

Perspective

Substance Abuse and HIV Infection

Substance abuse facilitates the spread of HIV infection and complicates its management. Successful treatment of HIV disease and other comorbidities in substance abusers requires treatment of substance abuse. At the Clinical Pathway of the Ryan White CARE Act 2002 All Grantee Conference held in Washington, DC, in August 2002, Henry Francis, MD, discussed characteristics of substance abuse in the United States and obstacles and approaches to successful treatment.

Who Are Substance Abusers?

Substance abuse can be defined as the repeated use of a substance even with the knowledge of its negative health consequences. Abused substances may be legal or illicit and thus include alcohol and nicotine as well as marijuana, cocaine, heroin, amphetamines, tranquilizers, hallucinogens, steroids, inhalants, and “club” drugs. Addiction plays a major role in substance abuse, and behavioral addictions, such as sex addiction, can also have important social, public health, and medical consequences.

The prevalence of drug use in the United States is shown in Table 1. The stigma attached to illicit drug abuse obscures the impact of abuse of legal substances on society. Nicotine is a highly addictive drug and cigarette smoking is associated with staggering health care costs. The total cost of crime, accidents, and destruction of property associated with illicit drug abuse in the United States is approximately \$50 billion over a 10-year period, which is one third less than costs for similar alcohol abuse-related damages over 2 years. The stigma attached to illicit drug abuse also prevents the recognition, or results from the failure to

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recognize, that underlying addiction is a chronic disease requiring treatment, rather than a social problem.

Illicit drug use according to age, sex, and ethnicity is shown in Table 2; alcohol use is shown in Table 3. Men tend to use illicit drugs more than women do. Incidence of drug addiction tends to be highest among African Americans, followed by Hispanic Americans and white Americans. White Americans, however, have greater rates of alcohol use and addiction. Although these demographic patterns of substance abuse and addiction are not completely understood, they at least partly reflect accessibility and social practices.

Important new drug abuse trends include the abuse of club drugs (see related article, page 25) and anabolic steroids among young people. Club drugs include methylenedioxymethamphetamine (MDMA, ecstasy), flunitrazepam (Rohypnol), gamma hydroxybutyrate (GHB), gamma butyrolactone (GBL), and ketamine. MDMA abuse increased from 5.8% to 8% among 12th-graders from 1998 to 1999. Methamphetamine addictions are replacing opiate addictions in several areas in the world and promise to become an even larger problem in the United States. Anabolic-androgenic steroid abuse increased from 2% to 2.7% among 10th-graders from 1998 to 1999. Because of increased pressure to perform in sports, abuse of steroids by young women rivals that of young men, and it is estimated that 175,000 high-school-aged women have used steroids at least once. Typical patterns of use include sharing needles for group injections with the aim of building muscle together, and these practices have been associated with substantial transmission of disease. Cessation of steroid use is associated with withdrawal symptoms.

The question “Who are substance abusers?” is thus not an easy one to answer. It may not be surprising that 53% of the general population in the United States have used illicit drugs at one time or another. However, some

aspects of the profile of the “average” injection drug user may be surprising: 60% are men, 45% are white, 43% have completed high school, and 53% are employed.

Drug Abuse and Disease

Among injection drug users in this country, some 40% to 45% are HIV-infected, 30% have a positive test result with tuberculin skin testing, 80% to 90% are hepatitis C virus (HCV)-seropositive, 40% are hepatitis B virus (HBV)-seropositive, and 60% use alcohol. The frequency of other sexually transmitted diseases (STDs) ranges from 0% to 80%, and STDs are more common in women than in men. Such data are known only for injection drug users, who account for approximately 10% of the estimated 6 million active drug users in the United States. Levels of such comorbidity in noninjection drug users are likely somewhere between those observed in injection drug users and those in the general population. However, it is also believed that the drug-using population is larger than estimated and that significant comorbidity occurs in the unaccounted-for segments of this population.

Comorbidity is the rule in substance abuse—drug users typically use more

Table 1. Prevalence of Drug Use in the United States

Drug	Current User Estimate
Alcohol	109,029,000
Tobacco	66,476,000
Marijuana	12,122,000
Cocaine	1,676,000
Hallucinogens	1,264,000
Inhalants	539,000
Stimulants	1,018,000
Heroin	123,000

Adapted from the 2001 National Household Survey on Drug Abuse of the Substance Abuse and Mental Health Services Administration.

Table 2. Estimated Illicit Drug Use (Percent of Population) By Age, Sex, and Ethnicity in the United States

Age (yrs)	White	Hispanic	African American
12-17	10.3	9.9	9.9
18-25	13.6	11.1	17.1
26-34	7.1	5.4	9.4
>35	3.2	3.5	4.8
Sex			
Male	7.7	7.7	12.0
Female	-	-	5.2

Adapted from the 1998 National Household Survey on Drug Abuse of the Substance Abuse and Mental Health Services Administration.

than 1 drug and have more than 1 disease—and it complicates patient management. A third of addicts have overt psychiatric comorbidity; in others, psychiatric problems become evident during treatment, with psychosis emerging in response to drug treatment in some. Often, psychiatric illness must be managed before the patient can begin treatment for medical illness and substance abuse. Disease contracted as a result of risk behaviors also complicates management. These diseases can be split into 2 conceptual categories: those that pose a public health threat, such as HIV disease, hepatitis, other STDs, and tuberculosis; and those that do not, such as cellulitis, endocarditis, and meningitis. In this latter context alone, billions of dollars are spent treating complications of drug abuse that could be prevented with rigorous adoption of a focus on treatment and prevention of drug abuse. Additional management complications stem from problems with interactions between drugs used to treat substance dependence and those that treat medical and psychiatric illnesses. Further, many substance abusers appear to have increased tissue and organelle injury that can complicate drug treatment.

With regard to HIV infection in substance abusers, injection drug users have a high rate of HIV disease, as noted above. In addition, approximately 25% to 30% of noninjection drug users have HIV infection. Drug-sharing and sex networks frequently overlap. Transmission of HIV can occur through needle sharing and sex, and the use of some noninjection drugs, such as crack cocaine, is associated with frequent unsafe sex

practices and increased risk of transmission of HIV infection and other STDs. Transmission can also occur in the absence of needle sharing through reuse of the cotton wads that are used to filter injected heroin or cocaine solutions. Virus-containing blood from the reused syringe of one person is deposited in the cotton wad and then washed into the drug solution to be injected by another person when the solution is filtered through the reused cotton wad. Persons infected in this manner may believe that they are at no risk for HIV transmission and can subsequently infect others through unprotected sex, which they perceive as “safe” because they do not share needles.

As noted, the prevalence of other STDs among drug users is highly variable, with prevalence and incidence varying in part according to the substance of abuse. Notable associations include those of syphilis and crack cocaine use; trichomoniasis in injection drug-using women, which is associated

with vaginal inflammation that may facilitate HIV transmission; and a high rate of sexual transmission of HBV (30%-50%) in injection drug users. Approximately 60% of the 4 million cases of HCV infection are in injection drug users, with sexual transmission accounting for less than 20% of cases. HCV transmission among drug users can be blood-borne, as a result of sharing razors and the straws used to snort drugs, which can cut the nasal mucosa and draw blood. Infection occurs in 50% to 80% of injection drug users within the first 2 years of use. Coinfection with HBV and HCV dramatically accelerates HCV disease progression in the drug-using population, with progression to severe liver disease occurring in 2 or 3 years in some cases. HCV infection is emerging as a substantial problem in younger persons in association with abuse of injection drugs, including steroids.

Medical and psychiatric drug therapy can be complex in patients receiving methadone for opiate addictions. Table 4 shows the effects of antiretroviral drugs on serum methadone concentrations, with the interactions primarily reflecting pharmacokinetic interactions between methadone and the nonnucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs) mediated by cytochrome P450 metabolism. It should be noted that measurable changes in serum levels of methadone with coadministration of these agents are not always accompanied by clinically significant effects (eg, withdrawal symptoms). Clinical effects have been observed with nevirapine and efavirenz among the NNRTIs and with nelfinavir among the PIs. Interactions of

Table 3. Estimated Alcohol Use (Percent of Population) By Age, Sex, and Ethnicity in the United States

Age (yrs)	White	Hispanic	African American
12-17	20.9	18.9	13.1
18-25	65.0	50.8	50.3
26-34	65.2	53.1	54.8
>35	56.2	47.7	38.3
Sex			
Male	61.2	56.8	49.0
Female	49.2	33.6	32.3

Adapted from the 1998 National Household Survey on Drug Abuse of the Substance Abuse and Mental Health Services Administration.

methadone with other commonly used drugs are shown in Table 5.

In treating medical and psychiatric disease in substance abusers, both substance abuse and concomitant disease must be identified and treated. Substance abuse is a chronic disease requiring chronic treatment, beginning with identification of the disease, detoxification, and stabilization.

Treating Substance Abuse

Treatment of substance abuse requires a global approach to the patient, necessitating access to and use of health systems focused on the mental, physical, and environmental aspects of disease. Thus, effective treatment must confront physical disease (mental and physical aspects), genetic disposition to addiction, family situation, and historical and social situation. It must also confront stigma and treatment bias. Resources required for effective treatment are shown in Figure 1.

It must be stressed that treatment with methadone, buprenorphine, or levomethadyl acetate does not cure addiction. First, these drugs are used to treat only opiate addiction. Second, the only proven effect of methadone is that it decreases the amount of craving by patients during treatment for addiction. Thus, the role of methadone and the other drugs is to provide a stabilizing influence so that interventions designed to alter the patient's thinking, behavior, and environment, or to prepare the patient for return to a negative environment, can be implemented over a period of time. Drug therapy alone for treatment of addiction has a very low success

Table 4. Effects of Antiretroviral Drugs on Serum Methadone Concentrations

Drug	Effects
Nucleoside Reverse Transcriptase Inhibitors	
Zidovudine	No change
Didanosine	No change
Zalcitabine	Not studied
Stavudine	No change
Lamivudine	No change
Abacavir	Increase in methadone clearance
Nonnucleoside Reverse Transcriptase Inhibitors	
Nevirapine	Decrease in methadone levels by 46%, opiate withdrawal common, potential heroin use relapse
Delavirdine	Increase (modest) in methadone levels
Efavirenz	Decrease in methadone levels by 48%, opiate withdrawal common, potential heroin use relapse
Protease Inhibitors	
Indinavir	No change
Ritonavir	Decrease in methadone levels (study design limits clinical utility of data)
Nelfinavir	Decrease in total (but not free) methadone levels
Saquinavir	Decrease in R-methadone levels when administered with ritonavir
Amprenavir	No effect on R-methadone levels
Lopinavir/ritonavir	Decrease in methadone levels, opiate withdrawal

Adapted with permission from Gourevitch, *Mt Sinai J Med*, 2001.

rate: about 1 in 10 patients.

It is commonly believed that injection drug users have a low rate of adherence to drug treatment and other thera-

peutic regimens. This belief results in substantial treatment bias—treatment may be withheld from such patients, or patients may become discouraged by biased attitudes of health care practitioners. However, history of injection drug abuse is actually a poor predictor of treatment adherence, as are race, sex, age, socioeconomic status, level of education, and occupation. Factors that accurately predict patient adherence include patient health beliefs, ease of access to health care practitioners, familiarity of treatment setting, existence of a social support system for the patient, perceived support from clinical staff, and simplicity of medication regimens (Williams, *J Assoc Nurses AIDS Care*, 1997; Huang, *Int Conf on AIDS*, 1989; Samuels et al, *J Acquir Immune Defic Syndr*,

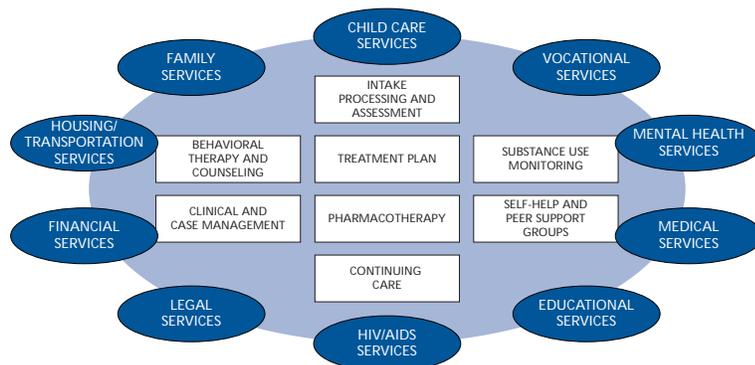


Figure 1. Components of a comprehensive substance abuse treatment program. Adapted from the National Institute on Drug Abuse, 1999.

Table 5. Effects of Other Commonly Used Drugs on Serum Methadone Concentrations

Drug	Effects
Rifampin	Decrease in methadone levels, severe opiate withdrawal
Rifabutin	No change, mild opiate withdrawal
Fluconazole	30% increase in methadone levels (unknown clinical significance)
Phenytoin	Decrease in methadone levels
Phenobarbital	Decrease in methadone levels
Carbamazepine	Decrease in methadone levels
Fluvoxamine	Increase in methadone levels by 20%-100%
Sertraline	Transient mild increase in methadone levels

Adapted with permission from Gourevitch, *Mt Sinai J Med*, 2001.

1990; Morse, *Soc Sci Med*, 1991). The patient's belief in the health system, which often must be encouraged and supported, is of enormous importance to adherence and treatment success in substance-abuse patients.

The goal of substance-abuse treatment is to return the patient to productive functioning. Treatment reduces drug abuse by 40% to 60%, reduces associated crime by 40% to 60%, and increases employment prospects by 40% (Craven et al, *J Acquir Immune Defic Syndr*; 1990; Morse et al, *Soc Sci Med*, 1991). Appropriate treatment for substance abuse is as successful as treatment of other chronic conditions such as diabetes, asthma, and hypertension.

Conclusions

Perhaps the greatest impediment to the effective treatment of substance abuse is the view that the condition is a social problem rather than a disease. The response to behaviors resulting from addiction is more frequently incarceration than renewed or intensified efforts at stabilizing and treating the substance abuser. The costs associated with substance abuse are enormous, including costs associated with the high frequency of HIV disease and other diseases in the substance-abusing population. Prevention of substance abuse prevents associated complications and reduces costs to society. In this regard, it bears noting that children between the ages of 8 and 12 whose parents or caregivers warn them about the dangers of drugs and

other abused substances are half as likely to become addicted to or engage in significant abuse of drugs as those who do not receive such direct attention.

It is important that health care practitioners have access to information on current trends in abused substances and their effects on those who use them. Web site addresses where such information is available are listed in Table 6.

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Table 6. Sources of Information on Substance Abuse, Its Treatment, and Abused Substances

www.nida.nih.gov	National Institute on Drug Abuse
www.whitehousedrugpolicy.gov	Office of National Drug Control Policy
www.dea.gov	US Drug Enforcement Administration
www.bluelight.nu	Descriptions of the experiences of adolescents taking various drugs; these descriptions can be helpful in identifying unusual clinical presentations associated with drug use
www.erowid.org	Up-to-date list of drugs used by young people, information on biochemistry of these drugs and their clinical effects

Suggested Reading

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