Perspective

Methamphetamine Use in Urban Gay and Bisexual Populations

It is estimated that the use of methamphetamine is 5- to 10-times more common in urban gay and bisexual men than in the general US population. Given its effects in stimulating energy, confidence, and libido, as well as its relative inexpensiveness, the drug can efficiently address serious problems in functioning among HIV-infected men, who may suffer significant symptoms of depression or fatigue associated with chronic illness and HIV-related drug treatments. Long-term methamphetamine use is associated with physical, psychologic, and social adverse effects. Increased use of the drug associates with more frequent sexual risk behaviors and increased risks for HIV transmission. Behavioral therapies, notably the approach of contingency management, are being investigated for reducing methamphetamine use and risk behaviors in the urban gay population. This article summarizes a presentation made by Steven Shoptaw, PhD, at the International AIDS Society–USA course in Los Angeles in February, 2006.

Methamphetamine is a long-acting stimulant. It goes by various street names, including crystal, tina, speed, and crank. It can be injected, insufflated (snorted), smoked (eg, by heating on aluminum foil and inhaling the vapor through a pen or straw), taken orally, or taken via "booty-bump" (anal insertion). Methamphetamine comes in forms that can range from a powder that can be white, yellow, orange, pink, or brown (depending on the chemicals used in processing and the expertise of the "cook") to an "ice" form consisting of high-purity methamphetamine crystals or coarse powder that is translucent to white, sometimes with a green, blue, or pink tinge. In general, the purity of methamphetamine on the street is very high, with coloring having little to do with potency of the drug.

Methamphetamine has a half-life of 9 to 12 hours, is inexpensive (approximately $25–$50 per gram), and is used by many different groups, including gay and bisexual men, blue-collar heterosexuals, and youth. There is an especially high prevalence of use in urban gay and bisexual men, estimated at 5- to 10-times that in the general population. Data from San Francisco and Los Angeles indicate methamphetamine use within the prior 6 months in 13% and 11%, respectively, of gay men (Stall et al, *Addiction*, 2001).

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Physical and Psychologic Effects of Methamphetamine

Acute physical and psychologic effects and chronic physical effects of methamphetamine use are listed in Table 1. Medical complications associated with use include: tachycardia, hypertension, tachypnea, hyperthermia, and central nervous system (CNS) excitation; rhabdomyolysis and cardiovascular events, including myocardial infarction and stroke, especially in young patients (29–45 years of age); impairment of CD8+ T-lymphocyte function; and acute pulmonary hypertension associated with smoking the drug. Methamphetamine use is also associated with "meth mouth;" this rotting of the teeth around the gums is related to neglect, xerostomia, decreased fluid intake and intake of high-sugar drinks, characteristics of the drug itself that result in shrinking of the gingival tissue, and bruxism.

Methamphetamine use in gay men is rarely casual, and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for dependence or abuse should be applied to determine the extent of the use problem once it is identified (Table 2). The acute physical

Table **1**. Acute Physical and Psychologic Effects and Chronic Physical Effects of Methamphetamine Use (see Peck et al, *J Addict Dis,* 2005).

Acute physical effects
Increases
Heart rate
Blood pressure
Pupil size
Respiration
Sensory acuity
Energy
Decreases
Appetite
Sleep
Reaction time
Acute psychologic effects
Increases
Confidence
Alertness
Mood
Sex drive
Energy
Talkativeness
Decreases
Boredom
Loneliness
Timidity
Chronic physical effects
Tremor
Weakness
Dry mouth
Weight loss
Cough
Sinus infection
Sweating
Burned lips; sore nose
Oily skin/complexion
Headaches
Diarrhea
Anorexia

and psychologic effects of methamphetamine, as well as its relative inexpensiveness and availability, make it easy to understand why this drug has practical vaue for addressing serious problems in functioning among HIV-infected men. Increased energy, confidence, and libido and improved mood are desirable, particularly among individuals who may be wrestling with the consequences of having a chronic illness such as HIV disease and who may therefore be socially withdrawn or depressed, or those who are suffering from drug treatment-related fatigue or other adverse effects of HIV drug therapy. However, there is often a high price exacted for these "benefits." In addition to the chronic physical effects and complications noted above, the dangers of use include significant risk for psychosis (risk that may persist for years after drug use has stopped), depression, violence, family and social disruptions, and criminal activity. Among men who have sex with men (MSM), methamphetamine abuse increases the likelihood of infection with HIV; in those infected with HIV, it may exacerbate neurotoxicity and other pathologic processes common to HIV infection and complicate the treatment of infection. Methamphetamine use, HIV infection, and HCV infection are each associated with neurocognitive functioning deficits, with additive deficits being found when the conditions are present together. Methamphetamine use also frequently occurs in tandem with the use of poppers (amyl nitrite), which has been independently implicated as a risk factor for transmission of sexually transmitted infections, such as HIV (including resistant virus) and HCV.

Methamphetamine is metabolized by the cytochrome P450 (CYP) 2D6 isoenzyme. It needs to be emphasized that the effect of the HIV protease inhibitor (PI) ritonavir on prolonging the methamphetamine high is well recognized on the street. PIs generally are metabolized via CYP3A4, but ritonavir also affects CYP2D6 and has been shown to increase levels of both methamphetamine and 3,4-methylenedioxy-N-methylamphetamine (MDMA, or ecstasy) by 3- to 10-fold. A few overdose deaths have been reported in HIV-infected patients using methamphetamine or MDMA, and all have occurred in patients taking ritonavir. The nonnucleoside analogue reverse transcriptase inhibitor (NNRTI) delavirdine also is partially metabolized via CYP2D6, and would be expected to slow metabolism of methamphetamine and MDMA. The risk of methamphetamine toxicity is increased in the approximately 3% to 10% of the white population that has a polymorphism in the CYP2D6 gene.

Table **2**. *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision, Criteria for Drug Abuse and Dependence

Abuse

Maladaptive pattern of use, clinically significant impairment or distress, and more than 1 of the following in the same 12-month period:

1. Failure to fulfill major role obligations
2. Use in physically hazardous situations
3. Recurrent legal problems
4. Continued use despite social and interpersonal problems

Dependence

Maladaptive pattern of use, clinically significant impairment or distress, and more than 3 of the following in the same 12-month period:

1. Tolerance
2. Withdrawal
3. Used for longer periods than intended
4. Inability to cut down or quit
5. Time spent getting, using, or recovering from drug
6. Decreased involvement in social, work, or recreation activities
7. Continued use despite knowledge of negative consequences

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders,* 2000.

Methamphetamine Use and HIV Risk

Data on methamphetamine use and prevalence of HIV infection among gay men suggest a time-to-response phenomenon, in which the longer or more heavily involved individuals are in using methamphetamine, the more likely they are to be HIV infected. As shown in Figure 1, a study in the Los Angeles area shows that the prevalence of HIV infection increases in a stepwise fashion from approximately 10% in occasional methamphetamine users, to more than 20% of regular users, more than 40% of chronic users, 60% of men in outpatient drug-free treatment, and 86% of men in a gay-specific social model recovery house (Reback, Report from the City of Los Angeles, AIDS Coordinator, 1997; Shoptaw et al, *Drug Alcohol Depend*, 2005). The increased risk of HIV infection with methamphetamine use is attributable to increased sexual risk behaviors. Some idea of the sexual disinhibition associated with methamphetamine use is provided by a study in a population of methamphetamine-abusing heterosexual men and women in San Diego (Semple et al, *Addict Behav,* 2004). In this population, the average number of episodes of vaginal sex within the past 30 days was 20, compared with a national average of 6 to 7 in the general population, and the average number of sex partners in the past 60 days was 11, compared with 1 to 2 in the general population.

Project EXPLORE in San Francisco found that at baseline among 736 initially HIV-seronegative gay men followed up for risk behaviors, approximately 35% had used poppers, approximately 20% cocaine, and approximately 25% methamphetamine within the prior 60 days (Colfax et al, *Curr HIV/AIDS*, 2005). Logistic regression analysis among 386

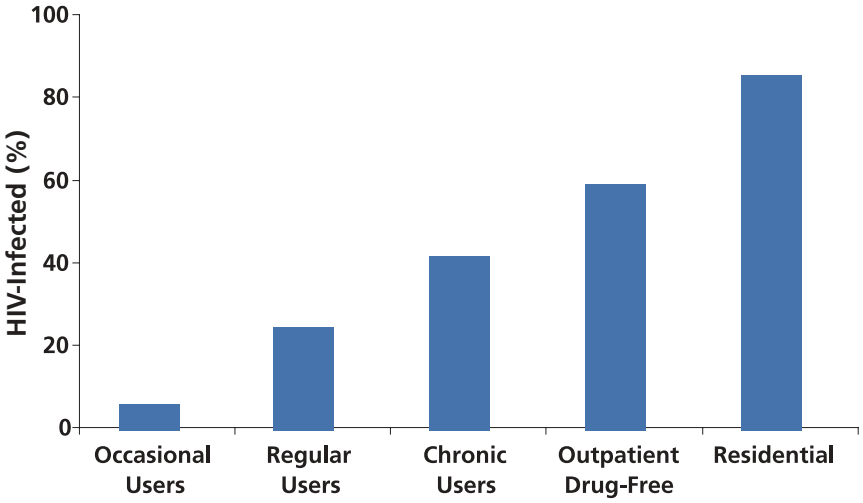

Figure **1**. Prevalence of HIV infection in different samples of men who have sex with men who report levels of methamphetamine use that range from occasional use to severe addiction. Data provided by S. Shoptaw.

participants, yielded odds ratios (ORs) for HIV-serodiscordant unprotected anal sex of 1.5 (95% confidence interval [CI], 1.1–1.9) for those using 1 of these drugs less than 1 week out of the month, 3.2 (CI, 2.2–4.7) for 2 drugs less than 1 week out of the month, 2.8 (CI, 1.6–4.9) for 3 drugs less than 1 week in the month, and 2.2 (CI, 1.5–3.4) for at least 1 drug used weekly. In a treatment study in methamphetamine-abusing MSM in Los Angeles, significant univariate predictors of HIV-seropositive status included prior treatment for methamphetamine use (OR, 4.3; $P = .0006$), as well as unprotected receptive anal intercourse (OR, 3.5; $P = .0046$), history of sexually transmitted diseases (OR, 1.5; $P = .0047$), suicidal or homicidal ideation at admission (OR, 6.5; $P = .0057$), and positive health insurance status (OR, 3.0; $P = .0060$; Peck et al, *Addict Dis*, 2005).

Intervention in Methamphetamine Use

Given the high prevalence of methamphetamine use in urban gay men, any clinical practice in such a setting should establish a routine for assessing methamphetamine use. Use of the 5 "A"s—Ask, Assess, Advise, Assist, and Arrange—is part of good practice in helping patients to stop any kind of substance abuse. For methamphetamine use, in particular, it is useful to ask *all* patients in such a setting the question: "How much methamphetamine have you used since your last visit?"

Behavioral treatments can have a dramatic effect on methamphetamine use (Shoptaw et al, *Drug Alcohol Depend,* 2005). One such treatment is that of contingency management, a behavioral therapy that shapes behavior change by the provision of immediate reinforcements when the desired behavior is produced. Contingency management strategies validated for use with stimulant abusers typically provide vouchers of increasing value for provision of successive methamphetamine-free urine samples. Vouchers are then exchanged for goods or services that promote a drug-free lifestyle (see Higgins et al, *Am J Psychiatry,* 1993). In an intervention study of 162 treatment-seeking methamphetamine-abusing gay men, contingency management resulted in significantly longer retention in treatment, significantly more drug-free urine samples, and significantly longer stretches of consecutive clean urine samples (Shoptaw et al, *Drug Alcohol Depend,* 2005). The study also showed that provision of this and other behavioral drug-abuse treatments resulted in prompt and sustained reductions in unprotected receptive and insertive anal intercourse (Figure 2). This type of sustained risk reduction is a rare finding in HIV prevention trials. Based on these results, contingency management was adopted into a San Francisco public health initiative called Positive Reinforcement Opportunity Project in an attempt to extend these benefits into the methamphetamine-abusing population not actively seeking drug-abuse treatment. The program permitted access to the intervention in nontraditional settings and, in effect, allowed individuals who were not necessarily interested in seeking help to nevertheless be linked into treatment. The program found that contingency management helped about half of MSM to reduce or eliminate methamphetamine use.

Currently, there are no effective pharmacologic methods available for treating methamphetamine abuse. Modafinil is a nonamphetamine-type stimulant that has shown some promise in treating fatigue in HIV-infected individuals. The drug has some favorable characteristics, including promoting wakefulness (it is currently approved for treating narcolepsy), improving cognitive function, and being only a mild inducer of CYP; it is a schedule IV drug with what is believed to be a low abuse potential. In a small study in HIV-infected individuals, modafinil reduced fatigue, reduced depression, and improved neuropsychologic functioning (memory, speed of processing, and executive function) and was associated with only mild side effects (Rabkin et al, *J Clin Psychiatry,* 2004). The National Institute on Drug Abuse is interested in assessing this drug as a treatment for methamphetamine abuse in HIV-seropositive patients, and is currently performing a phase II trial of the drug in patients with cocaine dependence. It would also be reasonable to evaluate the drug in the treatment of methamphetamine abuse in HIV-seronegative individuals. Other potential candidates for treating methamphetamine abuse

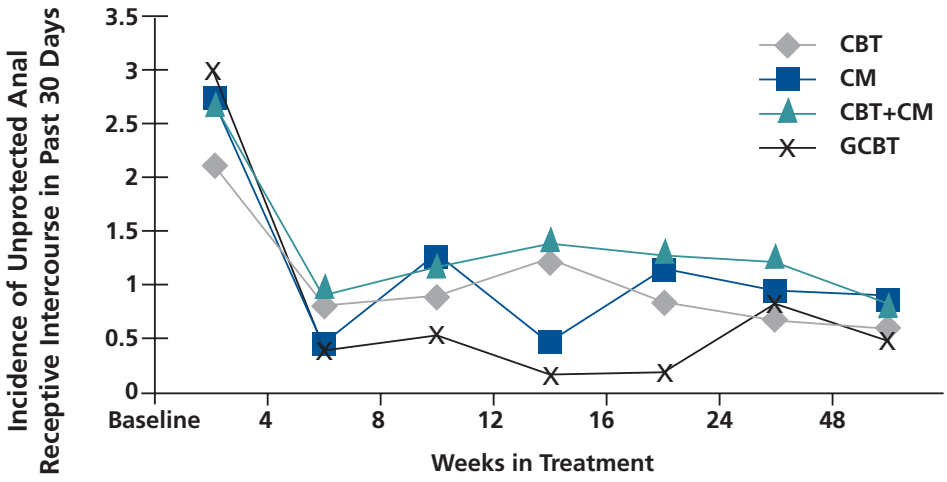

Figure **2**. Sustained reduction in unprotected anal receptive intercourse among men who have sex with men receiving treatment for methamphetamine abuse. CBT indicates cognitive behavioral therapy; CM, contingency management; GCBT, group CBT. $\chi^2_{(3)}=6.75$; $P<.01$. Adapted from Shoptaw et al, *Drug Alcohol Depend,* 2005.

include bupropion, which showed borderline effectiveness in reducing methamphetamine use in a recent phase II trial (Elkashef, *The Methamphetamine Menace,* 2005).

Summary

Methamphetamine use is very common in urban populations of MSM, and increased use is associated with increased risks of numerous adverse health consequences and increased prevalence of sexual risk behaviors for HIV transmission. Methamphetamine is a highly functional drug in this population, producing increased energy, confidence, and libido; for those with HIV infection, it helps the individual to temporarily forget about HIV infection, to feel poweful and attractive in his body and to reduce fatigue associated with chronic illness and HIV medications. Given the high prevalence of methamphetamine use among MSM, it is wise to screen all gay and bisexual patients in care settings for methamphetamine use at each clinic visit. At the very least, each contact with MSM should contain a brief intervention that includes a strongly worded message about the need to not start or to discontinue methamphetamine use that includes support and information for not starting or for quitting. Behavioral interventions, including contingency management, are successful in producing sustained reduction in methamphetamine use and HIV risk behaviors (Shoptaw et al, *Drug Alcohol Depend,* 2005). Investigation is underway to identify drug treatments that may help in reducing methamphetamine use.

Presented in February 2006. First draft prepared from transcripts by Matthew Stenger. Reviewed and updated by Dr Shoptaw in April 2006.

Financial Disclosure: Dr Shoptaw has no affiliations with commercial organizations that may have interests related to the content of this article.

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