

ASPECTS OF PRIMARY CARE FOR THE HIV-INFECTED SUBSTANCE USER

I. INTRODUCTION

Substance users are often affected by multiple co-morbid medical and psychiatric conditions, including HIV infection, viral hepatitis, tuberculosis infection, sexually transmitted diseases, other common chronic medical conditions, and depression. Yet despite their need for more intensive medical services, drug users' access to general and HIV-specific medical care is often diminished compared with that of the general population.

Routine medical care for HIV-infected substance users includes the same elements of routine medical care that are appropriate for HIV-infected persons in general. This chapter discusses selected conditions which may have greater prevalence among substance users, or which may have particular diagnostic, preventive, or therapeutic implications in this diverse patient population. Illnesses associated with injection drug use are emphasized in this chapter. A full review of the medical complications of drug abuse is beyond the scope of this chapter, but can be found in several recent references (see *Further Reading*). Risk reduction and related behavioral interventions are addressed in *Working With the Active User*.

II. VIRAL HEPATITIS

RECOMMENDATION:

All HIV-infected patients should be tested at baseline for evidence of hepatic injury. (II)

Key Points:

- Substance users are at high risk for infection with hepatitis viruses A, B, and C (HAV, HBV, and HCV).
- Infection among substance users may initiate and amplify hepatitis outbreaks.

Hepatitis A is transmitted primarily by way of fecal-oral contamination, hepatitis B by sexual contact and injection drug use, and hepatitis C by injection drug use. Hepatitis contributes substantially to morbidity and mortality among IDUs. IDUs may transmit hepatitis to both substance-using contacts and to non-substance-using sexual, household, and other close contacts.

It is particularly important to prevent viral hepatitis among HIV-infected substance users because HAV, HBV, and HCV co-infection(s) may have additional implications for HIV-infected patients. Furthermore, bidirectional interactions between HIV and hepatitis viruses may complicate the disease progression and treatment of both viruses. In addition, superimposed HAV and HBV may exacerbate liver disease among those with chronic HCV infection.

HAART has contributed to improvements in life expectancy for HIV-infected persons. Consequently, persons co-infected with HIV and HBV and/or HCV who are receiving HAART are more likely to survive to be at risk for the late sequelae of chronic HBV and HCV infection, including cirrhosis, end-stage liver disease (ESLD), and hepatocellular carcinoma.

A. Hepatitis A

RECOMMENDATIONS:

Clinicians should offer HIV-infected substance users who do not have antibody evidence of previous exposure (i.e., who are susceptible to hepatitis A) the hepatitis A vaccine. (II) The full series should be given (initial dose and a second dose 6 to 12 months later) to ensure maximal antibody response.

Routine post-vaccination antibody measurement is not recommended because of the generally high efficacy of the vaccine. (II)

Substance users are at risk for acquiring the primarily enterally transmitted hepatitis A virus and play a key role in HAV epidemiology. Outbreaks of HAV have been reported among IDUs and non-injection illicit substance users in numerous U.S. cities and numerous countries. HAV seropositivity among IDUs correlates with poverty but not with any specific drug use practice, previous STDs, or serologic evidence of HBV, HCV, syphilis, or HIV infection. Although fecal-oral transmission predominates among IDUs living in unsanitary conditions, HAV may be transmitted parenterally. Use of contaminated water for drug preparation may also contribute to hepatitis A transmission.

HAV infection has been shown to be more aggressive in patients with underlying liver disease, including chronic HBV and/or HCV infections. HAV also may result in significant flares of underlying liver disease in co-infected patients. The Advisory Committee on Immunization Practices recommends that all persons with chronic liver disease (e.g., HBV or HCV) and all IDUs be vaccinated against HAV.

Almost immediate protection may be obtained from the hepatitis A vaccine. However, vaccination rates among IDUs are low, most likely due to lack of previous engagement in longitudinal medical care that would have included vaccination. HAV vaccination is indicated for all HIV-infected substance users who are susceptible, and this may be particularly important for those co-infected with HCV.

Key Point:

Clinicians should periodically readdress vaccination with individuals who initially decline either hepatitis A or hepatitis B vaccination.

Although optimal benefit is obtained after complete courses of vaccine, there is significant clinical value to receipt of single doses which rapidly stop community outbreaks. Testing to confirm seroconversion after hepatitis A vaccine is unnecessary. Patients who are at increased risk for, and non-immune to, hepatitis A *and* hepatitis B infection may be given the combined hepatitis A and B vaccine in a total of three doses at 0, 1, and 6 months.

B. Hepatitis B

RECOMMENDATIONS:

Clinicians should offer the hepatitis B vaccine to HIV-infected substance users who have been identified by serology to be susceptible to hepatitis B. (II)

Clinicians should strongly encourage all HIV-infected patients who do not have serologic evidence of prior HBV infection, or who have not previously received the complete series of HBV vaccine, to receive the hepatitis B vaccination series. Serologic testing for anti-HBs 1 to 2 months after the third dose should be performed. If the patient did not respond to the vaccine series, the clinician should administer a second series when the patient's CD4 count is ≥ 200 cells/mm³.(III)

HIV-infected substance users who continue to inject drugs should receive counseling regarding the risk of HBV infection from non-sterile injection practices (see Table 1). These patients should be referred to sources of sterile injection equipment (such as syringe exchange programs and pharmacy sales). (II)

Clinicians should evaluate HIV-infected substance users chronically infected with hepatitis B (or co-infected with hepatitis B and C) for liver disease. These patients should be evaluated and offered treatment when medically indicated according to current guidelines. (I)

Clinicians should inform and advise HIV-infected substance users chronically infected with hepatitis B (or co-infected with hepatitis B and C) that sharing injection equipment and engaging in unprotected sex place their partners at risk for transmission of both HIV and viral hepatitis. (II)

Clinicians should advise HIV-infected substance users chronically infected with hepatitis B that drug-sharing, sexual, and household contacts may be at risk for hepatitis B. Such contacts should be advised to undergo medical evaluations and, if susceptible, should be offered HBV vaccination. (II)

The drug regimen of choice is currently unknown because no randomized comparative trials have been conducted in this patient population. Options include tenofovir, emtricitabine, interferon alfa-2b, lamivudine, or adefovir; there are insufficient data to recommend combinations of drugs at this time. If lamivudine is given for treatment of hepatitis B, it should never be used alone but in combination with other HIV-active antiretroviral agents as a component of HAART. (See Chapter 7B in *Criteria for the Medical Care of Adults With HIV Infection* manual for further treatment recommendations.)

HBV is similar to HIV in that it is spread primarily by sexual activity and injection drug use; however, transmission of HBV is more efficient via the sexual and percutaneous routes than HIV. HBV is generally found in very high concentrations in serum (10^8 – 10^{10} virions/mL), and HBV levels have been shown to be even higher in HIV-infected patients compared with those who are non-HIV-infected.

Key Point:

HBV vaccination is indicated for all HIV-infected substance users who are susceptible and may be particularly important for those co-infected with HCV.

HBV is preventable by vaccination but, like HAV, HBV vaccination rates among IDUs are low. Vaccination for hepatitis B is most effective after completion of a three-dose series at 0, 1 to 2 months, and 6 months. Lesser but still clinically significant protection may be conferred by incomplete vaccine courses, even by single doses. Some IDUs may not achieve the same geometric mean HBsAb serum antibodies as non-IDU healthy controls; however, overall seroconversion rates may be comparable in adherent IDUs. In HIV-infected individuals, the value of routine monitoring may be assessed on a case-by-case basis. Patients who are at increased risk for, and non-immune to, hepatitis A *and* hepatitis B infection may be given the combined hepatitis A and B vaccine in a total of three doses at 0, 1, and 6 months.

Ideally, hepatitis B vaccine should be administered early in the course of HIV disease, before severe immune suppression has occurred. However, advanced immune suppression is not a contraindication to vaccination, and vaccination of susceptible persons should not be deferred or delayed because of advanced immune suppression or in anticipation of expected immune recovery due to the effect of HAART.

Generally, when HIV-infected patients do not respond to the vaccine series, a rapid loss of induced antibody occurs. These patients are, therefore, at risk for HBV infection following exposure. The clinician should test for HBsAb 1 to 2 months after completion of the third vaccine dose. If no antibody is detected, a repeat vaccination series may be initiated, although its success is not likely. If a second vaccination series is being considered, HBV seroconversion may be enhanced by immune reconstitution (≥ 200 cells/mm³) prior to re-vaccination.

C. Hepatitis C

RECOMMENDATIONS:

Clinicians should perform annual HCV screening to detect recent infections for HIV-infected substance users who do not have antibody evidence of previous exposure (i.e., who are found to be susceptible to HCV) and who continue to engage in risk behaviors. (III)

HIV-infected substance users who continue to inject substances and who are found to be susceptible to hepatitis C should receive counseling regarding the risk of HCV infection from non-sterile injection practices. These patients should be referred to sources of sterile injection equipment (such as syringe exchange programs and pharmacy sales). (II)

Clinicians should evaluate HIV-infected substance users chronically infected with hepatitis C (or co-infected with hepatitis B and C) for liver disease. These patients should be evaluated and offered treatment when medically indicated according to current guidelines. (I)

HIV-infected substance users chronically infected with hepatitis C (or co-infected with hepatitis B and C) should be counseled to avoid sharing injection equipment or engaging in unprotected sex because their partners will then be at risk for transmission of both HIV and viral hepatitis. (II)

Substance-sharing contacts should be advised to undergo medical evaluations. (II) As part of this medical evaluation, all contacts should be offered testing for HIV and hepatitis C.

Clinicians should advise HIV/HCV co-infected patients and patients infected with HCV alone to discontinue consumption of alcohol.

Key Point:

HCV seems to be more easily transmitted parenterally than HIV.

HCV is primarily transmitted by the parenteral route. Injection drug use is now the major route of HCV transmission, accounting for at least 60% of all new infections in the United States. In some populations of IDUs, over 80% have been infected with HCV. However, lower prevalence has been found in other populations, particularly among younger users. It is estimated that 25% to 40% of HIV-infected patients are co-infected with hepatitis C, primarily through injection drug use. In New York City, the co-infection rate is estimated at approximately 40%, and the rate is presumably much higher among patients infected with HIV through injection drug use (~70%-90%). After 1 year of injecting drugs, 22% to 65% of IDUs were identified as being infected with HCV, whereas only 14% were infected with HIV.^{1,2} The ease with which HCV is transmitted may have important implications for how best to construct prevention strategies.

1. Prevention

HCV is currently only preventable by behavioral risk reduction because no vaccine is available. Thus, clinicians should discuss risk reduction methods (see Table 1) with patients. Outreach and educational interventions have been effective in reaching in- and out-of-treatment IDUs and their risk contacts and can also promote desired HIV risk-reducing behavior changes. HCV seems to be acquired more rapidly among IDUs than does HIV, driven in part by the higher prevalence of HCV than HIV among injection partners.³ The overlap in modes of transmission and risk behaviors means that many risk-reduction interventions geared at HIV may also help prevent viral hepatitis. However, the additional modes of transmission, greater infectivity of some hepatitis viruses, and higher background prevalence of HCV among IDUs contribute to the need for additional efforts to prevent HCV among IDUs. These and other data suggest that hepatitis prevention efforts should target both syringe-mediated transmission and sharing of other injection equipment (cookers and filtration cotton), as well as high-risk sexual behaviors among IDUs and their contacts.

Table 1
Viral Hepatitis Risk Reduction Guidance for Substance Users

- Stop using illicit drugs – substance users who wish to stop using drugs should be referred to substance abuse treatment when indicated.
- If unable to stop using illicit drugs, substance users should stop injection of illicit drugs.
- If unable to stop injection of illicit drugs, substance users should use a new, sterile needle for every injection.
- Substance users should use their own needle, syringe, filtration cotton, and cooker, without sharing with others.
- If assisting others with injections, the substance user should wash hands thoroughly between injections and use all new equipment.
- Substance users should know their own HIV, hepatitis B, and hepatitis C status, should not engage in unprotected sex, and should be advised to avoid sharing injection equipment.

Although syringe exchange programs have been documented to reduce HIV transmission, data regarding their effect on HCV transmission have been conflicting. Australia has a far more extensive network of syringe exchange programs yet continues to document high rates of HCV transmission, suggesting that these interventions are not sufficient.⁴ Still, other studies in Australia, Scotland, and Switzerland suggest a decreasing prevalence of HCV with the use of syringe exchange programs.⁵⁻⁷

Several reasons explain why syringe exchange programs and methadone maintenance treatment may not have as marked an effect on the transmission of HCV as on HIV transmission.⁸ IDUs frequently do not access these services when they first begin injection drug use, which is a time when they are at high risk for acquiring initial HCV. Furthermore, although the number of shared syringes among substance users has been significantly reduced, sharing of “cookers” (used to dissolve drugs for injection) and filtration “cottons” (used to filter particulate matter from dissolved drugs) has been implicated as a vehicle of transmission of HCV.⁹ Both IDUs and healthcare professionals need to be aware of this potential mode of transmission to promote behavioral risk reduction. IDUs assisting one another in injection may also facilitate contact with infected blood.¹⁰

2. Effect of Substance Use and Substance Use Treatment on HCV Disease Progression and Treatment

Alcohol consumption during HCV treatment reduces the likelihood of response in a dose-related manner.¹¹ However, the optimal duration of abstinence prior to treatment remains unclear. Patients actively using alcohol or injecting drugs may experience increased toxicity from HCV therapies. The treating physician should consider the inherent risks as well as potential benefits of treatment for HCV in these patients.

Although more studies would be useful, it is fairly clear that most illicit drug use is not by itself hepatotoxic, and there is no evidence that use of these drugs presents any pharmacological contraindication to anti-HCV treatment.^{12,13}

Methadone, the most widely used pharmacologic treatment for opioid dependence, does not have an effect on HCV progression, and a decrease in methadone dose is probably not necessary in HCV-infected patients.¹² There has been some clinical controversy as to whether the presence of HCV infection is associated with an increase or a decrease in methadone dose requirements, but definitive data about this issue have not been published. The effects of HCV infection on dose requirements for *buprenorphine*, approved for opioid dependence treatment in the United States in 2002, are also undefined.

Key Point:

Clinicians should be guided by patients' symptoms (e.g., opioid craving or oversedation) when considering whether a change in methadone or buprenorphine dose is indicated.

It is estimated that between 3% and 20% of patients with chronic HCV will develop cirrhosis over the course of 20 to 40 years, with higher rates and more rapid progression among HIV/HCV co-infected patients. However, persons infected through injection drug use may be less likely to progress.¹⁴⁻¹⁶ Heavy use of *alcohol*, which is common among users of other substances, is associated with more rapid progression of cirrhosis.

Concern that the similarities between the side effects of interferon treatment and the symptoms of opioid withdrawal might induce relapse in patients with opioid abuse histories has been expressed, but there is no evidence supporting such a connection. Nonetheless, clinicians, drug treatment staff, and patients should be aware of the potential for confusion of these symptoms, and individuals with symptoms should undergo a careful evaluation to determine the etiology of their symptoms.

3. Treatment and Adherence

The initial National Institutes of Health (NIH) Consensus Panel statement on management of hepatitis C suggested not treating substance users until abstinence had been achieved for at least 6 months; this was modified by the 2002 consensus statement. The new consensus statement suggests that substance users be targeted for HCV testing and be considered for treatment. Those interested in and ready for substance abuse treatment should be referred to substance abuse treatment programs, and those not ready for substance abuse treatment should be counseled on behavioral strategies to reduce their risks of re-infection. Recent studies have shown that in appropriate program models, substance users can complete and benefit from treatment for HCV.^{17,18}

Key Point:

Adherence to the HCV treatment regimen is difficult for all patients, not just substance users or those with HIV.

Two recent studies evaluating treatment outcomes were discouraging.^{19,20} Many potential patients were excluded because they did not adhere to the pre-treatment testing (57% and 37%,

respectively, did not complete testing); others were excluded based on relative and absolute medical and psychiatric contraindications (27% and 34%, respectively). Of the few patients treated, the sustained viral response was only 13%. Adherence to therapy is important in optimizing the outcomes of HCV therapy. Consequently, clinicians should identify potential barriers to adherence and consider measures to promote adherence.

For further guidance on management of HIV/HCV co-infected patients, including anti-HCV therapy and HAART interactions, refer to Chapter 7A in the *Criteria for the Medical Care of Adults With HIV Infection* manual.

III. TUBERCULOSIS

RECOMMENDATIONS:

Clinicians should perform a PPD tuberculin skin test at baseline for HIV-infected substance users. (II)

Clinicians should evaluate HIV-infected substance users who have a reactive tuberculin skin test and should obtain a chest radiograph to exclude active tuberculosis. (I)

HIV-infected substance users with active tuberculosis should receive expedited treatment (AI), and strong consideration should be given to directly observed therapy (DOT). (II)

Clinicians should evaluate HIV-infected substance users who have latent TB infection, and, in the absence of medical contraindications or previous completion of preventive therapy, these patients should be offered treatment for latent TB infection. (I)

To identify recent infections, clinicians should obtain annual PPD tuberculin skin tests in HIV-infected substance users whose skin test results were negative for tuberculosis at baseline. (II)

Substance users, with or without HIV infection, are at increased risk for tuberculosis (TB) infection and disease. Unlike bloodborne infections, skin and soft-tissue infections, or endocarditis, for which the risks are directly related to the act of non-sterile drug use, the increased risks of tuberculosis are related instead to a convergence of social and demographic TB risk factors (see Table 2).²¹

Table 2 Risk Factors Associated With Tuberculosis
<ul style="list-style-type: none">• Poverty• Unemployment• Homelessness• Incarceration• Foreign birth• HIV co-infection

Rates of TB infection among substance users increase significantly with both age and years of drug use. The latter is likely related to increased time spent in settings in which TB is transmitted.²² Among IDUs at a New York City syringe exchange program, positive tuberculin skin test rates were 5% among IDUs aged ≤35 with <5 years of drug use; 13% among those aged >35 with <5 years of drug use; 17% among those aged ≤35 with >5 years of drug use; and 21% among IDUs >35 with >5 years of drug use.²² This cumulative increased risk supports recommendations for serial TB screening in substance users.

HIV-infected substance users with latent TB infection should be evaluated to exclude active TB and, if excluded, should be offered treatment of latent TB infection. The preferred regimen for LTBI is 9 months of isoniazid 300 mg daily (or 900 mg twice weekly if directly observed) plus pyridoxine, 25 mg per day or 50 mg twice weekly, to prevent peripheral neuropathy. The currently recommended duration of isoniazid for the treatment of latent TB infection among HIV-infected persons is 9 months, although significant preventive therapy benefit is obtained from 6-month regimens. Because clinically relevant and significant hepatitis has been observed in persons receiving rifampin/pyrazinamide regimens, rifampin/pyrazinamide is not recommended for the treatment of latent TB infection.

Key Point:

Rifampin may increase the catabolism of opioids and can precipitate opioid withdrawal in opioid users or those on methadone maintenance regimens unless methadone doses are increased.

For patients who are receiving treatment for active TB disease and using opioids or receiving methadone maintenance regimens, the interaction of rifampin and opioids may contribute to non-adherence. This may be managed by discussing the potential for this interaction with the patient and monitoring for withdrawal symptoms. At the first sign of withdrawal following rifampin therapy in patients receiving methadone, methadone doses should be increased by 5 to 10 mg every 1 to 2 days beginning on the day the withdrawal symptoms were observed. Because of methadone's long half life (24-36 hours), care should be taken not to continue daily dose increases for more than 3 days at a time, at which time at least 2 days of stable dosing should follow before further dose increases are considered. Final methadone doses may be 50% greater than the initial dose prior to the introduction of rifampin. When rifampin is discontinued, the methadone dosage should be lowered to avoid over-sedation. Similarly, rifampin may increase the catabolism of certain protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs).

With isoniazid, there is no routine requirement for dose adjustments of any HAART regimen, and less frequent monitoring of serum liver enzymes (e.g., monthly) is required. For further guidance on management of HIV-infected patients with TB infection, refer to Chapter 7D in the *Criteria for the Medical Care of Adults With HIV Infection* manual.

Key Point:

Co-locating TB services may improve adherence and rates of treatment completion.

For substance users in methadone maintenance treatment programs, on-site DOT may be a valuable adherence-promoting strategy and can be both cost-effective and cost-saving from a

societal perspective.²³⁻²⁵ When feasible, incentives which offer positive reinforcement to substance users, including monetary incentives, seem to be both effective at increasing rates of adherence to TB services and justifiable on a cost basis. Similarly, DOT for latent tuberculosis infection may be used to increase completion rates in congregate settings (e.g., penal institutions, residential facilities, shelters) or in ambulatory clinical settings that are attended on a frequent basis (e.g., methadone maintenance programs, dialysis units).

IV. SEXUALLY TRANSMITTED DISEASES IN HIV-INFECTED SUBSTANCE USERS

RECOMMENDATION:

Clinicians should reinforce behavioral risk-reduction measures for STD prevention, including consistent condom use.

High rates of sexually transmitted diseases (STDs) are seen among both IDUs and non-injection substance users, such as crack cocaine users. STDs have been shown to be independent risk factors for the sexual transmission of HIV.

Although preventive vaccines are available for hepatitis A and B, the prevention of other STDs relies on behavioral interventions. Consistent condom use is highly effective for STD prevention. Young IDUs and IDUs who have recently begun to inject may be more likely to engage in unprotected intercourse with opposite sex primary partners than IDUs who have been injecting for longer periods of time.²⁶ This finding, along with the observations that the risk of HBV and HCV may be greatest among new injectors, emphasizes the importance of targeting new injectors for both sexual and injection risk-reduction efforts.²⁷

Key Point:

Primary care clinicians play an important role in reinforcing behavioral risk-reduction measures.

Among substance users, incidence rates for early syphilis range from 2.9 per 1000 person years to 1 per 100 person years,²⁸⁻³⁰ which is substantially higher than that in the general population. In recent U.S. outbreaks of primary and secondary syphilis, use of crack cocaine and the exchange of sex for money or drugs have been identified as major risk factors for syphilis as well as for HIV transmission.³¹⁻³³ Among IDUs, young age, multiple sex partners, and engaging in paid sex are associated with higher rates of syphilis.²⁹

The presence of genital ulcer disease has been associated with HIV transmission. Genital ulcers directly increase the likelihood that genital secretions will contain an infectious amount of HIV-1 and increase the potential for contact between HIV-1 in genital secretions and genital mucosal cells receptive to HIV-1 infection. Smoking crack cocaine may cause blisters and sores on the lips and oral mucosa that may also facilitate the transmission of infectious pathogens.

A. Screening for STDs in HIV-Infected Substance Users

RECOMMENDATIONS:

Clinicians should screen HIV-infected substance users for syphilis.

Clinicians should screen female HIV-infected substance users annually for cervical gonorrhea and chlamydia.

Urine-based testing for gonorrhea and chlamydia may be of value for both male and female substance users. The logistical ease of urine-based tests may increase patient acceptance and allow testing in community-based field sites.

B. Diagnosis of STDs in HIV-Infected Substance Users

The diagnosis of STDs among substance users differs little from that among non-substance users. However, clinicians need to be aware that false-positive syphilis non-treponemal tests can occur in IDUs and persons with HIV, HBV, and HCV, which emphasizes the importance of performing treponemal tests as well. Among HIV-infected persons, FTA antibody tests may fluctuate between negative and positive more frequently than among non-HIV-infected persons,³⁰ emphasizing the importance of both follow-up testing and making treatment decisions within a whole clinical context. Because hepatitis A and B can be transmitted by unprotected sexual practices, they are appropriately considered STDs.

For further guidance in managing STDs in HIV-infected patients, refer to Chapters 6 and 7 in the *Criteria for the Medical Care of Adults With HIV Infection* manual.

C. Alcohol and STD Treatment Interactions

Among the antimicrobial agents used to treat STDs, none are specifically contraindicated or problematic in substance users. For individuals receiving disulfiram for management of alcoholism, metronidazole may precipitate abdominal distress, nausea, vomiting, flushing, and headache. Liquid preparations of some antimicrobial agents, including some preparations of ritonavir, may contain alcohol that may also precipitate such reactions in persons receiving disulfiram.

V. SOFT-TISSUE DISORDERS

RECOMMENDATION:

Clinicians should counsel IDUs on risk reduction for soft-tissue infections (see Tables 3 and 4).

Abscesses are common among IDUs, with an incidence of 33/100 person years in one setting and a prevalence of 32% in another setting. The most common organisms are skin and oral flora, including *Staphylococcus aureus*, facultative gram-negative bacteria, and mixed anaerobic bacteria. This suggests that the contamination is usually related to the injection practices and not the drugs used. However, drugs or injection equipment may be contaminated with environmental organisms, such as *Clostridium tetani* or *C. botulinum*, and may cause cases or clusters of tetanus or wound botulism. Table 3 provides topics that clinicians should discuss with IDUs to reduce the risk of soft-tissue infections, and Table 4 presents risk factors associated with abscesses.

TABLE 3 TOPICS FOR CLINICIANS TO DISCUSS WITH IDUs FOR REDUCING SOFT-TISSUE INFECTIONS
<ul style="list-style-type: none">• Clean skin thoroughly before each injection• Use a sterile syringe for every injection• Rotate injection sites• Keep tetanus vaccinations up to date

- Avoid intramuscular injection of cocaine

TABLE 4
RISK FACTORS ASSOCIATED WITH ABSCESSES*
<ul style="list-style-type: none"> • Not cleansing the skin prior to injection • Use of dirty syringes • Subcutaneous injection • Being female • Cocaine injection

* HIV as a risk factor has been an inconsistent finding.
Data are from Ref. 34.

Pus-filled abscesses usually need to be drained and packed. Culture and sensitivity testing should be performed when pus can be obtained safely, because antimicrobial resistant organisms, including methicillin-resistant *Staphylococcus aureus*, are increasingly common among injectors. The clinician should be aware that subcutaneous injection may cause inflammation and swelling that is not infected and will resolve on its own. IDUs may also develop necrotizing skin and soft-tissue infections. See *Working With the Active User* for more information concerning safer injection.

VI. OVERDOSE

RECOMMENDATION:

Clinicians should counsel substance-using patients about the risk of overdose and how it may be prevented.

A. Heroin and Other Opioids

Key Point:

Methadone maintenance has been demonstrated to be an effective preventative measure for overdose.

Heroin use is associated with a significant increase in mortality, approximately half of which is due to overdose. The risk of overdose may be as high as 2% per year. Heroin overdose is characterized by respiratory depression primarily due to reduction in brainstem sensitivity to carbon dioxide, which may lead to death. Death usually occurs 1 to 3 hours after injection rather than suddenly.³⁵ In many cases of overdose, opioids are mixed with alcohol or benzodiazepines. Table 5 lists other risk factors associated with overdose; Table 6 identifies harm-reduction topics that clinicians should discuss with substance users.

TABLE 5
RISK FACTORS FOR HEROIN OVERDOSE
<ul style="list-style-type: none"> • Age: late 20s or early 30s • Using heroin for 5 to 10 years • Recent release from detoxification or correctional facility • Using heroin outdoors • Using heroin alone • Mixing heroin with alcohol or benzodiazepines • Concurrent serious medical conditions, particularly pulmonary and hepatic dysfunction

TABLE 6
HARM REDUCTION FOR HEROIN OVERDOSE
<p>Patients should be taught the following:</p> <ul style="list-style-type: none"> • the risks of mixing depressants with heroin • the risk of reinitiating heroin use after a period of abstinence • to recognize the signs of a possible heroin overdose in another user and to immediately call for medical help (many people who overdose are not alone)

It has been suggested that heroin users may benefit from training in resuscitation and the provision of naloxone, which can be administered to companions should they overdose.³⁶ The New Mexico Department of Health is piloting such a program.

B. Cocaine

Cocaine overdose is much more difficult to describe and quantify than heroin overdose. It may be more accurate to refer to it as cocaine-related mortality because there do not seem to be direct relationships among dose, tolerance, and mortality.

Potentially lethal reactions to cocaine include seizures, myocardial infarction, hypertensive crisis, cerebral hemorrhage, aortic dissection, and hyperthermia. It has been noted that more deaths are attributed to cocaine during hot weather when hyperthermia becomes more likely. Dysrhythmias may occur but are likely only lethal in the presence of previous myocardial damage.

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Rating Scheme For Clinical Practice Recommendations	
Rating	Definition
Quality of Evidence for Recommendation	
I	At least one randomized trial with clinical results
II	Clinical trials with laboratory results
III	Expert opinion