genotype 3a, which was the same genotype they had before treatment. Another study from Scandinavia reported 5-year follow-up evaluations of 27 injection drug users who had cleared HCV RNA with interferon therapy. Nine patients (33%) relapsed to drug use, but only 1 became reinfected, despite a total of 45

person-years of observation.⁴³ These data suggest that if steps are taken to help patients avoid high-risk injection practices, reinfection after successful therapy may be the exception rather than the rule.

In summary, few studies have reported results of treatment of chronic hepatitis C in active drug users, and more data are needed to determine optimal treatment strategies. The evidence to date does not bear out the concept that illicit drug use renders treatment futile. Although adherence, psychologic side effects, and the possibility of reinfection may limit the effectiveness of hepatitis C treatment in some drug users, treatment is successful in others despite ongoing drug use, moderate alcohol consumption, and significant psychiatric comorbidity. Treatment decisions should, therefore, be made by patients and their physicians on an individual basis.

Monitoring and Treating Injection Drug Users With Hepatitis C

Caring for drug users presents special challenges to the health care team requiring patience, experience, and tolerance. Fortunately, a substantial body of research and clinical experience exists on the prevention and management of chronic viral infections among injection drug users, especially HIV infection, and effective principles have been developed for engaging drug users in health care relationships (Table 2).⁴⁵⁻⁴⁸ Learning from this experience will be critical for efforts to control hepatitis C. Successful programs depend on a respectful approach to substance users, an understanding of the medical and behavioral sequelae of addiction, and an avoidance of moralistic judgments.

Harm reduction is the effort to help patients reduce high-risk behaviors without imposing unrealistic demands for global change.⁴⁹⁻⁵¹ If patients are unlikely to discontinue injection drug use, interventions with limited but practical objectives can and should be taken to help reduce the harmful consequences of continued drug use. Harm reduction is an approach that recognizes that people must set their own agenda for change; that emphasizes the benefits of incremental changes; that recognizes that drug users are motivated to improve their health and well being; and that emphasizes the importance of removing barriers to healthier behaviors and helping people find ways to be healthier that will work for them.^{52,53}

Medical care for drug users with hepatitis C should begin with strong linkages with prevention services, including community-based hepatitis C testing and counseling programs, so that drug users with hepatitis C can be identified and their entry into care facilitated. Success treating hepatitis C in injection drug users will require collaboration between experts in hepatitis and experts in

Table 2. Principles for Managing Health Care Relationships With Substance-Using Patients

Establish a climate of mutual respect
Maintain a professional approach that reflects the aim of enhancing patients' well being; avoid creating an atmosphere of blame or judgment
Educate patients about their medical status, proposed treatments, and their side effects
Include patients in decision making
If possible, establish a multidisciplinary team consisting of primary care physicians, HIV specialists, psychiatrists, social workers, and nurses
Have a single primary care provider coordinate the care delivered by such a team to maximize consistency and continuity
Define and agree on the roles and responsibilities of both the health care team and the patient
Set appropriate limits and respond consistently to behavior that violates those limits
Minimize barriers to participation (penalties for missed visits, and so forth)
Recognize that patients must set their own goals for behavior change and work with patients to achieve commitment to realistic goals for healthier behaviors
Acknowledge that abstinence is not always a realistic goal; emphasize risk-reduction measures for patients who continue to use drugs
Acknowledge that sustaining abstinence is difficult and that success may require several attempts
Be familiar with local resources for the treatment of drug users
Pitfalls to avoid
Unrealistic expectations
Frustration
Anger
Moralizing
Blame
Withholding therapy

Data from O'Connor et al.,⁴⁵ Batki and Sorensen,⁴⁶ Wartenberg,⁴⁷ and Selwyn and O'Connor.⁴⁸

substance use to create programs specifically designed for drug users. Collaboration between experts in HIV and experts in substance use has been stimulated by federal funding programs such as the Ryan White Care Act. Similar programs are needed for hepatitis C. Expertise working with drug users is available from a variety of sources, including public health and community workers with experience in HIV prevention and harm reduction, HIV treatment providers, substance use treatment providers, substance use researchers, and, probably most importantly, drug users themselves. A multidisciplinary team, with input from primary care physicians, hepatologists, nurses, psychiatrists, social workers, drug counselors, and psychologists, may be the optimal approach. A flexible attitude is necessary so that unrealistic expectations do not lead to frustration and resentment. The measure of success of this effort is how much patients are helped to be healthier, not whether a predetermined goal is achieved.

Caring for drug users also requires providing treatment for substance use. Proven effective treatments for substance use exist.^{54,55} Opiate agonist therapy (e.g., methadone maintenance therapy) has been shown to diminish and often eliminate opiate use and to reduce transmission of many infections, including HIV.⁵⁶⁻⁶¹ All patients with

hepatitis C, regardless of whether they are known to have injected drugs, should be asked about past or current drug and alcohol use. Treatment for substance use should be discussed with those who use drugs or alcohol and provisions made to provide treatment for those who want and need it. Alcohol treatment is particularly important because of the strong effect of heavy alcohol intake on the progression of hepatitis C. Hepatitis C and substance use can be treated simultaneously,⁴⁰⁻⁴² but there are no data on whether it is better to treat one or the other first, or both together. Attention should also be paid to assessing and treating mental health conditions, which are associated with both hepatitis C and substance use and may be induced or exacerbated by hepatitis C treatment. Medical services and mental health care should be integrated with substance use treatment.⁶²

Attention to ensuring optimal adherence is important for all patients, not just those who use drugs.²⁹⁻³¹ Patient readiness should be assessed before embarking on therapy, and adherence should be assessed and monitored regularly during therapy.³⁴ Effective strategies for improving adherence range from basic clinical practices—such as establishing a consistent, trusting physician-patient relationship, providing clear information about expected outcomes and side effects of medication, and paying careful attention to perceived side effects—to specialized tools such as electronic reminder systems, directly observed therapy, and cash incentives (Table 3).^{63,64} Simplifying complex treatment regimens, treating depression, or helping a homeless patient find housing can improve adherence. Patients also may benefit from counseling to help them incorporate the regimen into their daily lives.

Adherence to hepatitis C treatment often can be complicated by side effects, including depression. Thus, the management of side effects is critical to maximize the effectiveness of treatment for hepatitis C. The psychologic side effects of interferon are of concern in all patients, not just those who use drugs or those with preexisting psychiatric diagnoses. Interferon may have severe psychologic side effects in patients without preexisting psychiatric disorders.^{65,66} To minimize these effects, all patients should be screened for depression and other mental health conditions before undergoing hepatitis C treatment, treated for these conditions if necessary, and monitored (and treated if necessary) for them during hepatitis C treatment. Antidepressant medication may be helpful in a sizeable proportion of patients.

Caring for injection drug users should always include education and support for safe injection practices.^{67,68} Education is particularly important for drug users receiving hepatitis C treatment to reduce the

Table 3. Effective Strategies for Improving Adherence

Information about intended effects and side effects of medication
Attention to perceived side effects
Counseling addressing barriers to and facilitators of adherence
Respectful and nurturing provider-patient relationship
Treatment of depression if patient is depressed
Directly observed therapy
Cash incentives
Devices (pager reminders, pill organizer boxes, and so forth)

Data from Guidelines for using antiretroviral agents among HIV-infected adults and adolescents,³⁹ Friedland and Williams,⁶³ and Reiter et al.⁶⁴

chances of reinfection. The possibility of reinfection should be discussed with patients before starting hepatitis C treatment. Those who inject drugs after successful treatment for HCV infection may be able to avoid reinfection by using a new sterile syringe for each injection and by not using injection equipment that has been used by other persons. Physicians should refer patients who inject drugs to syringe exchange programs or, if necessary, directly prescribe syringes.⁶⁹⁻⁷¹ There are now more than 200 syringe exchange programs in more than 150 cities in 36 states in the United States, and these numbers are increasing yearly. For drug users without access to such programs, physicians in at least 46 states are allowed by law to prescribe syringes so that their patients can avoid acquiring and transmitting blood-borne infections.⁷⁰ Several studies have shown that injection drug users are able to master safe injection practices.⁷²⁻⁷⁴ When given access to sterile syringes, drug users readily make use of them, reducing their high-risk behavior and rates of disease transmission.⁷²⁻⁷⁷ Unfortunately, HCV may be more readily transmitted than HIV through the sharing of injection equipment other than syringes, such as cookers (bottle caps, spoons, and other containers used to dissolve drugs) and cottons (filters used to draw up the drug solution into a syringe),^{6,7} and probably through minor instances of blood contact, such as may occur when one person gives an injection to another.⁷⁸ During the HIV epidemic, injection drug users learned quickly about the risks of sharing syringes, and behavioral norms changed, which resulted in dramatic decreases in rates of syringe sharing.⁷²⁻⁷⁴ The sharing of other injection equipment is, unfortunately, still relatively common,⁷⁹ as is the practice of giving and receiving injections.⁸⁰ For these reasons, it is important for physicians to educate patients not just to avoid sharing syringes, but to avoid sharing any injection equipment, to wash hands before and after giving injections, and to avoid any contact with blood from other people (Table 4).^{67,68}

Table 4. Medical Advice For Persons Who Inject Illicit Drugs

Do not use illegal drugs
Receive substance use treatment
Never use syringes previously used by another person
Never use other injection equipment previously used by another person
Use a new, sterile syringe to prepare and inject drugs
Use a new or disinfected container (cooker) and a new filter (cotton) to prepare drugs
Wash hands and clean the injection site before injection
Wash hands before and after giving injections
Safely dispose of syringes after one use

NOTE. Handwashing added by author. Adapted from U.S. Public Health Service Medical Advice for Persons Who Inject Illicit Drugs.⁶⁸

Prevention of Hepatitis C in Injection Drug Users

Preventing morbidity and mortality from hepatitis C in injection drug users requires (1) reducing exposure to HCV, (2) reducing infection among those exposed, and (3) reducing disease among those infected.⁸ Injection drug use would be greatly reduced if all those who needed treatment for substance use treatment could get it (prevention of exposure). HCV spread can be prevented if drug users have access to sterile syringes and education in how they can avoid acquiring and transmitting the virus (prevention of infection). Finally, barriers to medical treatment must be overcome so that drug users can benefit from advances in HCV treatment (prevention of disease).⁹ HCV treatment also may reduce transmission (prevention of infection) because HCV-infected drug users are the source for most HCV transmission in the United States (Table 5).

Fully implementing measures to prevent hepatitis C among drug users will require changing public policies and instituting or expanding public health programs, but physicians and other health care providers can have a positive effect without waiting for these changes. Access to sterile syringes should be expanded through expansion of syringe exchange programs and the repeal of laws restricting syringe access.^{75,76} However, health care providers also can play a critical role by referring patients to syringe exchange programs, teaching them safe injection, and prescribing and dispensing syringes. Physicians and pharmacists should be educated to recognize that helping injection drug users gain access to sterile syringes and educating them in safe injection are potentially life-saving interventions,⁸¹⁻⁸⁴ and ones that cost little or nothing. All patients with hepatitis C should be warned that their blood may be infectious, even through trivial contact, and should be instructed in how to avoid transmitting the infection to others. Those who inject drugs should be given biohazard sharps containers or instructed to safely

dispose of injection equipment in puncture-resistant containers.^{85,86}

The capacity for substance use treatment should be expanded.^{56,57} The current capacity for drug use treatment is sufficient for only 15% to 20% of the drug users in the United States. This lack of availability may be responsible for more blood-borne disease transmission in the United States than any other deficiency except the failure to adequately fund needle exchange programs and to allow drug users access to sterile syringes. The shortage may be relieved somewhat if physicians in medical practice prescribe opiate replacement therapy, either through office-based methadone programs or the use of the recently approved opiate agonist buprenorphine for the outpatient treatment of opiate addiction. With these changes in public policy on opiate agonists, however, also must come changes in attitudes of physicians who will need to gain training and experience with these modalities and prescribe them, if they are to help. An immediate and substantial expansion of the substance use treatment capacity, through a variety of approaches, must be the cornerstone of any approach to reducing the harmful health consequences of substance use.

Community-based hepatitis C prevention programs are needed, to provide outreach, HCV testing and counseling, and education in safe injection, and to link patients who are found to be positive to medical care. Members of groups at high risk for HCV infection, such as injection drug users and incarcerated persons, should be regularly screened for HCV infection. Efforts are particularly important to identify persons with new HCV infections because treatment may be more effective during the acute phase than later, and those with advanced hepatic fibrosis, in whom treatment may reduce the incidence of hepatocellular carcinoma and improve survival.

Table 5. Strategies for HCV Prevention and Control in Injection Drug Users

Reducing injection drug use (prevention of exposure)
Evidence-based substance abuse prevention
Expansion of substance abuse treatment
Reducing HCV transmission among injection drug users (prevention of infection)
Access to sterile syringes and other injection equipment
Repeal of paraphernalia and syringe prescription laws
Establishment of syringe exchange and distribution programs
Education of physicians and pharmacists to provide injection drug users access to sterile injection equipment
Community-based outreach to injection drug users
Education in safe injection
Client-centered HCV counseling and testing
Reducing liver disease in infected injection drug users (prevention of disease)
Integration of prevention and care
Medical treatment for HCV infection
Integration of medical, mental health, substance use, and social services
Provision of services to incarcerated populations

Finally, correctional facilities provide an enormous opportunity to safely and effectively treat a large number of persons with hepatitis C and provide prevention services to persons at risk for hepatitis C.⁸⁷ Approximately one quarter of the nearly 2 million individuals incarcerated in state and federal correctional facilities in the United States have hepatitis C. Efforts are needed to ensure that therapy and education on prevention of hepatitis C are provided to prisoners. The medical issues involved in treating prisoners for hepatitis C are no different from those involved in treating any patient with this disease, and in many respects the logistical issues (such as adherence and interference of therapy with work and daily activity) are less problematic.⁸⁷ The withholding of hepatitis C prevention and treatment from incarcerated persons, although widespread, is unethical.⁸⁸ Federal, state, and local correctional departments must be given the resources to provide optimal therapy and means of prevention of hepatitis C to prisoners.

Conclusion

A sound policy for the control of hepatitis C will require implementing prevention and treatment programs designed for injection drug users, the group most severely affected by this infection.^{8,9} Controlling hepatitis C in the United States will require further research to develop and test effective strategies for prevention and treatment for persons who inject drugs. In the meantime, substantial progress can be made to control hepatitis C if existing knowledge and resources are brought to bear.

Future Research Needs

Research is needed to better understand the epidemiology and natural history of hepatitis C in injection drug users. The number of injection drug users in the United States who have hepatitis C is unknown, as is the number of those who become infected each year and the numbers who develop cirrhosis and die of hepatitis C annually. It has been estimated that 35,000 persons are newly infected with HCV each year in the United States, and that about 60% of infected persons are injection drug users.⁴⁴ These estimates, however, are derived from data from a surveillance system in 4 U.S. counties⁸⁹ and rely on estimates that 1 in 6 new infections in these counties manifest as acute hepatitis, and 42% of these cases are reported to the surveillance system.⁹⁰ It is rare, however, for HCV infection in drug users to be associated with a clinical illness that comes to medical attention and clinical cases of acute hepatitis among injection drug users often are not reported.⁹¹ Thus, the current estimates may underestimate the true number of drug users becoming infected with HCV in the United States. Ongoing programs to

assess the current rates as well as future changes in the incidence of HCV infection in injection drug users are needed to provide data on the size of this problem as well as the efficacy of control measures as they are introduced.

The natural history of hepatitis C among injection drug users needs to be better defined. There have been few longitudinal studies of hepatitis C in representative cohorts of injection drug users.⁹² The course and outcome of hepatitis C may be different in injection drug users than in other populations because of differences in size of the inoculum, the frequency of repeated exposure, concurrent nutritional status, coinfections (with known and unknown infectious agents), associated comorbidities, and other factors that affect the natural history of the disease. Community-based studies are needed because studies of clinical populations often overestimate the frequency of clinical disease.⁹³ Ultimately, decisions on therapy need to be based on an accurate understanding of the risk for serious disease in patients who are not treated.

Research is needed on strategies for treating hepatitis C in substance users. Studies are needed to define the optimal approach to therapy in patients who use various substances (opiates, stimulants, marijuana, alcohol) and are at various stages in recovery or relapse. Studies are needed to determine whether substance use is best treated before, during, or after treatment of hepatitis C. Of great importance is research on how to assess and manage mental health conditions in drug users with hepatitis C, improve treatment readiness and rates of treatment initiation, optimize adherence, and manage the side effects, particularly the psychological side effects, of interferon. Studies are needed to determine the safety and effectiveness of various treatment strategies, the rates of adherence that can be achieved, the risk of serious side effects, and the risk of reinfection. The pharmacokinetic interactions between therapies for hepatitis C and opiate agonists as well as illicit drugs need to be elucidated. Strategies need to be developed for treating hepatitis C in correctional facilities while preserving confidentiality, maximizing continuity of care after release, and preventing reinfection in prison and after release. Perhaps most importantly, research is needed on the prevention of hepatitis C among injection drug users. Of particular importance is the development of methods of reaching new initiates to injection before they become infected with HCV, with effective strategies to help them stop injecting or avoid engaging in high-risk injection practices. Perhaps most importantly, research is needed on the prevention of hepatitis C among injection drug users. Of particular importance is the development of methods of reaching new initiates to injection before they become infected with HCV, with effective strategies

to help them stop injecting or avoid engaging in high-risk injection practices.

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Commentary

Hepatitis C prevention and treatment for substance users in the United States: acknowledging the elephant in the room

Brian R. Edlin*

Center for the Study of Hepatitis C, Weill Medical College of Cornell University, New York, NY, USA

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Like many countries, the United States faces a major epidemic of hepatitis C virus (HCV) infection. Nearly 3 million Americans are estimated to be infected with HCV (Alter et al., 1999), and some 35,000 new infections are believed to occur annually (Williams, 1999). The virus causes chronic infection in about 85% of those infected, and among those chronically infected, cirrhosis may eventually develop in from 5 to 20% (Freeman et al., 2001; Liang, Rehermann, Seeff, & Hoofnagle, 2000). HCV infection is thought to result in 8000–10,000 deaths annually. It is already the most common cause of chronic liver disease and the most common reason for liver transplantation in the United States, and morbidity and mortality from HCV infection are rising and are expected to continue rising in the coming decades (Armstrong, Alter, McQuillan, & Margolis, 2000).

In the United States, as in many other developed countries, injection drug users (IDUs) constitute the largest group of persons infected with HCV, and most new infections occur in IDUs. Injection drug use predominates as a mode of transmission in most countries where the endemicity of HCV is low. There are probably a million or more current IDUs with HCV infection in the U.S.; of the estimated 1.2–1.3 million current IDUs in the U.S. (Normand, Vlahov, & Moses, 1995), some 80–90% have been infected with HCV (Lorvick, Kral, Seal, Gee, & Edlin, 2001; Thomas et al., 1995), although recent studies have shown that prevalence rates in young IDUs and recent initiates are now much lower (Garfein et al., 1998; Hahn, Page-Shafer, Lum, Ochoa, & Moss, 2001; Thorpe, Ouellet, Levy, Williams, & Monterroso, 2000). The incidence of new infections among IDUs is also quite high, however, generally ranging from 10 to 20% per year in the U.S. (Garfein et al., 1998; Hagan et al., 1999, 2001; Hahn et al., 2001; Thorpe et al., 2000).

The situation is similar in other developed countries (Crofts, Jolley, Kaldor, van Beek, & Wodak, 1997; Patrick et al., 2001; Van Ameijden, Van den Hoek, Mientjes, & Coutinho, 1993; van Beek, Dwyer, Dore, Luo, & Kaldor, 1998). Moreover, initiation of heroin use and injection drug use is increasing among young people (CDC, 2001a). Controlling the HCV epidemic, therefore, will require developing, testing, and implementing prevention and treatment strategies that will be effective for persons who inject drugs. Fortunately, substantial research and clinical experience exists in the prevention and management of chronic viral infections among IDUs, particularly because of the HIV epidemic. Learning from this experience will be critical for efforts to control HCV.

The public health response to the HCV epidemic in the U.S. to date has, unfortunately, fallen short of what is needed to stop the epidemic. Until recently, official documents produced by the U.S. Public Health Service about its response to the HCV epidemic were silent on most of the interventions described in this article (CDC, 1998; CDC, 2001b; NIH, 1997a). In 2002, NIH issued an updated Consensus Statement on the Management of Hepatitis C that took a substantially more comprehensive approach to the problem (NIH, 2002). This statement challenges the medical, scientific, and public health communities to address numerous problems that remain unsolved and continue to contribute to the HCV epidemic.

Preventing morbidity and mortality from HCV can be divided into primary, secondary, and tertiary prevention (Table 1). This paper summarises recommendations for effective prevention in each of these categories, and discusses some of the barriers that have hampered their implementation.

Primary prevention: reducing injection drug use

Because injection drug use is responsible for the majority of new infections, reducing the number of people who inject

* Present address: Center for the Study of Hepatitis C, Weill Medical College of Cornell University, 411 E. 69th Street, Room KB-322, New York, NY 10021, USA. Tel.: +1-212-746-4870; fax: +1-212-746-8544.
 E-mail address: bre2002@med.cornell.edu (B.R. Edlin).

Table 1
Strategies for HCV prevention and control

Primary prevention (preventing exposure): reducing injection drug use
1. Evidence-based substance abuse prevention
2. Expansion of substance abuse treatment
Secondary prevention (preventing infection): reducing HCV transmission among IDUs
3. Access to sterile syringes and other injection equipment
a. Repeal of paraphernalia and syringe prescription laws
b. Establishment of syringe exchange and distribution programs
c. Education of physicians and pharmacists to help IDUs gain access to sterile injection equipment
4. Community-based outreach to IDUs
5. Client-centered HCV counselling and testing
Tertiary prevention (preventing disease): reducing liver disease in infected persons
6. Medical treatment for HCV infection
7. Integration of medical and social services
8. Provision of services to incarcerated populations

drugs is an important way to prevent the spread of HCV (Alter & Moyer, 1998).

Substance abuse prevention

HCV can be rapidly acquired after the onset of injection drug use (Garfein, Vlahov, Galai, Doherty, & Nelson, 1996; Lorvick et al., 2001). Efforts to control hepatitis C, therefore, must include a commitment to help people who do not inject drugs avoid starting to do so. Unfortunately, few drug use prevention programs have been rigorously evaluated and shown to be effective (Gerstein & Green, 1993). Nevertheless, evidence-based principles of effective strategies have been identified (Sloboda & David, 1997; Tobler, 1997). Effective strategies for preventing drug use among youth include educating and training parents, strengthening families, providing alternative venues for building skills and confidence, mobilizing and empowering communities, and other structural approaches (CSAT, 1994). Unfortunately, public spending has often not been directed toward programs that use those strategies (Ennett, Tobler, Ringwalt, & Flewelling, 1994; Gerstein & Green, 1993; Gorman, 1998). Moreover, to be effective, programs must be supported by structural social and economic change to reduce social inequality and economic disparity, create supportive social environments, and increase economic opportunities for young people, particularly in economically disadvantaged communities (Aguirre-Molina & Gorman, 1996; World Health Organization, 1986).

Substance abuse treatment

Opiate agonist therapy is effective treatment for opiate addiction (Lowinson et al., 1997; Strain & Stitzer, 1999). It has been shown to diminish and often eliminate opiate use and reduce transmission of many infections, includ-

ing human immunodeficiency virus (HIV) (Ball & Ross, 1991; Gerstein & Lewin, 1990; Hartel & Schoenbaum, 1998; Metzger, Navaline, & Woody, 1998; NIH, 1997b; Sorensen & Copeland, 2000). Yet while substance abuse is generally recognised as a major problem facing the nation, and enormous public resources are expended for interdiction and the arrest, prosecution and incarceration of those engaging in illegal drug use, sufficient resources have not been allocated to provide access to substance abuse treatment to those who need it (Amaro, 1999; NIH, 1997b). The availability of substance abuse treatment is severely limited and large numbers of substance users do not have access to treatment. Methadone maintenance treatment in the U.S. is hobbled by both underfunding and onerous federal regulations; the current capacity is enough for only 15–20% of heroin users in the U.S. (Institute of Medicine, 1995). Unfortunately, funding for the support of substance abuse treatment programs has eroded during the course of the AIDS epidemic. There are now actually fewer treatment programs available and, within programs, fewer services (Etheridge, Craddock, Duntzman, & Hubbard, 1995; Metzger et al., 1998). Substantial expansion of substance abuse treatment capacity, to allow drug users who wish to stop or reduce their drug use access to treatment, will be critical to reduce the spread of HCV infection (Alter & Moyer, 1998). Resources must be provided for long-term methadone maintenance; time-limited “detoxification” is not a treatment for substance abuse (Gerstein & Harwood, 1990). Particular efforts are needed to design programs for young IDUs and recent initiates to injection, many of whom have not yet become infected with HCV. Substance abuse treatment for HCV-infected IDUs, on the other hand, can reduce the further spread of the infection (secondary prevention).

Secondary prevention: reducing HCV transmission

At least 60% of new HCV infections in the United States are thought to occur in persons who use illicit drugs by injection. To stop the transmission of HCV among IDUs, several types of interventions are needed.

Access to sterile syringes

Persons who inject drugs need access to sterile injection equipment in order to avoid acquiring and transmitting HCV and other bloodborne infections (U.S. Public Health Service, 1997). To accomplish this goal, several steps are needed. First, paraphernalia and prescription laws, which prohibit public health workers and pharmacists from making syringes available to drug users through syringe exchange programs and pharmacy sales, must be repealed (Gostin, Lazzarini, Jones, & Flaherty, 1997). Second, syringe exchange and distribution programs must be widely expanded and publicly supported and funded (Heimer, 1998; NIH,

1997c; Normand et al., 1995; Strathdee & Vlahov, 2001; Vlahov & Junge, 1998). Police, for example, must not interfere with drug users attending needle exchange programs (Grund, Heckathorn, Broadhead, & Anthony, 1995). And finally, physicians and pharmacists must be educated to understand that providing access to sterile syringes is a lifesaving intervention for persons who inject drugs (Burris, Lurie, Abrahamson, & Rich, 2000; Case, Beckett, & Jones, 1998; Gleghorn, Gee, & Vlahov, 1998; Rich, Macalino, McKenzie, Taylor, & Burris, 2001; Singer, Baer, Scott, Horowitz, & Weinstein, 1998; Wright-De Agüero, Weinstein, Jones, & Miles, 1998). Health care professionals do their patients a disservice if they withhold access to sterile injection equipment in order to enforce the “War on Drugs” at the expense of their patients’ health and safety.

It should be noted that syringe exchange programs (Kaplan, 1995; Laufer, 2001) and increased access to sterile syringes (Holtgrave, Pinkerton, Jones, Lurie, & Vlahov, 1998) have already been shown to be cost-effective and cost-saving to society because they enable drug users to prevent HIV transmission. The prevention of HCV transmission results in even greater savings. Legalizing over-the-counter sales of syringes in pharmacies, moreover, would not cost the public anything.

Outreach to injection drug users

Community-based outreach programs are effective at helping drug users reduce their risk behaviours for acquiring bloodborne viral infections (Booth & Wiebel, 1992; Broadhead et al., 1998; Coyle, Needle, & Normand, 1998). To prevent HCV transmission, it will be particularly important to implement programs specifically designed for young IDUs and those who have recently begun injecting. IDUs know considerably less about hepatitis C than about HIV (Seal, Ray, Lorvick, Kral, & Edlin, 1999). Outreach programs must (1) educate IDUs about how to avoid acquiring and transmitting HCV infection, (2) support behaviour change to reduce high-risk behaviour, (3) provide client-centered counselling and (4) provide linkages to services, including HCV testing and care for infected persons.

HCV counselling and testing

Client-centered counselling and testing have been shown to reduce HIV risk behaviours and HIV incidence (Holtgrave, Qualls, & Graham, 1996; Kahn, 1998; Kamb et al., 1998). Identifying persons with HCV infection is also important to allow them to make decisions about seeking treatment. Persons who are HCV antibody positive require a test for HCV RNA to determine whether they are currently infected or not. IDUs who are HCV antibody negative should be re-tested every six months, because the treatment of persons with new HCV infection is more than 90% effective at eradicating virus (Jaekel et al., 2001). To

meet these goals, HCV counselling and testing programs and services will need to be greatly expanded.

Reducing injection equipment sharing

Efforts to reduce HIV spread among IDUs in some locations appear to have reduced HCV transmission as well (Edlin et al., 2000). It should be noted, however, that HCV may be more readily transmitted than HIV through the sharing of injection equipment other than syringes, such as cookers, cottons, etc. (Hagan et al., 2001; Thorpe et al., 2000), raising the standard for safer injection practices. Syringe exchange programs have been effective in allowing IDUs to avoid sharing syringes but less effective at helping them avoid sharing other injection equipment (Bluthenthal, Kral, Erringer, & Edlin, 1998). HCV may be transmitted if blood contact occurs during the giving and receiving of injections (Flynn, Anderson, Clancy, & Britton, 1996; Kral, Bluthenthal, Erringer, Lorvick, & Edlin, 1999), which may be especially common the first time drugs are injected. To prevent HCV transmission, programs must emphasise reducing the sharing of all injection equipment and avoiding any blood contact between persons (U.S. Preventive Services Task Force, 1996; U.S. Public Health Service, 1997).

Tertiary prevention: reducing liver disease in infected persons

Medical treatment for HCV infection

Current antiviral therapy for HCV infection can eliminate the virus from as many as 40–80% of infected persons, depending on the viral genotype (Manns et al., 2001). Because injection drug users constitute the largest number of chronic HCV infections and are the source of most new infections in the United States, controlling hepatitis C will require treatment strategies that are effective in persons who inject drugs (Edlin et al., 2001). Recent advances in HCV treatment regimens now allow effective treatment of HCV in some persons with as few as 48 doses of pegylated interferon (Zeuzem et al., 2000). This is fewer than the number of preventive therapy doses required for the treatment of latent tuberculosis infection (CDC, 2000). Many studies have shown that active drug users can complete preventive tuberculosis therapy in programs that take into account the circumstances of their lives (Chaisson et al., 2001; Lorvick et al., 1999; Salomon et al., 1997; Smirnoff, Goldberg, Indyk, & Adler, 1998; Tulskey, Pilote, & Hahn, 2000).

HCV treatment is more complex and less effective than preventive TB therapy. Adherence, psychological side effects, and the possibility of re-infection present challenges to effective treatment for some drug users. Fortunately, an array of effective strategies exists to overcome each of these challenges (Edlin et al., 2001). Before discussing these in more detail, however, it should be emphasised that for most

patients, HCV treatment should be considered elective at this time. Treatment can be more definitely recommended for patients with relatively advanced hepatic fibrosis, in whom the clinical sequelae of advanced liver disease may be imminent (Yano et al., 1996; Heathcote et al., 2000). The treatment of patients who already have cirrhosis has been shown to reduce the incidence of liver cancer and probably death. Patients with acute HCV infection should also be informed that treatment may be more effective at eradicating virus when started shortly after acquiring the infection (Jaeckel et al., 2001; Quin, 1997). For most patients, however, who are not in one of these categories, the benefits of antiviral treatment for HCV infection do not unequivocally outweigh the disadvantages. Most patients will never develop cirrhosis or liver cancer. Clinical trials have demonstrated sustained viral clearance in 40–80% of treated patients (Manns et al., 2001), and histological damage appears to improve in treated patients (McHutchison, Gordon, & Schiff, 1998; Sobesky et al., 1999), but trials have not examined the effects of treatment on clinical endpoints—symptomatic disease or death—which would require many years of follow-up. Because treatment appears to provide histological and virological benefits, patients should have access to it. Histological benefit would be expected to translate into clinical benefit; and, most infected people would undoubtedly want to clear the infection, which appears to mean that they are rid of the virus, even if clinical benefit has not been proven. But the absence of data on clinical outcomes makes it impossible to know how likely treatment is to reduce the risk of developing clinical disease. It is still entirely possible that the patients who achieve sustained viral clearance after treatment are not those who would have developed cirrhosis or liver cancer had they not been treated. When the benefit of treatment is uncertain, the side effects can be severe, disease progression will not occur in most untreated patients, and better therapies are likely to be developed in coming years, the decision to undergo treatment in patients must depend highly on patients' personal preferences, such as their desire to be rid of the virus.

From the public health standpoint, however, providing therapy for HCV-infected drug users who opt for it is beneficial, because viral clearance would appear to mean that a person can no longer transmit the infection. Unfortunately, significant barriers to treating HCV infection in active drug users exist. Many do not have a trusting relationship with a physician who can help them endure the difficulties of HCV therapy. Patients must work at adhering to the regimen, physicians must be responsive to patients' experiences of side effects, and both parties must be able to communicate openly about their expectations and frustrations. Many drug users do not have relationships with providers that will support this kind of collaboration. Many physicians become frustrated with drug users who fail to follow through with medical advice, appointments, and prescribed medication. And users, for their part, often feel that they encounter treatment in health care systems that is judgmental and unresponsive to their needs (Batki & Sorensen, 1999; Lewis, 1997; Shine, 1996; Wartenberg, 1991).

Fortunately, however, extensive experience treating IDUs for medical conditions, especially HIV infection, has led to the development of effective principles for engaging drug users in health care relationships (Table 2). Successful programs invariably adopt a respectful approach to substance users, understand the medical and behavioural sequelae of addiction, and refrain from moralistic judgments (Bamberger et al., 2000; Batki & Sorensen, 1999; Marlatt, 1998; O'Connor, Selwyn, & Schottenfeld, 1994; Robertson, 1998; Selwyn & O'Connor, 1992; Wartenberg, 1991). These strategies embody a harm reduction approach (Des Jarlais, Friedman, & Ward, 1993; Marlatt, 1998). Harm reduction stresses implementing interventions and making changes that are attainable and beneficial when the elimination of all harm is not possible in the short run. For drug users who cannot or will not make the global behaviour change of stopping drug use entirely, many measures can nevertheless reduce the harmful consequences of drug use. Harm reduction strategies, not "zero tolerance", are accepted medical

Table 2
Principles for managing health care relationships with substance-using patients

1. Establish a climate of mutual respect.
2. Maintain a professional approach that reflects the aim of enhancing patients' well-being; avoid creating an atmosphere of blame or judgment.
3. Educate patients about their medical status, proposed treatments, and their side effects.
4. Include patients in decision making.
5. If possible, establish a multidisciplinary team consisting of primary care physicians, HIV specialists, psychiatrists, social workers, and nurses.
6. Have a single primary care provider coordinate the care delivered by such a team to maximise consistency and continuity.
7. Define and agree on the roles and responsibilities of both the health care team and the patient.
8. Set appropriate limits and respond consistently to behaviour that violates those limits.
9. Minimise barriers to participation (penalties for missed visits, etc.).
10. Recognising that patients must set their own goals for behaviour change, work with patients to achieve commitment to realistic goals for healthier behaviours.
11. Acknowledge that abstinence is not always a realistic goal; emphasise risk reduction measures for patients who continue to use drugs.
12. Acknowledge that sustaining abstinence is difficult and that success may require several attempts.
13. Be familiar with local resources for the treatment of drug users.

Adapted from O'Connor et al. (1994), Wartenberg (1991), Selwyn and O'Connor (1992), Marlatt (1998) and Robertson (1998).

and public health practice for health behaviours other than illicit substance abuse, such as diet, exercise, smoking and medication adherence.

Success treating HCV infection in IDUs requires collaboration between experts in hepatitis and substance use to create programs specifically designed for drug users (Backmund, Meyer, Von Zielonka, & Eichenlaub, 2001; Sylvestre, 2002). Particular efforts are required to address the challenges posed by adherence, psychological side effects, and the potential for re-infection (Edlin et al., 2001). Effective strategies for improving adherence range from basic clinical practices—such as establishing a consistent, trusting physician-patient relationship, providing clear information about intended effects and side effects of medication, and paying careful attention to perceived side effects—to specialised tools such as electronic reminder systems, directly observed therapy, and cash incentives (Friedland & Williams, 1999; Lorvick & Edlin, 2000; Lorvick et al., 1999; Panel on Clinical Practices for Treatment of HIV Infection, 2001; Reiter et al., 2000). Simplifying complex treatment regimens, treating depression, or helping a homeless patient find housing can help improve adherence. Patients may benefit from individual counselling addressing barriers to and facilitators of adherence. To minimise psychological side effects, patients should be screened for depression and other mental health problems before HCV treatment, treated if necessary, and monitored for these problems during HCV treatment. Patients wishing substance abuse treatment must have access to it, and medical services should be integrated with substance abuse treatment (Weisner, Mertens, Parthasarathy, Moore, & Lu, 2001). Alcohol treatment is particularly important because of the strong deleterious effect of heavy alcohol intake on the progression of hepatitis C. Finally, because those successfully completing HCV therapy may be at risk for re-infection (Proust et al., 2000), drug users need detailed counselling and support to avoid risky injection practices, including referral to syringe exchange or prescriptions for syringes if necessary (Burris et al., 2000; CDC, 2002; Rich et al., 2001), in case they continue or return to injecting drugs. IDUs can master safe injection practices and many do inject safely.

Integration of medical and social services

HCV prevention must be provided, either on site or by referral, in all public programs and institutions serving illicit drug users, including public health clinics and hospitals, substance abuse treatment programs, correctional institutions, programs for high-risk youth, HIV counselling and testing sites, STD clinics, mental health clinics, and the like. Likewise, HCV treatment must be provided in the context of comprehensive medical and social services. Attention must be paid to important unmet needs, including hunger, housing, and untreated mental health conditions.

Provision of services to incarcerated populations

Substance abuse, including injection drug use, is prevalent in prison populations, in no small part because so many people are incarcerated for drug-related crimes. Prison offers an ideal opportunity to provide HCV treatment in a setting where barriers to adherence can be eliminated or minimised (Allen et al., 2003).

Social and political barriers to prioritising and implementing effective HCV prevention for drug users in the United States

The U.S. National Institutes of Health (NIH) and Centers for Disease Control and Prevention (CDC) have published guidelines for the prevention and treatment of hepatitis C (CDC, 1998; NIH, 1997a). CDC has also released a National Hepatitis C Prevention Strategy (CDC, 2001b). Until 2002, the documents produced by both agencies virtually ignored the need for prevention and treatment strategies for IDUs. None of these documents discussed developing hepatitis C prevention or treatment programs for IDUs. None set forth recommendations or plans for expanding substance abuse prevention or treatment, implementing syringe exchange programs, removing the legal barriers to syringe access, conducting community-based outreach, or organising HCV counselling and testing programs or treatment programs for IDUs or incarcerated persons. In fact, both NIH (1997a) and CDC (1998) guidelines recommended that persons who inject drugs not be treated for hepatitis C (and in the NIH guidelines, this provision was applied, inexplicably, not just to IDUs but to all illicit drug users). It was as though the needs of drug users, the burden of disease that they bear, and the importance of providing services to them in order to control the HCV epidemic had somehow been rendered invisible in the formulation of these policy documents. Like the proverbial elephant in the living room (Hastings & Typo, 1984), it is impossible not to notice the enormous need for HCV prevention and treatment for IDUs, and yet there seems to have been a tacit and perhaps unconscious agreement in the conference room that their needs would not be spoken of. As a consequence, recommended measures skirted the margins of the HCV problem, rather than addressing its core, and those most severely affected by the HCV epidemic received no help. How did we get into this state of affairs?

The withdrawal of rights and withholding of needed services from drug users is normative in public policy in the United States outside the health care setting. In public discourse, users of illicit drugs are often portrayed as perpetrators of social ills (Massing, 2000; Musto & Korsmeyer, 2002). This portrayal supports punitive public policies, which, in turn, reinforce the stigmatisation (Currie, 1993; Reinerman & Levine, 1997). The United States, for example, spends tens of billions of dollars annually on incarcerating

drug users (Office of National Drug Control Policy, 2000) but only a fraction of this amount on treating substance abuse (Coffey, Mark, & King, 1997; Murphy, Davis, Liston, Thaler, & Webb, 2000). As a consequence, the doors to prison are wide open for illicit drug users, while the door to substance abuse treatment is all too often firmly shut (Gerstein & Harwood, 1990). The persecution of drug users with the force of law in the U.S. probably warrants terms like “narcophobia” or “addictphobia” (Jones & Anderson, 1999) that have been applied to these policies to describe their irrational and pernicious nature. For example, a provision passed by the U.S. Congress as part of so-called “welfare reform” prohibits anyone convicted of a drug offense from ever receiving food stamps for the rest of their lives, regardless of whether they ever use drugs again (United States Code, 1999). Other provisions deny housing and education benefits to current and former drug users. Such “zero tolerance” policies place a higher value on penalising unwanted behaviour than on actually reducing it. They are aimed not at curbing drug use but at punishing the drug user (Gostin, 1990). The goal is ostensibly to decrease drug use by increasing the personal cost to drug users of their use, but while this approach is demonstrably ineffective (Drucker, 1999; Nadelmann, 1989) it has received priority over interventions that have been demonstrated to be effective (Ball & Ross, 1991; NIH, 1997b). Unfortunately, the drive to punish wrongdoers may be a deeply rooted human urge (Fehr & Gächter, 2002).

In this environment, it is particularly important that “zero tolerance” attitudes and policies be avoided in the health care system, whose mission is not to control behaviour but to provide relief from suffering. Intolerance, unfortunately, can find its way into the health care setting, where it can interfere with effective and compassionate care. Drug users are difficult to care for, and physicians rarely receive training in caring for them. Drug users may fail to follow their physicians’ advice, fully and truthfully disclose their lifestyles and behaviours, or keep their appointments. Physicians often find caring for drug users frustrating and, not understanding or approving of their behaviour, may respond with aversion, malice, or neglect (Chappel & Schnoll, 1977; Gorlin & Zucker, 1983; Groves, 1978; Jecker, 1996). Most physicians do not feel comfortable caring for injection drug users (Gerbert, Maguire, Bleeker, Coates, & McPhee, 1991). Indeed, half the physicians in a survey of one large urban hospital believed that patients who engage in self-destructive behaviour are not entitled to health care (Gross, 1999). Better education of physicians and health care providers in substance use and addiction, and exposure to models of compassionate care, are needed to overcome these barriers (Lewis, 1997; O’Connor et al., 1994; Shine, 1996).

Other factors may influence policies toward drug users with HCV infection as well. Scientists and health professionals who have been working on HIV/AIDS have had two decades of experience learning about the complexities of addressing difficult problems affecting disenfranchised com-

munities. They have learned many lessons, often the hard way, about the necessity of overcoming prejudices, bridging cultural gaps, and avoiding discrimination in order to effectively serve marginalised populations. They have learned to recognise the role of social, cultural, and behavioural factors in disease transmission and control. Hepatitis C treatment experts may benefit from the lessons learned and the experience gained by several groups of professionals during two decades of responding to HIV. Substance abuse treatment professionals have expertise working with drug users in treatment. Harm reduction workers and substance abuse researchers have expertise working with out-of-treatment drug users. And many AIDS medical providers have expertise providing medical care to drug users both in and out of substance abuse treatment. Involvement of these professionals in HCV prevention and treatment efforts will greatly improve their effectiveness.

Moreover, while gay communities effectively mobilised to demand attention to the emerging AIDS epidemic, drug users have not organised to bring political pressure to bear to make the system responsive to their needs. Federal support through the Ryan White Comprehensive AIDS Resources Emergency Act provided funding for indigent persons to receive HIV treatment and for a national education and training network to educate healthcare providers about such care. Similar support for the needs of persons with HCV infection could foster the collaboration between experts in viral hepatitis and experts in substance abuse that is needed to address the HCV epidemic.

Finally, in the public health arena, the fear of political opposition to programs such as syringe exchange has paralysed public health departments and agencies in many jurisdictions. In a study of HIV prevention policies and practices for IDUs in six U.S. communities, public health departments in some cities where syringe exchange had not been implemented had never even had discussions about such programs, and many public health officials were uncomfortable or unwilling even to discuss their policies with study staff (Downing et al., 2002). The inertia created by this fear was often a greater barrier than any organised opposition to these programs. Once certain issues were considered off limits, public health workers grew so used to the restrictions that they did not notice them anymore, like the proverbial elephant in the living room. In communities that had overcome this inertia, it was often the presence of political or public health figures who exercised leadership on HIV prevention for IDUs who were able to effectively change the debate. Such leadership was often instrumental in implementing prevention interventions (Downing et al., 2002). Once programs were initiated, many fears were simply proven unfounded.

New, more comprehensive NIH statement

In 2002, NIH reconvened its consensus conference to update its guidelines because of new advances in medical

Table 3
Recommendations for IDUs in NIH hepatitis C consensus statement, 2002 (NIH, 2002)

Treatment
1. Treatment decisions for active IDUs should be made on a case-by-case basis.
2. Active IDU in and of itself is not a reason to exclude patients from antiviral therapy.
3. Active IDUs can be successfully treated for hepatitis C.
4. Methadone is not a contraindication to HCV treatment.
5. Treatment for drug and alcohol abuse should be made available to all patients who want and need it.
6. Experts in HCV and substance abuse should collaborate to treat patients.
7. Patients' adherence should be assessed, monitored, and supported.
8. Patients' psychological conditions, especially depression, should be assessed and treated and should be monitored while on hepatitis C therapy.
9. Alcohol abuse and dependence should be diagnosed and treated.
Access
10. The availability of treatment for IDUs and patients with psychological conditions should be increased.
11. The availability of diagnosis and treatment should be increased for African American and Hispanic populations and persons who are uninsured or have publicly funded healthcare.
12. Programs should be established to prevent, diagnose, and treat hepatitis C in correctional facilities.
Prevention
13. Substance use treatment capacity should be expanded.
14. IDUs should have access to sterile syringes through needle exchange programs, physician prescription, and pharmacy sales.
15. Physicians and pharmacists should be educated to recognise that providing IDUs with access to sterile syringes and education in safe injection practices may be lifesaving.
16. IDUs should be educated not to use others' injection equipment, to wash hands before and after injecting, and to avoid any contact with blood from other persons.
17. Community-based education and support programs for IDUs are needed.
18. HCV prevention education in correctional settings is a high priority.
19. IDUs and incarcerated persons should be screened for HCV.
Research
20. Strategies are needed to make treatment available to drug users, drinkers, prisoners, and patients with HIV co-infection or major psychiatric illness.
21. Research is needed on managing side effects and methods of increasing patient adherence.
22. Studies of the prevalence and management of hepatitis C in populations with publicly funded healthcare or no health insurance are needed.
23. The natural history of fibrosis in various groups, including IDUs, should be studied.
Collaboration
24. A comprehensive approach to collaboration among health professionals concerned with management of addiction, primary care physicians, and specialists involved in various aspects of hepatitis C is needed to deal with the complex societal, medical, and psychiatric issues of IDUs afflicted by the disease.

regimens for hepatitis C (NIH, 2002). The 2002 Consensus Panel included several AIDS scientists, and a researcher with experience in AIDS and substance abuse was asked to address the conference (Edlin, 2002). The new Consensus Statement took a substantially more comprehensive approach than previous Public Health Service documents, raising important social and behavioural issues and challenging the medical, scientific, and public health communities to address the critical needs of injection drug users and other underserved and disenfranchised populations (Table 3). The new guidelines not only rescind the proscription against treating drug users, recommending instead a case-by-case approach, but now also comment specifically on a variety of critical issues that were not previously addressed in official statements or guidelines on hepatitis C. These issues include the importance of attention to mental health issues in the treatment of hepatitis C, the importance of attention to patients' adherence to medication, patient participation in decision making, addressing hepatitis C in correctional facilities, and, most notably, hepatitis C prevention in drug users. The onus is now on scientists, providers, policymak-

ers, insurers, and government funders to implement the Panel's recommendations (Table 3).

Conclusion

Substantial research and experience exist to inform efforts to address the enormous hepatitis C epidemics in developed countries such as the United States. Since transmission through contaminated injection equipment accounts for most HCV transmission, efforts must focus on preventing and treating substance abuse and providing services to drug users, including community-based outreach, access to sterile syringes and injection equipment, counselling and testing, and antiviral treatment. A major effort is needed to increase substance abuse treatment capacity in the U.S. Prevention programs for IDUs must emphasise the importance of avoiding all blood contact and the sharing of any injection equipment. Treatment will require programs designed specifically for drug users in which experts in both hepatitis and substance abuse collaborate. Physicians must

recognise the value of gaining expertise and experience in caring for persons who use drugs. Providing services to drug users conflicts with social policies designed to increase the personal costs of drug use to users. But such policies are not consistent with the goals of medicine or public health. Public health professionals must provide policy makers and the public with the best possible advice about effective strategies to combat major public health problems such as the HCV epidemic. Public health officials must exercise leadership and prioritise needed interventions, regardless of the political climate. Advocates for harm reduction must organise to bring pressure to bear, in both the political and public health arenas, in support of sound hepatitis C prevention and control policies.

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Overcoming Barriers to Prevention, Care, and Treatment of Hepatitis C in Illicit Drug Users

Brian R. Edlin,¹ Thomas F. Kresina,⁴ Daniel B. Raymond,³ Michael R. Carden,¹ Marc N. Gourevitch,² Josiah D. Rich,⁷ Laura W. Cheever,⁶ and Victoria A. Cargill⁵

¹Center for the Study of Hepatitis C, Weill Medical College of Cornell University, ²Division of General Internal Medicine, New York University School of Medicine, and ³Harm Reduction Coalition, New York, New York; ⁴Center on AIDS and Other Medical Consequences of Drug Abuse, National Institute on Drug Abuse, and ⁵Office of AIDS Research, National Institutes of Health, Bethesda, Maryland; ⁶HIV/AIDS Bureau, Health Resources and Services Administration, Department of Health and Human Services, Washington, DC; ⁷Miriam Hospital, Brown University School of Medicine, Providence, Rhode Island

Injection drug use accounts for most of the incident infections with hepatitis C virus (HCV) in the United States and other developed countries. HCV infection is a complex and challenging medical condition in injection drug users (IDUs). Elements of care for hepatitis C in illicit drug users include prevention counseling and education; screening for transmission risk behavior; testing for HCV and human immunodeficiency virus infection; vaccination against hepatitis A and B viruses; evaluation for comorbidities; coordination of substance-abuse treatment services, psychiatric care, and social support; evaluation of liver disease; and interferon-based treatment for HCV infection. Caring for patients who use illicit drugs presents challenges to the health-care team that require patience, experience, and an understanding of the dynamics of substance use and addiction. Nonetheless, programs are successfully integrating hepatitis C care for IDUs into health-care settings, including primary care, methadone treatment and other substance-abuse treatment programs, infectious disease clinics, and clinics in correctional facilities.

Injection drug users (IDUs) constitute the largest group of persons infected with the hepatitis C virus (HCV) in the United States, and most new infections occur in IDUs. The prevalence of HCV antibody in most studies of older IDUs is 80%–90% [1–3], and uninfected IDUs generally become infected at rates of 10%–20%/year [3–7]. Controlling the HCV epidemic, therefore, will require developing, testing, and implementing strategies for the prevention, care, and treatment of hepatitis C that will be effective for IDUs [8]. Substantial barriers to providing effective care and treatment for IDUs with hepatitis C stem from characteristics of the disease, patients, providers, and the health care system. As a result, although a large proportion of IDUs with hep-

atitis C express willingness to undergo treatment, a disproportionately low number of IDUs have actually received antiviral therapy for HCV infection [9]. Fortunately, clinicians undertaking hepatitis C care can draw upon a substantial body of research and clinical experience in the prevention and management of chronic viral diseases among IDUs [10, 11]. This article addresses the scope of hepatitis C care and the challenges and barriers faced by health-care providers and IDUs in the medical management of HCV infection.

INJECTION DRUG USE AND HEPATITIS C RISK BEHAVIOR

Drug use is a complex behavior with multidimensional determinants, including social, psychological, cultural, economic, and biological factors [11–13]. The 2002 National Survey on Drug Use and Health [14] reported that 3.7 million Americans >12 years have experimented with heroin use. An estimated 1.0–1.5 million Americans actively use illicit drugs by injection [15]. Bloodborne viral infections, including HCV, hepatitis

Reprints or correspondence: Dr. Victoria A. Cargill, Minority Research, Clinical Studies, Office of AIDS Research, National Institutes of Health, 2 Center Dr., Rm. 4E20, Mail Stop 0255, Bethesda, MD 20892 (vc52x@nih.gov).

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B virus (HBV), and HIV, are transmitted when uninfected IDUs use injection equipment, especially syringes, that have previously been used by an infected person [15]. The transmission of HCV is estimated to be 10 times more efficient than that of HIV [16] and can probably result not only from the sharing of syringes but also from the sharing of other injection equipment, such as “cookers” (i.e., bottle caps, spoons, and other containers used to dissolve drugs) and “cottons” (i.e., filters used to remove particulate matter while drawing up the drug solution into a syringe) [3–5]. Transmission can probably also occur through minor instances of blood contact, such as when one person administers an injection to another [17].

The HIV epidemic led to significant changes in injection practices. Beginning in the 1980s, as IDUs learned of the risks of disease transmission through sharing syringes, behavioral norms changed, and rates of syringe sharing dropped dramatically [18–20]. HIV prevention programs, including needle exchange, outreach, and peer education, have strengthened and supported reductions in needle sharing while increasing the availability of sterile syringes and injection equipment. When given access to sterile syringes, IDUs readily made use of them, reducing needle sharing [18–20] and rates of disease transmission [15, 21, 22]. The sharing of other injection equipment, however, remains relatively common [19, 23], as does the practice of giving and receiving injections [24]. Historically, HCV was usually acquired very soon after a person began injecting drugs [2, 25]. Recent studies have shown, however, that, since the introduction of needle exchange and other HIV prevention interventions for IDUs, the prevalence and incidence of HCV infection among young IDUs and recent initiates have declined substantially [5, 6, 7, 22]. Thus, although the incidence of HCV infection among IDUs remains unacceptably high [3–7], the evidence suggests that prevention efforts can be successful.

NATURAL HISTORY OF HCV INFECTION

Infection with HCV may result in 1 of 3 outcomes: infection may spontaneously resolve during the acute phase and never progress to chronic infection, infection may become chronic without medical complications or end-organ disease, or infection may become chronic, with progressive medical complications, such as cirrhosis, hepatocellular carcinoma, or end-stage liver disease. The virus-host interactions that result in the resolution of HCV infection are not well understood [26], but it has been shown that treatment of acute HCV infection can result in high rates of successful clearance of the virus [27–29]. Thus, regular testing for HCV of uninfected persons at high risk for infection—particularly young IDUs and recent initiates to injection drug use—is an important strategy for secondary prevention of chronic HCV infection in persons who acquire the infection acutely. On the other hand, the long period of

clinical latency before chronic HCV infection causes severe liver disease and the low but variable proportion of infected persons who will develop severe liver disease make it impossible to predict the clinical sequelae of untreated HCV infection in any particular individual. This complicates the assessment of the benefits of treatment when counseling infected patients.

HEPATITIS C CARE FOR ILLICIT DRUG USERS

Care for hepatitis C is a vital component of a comprehensive health program for persons who use illicit drugs. Such care includes screening for transmission risk behavior, prevention counseling and education, testing for HCV antibody and RNA, vaccination against hepatitis A virus (HAV) and HBV, and evaluation for comorbidities, including HIV infection. IDUs who are found to have chronic HCV infection should be assessed for the presence and degree of liver disease and evaluated for treatment for HCV. This evaluation should include determining the need for substance abuse services, psychiatric care, and social support and an effort to engage the patient in primary care.

Patient-provider relationships. Caring for drug users presents special challenges to the health-care team and requires patience, experience, and tolerance. Comorbid psychiatric conditions are common, including major depression, anxiety disorders, posttraumatic stress disorder, and bipolar disorders. In addition, many drug users have had negative experiences with the health-care system and its providers [30, 31]. IFN therapy has a number of reversible neuropsychiatric adverse effects, including impairment in concentration, depression, insomnia, and irritability [32]. Successful treatment for hepatitis C requires a trusting relationship with a health care provider who can help patients anticipate, plan for, and endure the difficulties of therapy for HCV infection. Patients must work at adhering to the regimen, physicians must be responsive to patients' experiences of adverse effects, and both parties must be able to communicate openly about their expectations and frustrations. Physician-patient relationships that support this kind of collaboration are based on mutual trust and respect and take time to develop. Drug users often believe that the health care they receive is judgmental and condescending, unresponsive to their needs, and delivered without respect. For their part, persons actively using drugs may fail to follow through with medical advice, appointments, and prescribed medication [10, 11, 12, 33]. These problems can lead to a dynamic of mistrust and lack of cooperation between the patient and provider.

The extensive experience gained from treating IDUs for medical conditions, especially HIV infection, has led to the development of effective principles for engaging drug users in health-care relationships (table 1) [11, 34–36]. Successful programs invariably adopt a respectful approach to substance users, un-

Table 1. Principles for managing health-care relationships with substance-using patients.

Establish a climate of mutual respect
Maintain a professional approach that reflects the aim of enhancing patients' well-being; avoid creating an atmosphere of blame or judgment
Educate patients about their medical status, proposed treatments, and their adverse effects
Include patients in decision making
If possible, establish a multidisciplinary team consisting of primary care physicians, HIV specialists, psychiatrists, social workers, and nurses
Have a single primary care provider coordinate the care delivered by such a team, to maximize consistency and continuity
Define and agree on the roles and responsibilities of both the health-care team and the patient
Set appropriate limits and respond consistently to behavior that violates those limits
Minimize barriers to participation (e.g., allow flexibility in adherence to appointment schedules and allow drop-in visits, to the extent possible)
While recognizing that patients must set their own goals for behavior change, work with patients to achieve commitment to realistic goals for healthier behaviors
Acknowledge that abstinence is not always a realistic goal; emphasize measures to reduce risks for patients who continue to use drugs
Acknowledge that sustaining abstinence is difficult and that success may require several attempts
Be familiar with local resources for the treatment of drug users
Pitfalls to avoid
Unrealistic expectations
Frustration
Anger
Moralizing
Blame
Withholding therapy

NOTE. This table is adapted from [102] and is reprinted with permission from Wiley.

derstand the medical and behavioral sequelae of addiction, and refrain from moralistic judgments [10, 11, 35–37]. They use client-centered approaches and, often, multidisciplinary teams. Providers can be effective by working with clients individually to identify changes they are motivated to make to enhance their health and well-being. This client-centered approach recognizes that, when global behavior change (such as ceasing all drug use) is not possible or likely in the short term, many other measures can nevertheless reduce the harmful medical consequences of high-risk behavior [36, 38].

Education about prevention of HCV infection. Education and counseling aimed at reducing the transmission of HCV and other bloodborne pathogens are integral components of all health-care services for IDUs. The primary goal of prevention education and counseling for patients who continue to inject drugs is to support safer injection practices [39, 40]. IDUs

should be encouraged to use a new, sterile syringe for each injection and to avoid sharing injection equipment with other users, practices that can reduce the risk of acquisition of HCV by uninfected persons and help those who have received successful antiviral treatment to avoid reinfection. Health-care providers can also facilitate access to sterile syringes by prescribing syringes [41] and by referring patients to syringe exchange programs and pharmacies that sell syringes without a prescription [42, 43]. Physicians in at least 46 states are allowed by law to prescribe syringes to IDUs to reduce transmission of blood-borne infections [44]. A survey of knowledge and attitudes among health-care providers about prescription of syringes showed uncertainties about legal issues but substantial willingness to prescribe syringes to IDUs [45]. Prescribing syringes to patients who inject drugs can strengthen patient-provider relationships and facilitate retention in care.

Where possible, IDUs should also be referred to local syringe exchange programs and pharmacies that sell syringes without a prescription. Currently, there are >200 syringe exchange programs in >150 cities in 36 states in the United States. A majority of syringe exchange programs provide a range of ancillary services, including education, support groups, and case management. Pharmacies are more widely accessible than are syringe exchange programs, operating in more locations and for more hours. At present, pharmacies in 46 states may legally sell syringes without a prescription, because they either do not have laws requiring prescription for syringes [46, 47] or have recently amended them [42, 43, 48, 49].

Health-care professionals can provide education and support for safer injection practices at relatively little cost. Only a limited number of public health departments offer HCV education [50]. In addition, a recent report indicated that only 54% of treatment programs for substance abuse provide education about HCV to all of their patients [51]. Thus, there is a need to increase education about HCV for IDUs and other high-risk populations. Incorporating education initiatives regarding HCV into existing and widely available HIV prevention programs and substance-abuse treatment programs is an optimal and cost-effective strategy to address the growing need for education about HCV through the use of existing resources. Continuing education programs can help physicians and pharmacists, who have traditionally been trained to make every effort to keep syringes from being used for nonmedical purposes, recognize that providing access to sterile syringes and education about sterile injection methods can be lifesaving interventions [52].

Screening and testing for HCV infection. A comprehensive health care program for IDUs should include strong linkages with hepatitis C prevention services, including community-based programs of counseling and testing for HCV, so that IDUs infected with HCV can be identified and their entry into

care facilitated. Testing for HCV antibodies should be accompanied by client-centered counseling based on individualized behavioral risk assessments. Such services should be available either on-site or by referral [53] in all public programs and institutions serving illicit drug users, including public health clinics and hospitals, syringe exchange and HIV prevention programs, substance-abuse treatment programs, correctional institutions, programs for high-risk youth, HIV counseling and testing sites, sexually transmitted disease clinics, mental health clinics, and psychiatric hospitals. Regardless of where HCV testing occurs, counseling and testing provide a critical opportunity to connect IDUs to comprehensive medical and social services addressing other core issues, such as primary care, untreated mental health conditions, housing, and hunger.

Existing testing programs outside of medical facilities generally provide only testing for HCV antibody and do not offer tests for HCV RNA. HCV RNA testing is necessary to distinguish between persons with chronic infection and those who have cleared their infection spontaneously. Without HCV RNA testing, persons who have positive antibody test results do not learn whether they are actually infected, and many who are not infected may assume that they are [54]. Persons whose HCV infection resolved spontaneously during the acute phase are susceptible to reinfection [55, 56]. Therefore, programs of counseling and testing for HCV require strong referrals to medical care for confirmatory testing for HCV RNA and appropriate evaluation and follow-up. If negative HCV RNA test results reveal cleared infection, IDUs can be so informed, counseled on strategies to reduce the risk of reinfection, and referred to prevention services.

Vaccination against HAV and HBV. HAV and HBV are important public health concerns for IDUs infected with HCV, because of the increased risk of severe liver disease due to superimposed chronic HBV infection [57] or acute HAV infection [58]. Vaccinations against HAV and HBV are recommended for persons at high risk, including IDUs and persons with HCV infection [59]. Thus, vaccination strategies for HAV and HBV are an important component of hepatitis C care [60]. To maximize their effectiveness, vaccination strategies should take into account issues such as seroprevalence [61, 62], knowledge of immunity status [63], adherence to follow-up visits [64], vaccine schedule [65], current medical services [66], and the need for social services [65]. Targeted vaccinations for IDUs have been shown to be effective when done at methadone clinics [67], as part of infectious disease prevention services at a syringe prescription program [68], or in other community-based settings [69]. Of note, even if a vaccine series is not completed or not completed on schedule, partial protective immunity may still be conferred [59].

Substance-abuse treatment and hepatitis C care. Hepatitis C care also requires providing access to treatment for substance

use and abuse. Numerous treatment modalities for substance dependence have demonstrated effectiveness [70–72]. Therapy with opioid agonists, including methadone maintenance treatment, has been shown to diminish and often eliminate opioid use and reduce transmission of many infections, including HIV [73–75]. The recent approval of buprenorphine makes office-based pharmacotherapy for opioid addiction possible [72]. Physicians who complete a defined training [76] can apply for a waiver to the Drug Addiction Treatment Act of 2000 and prescribe buprenorphine to opioid-dependent patients. This new treatment modality not only expands the accessibility of pharmacotherapy for opioid dependence but also mitigates the stigma associated with receiving substance-abuse treatment by integrating it into routine general medical practice.

Care for hepatitis C must also address the risks of alcohol use. All patients with HCV infection should be counseled to refrain from the consumption of alcohol, because heavy alcohol intake [77] accelerates the progression of HCV-related liver disease and increases the risk of developing hepatocellular carcinoma [78, 79]. Blood levels of HCV RNA are commonly elevated in infected patients who regularly consume alcohol, presumably because of enhanced viral replication in hepatocytes, which has been observed in *in vitro* models [80–82]. Both the consumption of alcohol during treatment and higher baseline HCV RNA levels have been associated with a decreased rate of therapeutic response to IFN-based treatment regimens. Consumption of alcohol compromises the responses of endogenous IFN- α to HCV infection [82] and is associated with poor adherence to medications [79, 82, 83].

Brief interventions by medical providers focused on problem use of alcohol have been shown to produce positive results in a variety of settings [84–86]. This approach consists of delivering brief, client-centered counseling within the context of the medical relationship, by using reflective listening while assuming a nonjudgmental demeanor. Core elements of brief interventions include assessing current levels of consumption of alcohol, providing education regarding risks, assessing and facilitating motivation to alter alcohol consumption, problem solving and developing strategies for change, setting goals, and discussing progress during scheduled follow-up visits [87]. Although brief interventions in the medical context have usually been used to help patients reduce alcohol consumption, the approach can easily be adapted to address any number of potentially harmful behaviors, with the quality of the patient-provider relationship being a fundamental determinant of the approach's effectiveness.

Naltrexone and acamprosate are US Food and Drug Administration–approved pharmacotherapeutic modalities that have been shown to be safe and efficacious in treating alcohol addiction in an outpatient setting [88]. Acamprosate and naltrexone have different mechanisms of action and modify dif-

ferent behavioral aspects of addiction. Acamprosate is a long-acting agent that prolongs periods of abstinence by normalizing glutamateric neurotransmission, which is dysregulated during chronic consumption of alcohol and withdrawal. Naltrexone is a fast-acting opioid receptor antagonist that reduces heavy consumption of alcohol by decreasing the rewarding effects of ethanol. The safety and efficacy of combination treatment with both drugs for alcohol addiction has been demonstrated in double-blind studies, although no studies have addressed concurrent HCV infection or IFN-based antiviral treatment.

Antiviral treatment. Optimal antiviral regimens for HCV infection are discussed elsewhere [89, 90]. Not all IDUs will want or need antiviral therapy, given the toxicity and limited efficacy of current regimens and the variable natural history of untreated infection, but none should be denied therapy solely on the basis of their addiction. The 2002 National Institutes of Health Consensus Statement on the Management of Hepatitis C [89] and the 2004 Practice Guidelines for the Management of Hepatitis C endorsed by the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America [90] recommended that decisions about treatment of hepatitis C in IDUs be made on a case-by-case basis and advised that drug use itself was not an absolute contraindication to antiviral therapy for HCV infection. Several groups have now reported success in providing antiviral treatment for HCV infection to IDUs, even those who were not abstinent from illicit drugs [91–99]. Correctional facilities provide an opportunity to offer treatment to a large number of persons with hepatitis C through existing infrastructure, as discussed elsewhere in this supplement issue of *Clinical Infectious Diseases* [100].

Successful treatment of IDUs with hepatitis C by means of IFN-based treatment regimens must be considered in the context of overall health care of IDUs and requires collaboration between experts in hepatitis, substance use and addiction, and mental health to create treatment models specifically designed for IDUs. An optimal multidisciplinary team would represent the perspectives of primary care physicians, hepatologists, nurse practitioners, nurses, psychiatrists, psychologists, addiction specialists, social workers, and drug counselors. Backmund et al. [91] demonstrated the success of this approach, which has been replicated by others. Particular efforts are needed to address the challenges faced by IDUs with respect to adherence to medications, psychological adverse effects, and the potential for reinfection [101, 102].

Adherence to treatment. Active use of psychoactive substances, particularly alcohol or stimulants, is often associated with reduced adherence to medical interventions [103, 104]. Individualized programs designed to address the particular needs of IDUs, however, can achieve rates of adherence as high as those in other patient populations [8, 91, 92, 96, 105, 106].

Adherence to medications can be optimized by integrating medical care and treatment for substance abuse [98]. Patients who are engaged in methadone maintenance treatment programs or have a history of injection drug use or psychiatric disorders show rates of discontinuation of treatment for HCV that are similar to those of control groups [91, 107]. Methadone maintenance treatment, coupled with multiple support interventions, improves rates of adherence to medications and reduces the risk of HIV infection [108].

The most effective interventions for improving adherence among IDUs are multidimensional and target several aspects of adherence behavior [109, 110]. In one study of HIV-positive IDUs, treatment with buprenorphine had a significant effect on adherence to treatment for HIV; 78% of IDUs receiving treatment with buprenorphine were adherent to therapy for HIV, compared with 65% of former IDUs and 42% of active IDUs [111]. Similarly, the identification and treatment of depression associated with injection drug use, whether comorbid or antecedent, has been associated with improved adherence to treatment [112]. Providing essential support services, such as case management and transportation, has also been shown to improve retention in care, a critical component of treatment for HIV [113]. Helping a homeless patient find housing can improve adherence.

Additional effective strategies for improving adherence include basic elements of good clinical care, such as establishing a consistent, trusting physician-patient relationship, providing clear information about intended effects and adverse effects of medication, and paying careful attention to perceived adverse effects. Individual counseling that addresses barriers to and facilitators of adherence may be of benefit. Specialized tools, such as electronic reminder systems, directly observed therapy, and cash incentives for attending scheduled medical appointments, have also been shown to improve adherence [106, 114–117]. Directly observed therapy is highly effective in improving rates of adherence to preventive treatment for tuberculosis among IDUs [118] and may have a place in the treatment of hepatitis C for IDUs, especially in combination with pharmacotherapy for substance dependence.

Mental health assessment, monitoring, and treatment. When considering treatment for IDUs with hepatitis C, particular attention must be paid to mental health conditions, which are associated with both hepatitis C and substance use and may be induced or exacerbated by treatment for hepatitis C [95, 119–122]. As a group, IDUs exhibit higher rates of comorbid psychiatric disorders than do the general population [31, 123]. IFN-based regimens for hepatitis C are often complicated by neuropsychiatric adverse effects, including depression, insomnia, and irritability [120–122]. Patients should be screened for depression and other mental health problems before beginning treatment with IFN, treated if necessary, and

monitored for these problems during treatment for HCV. Strong linkages with mental health services, whether on-site or within the community, are a vital component of comprehensive health programs for IDUs and are particularly important during treatment for hepatitis C. Past episodes of depression or other psychiatric disorders are not absolute contraindications to treatment for HCV infection. Persons with psychiatric histories may adhere to and complete treatment for HCV infection at rates as high as those of other patient groups [92, 93], if their mental health status is closely monitored and treated. Some authors have recommended prophylactic antidepressant therapy before beginning treatment for HCV in patients thought to have a high risk of depression [124].

Morbidity due to concurrent infectious diseases. HIV infection may complicate hepatitis C care. HIV infection modifies the natural history of HCV infection [125], reducing the ability of the host to clear or resolve HCV infection. Clearance of HCV viremia occurs less often in persons coinfecting with HIV than in HIV-uninfected persons and occurs less frequently in those with low CD4 lymphocyte counts. Patients coinfecting with HCV and HIV have higher levels of HCV RNA and more rapid progression of cirrhosis to end-stage liver disease and death than do HCV-monoinfected persons [126]. Liver disease due to HCV infection has become a major cause of morbidity and mortality among persons living with HIV infection. In addition, HCV coinfection increases the frequency of drug-induced hepatotoxicity in HIV-infected persons, thus complicating the medical management of HIV infection [127]. HIV-coinfecting patients are less likely than are HCV-monoinfected persons to achieve a sustained virological response to treatment for HCV infection, although combination therapy with pegylated IFNs and ribavirin have improved treatment outcomes in this population [128, 129]. HIV-infected IDUs with chronic HCV infection should be considered to be candidates for anti-HCV therapy, especially given their higher risk of progression to end-stage liver disease and the higher risk of liver toxicity after beginning antiretroviral therapy. However, this decision should be considered in the wider context of the patient's presentation, including stable antiretroviral therapy, ongoing psychosocial needs (nutrition, housing, and support), underlying psychiatric diagnoses, immunologic status (CD4 lymphocyte count), and the education and motivation of the patient. This is clearly an area in need of further study.

STRUCTURAL CHALLENGES TO PROVIDING CARE FOR IDUs WITH HCV INFECTION

Poverty, homelessness, addiction, mental health disorders, social marginalization, fear of arrest and prosecution, mistrust of the health-care system, and limited involvement in stable primary care relationships represent challenges to effective

hepatitis C care. Other barriers may include the social instability and comorbidities associated with drug use, insufficient access to expertise about HCV, and the high cost of comprehensive care and treatment. Physicians rarely receive meaningful training in addiction medicine or effective strategies for managing the difficulties often encountered in providing care for drug users. Consequently, unrealistic expectations, coupled with judgmental attitudes, can lead to frustration and resentment for both physician and patient. Drug users, similar to non-drug using patients, may fail to follow their physicians' advice, be reluctant to fully and truthfully disclose their lifestyles and behaviors, and/or experience difficulty keeping their appointments. Physicians caring for IDUs often experience this behavior as frustrating and specifically related to drug use and may respond with aversion, malice, or neglect [130]. Indeed, most physicians do not feel comfortable caring for IDUs, preferring to relegate this task to an addiction specialist or a drug treatment facility [131]. A growing number of programs are successfully integrating hepatitis C care into a variety of health-care settings, including primary care, methadone maintenance treatment programs and other substance-abuse treatment programs, infectious disease clinics, and clinics in correctional facilities. Better education of physicians and health-care providers about substance use and addiction, and exposure to models of compassionate care, are needed to improve their understanding of problematic substance use as a treatable disorder. Expanding the capacity of hepatitis specialists to manage care for substance users, and of addiction specialists to manage treatment of hepatitis C, will be necessary to overcome these challenges.

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