

## Substance Use and HIV

Much of ACRIA's HIV treatment education work is provided for people who are active drug users or in various states of recovery. We regularly conduct workshops at syringe exchange programs and other harm reduction sites. But until now, we haven't devoted an issue of *ACRIA Update* specifically to HIV and substance use. Misconceptions and assumptions about the relationship between drug use and HIV disease come up all the time during our workshops. Although there are only partial answers to many questions about drug use and HIV, a lot of data exist that can give us a better understanding of the relationship between the two.

We hope that the articles in this issue of *ACRIA Update* will help you better understand and

address the concerns of many people with HIV. In addition to articles about crystal meth, the effect of drug use on HIV disease progression, and how HIV treatment works for active users, we've included a list of known and potential interactions between HIV-related medications and street/recreational drugs as well as interactions with methadone.

The information is meant to help HIV-positive drug users understand the possible risks of combining various drugs and, if they choose to do so, to be as safe as possible. This is the essence of harm reduction – to reduce harm. We thank our colleagues at the Harm Reduction Coalition for their invaluable assistance with this issue of *ACRIA Update*.

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## HIV Care and Treatment as Harm Reduction

by Daniel Raymond

*"As someone who . . . worked in one position or another as an advocate for the health care needs of illicit drug users for the past ten years, I was intimately aware of the incredible stigma, discrimination, and outright hostility and disgust injection drug users routinely face when attempting to seek health care services of any kind. Suddenly, I was my own client, and all those years I'd spent advocating for other drug users . . . did not prepare me for the treatment I would also receive as a heroin injector with AIDS."*

From *One Junky's Odyssey* by I. Thaca. *Harm Reduction Communication*, Fall 1997

The struggles to keep drug users alive and healthy in the midst of the AIDS epidemic have yielded many stories of survival and innovative models of healthcare delivery. Pioneering clinics and service agencies integrated HIV care, addiction treatment, mental health, support, and education. Current and former drug users pooled their knowledge about HIV, shared tips on coping with side effects, and became educators and adherence counselors. HIV transformed drug users and the systems entrusted with their care and welfare and challenged everyone to adapt and grow stronger. And final-

ly, after nearly two decades of AIDS-related illness and deaths among drug users, the years 1996-7 brought new hope in the form of effective, three-drug combination treatment for HIV, or HAART (Highly Active AntiRetroviral Therapy).

But for too many drug users, the words quoted above, written on the cusp of the HAART era, still ring true today. HAART has certainly kept a lot of HIV-positive drug users alive and relatively healthy. But it is increasingly obvious – on the street, in needle exchanges and health clinics, at

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ACRIA is an independent, non-profit, community-based AIDS medical research and treatment education organization dedicated to rapidly improving the length and quality of life for people living with HIV/AIDS. Bulk copies of *ACRIA Update* are available free to agencies that provide services to people living with HIV/AIDS. For more information, call 212-924-3934 ext. 120.

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## GW-873140 for Treatment-Naïve Adults

People who have not taken anti-HIV drugs (or for less than 2 weeks) will take one of several doses of GW873140 (a CCR5 antagonist) and take Combivir, for 96 weeks. Participants must be 18 or older and have a viral load of at least 10,000 and CD4 count greater than 100. Study participants will be reimbursed \$25 for each regular visit and \$200 for one 12-hour PK visit.

## UK-427,857 for Drug-Resistant HIV

People who have taken anti-HIV drugs from three of the four classes of drugs will take either UK-427 (an experimental HIV CCR5 attachment inhibitor) with an optimized regimen of anti-HIV drugs, or take a placebo (dummy pill) with the optimized regimen, for 11 months. Participants must be 16 or older and have a viral load of at least 5,000.

## The Effect of Reyataz on Cholesterol Levels

People who have high cholesterol levels and a viral load below 50 while taking Kaletra will either switch to Reyataz or continue taking Kaletra. The study will last 12 months. Study participants will be reimbursed \$25 for each visit.

## Reyataz Compared to Kaletra

People whose viral load has risen to over 1,000 while taking an NNRTI as part of their first HAART regimen will switch to either Kaletra, or to Reyataz / Norvir. Everyone will also take Viread and either Videx EC or Zerit XR. The study will last for 22 months. Study participants will be reimbursed \$25 for each visit.

## One-day study of Reyataz Resistance

People whose viral load has risen to over 1,000 while taking Reyataz will have blood tests for resistance, CD4 and viral load. Study participants will be reimbursed \$25.

**For the above trials, contact Dr. Douglas Mendez at 212-924-3934 ext. 126 or Dr. Yuriy Akulov at ext. 124.**

## Research on Older Adults with HIV: ROAH PROGRAM

People in this large study of older adults with HIV will fill out a survey about physical and behavioral health, social networks, quality of life and spirituality. Participants must be 50 or older and be able to read and complete a questionnaire. Study participants will be reimbursed \$25 for one visit.

**For the ROAH Program, contact Andrew Shippy at 212-924-3934 ext. 104.**

### Editor's Notes

- All material in *ACRIA Update* is presented for educational and informational purposes only, and is not intended as medical advice. All decisions regarding one's personal treatment and therapy choices should be made in consultation with a physician.
- *ACRIA Update* refers to most drugs by both their commercial and scientific names upon their first reference in an article. Thereafter in the article, they will be identified with the name by which we feel they are most commonly known, either commercial or scientific.

## HIV Care and Treatment as Harm Reduction *(continued from first page)*

conferences, and in scientific journals – that drug users are not benefiting enough from the new treatments. People are still getting sick, and people are still dying – fewer people, but still too many. The full gains of the HAART era have not yet trickled down to drug users living with HIV.

### From Biology to Sociology

Several factors may explain why drug users fare less well on the spectrum of sickness to survival. In crude terms, explanations have fallen into two camps – biology and sociology. According to the biology camp, mixing drugs and HIV in the same person is a recipe for disaster. Early discussions of drug use and AIDS imagined drug users' bodies as something like an anatomical state of anarchy. The presence of cocaine supposedly made HIV replicate like wildfire, preying on an immune system already weakened by both the "addict lifestyle" and the suppressive properties attributed to substances such as heroin and alcohol. This imagery quickly became entrenched in how all types of people – healthcare professionals, substance abuse counselors, HIV educators, drug users themselves – thought and talked about AIDS. Proponents of this view seized upon esoteric data – "Cocaine makes HIV replicate 25 times faster!" – derived from *in vitro* (laboratory) studies.

Test-tube-and-microscope-style science took on a quasi-religious authority, even though nobody knew whether the findings of lab research bore any resemblance to what goes on in actual people's bodies. Indeed, clinical data from long-term studies of drug users living with HIV contradict assumptions that drug use itself inevitably hastens or worsens the course of HIV disease. According to data from the Women and Infants Transmission Study (WITS), a large group (also called a cohort) of primarily African-American and Latina HIV-positive women in the United States, women categorized as 'hard drug users' (cocaine, crack, heroin, or any injection drug), did not differ from other women with HIV in CD4 cell percentage, HIV viral load, or survival. Hard drug users did, however, experience more

AIDS-defining opportunistic infections, primarily tuberculosis and recurrent pneumonia, infections common in drug users regardless of HIV status.

A smaller but similar study was published in the journal *AIDS* in September 2004. Fifty-one injection drug users (IDUs) in Amsterdam were followed since they became infected in the 1980s. The study found that differing rates of disease progression in this group reflected variations in immune status at the time of infection, rather than drug use itself. In fact, while the duration of drug use did not predict disease progression, those drug users who had been injecting most frequently when they became infected actually experi-

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***“Earlier HAART  
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enced slower declines in CD4 cell counts than IDUs who were injecting less often.

Yet these data do not warrant complacency for the state of HIV care for drug users. A report from Baltimore published in the *Journal of AIDS* in January 2004 echoed the results of the WITS study. Researchers observed that, while rates of AIDS-defining illnesses have decreased in all groups since the introduction of HAART, these declines were substantially lower among HIV-positive injection drug users. Moreover, a review of data from a large group of people with HIV followed in Switzerland found that death rates (including non-AIDS-related deaths) were substantially higher in HIV-positive injection drug users in the HAART era than in non-IDUs, perhaps related to poorer access to HIV treatment.

The sociology camp, therefore, discounts the clinical relevance of hypothetical interactions between drugs and HIV and/or the immune system. Instead, they point to common themes that determine how well HIV-positive people do in the HAART era: access to care, quality of care, and adherence. People that don't score highly on these criteria have poorer health, lower CD4 cell counts, and less likelihood of having undetectable viral loads. Ample research demonstrates that HIV-positive drug users face high barriers on all three counts, and these problems in turn reflect systemic gaps and shortfalls in broader systems of care that include a lack of housing and support for treatment of drug addiction and psychiatric problems.

### Too Little, Too Late?

Roughly half the people with HIV in New York City have been classified as 'delayers' – people who test positive for HIV within a year of an AIDS diagnosis and/or enter HIV care late in the course of HIV disease. Not surprisingly, the primary factors associated with delayed testing and care are the interlocking issues of substance use, mental illness, and homelessness. While even 'delayers' can respond well to HAART, they may have more difficulty tolerating side effects due to advanced HIV disease, while remaining vulnerable to opportunistic infections until returning to higher CD4 cell levels.

Illicit drug users are, by definition, a class of outlaws – the drugs they use are illegal, and drug users face a range of sanctions from moral disapproval to police harassment, from losing jobs, custody of children, and homes, to ostracism and imprisonment. The healthcare profession both challenges and reinforces the marginalization of drug users. On the one hand, the medicalization of addiction effectively counters claims that drug use reflects moral weakness by viewing addiction as a disease that requires treatment. But treatment requires bringing drug users under the supervision of qualified experts capable of diagnosing the "truth" of addiction and prescribing the appropriate remedy. In its most extreme, least humanistic forms, the medical model of addiction too

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## HIV Care and Treatment as Harm Reduction

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often presumes that all illicit drug users live in thrall to their disease, incapable of exercising their wills towards any goal but inherently self-destructive drug-seeking behavior. Thus, even today, the pervasive legacies of stigma and discrimination still keep people away from even the most enlightened, non-judgmental medical providers.

Moreover, simply characterizing HIV-positive drug users as in or out of care fails to capture the fluid dynamics of many drug users' lives, which could be better described as in and out of drug treatment, in and out of jail, in and out of stable housing and employment, and in and out of chaotic patterns of drug use – sometimes within the space of a single year. As these trajectories bring drug users into contact with disparate systems and services, few programs are equipped to maintain on-going contact with people, much less offer continuity in HIV care. Adequate and appropriate substance use counseling and treatment, mental health care, and permanent housing can provide a crucial foundation of stability and enable further support. Yet these cornerstones of care are precisely those services that are in short supply.

The impact of delayed testing and treatment may have particularly detrimental consequences for drug users. A recent study reopened the question of when to begin HIV treatment, which federal guidelines recommend starting when CD4 cell counts fall below 350. A review of clinical data from a large group of primarily African-American injection drug users in Baltimore – the AIDS Linked to the Intravenous Experience (ALIVE) cohort – compared survival rates of HIV-positive and HIV-negative IDUs. In general, HIV-positive drug users had poorer survival rates than the HIV-negative group, as would be expected. However, HIV-positive IDUs who began HAART when their CD4 cell count exceeded 350 had survival rates comparable to HIV-

## Strategies to Improve HIV Care for Injection Drug Users

- Provide “one-stop” services wherever possible – medical care for HIV, psychiatric care, substance use treatment and harm reduction, education, case management, and other support services.
- Familiarize healthcare staff (including non-medical personnel) with drug users' needs and issues and harm reduction models.
- Strengthen linkages between community-based programs, hospitals and clinics, methadone and other substance abuse treatment programs, and jails and prisons to increase continuity of care.
- Improve the capacity of harm reduction and substance abuse treatment programs to provide support and education for HIV-positive drug users.
- Advocate within Ryan White Planning Councils for service models that can support access and maintenance in care for drug users and develop collaborations between programs funded through Ryan White monies and SAMHSA (Substance Abuse and Mental Health Services Administration) grants to states.
- Explore new models of care and support for HIV/HCV co-infection and for prescribing buprenorphine within HIV clinics.

negative drug users. Notably, the gains in survival from beginning HAART at higher CD4 cell levels were most pronounced in a reduction in non-AIDS-related causes of death, including drug overdose as well as viral or bacterial infections such as endocarditis and sepsis associated with injection drug use but not HIV. The study authors suggest that drug users may gain from beginning HIV treatment at a higher CD4 cell level than current guidelines recommend. By implication, earlier HAART may indirectly reduce other health risks associated with drug use, perhaps by strengthening engagement in medical care and other forms of support.

The Baltimore study raises interesting questions when compared to another large cohort of HIV-positive veterans, primarily African-American men, receiving care at the Atlanta Veteran Affairs Medical Center. The Atlanta study, published in the journal *Clinical Infectious Diseases* in November 2004, compared survival rates according to hepatitis C (HCV) infection, a blood-borne virus found in up to 90% of people who became infected with HIV through injection drug use. The full effects of hepatitis C co-infection on HIV disease progression and response to HAART remain

controversial. Yet ample research indicates that HIV infection can accelerate progression of hepatitis C, and hepatitis C-related liver disease has become a leading cause of death in people with HIV. The Atlanta cohort found that people co-infected with HCV had poorer survival rates than those with HIV alone. Survival differences couldn't be explained solely by the increased risk of death from liver disease in the co-infected group. The co-infected group, overwhelmingly comprised of African-Americans with histories of injection drug use, was less likely to receive HAART. However, those who were on HAART responded to treatment as well as those with HIV alone.

Together, these analyses reinforce the argument that HIV-positive drug users aren't receiving adequate HIV care and treatment and strengthen the call for more aggressive efforts to engage IDUs in appropriate HIV care (see box above). Activists and advocates must focus on fundamental issues of equity and structural change in order to increase access to care and quality of care.

*Daniel Raymond is the Hepatitis C Policy Analyst for the Harm Reduction Coalition.*

# Much Ado About Meth

by *Tim Horn*

“Huge Sale! Buy Crystal, Get HIV Free.” This was the text of a provocative ad that appeared on Verizon phone booths in the Chelsea neighborhood of New York City in January 2004. The ads were conceived and paid for by Peter Staley, a longtime AIDS activist and recovering crystal meth addict. Staley contends that the ads were meant to provoke discussion and, ultimately, action by others. This mission was accomplished, judging by the recent upswing in media attention focusing on the use of crystal meth (and its connections to HIV), the appearance of public service announcements by Gay Men’s Health Crisis and other groups, and a slew of well-attended community forums focusing on the widely unacknowledged crystal meth problem in New York City.

What is all the fuss about? This article reviews much of what we do – and don’t – know about crystal meth, including its relationship to HIV infection. There are few black-and-white conclusions, given that research into crystal meth and the negative effects it can have on individuals and public health is limited. It is hoped, however, that the increased attention now being placed on the potential dangers of crystal meth will yield the necessary information needed to curb the use and abuse of this drug.

## **Party Now, Pay Later**

The ease with which crystal meth can be manufactured is a major contributing factor to the increase in its use. Law enforcement officials identify and close hundreds of clandestine methamphetamine labs each year. Large operations produce methamphetamine in Mexico and California. Outside of these areas, small rural laboratories are more common. Rural areas are popular sites for production because strong odors are produced in the process of “cooking” the drug, which can draw immediate attention to the manufacturing operation.

The manufacturing of crystal meth begins with large quantities of ephedrine or pseudoephedrine, a chemical found in numerous over-the-counter cold medica-

tions. It is then cooked with a variety of other readily available substances, including red phosphorous, hydrochloric acid, drain cleaner, battery acid, lye, paint thinner, Freon, and/or antifreeze (every pound of crystal meth produced leaves behind five to six pounds of toxic waste). And because it is so easily and rapidly produced, it remains one of the cheapest drugs available.

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With the manufacturing process completed, crystal meth is bagged and sold as shiny yellowish-white rocks of various sizes or as a crystalline powder resembling small fragments of glass. It can be ingested by snorting or smoking, or dissolved in water to be swallowed, inserted into the rectum (“booty bump”), or injected into muscle or a vein. On the street, it goes by a variety of names, including crystal, glass, crank, Tina, Crissy, and ice (in its rock form).

Upon being ingested, the drug rapidly and aggressively stimulates cells in the brain to produce high levels of dopamine, the “pleasure” neurotransmitter, and norepinephrine, the “alertness” neurotransmitter. The flood of these chemicals amplifies sensory perceptions and induces a

long-lasting rush of euphoria, energy, elation, and confidence. However, what goes up must come down.

Six to eight hours after the drug is taken, the flood of dopamine and norepinephrine in the brain dries up, leading to the inevitable “crash and burn.” Energy levels drop and the feelings of joy, happiness, and pleasure are replaced with feelings of paranoia, anxiety, fatigue, aggression, and self-doubt. And the greater or longer the high, the greater the depletion of dopamine and norepinephrine levels afterwards.

With persistent use, natural dopamine production decreases, either because of permanent damage to dopamine-releasing terminals in the brain or because of physical dependence on the drug. In other words, life’s basic pleasures – watching an enjoyable movie, indulging in a gourmet meal, spending time with friends or a loved one, etc. – will no longer trigger the natural dopamine production that our bodies depend on to interpret these experiences as rewarding.

Side effects of crystal meth don’t end with the central nervous system. Other short-term effects, brought on through the release of norepinephrine, include: irregular, rapid heartbeat; elevated blood pressure; trouble sleeping; increased body temperature; and dehydration. What’s more, there have been numerous anecdotal reports of methamphetamine use sending individuals to the hospital with heart attack symptoms and rhabdomyolysis (the rapid breakdown of muscle fibers resulting in the release of muscle fiber contents into the bloodstream, which can be highly toxic to the liver and kidneys).

Long-term use of crystal meth is associated with an increased risk of heart attacks, stroke, cardiomyopathy (swelling of the heart), and pulmonary hypertension (a buildup of pressure in the pulmonary artery). Periodontal disease and dental problems are also frequent among crystal meth users.

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## Much Ado About Meth *(continued from previous page)*

### **Crystal Meth and the Risk of HIV and STD Infections**

While crystal meth users cite a number of different reasons for using the drug – use among suburban teens, as well as students, professionals, and homemakers who work long hours isn't uncommon – its use in the context of sexual activity has been of particular concern, especially among men who have sex with men (MSM). For many users, the biochemical effects of crystal meth dramatically reduce inhibitions while increasing sexual desire and feelings of invincibility, making it a powerful drug in terms of initiating, enhancing, and prolonging sexual activity. However, crystal meth intoxicification is also associated with serious lapses of judgment.

Various research teams have documented that, when crystal meth is used in association with sexual activity, condoms are more likely to be abandoned, numerous sex partners are more likely to be had, and trauma to the lining of the anus is more likely to be experienced (which greatly increases the risk of HIV transmission). This has many community activists, public health officials, and healthcare providers very worried about the possibility of increased HIV and sexually transmitted infection among individuals using crystal meth as a component of sex.

Recent data collected by the Center for HIV/AIDS Education Studies and Training (CHEST) at New York University indicate that, in New York City, MSM who use crystal meth are three times more likely to contract HIV through receptive anal intercourse than MSM who do not use the drug. Moreover, the CHEST study found that, among gay or bisexual male “party drug” users, approximately 62% indicated significant and frequent use of crystal meth. This is an increase from the early 1990s when usage rates among gay and bisexual men ranged between 5% and 25%. CHEST also found that MSM who reported crystal meth use were diverse in terms of ethnicity, age, income, and HIV status; 45% of the samples were men of color, and

half the men reported being HIV-positive. Researchers with the San Francisco Department of Public Health (SFDPH) have also found that MSM who used crystal and Viagra together were six times more likely to be diagnosed with syphilis than those who didn't use either drug. In another study from SFDPH, researchers found that 17.4% of 1,263 MSM who attended the city's public STD clinic had used crystal in the month before their visit. Those who used the drug were more than twice as likely as non-users to be HIV-positive, four times as likely to be diagnosed with syphilis, and almost twice as likely to test positive for gonorrhea.

Some experts argue that these numbers may only be the tip of the iceberg. Presently, most city and state departments of health do not routinely track crystal meth use among people newly infected with HIV, leading to an incomplete picture of the extent of the role of crystal meth use on HIV infection statistics. Organizations like the New York AIDS Coalition argue that, in order for community-based organizations and departments of public health to be able to provide effective prevention interventions to crystal meth-using populations, prevention experts must first gain a better understanding of who is using crystal meth and its prevalence among MSM and people infected with HIV.

### **Crystal Meth and HIV Disease Progression**

A frequent concern is that crystal meth speeds up disease progression in people who are already infected with HIV. Does crystal meth have a negative effect on immune function? Does crystal meth increase viral load? The short answer to these questions is that we don't really know.

There haven't been any studies documenting the effects of crystal meth on immune function in HIV-positive people, most notably its effects on CD4 cell counts. Most studies completed to date have been test tube or rodent experiments. One test tube study published in 1994 suggested that methamphetamine can

reduce interleukin-2 levels, a cytokine that promotes immune function in the body and plays a significant role in the immune system's response to HIV infection. It was also shown to decrease the function of CD8 cells, which play a role in the control of HIV replication, particularly during the early stages of infection. Another study involving retrovirus-infected rats, published in 2002, demonstrated a significant increase in tumor necrosis factor (TNF), an inflammatory cytokine that can negatively affect the immune system's response to HIV and increase viral replication. While these studies pave the way for further investigation, they do not conclusively answer whether crystal meth speeds up immune suppression in HIV-infected people.

As for the effect of crystal meth on viral load, one study published in 2003 in the *Journal of Infectious Diseases (JID)* compared HIV levels in HIV-positive individuals who were currently using meth to HIV-positive people no longer actively using the drug and HIV-positive people with no history of crystal meth use. Among those who weren't on any antiretroviral therapy, viral loads were similar among the three groups. In other words, HIV levels in the active crystal meth users were not significantly higher than the non-using individuals in the study. However, among those who *were* taking antiretroviral therapy during the study, the active crystal meth users had significantly higher viral loads than the non-using individuals. In simpler terms, active crystal meth users were significantly less likely to have undetectable viral loads in response to antiretroviral therapy than HIV-positive folks not using crystal meth.

This is a potential source of concern, given that a detectable viral load in someone on antiretroviral treatment is often a sign of drug resistance and treatment failure. Given the limitations of this study, it wasn't possible to determine why the active crystal meth users taking antiretroviral therapy had higher viral loads than the non-using study participants. However, two possible explanations were

offered by the study authors: poor adherence and/or a negative interaction between the crystal meth and the antiretrovirals being taken.

### **Crystal Meth and Treatment Adherence**

Studies have been extremely limited with respect to documenting adherence in HIV-infected individuals using crystal meth. However, there is no shortage of data from other studies evaluating the pill-taking habits of HIV-positive folks actively using other drugs and alcohol to know that adherence may be a problem among HIV-positive individuals actively using crystal meth. Common sense also dictates that a drug like crystal meth, a spontaneous and impulsive activity, doesn't mix well with antiretroviral medication adherence, which requires forethought and planning. The fact that crystal meth keeps individuals awake for long hours, away from food, provides a feeling of "liberation" from all responsibilities (to themselves and to others), and engaged in behavior that won't be conducive to stopping for regular medication dosing, may not exactly support the strict adherence needed to maintain the effectiveness of antiretroviral treatment.

One interesting adherence study, published in *AIDS Care* in 2003, surveyed 23 HIV-positive individuals in recovery for crystal meth addiction about their antiretroviral adherence practices while they were actively using. All 23 reported missing doses of their antiretroviral therapy. Approximately half of the survey volunteers reported taking "planned" breaks in therapy, defined as a conscious decision to stop medications while using crystal, either because it would interfere with their ability to enjoy whatever it was that they were doing while high or because they feared a negative drug interaction (with their antiretrovirals or other illicit drugs they were using). The other survey volunteers reported "unplanned" breaks in their therapy because their crystal meth use interfered with their ability to maintain a schedule, keep track of time, eat and drink regularly, and sleep.

Even though these 23 study participants did not take their medications according

to prescribed directions, they did not interpret skipping, stretching, or modifying their medication doses as non-adherence. For some, these medication adjustments were viewed as a positive coping strategy to create a sense of control over their lives and activities while using crystal meth. Other study participants believed that if they caught up with missed doses by increasing their dosage for two or three days following a treatment interruption, they would still qualify as adherent.

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### **Crystal Meth and Drug Interactions**

It is possible that crystal meth does not mix well with some antiretroviral medications. All of the amphetamines – including crystal meth and ecstasy (MDMA) – are metabolized (broken down) by one of the liver enzymes responsible for metabolizing Norvir (ritonavir) and all three approved non-nucleoside reverse transcriptase inhibitors (Sustiva, Viramune, and Rescriptor). There have been a few case reports – but no comprehensive studies – involving individuals who died as a result of high blood concentrations of methamphetamine after taking ecstasy or crystal meth with one of these antiretrovirals. What we don't yet know is to what extent antiretrovirals affect methamphetamine drug levels, nor do we know to what

extent methamphetamine affects antiretroviral drug levels in the body. If a decrease in antiretroviral drug levels occurs, this could translate into premature treatment failure, drug resistance, and disease progression.

### **Crystal Meth and HIV-Associated Dementia**

One of the most significant concerns surrounding crystal meth use in HIV-positive people is the possibility of an increased risk of HIV-associated dementia (HAD). HAD normally occurs in approximately 20% to 35% of people with advanced HIV disease and is one of the few AIDS-related complications that can be caused by HIV itself (HIV can damage nerve cells in the brain, although researchers don't totally understand how this happens). Symptoms of HAD include slower reaction times, poorer decision-making abilities, and poorer performance on measures of memory, attention, and concentration – many of the same problems seen in chronic crystal meth users.

Studies have demonstrated that HIV – most notably its gp120 and Tat proteins – can damage dopamine receptors in the brain. As discussed above, crystal meth can also have a profound effect on dopamine in the brain, which, some experts argue, could exacerbate or increase the risk of HAD as HIV disease progresses.

In a 2003 issue of the *Journal of Acquired Immune Deficiency Syndromes*, researchers found that methamphetamine users with advanced HIV infection had evidence of a specific type of brain damage not usually seen in HIV-infected patients with HAD: the loss of a specific group of neurons (nerve cells) and an increase in the number of glial cells (cells that repair damaged neurons).

It's also possible that crystal meth fuels HIV replication in the brain, leading to an increased likelihood of HAD and other neurological problems. There have been studies demonstrating that crystal meth can damage the walls of blood vessels in the head, allowing HIV to enter the brain much more easily. In a 2002 issue of the *Journal of Neurovirology*, researchers

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## Much Ado About Meth *(continued from previous page)*

found that crystal meth increased replication of the feline version of HIV (FIV) five to fifteen times in test tubes containing astrocytes (a type of glial cell). However, in the 2003 *JID* article discussed above, HIV levels were not significantly higher in the cerebrospinal fluids (CSF) of HIV-infected individuals actively using crystal meth, compared to HIV levels in the CSF of their non-using HIV-infected counterparts.

Additional data from studies exploring the impact of crystal meth on the central nervous systems of HIV-positive people are just now beginning to surface.

### **Treatment of Crystal Meth Addiction**

At the present time, there is no pharmacological treatment for crystal addiction, like methadone or buprenorphine for opiate (heroin) addiction. Anecdotal reports suggest that available psychotropic and anti-anxiety medications – including Bupropion, Celexa, Ambien, Depakote, Zyprexa, and Risperdal – may be useful in terms of managing some of the psychiatric complications that frequently arise upon stopping crystal meth. However, the effectiveness of these medications for this purpose has not been evaluated in clinical

trials. One pharmacological treatment currently being studied is Abilify (aripiprazole), approved for the treatment of schizophrenia. Abilify may reduce crystal meth cravings among individuals who are dependent on it.

The majority of crystal meth users end up seeking help through cognitive behavioral therapy (CBT) programs, motivational enhancement therapy (MET) programs, or 12-step programs like crystal meth anonymous (CMA). CBT programs usually involve a therapist or counselor, in one-on-one or group sessions, to help explore the causes, symptoms, and results of crystal meth use. CBT focuses on personal examinations of the events leading up to dependency on crystal meth. MET programs also involve a therapist or counselor and focus on a client's perceptions of his or her current drug-using behavior and the personal goals that he or she has for himself. Emphasis is placed on eliciting self-motivational statements of desire for and commitment to change.

CMA has become an increasingly popular approach to recovery by many crystal meth users ([www.crystalmeth.org](http://www.crystalmeth.org)). Some choose to go the CMA route without

other forms of intervention, while others use CMA to supplement other forms of addiction therapy. In short, CMA embraces a peer-support approach to recovery – similar to the Alcoholics Anonymous (AA) model – encouraging members to confront their addiction, surrender to a higher power, and empower themselves as a way of overcoming their addiction. Numerous CMA groups have sprouted up all over the United States, including groups focusing exclusively on gay and bisexual men and HIV-positive individuals.

Of course, recovery varies from person to person. The effects of withdrawal can linger for several weeks or months for casual users and years for chronic, heavy users. Sadly, the relapse rate is very high – one of the highest relapse rates of any illicit drug addiction. But help is available and, as the saying goes, it's about taking things one day at a time.

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## ACRIA Begins New HIV Over 50 Study

HIV Over 50 research at ACRIA has a new name. The **Research on Older Adults with HIV: ROAH Program** is beginning and we need your help. The purpose of this study is to better understand the unique personal resources and challenges that older adults with HIV face in their daily lives.

You may qualify for this study if you are age 50 or older, live in or receive healthcare in New York City, and can complete a questionnaire about your experiences. Participants in the ROAH Program will fill out a questionnaire that will take approximately 90 minutes to complete. Participation is confidential – your name and identifying information will be protected. You will receive \$25 for your time and travel expenses. You may be chosen to participate in more detailed interviews about stigma and/or cognitive function.

If you have questions about this study, contact Andrew Shippy at 212-924-3934 ext. 104 or if you would like to enroll, contact Philana at 212-924-3934 ext. 125.

# Drug Interactions: HIV Medications, Street Drugs and Methadone

by James Learned and Maia Szalavitz

A drug interaction is what happens when one drug that you take affects the way another drug you take works in your body. An interaction can affect your body's ability to break down one drug or both drugs. It can also affect the strength or effectiveness of one drug or both drugs. Drug interactions become more complicated – and more likely to happen – the more drugs you take. In many cases, interactions aren't a problem. There are lots of drugs that don't affect each other at all. But some medications should never be used together because they combine to create a toxic reaction. Such interactions are dangerous, even life threatening.

***“Drug interactions become more complicated – and more likely to happen – the more drugs you take.”***

The liver breaks down and absorbs (metabolizes) antiretrovirals for HIV, methadone, alcohol, street drugs like cocaine and heroin, prescription and over-the-counter medications, herbs, vitamins – the works. The liver has primary responsibility for drug metabolism, but the kidneys also play a role, mostly by eliminating drugs. Specific pathways of enzymes in the liver metabolize different drugs, but many drugs are metabolized by the same pathways. This is where interactions can occur.

The liver can only do so much work at one time. If you take two or more drugs at once, they can compete for the same enzymes in the liver in order to be broken down. This competition can affect the way the drugs are metabolized. One drug might be metabolized faster than usual, reducing levels of the drug in your blood and making it less effective. This could be a problem with a number of drugs. If your methadone levels are too low, for example, you could experience serious withdrawal symptoms. And if your anti-HIV drug is at low levels, it won't work as well and could allow your virus to become resistant to that drug and, perhaps, others as well.

Another kind of interaction can cause one of the drugs you're taking to be metabolized more slowly than usual. You could end up with a dangerously high dose of the drug in your system because it isn't being broken down and absorbed properly. In essence, this could cause an overdose and, depending on the drug, could be fatal.

It might be useful to think of the liver as a funnel – or many funnels, some of them having funnels within them. If drug A and drug B compete with one another for the same funnel, for example, a number of possibilities could occur:

- The levels of both Drug A and Drug B could *increase* in your system;
- The levels of both Drug A and Drug B could *decrease* in your system;
- Drug A levels could *increase* in your system and Drug B levels could *decrease*;
- Drug A levels could *decrease* in your system and Drug B levels could *increase*;
- Drug A levels could *increase* in your system and Drug B could remain at normal levels;
- Drug A levels could *decrease* in your system and Drug B could remain at normal levels;
- Drug A could remain at normal levels in your system and Drug B levels could *decrease*;
- Drug A could remain at normal levels in your system and Drug B levels could *increase*; or
- Both Drug A and Drug B could remain at normal levels in your system.

The more drugs you add to the mix, the more difficulty the funnels may have metabolizing them properly. There are many possible interactions – some of them may not cause a problem, but others certainly could.

The following pages describe known and potential drug interactions that involve medications to treat HIV or prevent and treat opportunistic infections. Some of this information is based on studies that have been conducted in test tubes, animals, or people; some of it is based on case reports – incidents that have actually happened to people; and some of the information is theoretical, based on what we know about how different drugs are metabolized – which pathways they use and how they use them.

(continued on next page)

## HIV Medications and Street/Recreational Drugs

There hasn't been much research on how illegal street drugs and HIV medications interact. Certainly, your best bet is not to use street drugs at all if you're taking HIV medications. But some interactions are known to be more dangerous than others.

It's difficult to study interactions between illegal drugs and anti-retrovirals. Some people have a higher tolerance to some drugs than other people do. Also, there are too many different kinds of cuts put on drugs, especially heroin and cocaine, which are hardly ever pure. So laboratory tests using pure heroin or cocaine, for example, wouldn't necessarily tell us what might happen in your body with drugs bought on the street.

We have more information about interactions with prescription drugs that are used recreationally. But even then, some drugs that are available by prescription, when bought on the street, may be cut with other substances that could cause unexpected interactions with other drugs.

### Alcohol

- **Videx** (ddI) can increase the risk of pancreatitis, and so can chronic alcohol use. So if you're using alcohol regularly, inform your healthcare provider and consider alternatives to Videx. There are other nucleosides to choose from.
- Alcohol increases **Ziagen** (abacavir) levels in your blood. A small study showed that consuming the equivalent of five alcoholic drinks with Ziagen resulted in up to a 41% increase in Ziagen levels. The increase isn't a good thing. Regular Ziagen dosing (300 mg every 12 hours) gives you enough of the drug to do the job. Increasing the amount won't fight HIV any better – but it could increase your risk of side effects. Ziagen is also in the combination pills **Trizivir** and **Epzicom**.
- Alcohol should not be used with **Agenerase** (amprenavir) *oral* solution (the liquid version) because it has propylene glycol in it, which can cause side effects when it's mixed with alcohol.
- The protease inhibitor **Reyataz** (atazanavir) can increase levels of bilirubin in some people, which can cause jaundice (yellowing of the skin and whites of the eyes). If you start taking Reyataz, be sure to have liver function tests performed regularly, including checking bilirubin levels. People with liver disease, such as chronic hepatitis B or hepatitis C, or liver damage caused by alcohol use may be more likely to experience high bilirubin levels, but no differences have been reported so far in people with mild to moderate liver damage.
- Occasional and light use of alcohol is not known to interact with other HIV medications, but regular, heavy alcohol use

can damage your liver, which might make it more difficult for your liver to properly break down some anti-HIV drugs, particularly protease inhibitors and non-nucleosides. The result could be levels of these antiretrovirals that are too low to slow down HIV replication the way they're supposed to. That could result in a higher viral load, lower CD4 count, and the development of drug-resistant HIV. Liver damage can also work the opposite way, allowing some drugs to build up in your system, which could cause worse side effects or an overdose.

- Since alcohol can cause dehydration, be sure to drink a lot of water to help your body deal better with any alcohol you drink.

### Amphetamines (speed, methamphetamine, crystal meth [Tina, ice])

- **Norvir** (ritonavir) – at full dose or the much lower doses used to “boost” other protease inhibitors – could increase amphetamine levels in the blood significantly. Kaletra, which contains a small amount of ritonavir, could have the same effect. This increase isn't a good thing. It could have serious consequences, including a faster heart rate and higher blood pressure, possibly even death. The other protease inhibitors and the rarely used non-nucleoside Rescriptor (delavirdine) could have less of an impact, but might still have some. There's no sure way to predict what might happen with these combinations.
- Taking amphetamines and certain antidepressants called SSRIs (Prozac, Paxil, Luvox, or Zoloft) together could, at least hypothetically, lead to a condition called “serotonin syndrome,” which can be life-threatening. When serotonin levels increase too much, confusion, agitation, coma, anxiety, and seizures can occur.

### Cocaine (coke, blow, crack)

- There have been no reported interactions between cocaine and HIV medications.
- You may have heard reports that cocaine significantly speeds up HIV reproduction in lab cultures. There have also been studies showing that mice infected with HIV and then injected with cocaine had significantly more virus and fewer CD4 cells than mice infected with HIV but no cocaine. This could certainly mean that cocaine use speeds up HIV disease progression in people, although what actually happens in the human body isn't clear.

### Ecstasy (MDMA, X)

- There was one death in England, which resulted from a single dose of Ecstasy taken with Norvir. Norvir slows down

the liver enzyme that breaks down Ecstasy, so Ecstasy accumulates in your system, making it 5 to 10 times stronger. In addition, up to 10% of Caucasians (the figure for other populations isn't known) have a deficiency in this enzyme, which may be why some people could overdose on what would be a non-toxic dose for others. If you're taking any protease inhibitor or non-nucleoside, Ecstasy can be extremely dangerous. Of these, Norvir seems to be the most dangerous, while Viracept (nelfinavir), Viramune (nevirapine), and Sustiva (efavirenz) may be less so. But drug interactions in the test tube are sometimes opposite to those seen in the body, so, again, this is hard to predict.

- If you *do* take Ecstasy with a protease inhibitor, wait as long as possible after taking the medication before taking the Ecstasy. And be sure to have someone with you who knows what you've done in case you have difficulties. It's really better not to mix these drugs! If you do, think about taking less Ecstasy than you might normally take – maybe 25% of your usual amount. Be sure to take regular breaks from dancing and other physical activity, drink plenty of fluids, and avoid alcohol – alcohol causes dehydration.
- If you *aren't* dancing or exercising, however, don't drink large quantities of water after taking ecstasy. It's actually possible to fatally overdose on water this way, because Ecstasy can also slow the body's ability to expel water as urine. Basically, drink to quench your thirst.

**GHB (gamma-hydroxy-butyrate, grievous bodily harm, liquid X, G)**

GHB is potentially dangerous with protease inhibitors, especially Norvir (full dose or lower doses), as well as the non-nucleosides Rescriptor and, possibly, Sustiva. And never mix GHB with alcohol.

**Heroin (dope, smack, brown, junk, China White)**

- Some people who use heroin and are prescribed antiretrovirals for their HIV may be afraid to take their HIV medications regularly for fear that they'll interact with the heroin. There are no documented interactions between antiretrovirals and heroin, although there are some theoretical ones. If you're using heroin, it's probably fine – and better for your health – to take your anti-HIV medications as well.
- Most protease inhibitors – Norvir, Kaletra, Agenerase, Lexiva, and Viracept in particular – as well as the non-nucleosides Rescriptor and Sustiva may reduce heroin levels, although

this is only based on theoretical research about the way your body breaks down heroin and these particular drugs. If this *is* true, it could lead to withdrawal symptoms. You might need more frequent doses of heroin to avoid withdrawal – one big dose won't last longer and could be an overdose. Be careful.

- Some synthetics sold as heroin (fentanyl, alpha-methyl-fentanyl) are potent in tiny doses and could be deadly if combined with another drug.

**Ketamine (Special K)**

- When combined with some anti-HIV medications, Special K can lead to “chemical hepatitis,” inflammation of the liver that could require hospitalization. The inflammation usually goes away in several weeks, but anything that damages the liver can be a serious problem for people with HIV. Norvir, Kaletra, Viracept, Agenerase, Lexiva, Rescriptor, and Sustiva are the antiretrovirals with the greatest potential to cause ketamine toxicity.

**LSD (acid, blotter)**

No known interactions. But it's possible that some anti-HIV medications, especially Norvir, could lead to a longer or more intense trip than planned or desired.

**Marijuana**

- According to one study, smoked marijuana slightly lowers levels of the protease inhibitors Crixivan and Viracept, although the decreased levels weren't enough to affect the antiretrovirals' activity. Protease

inhibitors may also increase THC levels, the active ingredient in marijuana – so smaller doses may make you more stoned. The same is true of the synthetic version, **Marinol** (dronabinol), which contains THC and is used to treat nausea and increase appetite. This interaction doesn't seem to be dangerous – although you should consider it if you're planning on being coherent!

- **Sustiva** makes many people feel at least somewhat disoriented. Using marijuana might heighten these feelings – and not necessarily in a good way.

**PCP (angel dust, rocket fuel)**

Levels of PCP may increase due to interactions with protease inhibitors or the non-nucleosides, Rescriptor and, possibly, Sustiva. These interactions could cause PCP toxicity. If you're on anti-HIV medications and using PCP, think about using less PCP than you might otherwise to avoid a possible interaction.

*(continued on next page)*

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**“Drug interactions in the test tube are sometimes opposite to those seen in the body...”**

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## HIV Medications and Street/Recreational Drugs *(continued from previous page)*

### **Poppers (amyl nitrate or butyl nitrate)**

Be sure not to use poppers if you take **Viagra**, **Levitra**, or **Cialis**. Poppers increase levels of these drugs, lowering your blood pressure enough to cause serious, even lethal, reactions (see next page for more detail).

### **Ritalin (methylphenidate)**

There are no known interactions between Ritalin and any medications specific to HIV.

### **Sedatives & Tranquilizers:**

Interactions between barbiturates, benzodiazepines and anti-retrovirals, especially the protease inhibitors and non-nucleosides, are tricky. There are many possible variables that could affect the interactions listed below, including other drugs that you might be taking.

#### ***Barbiturates (barbs, downers)***

Barbiturates are rarely used on the street since they don't provide much of an attractive high or down. But if you *are* taking barbiturates, there are some things that could be helpful to know:

- Combining a barbiturate – **Amytal** (amobarbital), **Nembutal** (pentobarbital), or **Seconal** (secobarbital), for example – with many of the protease inhibitors or non-nucleosides can lower levels of the anti-HIV medication. This interaction can reduce or eliminate the benefit of the anti-HIV drug and possibly cause HIV to develop resistance to the drug.
- High doses of barbiturates can cause unconsciousness, even death.
- The combination of barbiturates with **alcohol** or any other central nervous system depressant, including heroin, is *extremely* dangerous. Alcohol intensifies the sedative effect of the barbiturate, which can cause abnormally slow and shallow breathing, coma, and death. Even the normal dose of a barbiturate can be lethal if it's combined with alcohol.

#### ***Benzodiazepines (bennies, benzos, downers)***

- Taking the sedatives **Halcion** (triazolam) or **Versed** (midazolam) with *any* of the available protease inhibitors or the non-nucleosides Rescriptor or Sustiva could lead to a very dangerous, even deadly interaction, raising Halcion or Versed

levels so much that serious sedation could result, possibly stopping your breathing.

- Taking **Ambien** (zolpidem) with full-dose Norvir could cause a similar reaction, but low-dose Norvir, which is usually prescribed now, doesn't seem to significantly increase Ambien levels.
- **Valium** (diazepam) and **Tranxene** (clorazepate) levels can also increase when used with some of these same anti-HIV medications – particularly Invirase, Fortovase, Norvir, Agenerase, and Lexiva – but the interaction doesn't seem to be as severe or as potentially dangerous as that of Halcion or Versed.

- Norvir may *increase* **Klonopin** (clonazepam) levels, while Viamune and Sustiva may *decrease* Klonopin levels, possibly leading to symptoms of benzodiazepine withdrawal.

- Norvir slightly *decreases* **Xanax** (alprazolam) levels, while Invirase, Fortovase, Agenerase, Lexiva and Rescriptor *increase* Xanax levels. Except for Rescriptor, which greatly increases Xanax levels, the degree that these other antiretrovirals raise Xanax levels isn't clear.

- Invirase, Fortovase, Agenerase, Lexiva and Rescriptor may increase **Dalmane** (flurazepam) levels as well, but not as significantly as with Halcion or Versed.

- Physical dependence on benzos can develop. Withdrawal should be medically supervised because of the risk of seizures.

- Combining benzodiazepines with **alcohol** can be life threatening. Alcohol intensifies the sedative effect of the benzodiazepam, which can lead to coma or death. Benzos can also interact with opiates such as heroin, methadone or **OxyContin** (oxycodone) to cause increased, possibly lethal sedation.

**Bottom line:** *Mixing downs can be very dangerous. Mixing depressant drugs – alcohol and opioids; alcohol and barbiturates; alcohol and benzodiazepines; or a combination of depressant drugs – is the cause of most overdose deaths.*

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**“Mixing  
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**Viagra (sildenafil), Levitra (vardenafil), and Cialis (tadalafil)**

- These three drugs, marketed to help with impotence (erectile dysfunction), are often used recreationally by men to help get and keep an erection. None of them increase sexual desire. Although these are prescription drugs, people often get them through friends, on the street, or through the Internet. This means that what looks like Viagra, for example, may be Viagra – then again, it may not be. The three available medications have similar interactions with other drugs.
- There has been at least one documented death caused by the interaction of a protease inhibitor and Viagra (sometimes called blue diamonds or Vitamin V). The man had a heart attack. Protease inhibitors increase the blood concentrations of Viagra, which raises the likelihood and severity of side effects – extremely low blood pressure, dizziness, fainting, changes in your vision, and prolonged erection (meaning hours – *not* a good thing). **Norvir** (ritonavir) increases Viagra concentrations the most, while **Fortovase** (soft-gel saquinavir) and **Invirase** (hard-gel saquinavir) seem to have the least effect on Viagra blood levels. Other medications that increase Viagra blood levels include the non-nucleoside **Rescriptor**, the antifungals **Nizoral** (ketoconazole) and **Sporanox** (itraconazole), and the antibiotic **erythromycin**.
- Levitra and Cialis have similar interactions with these same drugs. Although not every drug has been studied with each of these medications to figure out every conceivable interaction, the way that they're broken down by the liver gives us a good idea of the possible interactions.
- The usual dose of Viagra is 50 mg once a day (at most). The usual dose of both Levitra and Cialis is 10 mg, also once a day at most. Based on what's known and what can be assumed, take a lower dose of Viagra, Levitra, or Cialis – and take it less often – to avoid a possibly dangerous drug interaction if you're also taking one of the drugs listed above. Some examples:
  - If you're on a protease inhibitor, don't take more than one 25 mg dose of Viagra within a two-day period.
  - If you're on a protease inhibitor-containing regimen that doesn't include Norvir, the highest dose of Levitra should be 2.5 mg within a 24-hour period.
  - If you're taking Kaletra or Norvir (even at a low dose) as part of your regimen, the highest dose of Levitra should be 2.5 mg and it shouldn't be taken again for three days.
  - If you're taking erythromycin, don't take more than one 5 mg dose of Levitra in a 24-hour period.
  - If you're taking 200 mg of Nizoral a day, your dose of

Levitra shouldn't be more than 5 mg in one day; and if you're taking 400 mg of Nizoral a day, your dose of Levitra shouldn't be more than 2.5 mg in one day.

- If you're taking Norvir (including low-dose Norvir), Nizoral, or Sporanox, your dose of Cialis should be 10 mg no more than once in three days.
- **Grapefruit juice** could increase levels of Cialis in your blood, so avoid it if you take that drug.
- Levitra can decrease levels of the protease inhibitor Crixivan, so if you're taking Crixivan three times a day (which is rare), it would be safer to use Viagra or Cialis at lower doses than usually recommended.
- **Warnings:**
  - Using **poppers** (amyl nitrate or butyl nitrate) with Viagra, Levitra, or Cialis can cause a severe decrease in blood pressure – low enough to cause you to fall down or faint, perhaps hurting yourself. Even more serious reactions due to the drop in blood pressure include stroke, heart attack, and death.
  - If you take one of these drugs and have an erection that lasts for more than four hours, go to the emergency room. If you don't get treated, this can result in the permanent loss of erectile function.
  - Combining Cialis with significant amounts of **alcohol** can increase the side effects of Cialis, perhaps to a dangerous degree. Combining alcohol with Viagra or Levitra doesn't seem to have the same effect.
  - If you have liver damage due to viral hepatitis, alcohol use, or for any other reason, be careful if you use any of these drugs. If you have mild to moderate liver damage, use a low dose (25 mg of Viagra, 5-10 mg of Levitra, or no more than 10 mg of Cialis). Higher doses could cause serious side effects. We don't know what happens if someone with severe liver damage takes one of these drugs. If you're on a protease inhibitor *and* have liver damage, your safest bet is not to use them at all – in that situation, there would be a lot going on at once and unpredictable things could happen.
  - If you have kidney damage and plan to use one of these drugs, either take Levitra (which kidney damage doesn't seem to affect) or a low dose of Viagra (25 mg) or Cialis (5 mg).
- Levitra and Cialis are relatively new compared to Viagra, which has been on the market since 1998. As more people use these drugs and further studies are conducted, we'll learn more about their safety and other possible interactions.

*(continued on next page)*

## HIV Medications and Methadone

The same liver enzymes that metabolize methadone break down many medications for HIV and drugs that prevent and treat opportunistic infections. So these drugs can cause changes in the way you respond to your methadone dose. Some can increase the effects of methadone; others can decrease it. Methadone can have an effect on the strength of some anti-HIV drugs, too.

It's best to tell both your HIV healthcare provider and the provider at your methadone clinic about all the medications you're taking. But if you don't share the information, at least know the drugs that you're on. Most of the important methadone-medication interactions *decrease* the effect of the methadone. If your dose isn't comfortable for you, it isn't "addictive behavior" to want one that is.

People considering detoxing from methadone should be aware that this might not be a good idea for some people with HIV, particularly if your CD4 count is low. Methadone-maintained people have fewer hospitalizations and are more likely to receive anti-HIV medications than many heroin users who aren't on methadone. When lowering your methadone dose it may be safest to go slowly and wait until you've adjusted to each decrease before moving on to the next one.

The following are some of the known drug interactions with methadone. There may be others. This area, like most involving drug users, hasn't been thoroughly studied – although, because methadone is legal, the information about possible drug interactions is more complete and there's more of it compared to that for illegal drugs. If you start a new medication and find that your methadone dose isn't "holding" you or that it makes you feel drowsy or over-medicated, talk to the provider at your clinic. If they refuse to adjust your methadone to meet your needs, ask your HIV care provider to discuss it with them. You shouldn't have to suffer because of ignorance about drug interactions from some clinic staff.

### DRUGS THAT MAYMAKE METHADONE STRONGER (MORE POTENT)

- Many medications can increase methadone levels to varying degrees. In most cases, the increase is minimal and might not have any noticeable effect. But if the increase is substantial enough, you could become over-medicated, although this is rare.
- **Diflucan** (fluconazole), used to treat fungal infections, can raise methadone levels in the blood by up to 35%. In one study of this effect, no symptoms of overdose were reported in the thirteen people who took Diflucan with methadone. **Nizoral** (ketoconazole), another anti-fungal, can have a similar effect.
- The antidepressants **amitriptyline** (**Elavil** and generic versions) and **fluvoxamine** (various brand names including

**Luvox**) can also increase the amount of methadone in your system. Fluvoxamine can raise methadone levels by anywhere from 20% to 100%. An increase above 30-50% could make you dangerously over-medicated. Then, if you stop taking fluvoxamine and your methadone levels suddenly go down again, you could suffer symptoms of withdrawal.

- Using anti-anxiety medications such as **Valium** (diazepam), **Xanax** (alprazolam), or **Halcion** (triazolam) with methadone can have a "synergistic" effect – you can become more sedated than each individual drug would cause (1+1= 3).
- **Tagamet** (cimetidine), used to treat ulcers and acid reflux (heartburn), can slightly increase methadone levels, as can urinary alkalinizers (**Bicitra**, **Polycitra**) used to treat gout and kidney stones.
- **Rescriptor** (delavirdine), the rarely used non-nucleoside, increases methadone levels slightly but, for most people, the increase isn't enough to require a decrease in their methadone dose.
- **Grapefruit juice** could slightly increase methadone levels in the blood, but the effect doesn't seem to be significant.
- **Cipro** (ciprofloxacin), an oral antibiotic sometimes used to treat MAC (Mycobacterium Avium Complex), bacterial pneumonia, and many common bacterial infections, can cause significant increases in methadone levels. This increase could possibly lead to serious sedation and even overdose for some people.

### DRUGS WITH MIXED OR CONTRADICTIONARY EFFECTS

- **Agenerase** (amprenavir), a protease inhibitor, significantly decreases methadone levels. Methadone decreases levels of Agenerase, as well, so this combination makes both drugs less effective. It's probably best *not* to take a combination that includes Agenerase if you're on methadone.
- Soon after the protease inhibitors **Norvir** (ritonavir) and **Crixivan** (indinavir) were approved, *in vitro* (laboratory) studies were conducted to see what affect these antiretrovirals might have on methadone. These test tube studies showed that both drugs increased the potency of methadone. But in the body, **Norvir** seems to have the opposite effect. It can *decrease* methadone blood levels by as much as one third and may require a slight increase in your methadone dose to avoid symptoms of withdrawal. A more recent study looking at the interaction between low-dose Norvir and methadone found that Norvir slightly and insignificantly *increased* methadone levels. If you're taking full- or low-dose Norvir and your methadone isn't holding you, report it and ask for a raise in your methadone dose.

- Although **Crixivan** increases methadone levels in the test tube, it doesn't affect methadone in the body.
- **Alcohol**, mixed with methadone, can increase sedation at first and later cause methadone to be metabolized quicker. After the effects of the alcohol wear off, you could feel withdrawal symptoms, possibly leading to relapse.

#### DRUGS THAT MAKE METHADONE WEAKER (LESS POTENT)

- **Sustiva** (efavirenz) and **Viramune** (nevirapine), two non-nucleosides, are the antiretrovirals that reduce methadone levels the most – possibly giving you the feeling that your anti-HIV meds are “eating” your methadone.
- **Sustiva** significantly reduces methadone levels in your blood. Based on small studies, the reduction varies a lot from person to person. Some have as much as a 50% reduction in methadone levels. Withdrawal signs and symptoms usually occur after seven days of starting Sustiva. Your methadone dose may need to be raised gradually – 5-10 mg daily – in order to be effective. In one study, the average increase in methadone dose required to avoid withdrawal symptoms was about 20%. Communicate with your provider!
- **Viramune** may also require an increase in your methadone dose. As with Sustiva, your methadone dose may need to be raised 5-10 mg daily to be effective after starting a combination that includes Viramune. In one study, almost one-third of the people on Viramune required an increase in their methadone dose. A very small study showed similar results, with some people experiencing serious withdrawal symptoms one to two weeks after starting Viramune.
- After measuring methadone levels in the blood of people taking either Sustiva or Viramune, a group of researchers in Ireland and England suggested that methadone doses might need to be increased in increments of 10 mg 8-10 days after starting either non-nucleoside.
- **Kaletra** (lopinavir/ritonavir), a protease inhibitor, reduces methadone levels significantly enough to require an increase in some people's methadone dose to avoid withdrawal. The reduced methadone levels are caused by the lopinavir in Kaletra rather than by the small amount of ritonavir Kaletra contains.
- Other antiretrovirals can also reduce methadone levels, including **Ziagen** (abacavir), **Viracept** (nelfinavir), **Agenerase** (see above), and **Lexiva** (fosamprenavir). Methadone dose increases might be necessary for some people, but probably not for most. The extent of these interactions varies from person to person and could depend on your methadone dose.
- **Rifampin** (used to treat tuberculosis) can significantly decrease the length of time methadone stays in your system. Methadone doses may need to be raised significantly in order to remain effective for some people who are also taking Rifampin. If you're taking Rifampin, be sure to report it to your clinic. And if you feel like you're having withdrawal symptoms, talk to your provider about increasing your methadone dose.

- The anti-seizure medications **Tegretol** (carbamazepine), **Dilantin** (phenytoin), and **phenobarbital** can also weaken methadone's effects.
- Doses of **Vitamin C** high enough to make the urine more acidic can reduce methadone levels and effects. So be careful not to overdo the Vitamin C!

#### DRUGS THAT METHADONE MAKES WEAKER

- Methadone seems to decrease the absorption of **Zerit** (d4T, stavudine) and the buffered tablet version of **Videx** (ddI, didanosine) – the decrease in Videx levels is quite significant, but the decrease in Zerit levels isn't. If you're on methadone, the amount of Videx getting into your system may not be enough to do its job. The low levels of Videx could also potentially lead to development of resistance.
- Instead of increasing the daily dose of Videx buffered tablets, it's probably best to switch to Videx EC, the enteric-coated formulation of the drug. Methadone doesn't seem to interact with Videx EC.
- Neither Videx nor Zerit seem to decrease the effect of methadone.

#### DRUGS THAT METHADONE MAKES STRONGER

- **Retrovir** (AZT) levels in the blood can be increased by as much as 40% when it's taken with methadone. This means that if you take less AZT than someone who isn't on methadone, you may get the same anti-HIV effect, although routine dose reductions aren't recommended. If you're having bad side effects from AZT, this could be due to this interaction – you may have too much AZT in your system. These increased side effects can be similar to opiate withdrawal (nausea, vomiting, headaches, etc.), so it can be hard to tell what's going on. Lowering your AZT dose may be in order, but don't lower it on your own. If you're taking AZT (or **Combivir** or **Trizivir**, both of which contain AZT), work closely with your healthcare provider to get the maximum benefit of your antiretrovirals, avoid developing drug-resistant HIV, and deal with possible side effects.

*James Learned is Director of Treatment Education at ACRIA and Editor of ACRIA Update.*

*Maia Szalavitz is the co-author of Recovery Options: The Complete Guide: How You and Your Loved Ones Can Understand and Treat Alcohol and Other Drug Problems (Wiley, 2000).*

*Thanks to Carlos Santiago and Constance T. Chang for their research assistance.*

A list of primary and secondary sources that were used to develop this material can be found on ACRIA's website: [www.acria.org](http://www.acria.org).

## ***Personal Perspective:*** Living With(out) Crystal Meth

by **Eddie Young**

Take some ephedrine, add just the right amount of drain cleaner, battery acid, and antifreeze, toss in assorted other easy-bake compounds, and you have the recipe for crystal meth. *Bon appétit.*

I had heard rumors about the ingredients, but didn't care. It looked clear and pure enough, especially after the first hit. I had also heard (from another addict) that an Australian study had shown that regular crystal use would lower the amount of HIV in the body. It's amazing how much an addict – no matter how educated – is willing to suspend disbelief to indulge his habit. Though I knew that this supposed finding from the Australian study wasn't true, the excuse was convenient and compelling. And some things were absolutely certain – crystal made me feel good, made sex fabulous, and put me on somebody's A-list. All it took was a harmless bump up my nose ... at first.

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I tested HIV-positive in November 1992, after waking up one morning blind in one eye. What few people know is that I had been using cocaine for about three years at that time and was just coming off a binge. Full-blown AIDS, shingles, presumptive toxoplasmosis, and optic neuropathy were diagnosed in a matter of days. I was put on a separate drug regimen for each of those conditions, which meant at least a couple of handfuls of pills a couple of times a day. I was farmed out to an eye specialist and was poked and prodded by an assortment of other interested doctors, becoming a guinea pig of sorts. Apparently, mine was the first presentation of toxo so affecting the optic nerve in the Atlanta area and created quite the buzz. The names of all of the prescribed meds

are gone from memory, but the panic, fear, and sense of impending death are very much with me today. On the up side, I stabilized with treatment, began attending HIV support group meetings and, in partnership with my physician, chose to stop the antiretroviral meds until circumstances dictated otherwise.

I also stopped using cocaine cold turkey – for about three months. The consequences of using were such that I thought I would never want to use again.

But addicts are great forgetters. True to form, I quickly forgot those consequences, and began to romanticize the drugged-out past. The party started again at the 1993 March on Washington for LGBT Equality. I ended up missing most of the March, but made it to many of the parties. *So much for gay pride.* Cocaine never took complete hold again, but I certainly gave myself permission to binge occasionally and to dive head-first back into alcohol, which had been my first drug of choice.

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How did I get to that point, and why wasn't that initial AIDS diagnosis the end of my addictive behavior? After all, I had been given a sort of second chance at life. Complete answers are too complex for this article, implicating everything from a dysfunctional family and childhood, to homophobia, to internalized shame about being HIV-positive (if not my own, then the shame that others projected onto me), to my own physiology. Perhaps, in twisted thought of death, I just wanted to go out with a bang. But the distilled answer is this: I felt lonely, I wanted to escape, and I desperately needed to feel

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*“I was only a binge user – getting high only after finding and blocking off a long weekend on my calendar.”*

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that I belonged – somewhere, anywhere. Add to that the drive of my inner addict – the obsession to use, and the compulsion to use more. After I took that first drug or drink, I had to have another and another. The nature of addiction is that one is too many and a thousand never enough.

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Early on, I refused to consider that I had a problem, much less that I was an addict. Addicts were “those” people, not me. They are not board presidents and bandleaders, law school graduates and community activists. I had only missed a few committee meetings over the years, didn’t lose my house or car and kept a healthy amount of money in the bank. I was only a binge user – getting high only after finding and blocking off a long weekend on my calendar. Or maybe I’d reschedule a meeting here or there to create a long weekend, or maybe I’d just do a little less meth on a two-day weekend so that I could be sure to eat before Monday. Or maybe I would use on the occasional weeknight, but take a sleeping pill to make sure I got enough rest. I couldn’t see a problem. Addicts use every day, I told myself. Anyway, meth was a relatively recent phenomenon for me. I had abused alcohol since college days in the early 80’s, and then added cocaine at the end of that decade. With time, though, I moved on to sample X and the other letters of the drug alphabet, finally adding crystal in early 2002.

The reality was that, as my addiction progressed, I was online almost every day, hunting for party and play (PnP) men. I would plan trips out of town just so that I would not use on a given weekend. Looking back, it’s clear that I wanted out; I just didn’t know how to get out. A close friend accused me of being a tweaker. He said that I had changed, that I never called him. He told me that I no longer spent time with him and that I was short-tempered, even belligerent, on the phone.

I was indignant and denied every word of this truth. Okay, so maybe I chose the escape route of alcohol and drugs when my former partner was diagnosed with cancer. Maybe I never made it across the street to a friend’s pool after 16 invitations one summer

because I was busy, busy, busy cruising online, snorting and smoking meth. And maybe I had convinced myself to sell my house and move to a condo because I just didn’t have time to mow the lawn. And maybe I was hanging out at my dealer’s place several nights a week, spending more money on meth than I was on food, and driving my car when high, and allowing groups of strangers into my home and into my bed. And maybe I engaged in other acts of incomprehensible demoralization that I now find difficult even to consider. And yes, maybe nothing came before the supply run to the dealer, as I always prudently planned ahead so that I would have enough for the next binge. And okay, so I stopped looking people in the eye. Who would want to look at me, anyway? Given another day or so of using, I would have slammed crystal into my veins with a needle. I had already planned it. The real horror is that this all seemed normal.

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After that first bump of meth, during an online hookup, I never wanted to go back. Crystal made me confident, even fearless – something alcohol and cocaine could never do. I felt validated through meth-infused sex. A few hours of illusory intimacy were better than days of emptiness. Instead of always being the best little boy in the world, I could run, if only for a few hours at a time, with the fast crowd – the fabulous people.

But none of that was real. Quickly after that first bump, I began to neglect and abuse my body, not wanting to eat, unable to sleep for days at a time. I so weakened my immune system that I simultaneously developed Kaposi’s sarcoma as this latest addiction took hold. I lost weight and exposed myself to other sexually transmitted diseases including hepatitis B and, eventually, syphilis – which brought with it the personal humiliation of partner notification. Recall that shortly after my 1992 HIV diagnosis and before finding meth – a span of ten years – I had not been on any HIV medications. But the KS diagnosis was the writing on the wall. I immediately started on HAART, enduring severe anemia before finding the right drug combo. The treatment cured the KS, but I remain on an ever-evolving drug cocktail. I’ve yet to

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## **Personal Perspective:** Living With(out) Crystal Meth

achieve an undetectable viral load. And the scar on my stomach from the KS biopsy will never disappear. Still, I didn't enter recovery for more than two years after first using crystal. In the meantime, I tried to stick to my dosing schedule, but, inevitably, at the end of the month, some bottles would have a few more pills than others. The worst moments were when, within minutes of taking a dose, I could not remember whether I had in fact taken that dose. Under-dosing and over-dosing were common. My doctor always asked about adherence and I always lied. Life was still an unbroken circle of using and denial.

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I often wonder whether anything would have been different had I disclosed my addiction to my doctor while still using. The real question is whether, as an active user, I was capable of that kind of honesty when I otherwise lived in a world replete with denial. In a "could have, should have" sense, disclosure might have meant avoiding KS, STDs, and the need to begin antiretroviral therapy. For me, though, honesty could only come when the pain became great enough.

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*If you think you may have a problem with crystal meth, you probably do have a problem with crystal meth.*

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Deep into my addiction, I became paranoid, skeptical, mistrustful and isolated. I felt hopeless and full of despair and came to rely more on meth to escape feelings of not belonging, of shame, and of worthlessness. I was caught in the vicious cycle of

addiction. I was also at my personal bottom – that point which all addicts hope to reach, before dying, when we're ready to try something different. In March 2004, a former party buddy ran up to me and whispered in my ear that he had entered recovery and had been clean for a few months. He planted a new seed in my mind. I saw him a couple of weeks later and knew that I had to find the

courage to ask about his new life. As a wise man once said, "Courage is the first of human qualities, because it is the quality that guarantees all the others." My friend said that with a little bit of willingness and an open mind, I, too, could find hope for a different way of living. I considered the possibility that I may have a problem.

We drove together to my first 12-step meeting, where I found recovering crystal meth addicts talking about what using did to their minds, bodies, careers and relationships. They talked about

how they got and stayed clean and how they are living their lives today. I realize now that I am not the eternally unique outsider, as I had so selfishly believed. I now know that I am more like other people than different. I've also learned that I am only as sick as my secrets. To stay sober, I must let people know who I am, warts and all. As people get to know me, I no longer feel lonely and want to escape. The vicious cycle is broken. Crystal meth addiction is progressive and fatal, but today I know that there is a solution. Today, I carry the message and not the mess.

*Eddie Young is a board member and immediate past president of AIDS Survival Project in Atlanta, Georgia. Mr. Young expanded this perspective from his article published in the March/April 2005 issue of AIDS Survival Project's newsletter, Survival News.*

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*"My doctor always asked about adherence and I always lied. Life was still an unbroken circle of using and denial."*

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# Drug Use: The Effect on HIV Progression, Adherence and the Relationship with Medical Providers

by Sharon Stancliff, MD

Injection drug use accounts for about a third of HIV cases in the United States, and alcohol and other drug use is common among many people living with HIV. In 2001, the *Archives of General Psychiatry* published the results of a national survey of 2,864 people with HIV who were accessing medical care. Nearly 40% reported using an illicit drug other than marijuana during the previous year, and over 12% reported drug dependence. Questions arise about the influence these substances may have on the progression of HIV and about the impact substance use may have on access, adherence, and response to treatment.

## Progression of HIV

Most long-term studies of HIV-positive people in the pre-HAART (Highly Active AntiRetroviral Therapy) era find no difference in the progression of HIV to AIDS and death between those who use illicit drugs, including the injection of heroin and cocaine, and non-drug users, although there are a few *in vitro* (laboratory based) studies suggesting that drugs, including heroin and cocaine, increase HIV replication.

A study published by Rompalo and colleagues in the *International Journal of STD and AIDS* in 2004 is particularly convincing as the analysis distinguishes between former and current drug injectors. About 640 HIV-positive women were followed for up to seven years – 52% had injection drug use as a risk factor, and 35% injected drugs during the study period. The analysis factored in the effect of initial CD4 count, viral load, and age. Over the seven years, there wasn't a difference in progression between the women who had past, current, or no history of injection drug use.

It is common for drug users to be told that they've made their HIV worse by taking drugs, further stigmatizing drug users; however, there is no good evidence that these illicit drugs actually do this. Past

and current injection drug use has not been found to be associated with progression of HIV disease, thus initiation of treatment can be based on standard guidelines including clinical indications and readiness for treatment among drug users.

The recent case of rapidly progressive, multi-drug resistant HIV in New York City has raised speculation that metham-

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**“Past  
and current  
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associated with  
progression of  
HIV disease...”**

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phetamine use may lead to more rapid progression of HIV. However, a 2003 study in the *Journal of Infectious Diseases* comparing HIV viral loads among users and nonusers of methamphetamine found that HIV viral loads weren't different between the two groups unless the subjects were taking HAART. When comparing those taking HAART, the methamphetamine users had significantly higher viral loads. This is consistent with a behavioral or biological impact of methamphetamine on HAART, but not on viral replication. Similarly, studies of the impact of alcohol on HIV sometimes find that alcohol may promote viral replication in the lab but, in the real world, it appears to have more impact on

the ability to take or have a good response to HAART than on the virus itself. Marijuana has not been found to have an unfavorable impact on HIV progression.

To conclude, there is no strong evidence that alcohol and other drugs by themselves have a significant biological impact on the progression of HIV disease. But several of these studies suggest that some substances have a negative effect when HAART enters the picture, implying that drug users may have difficulty obtaining, adhering to, and/or benefiting from treatment.

## Drug Users' Access to HAART

Numerous studies have found that alcohol and injection drug users (IDUs) are less likely to be prescribed HAART even when their CD4 counts and viral loads indicate that it's time to start HIV treatment. There are many reasons why this may be so, including poor access to medical care, reluctance on the part of providers to prescribe to these populations because of concerns about adherence, and, perhaps, the users' refusal to take the medications. Little is known about drug users' beliefs about HAART, but at least one study suggests that there may be fear about dangerous interactions between HIV medications and illicit drugs and alcohol, causing at least some people to refuse medication or to adhere poorly to the medications if they're prescribed.

Hepatitis C may pose another barrier to the receipt of HAART. Hepatitis C (HCV) is extremely common among HIV-positive injection drug users, and people with HCV are found to be somewhat less likely to receive HAART. However, HIV/HCV co-infected patients can benefit from HAART; while liver inflammation is a risk, it is rarely a cause for discontinuation of HAART. HCV infection isn't a valid reason to delay or defer therapy; in fact, data from a study published in *Hepatology* in January 2005 suggest that maintaining higher CD4 counts with HAART may delay progres-

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## Drug Use: The Effect on HIV Progression *(continued from previous page)*

sion of HCV, underlining the importance of treating injection drug users for HIV in a timely manner. Given that many co-infected patients are unlikely to have a successful response to HCV treatment, HAART may be particularly important in helping to prevent progression of liver disease caused by HCV.

### **Adherence to and Benefit from HAART**

There appears to be a hesitancy on the part of at least some medical providers to offer HAART to active drug users. To some extent, this hesitation is based on literature which shows that, as a group, active users are significantly less likely to report good adherence or to achieve undetectable viral loads. On the other hand, most studies also find that many users are highly adherent and successful in achieving undetectable viral loads with the expected clinical benefit of slower HIV disease progression.

This was well illustrated in an article published in the *Journal of Acquired Immune Deficiency Syndromes (JAIDS)* in 2001 because the study differentiated between current and past drug users. The study followed a group of 764 patients over the course of a year, looking at both self-reported adherence to HAART and virological response to treatment. While a significantly lower number of injection drug users adhered to medication and achieved an undetectable viral load compared to former users and nonusers, fully one third of the users did so.

In 2004, another study in *JAIDS* compared disease progression while on anti-retrovirals among 827 IDUs and 1,314 non-IDUs. The study found that, while the incidence of AIDS-defining illness was higher among the IDU group compared to the non-IDU group, this was not true for the IDUs with undetectable viral loads. These findings indicate that, given equal access to care, IDUs are less likely to have undetectable viral loads, suggesting other barriers to successful treatment. However, over 40% of the IDUs were

successful in achieving undetectable viral loads which were durable over more than one measurement, and this group experienced the same positive clinical impact as nonusers.

Active methamphetamine users have also been noted to be significantly less likely to achieve an undetectable viral load. In the study discussed above, only 39% of current methamphetamine users did so compared to about 60% of past and nonusers. As with heroin and cocaine, we see that many methamphetamine users can, indeed, achieve an undetectable viral load, though less do so.

There are few studies of the impact of alcohol on adherence. It appears that heavy drinking is associated with a lower likelihood of adherence, but the level of safe drinking hasn't been determined. A couple of studies have found little impact of light to moderate alcohol use, while a publication in *Alcoholism: Clinical & Experimental Research* in 2003 reported that any alcohol use, at least in people with a history of problem drinking, could decrease adherence.

There are also few studies that address the impact of marijuana on adherence. Two studies found that marijuana use is associated with poorer adherence, while one found that use of marijuana to control nausea may have a positive impact on adherence.

In summary, it appears that commonly used illicit substances and alcohol don't have a direct impact on the progression of HIV or on the response to HAART. However, for some patients, substance use will interfere with adherence to medication. Those patients will have reduced or no benefit from HAART, leading to a poor clinical outcome.

### **The Role of Stigma**

We have little information about what differentiates those drug users who are able to adhere to their medications from those who aren't. Certainly, the level and

patterns of drug use, as well as those factors that affect adherence in drug and non-drug users alike, such as housing and mental health, all play a role. But drug use may also have an impact on individuals' interactions with healthcare providers, as drug use is often stigmatized and associated with many stereotypes. Physicians and probably other healthcare providers are poorly equipped to care for many substance users. A paper published in *Academic Medicine* in 2001 outlined many of the reasons why. Medical schools provide little education about drug use and addiction, and there are few role models in providing care for these patients. Like the general public, physicians often have negative attitudes about substance users, making it difficult to develop strong, beneficial patient-provider relationships.

It is widely believed that a good relationship between the healthcare provider and patient has a positive impact on adherence. A 2004 study published in the *Journal of General Internal Medicine* lends support to this belief. A survey of 554 patients in 22 HIV practices examined satisfaction with healthcare providers on a variety of qualities and the subjects' self reported adherence. It was found that various patient-provider relationship qualities, including trust and communication, were significantly associated with adherence.

To summarize, many (but not all) studies find that patients who use heroin, cocaine, methamphetamine, and/or alcohol are less likely to adhere successfully to HAART. But these studies also find that a substantial number of users have excellent adherence.

### **Promoting Adherence**

Opioid maintenance such as the provision of methadone can be an important tool in promoting adherence among heroin users. Among HIV-positive patients with a current or past history of heroin use, methadone maintenance is associated with more consistent use of HIV medications and fewer hospitaliza-

tions. However, because methadone is available only in specialized clinics and has long been stigmatized as “just another drug of addiction,” many patients are reluctant to access or continue to use methadone despite the significant benefit it offers.

Buprenorphine is a new option for treating heroin addiction. It is similar to methadone in that it prevents withdrawal symptoms, blocks the effect of heroin, and reduces opioid craving. Because it’s more difficult to misuse and it’s very hard to have a fatal overdose on this medication, it may be prescribed by physicians outside of the methadone clinic system who apply for a waiver after completing an eight-hour training. As yet, there is little experience with buprenorphine in the United States, but a 2000 study by French researchers published in *AIDS* showed buprenorphine maintenance to have a positive impact on adherence and on viral suppression.

The U.S. Health Resources and Services Administration has shown support for the use of buprenorphine in HIV settings by funding a Special Project of National Significance to lead the way to integrating the use of this intervention into primary care. The option for physicians to prescribe buprenorphine can both reduce the need to rely on a completed referral to specialty care and, perhaps, promote the development of a trusting relationship as drug treatment becomes normalized. Further information can be found at [buprenorphine.samhsa.gov](http://buprenorphine.samhsa.gov).

We have seen that many drug users can adhere to their HIV therapy without intensive support, but, for those who can’t, there are interventions. There have been numerous successful studies using modified Directly Observed Therapy (DOT) programs, which observe patients take their antiretroviral doses daily or less frequently in methadone maintenance treatment clinics. Of note, good results have been achieved with methadone patients who are also cocaine users.

Not all drug users requiring additional support are in maintenance drug treat-

ment. For example, a program in Boston reported on in *Clinical Infectious Diseases* in 2004 trains peers from the community to work with patients, including drug users, who have very poor adherence to treatment. In varying levels of intensity, the peers accompany patients to medical appointments to facilitate the patient-provider relationship, provide education, and offer adherence assistance that may include DOT, risk reduction, and crisis intervention. According to the study, among the first 15 patients enrolled, 11 achieved a persistently undetectable viral load. While

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**“Substance use shouldn’t be used as the single factor in determining the ability of an individual to adhere to medications.”**

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this approach is labor intensive, a recently presented cost benefit analysis found that the cost of the intervention is less than the projected costs of the treatment of complications of AIDS expected with disease progression.

#### **Reducing Transmission**

Access to sterile syringes is key in preventing transmission of HIV and other blood-borne diseases. Syringe exchange is highly effective in reducing the transmission of HIV. Gibson and colleagues published an excellent review of studies of syringe exchange programs in the journal *AIDS* in 2001. Syringe exchange is not the only modality for providing access

to sterile syringes. In many states, syringes can be purchased at pharmacies or prescribed by physicians. A helpful guide to syringe access in the United States can be found at [www.temple.edu/lawschool/aidspolicy](http://www.temple.edu/lawschool/aidspolicy). In addition to preventing HIV, provision of syringes can assist in developing a good patient-provider relationship as the patient realizes that the provider is willing to work within the patient’s priorities.

Opioid maintenance is also essential in HIV prevention. Heroin users maintained on methadone have been found to be four to six times less likely to become infected with HIV, either because they stop injecting heroin or are able to have greater control over their heroin use because they aren’t constantly avoiding withdrawal symptoms. It’s easier to say no to the used syringe or to avoid unsafe transactions of sex for drugs if one isn’t fearful of withdrawal. It is likely that buprenorphine will have a similar effect as a tool in prevention of transmission of HIV.

#### **Conclusions**

Substance use does not appear to have a biological impact on the progression of HIV, but it is associated with barriers to access and adherence to HAART. In some cases, it may be appropriate to delay the initiation of HAART while patients stabilize a variety of complications in their lives such as substance use, housing and mental health issues, but it is clear that active substance use is not a contraindication to HAART—large numbers of substance users successfully achieve full viral suppression. In fact, timely initiation of therapy may be vital in HCV co-infected patients.

Primary care providers may be able to improve patient-provider relationships and promote adherence by becoming knowledgeable about substance use as well as by examining their own stereotypes and attitudes about substance use.

*Sharon Stancliff, MD is Medical Director of the Harm Reduction Coalition in New York City and has worked with HIV+ drug users in primary care, drug treatment and harm reduction.*

# Buprenorphine: The New Kid on the Block

by Donna M. Kaminski

Many heroin users who want to and are ready to stop using may not be aware that there is a pharmaceutical alternative to methadone that can help them achieve their goal. Buprenorphine, a drug that's a derivative of opium, was approved in 2002 by the Food and Drug Administration to treat opioid addiction. Injectable buprenorphine has been available for many years to help manage pain under the brand name Buprenex.

## What It Is and What It Does

Buprenorphine for the treatment of opioid addiction comes in two formulations – Subutex, which contains only buprenorphine, and Suboxone, which is a combination product that includes both buprenorphine and naloxone, a drug that causes very quick opiate detoxification. Both formulations come in tablets that contain 2 or 8 mg of buprenorphine. Suboxone tablets also contain 0.5 or 2 mg of naloxone. The naloxone in Suboxone makes you experience withdrawal if you were to crush the tablets for injection. You put the tablets under your tongue, and they dissolve in a few minutes. Buprenorphine doesn't work if it's chewed or swallowed, which is a plus if you live with or are around children.

Buprenorphine blocks the effects of heroin and prevents both withdrawal symptoms and cravings. If you aren't a regular opioid user, buprenorphine gives you a minor high – much less than either heroin or methadone. If you use heroin while taking buprenorphine, you won't get the high that you'd normally expect. In fact, in high doses, buprenorphine is extremely unpleasant to take if you're on heroin, methadone, or another opiate because combining the drugs causes severe withdrawal symptoms.

Buprenorphine begins to work a half-hour to an hour after it's taken, and the effect lasts anywhere from one to three days, depending on the dose and the individual. The standard dose ranges from 4 to 32 mg/day. Starting doses might begin at 2-4 mg and are often stabilized at 12-24 mg a day.

Buprenorphine has what's called a "ceiling effect." Once you're taking a certain amount of the drug, higher doses don't produce a greater effect. Because of this, people aren't likely to need their dose increased above 32 mg. This makes it much more difficult to overdose on buprenorphine than on heroin, methadone, or other opiates. So, while buprenorphine works similarly to methadone, it is considered safer. It also has a much lower street value. Some people choose to switch from methadone to buprenorphine as maintenance therapy.

## Does it Work?

Buprenorphine has been widely used in other countries for many years. In France, for example, about 80,000 people have used it in primary care, resulting in a decrease in heroin overdose and an improvement in health and social function. A French study published in *AIDS* in 2000 found that individuals on buprenorphine

maintenance were more likely to adhere to their HIV medications and were able to keep their viral loads low. While experience with buprenorphine in the U.S. is comparatively limited, studies and experience with buprenorphine in France and other countries suggest that it is safe and has a positive impact on HIV adherence and viral load suppression.

## Side Effects

The initial side effects of buprenorphine are similar to those of other opiates and may include headache, nausea, vomiting and constipation, though if you are moving from heroin to buprenorphine you may have no side effects. When you start buprenorphine it is *very* important that you have been away from heroin, methadone and all other opioids long enough to be feeling moderate withdrawal symptoms – at least 8 hours with heroin and 24 or more hours with methadone. Otherwise you will be thrown abruptly into withdrawal and feel miserable.

## Interactions with Other Drugs

HIV medications such as the protease inhibitors Norvir, Kaletra, Crixivan, Invirase, and Fortovase and the non-nucleoside Rescriptor may increase buprenorphine blood levels and, therefore, its effects. The other non-nucleosides, Sustiva and Viramune, may decrease buprenorphine levels. These particular interactions don't appear to be dangerous, but buprenorphine dose adjustments may be necessary. Other drugs that aren't specific to HIV may also interact with buprenorphine.

Several overdoses have been reported in France when buprenorphine was injected with a benzodiazepine like Xanax.

## Where to Get It

Unlike methadone, you don't have to go to a specialized clinic to receive buprenorphine. It can be prescribed by your doctor, provided that she or he has been certified through an eight-hour training and has a permit to administer buprenorphine. Each approved doctor in private practice and any facility with an approved doctor on site can provide buprenorphine to a maximum of 30 people – although there is lobbying to increase these limits. The availability of buprenorphine in an office setting may help integrate substance use treatment into primary care, helping people who are wary of the restrictive, infantilizing atmosphere of some methadone clinics take advantage of this option. However, many doctors in private practice don't have experience in addiction issues or the capability to provide supportive services for drug users.

If you're interested in exploring this option, talk to your health-care provider to see if buprenorphine treatment is appropriate for you.

*Donna M. Kaminski is Associate Director of Treatment Education at ACRIA.*

### ACRIA Launches Largest Over-50 Study Ever

Following on its 2003 study of people over the age of 50 with HIV, ACRIA's Research Department has begun work on the ROAH (Research on Older Adults with HIV) Program. The 1,000-person cohort study, the largest ever conducted on this often overlooked segment of the HIV population, will begin three months of data collection in mid-April. The study will investigate the type and adequacy of the health support networks available to older HIV-positive individuals. It will examine such issues as caregiving, stigmatization, depression, and understanding medical tests, as well as the availability and quality of medical, mental health, and social services and the organizations that provide them. ROAH will mark the first time that detailed data on sexual and drug-using behaviors will be collected from this age group. ROAH study participants are from New York City, where people over 50 now account for 27 percent of those living with the virus, and their demographics mirror that population.

### ACRIA and FIAR Submit Grant to Study Lipids

ACRIA and FIAR (Foundation for Integrative AIDS Research) recently submitted a grant proposal to the National Center for Complementary and Alternative Medicine (NCCAM) to study alternative treatments for high lipid levels in people using HAART. The proposed study would compare the effects of a combination of herbal and nutritional supplements that may lower lipid levels with a commonly used lipid lowering drug (pravastatin). If funded, this one-year cross-over study will be conducted at ACRIA.

### Training Scheduled for Charlotte, North Carolina

In June, ACRIA Treatment Educators will journey to North Carolina to conduct four days of intensive HIV treatment education training for 25 peers and professionals from AIDS service organizations in and around the city of Charlotte. The

training, which we have conducted in regions across the country, is part of ACRIA's National HIV Treatment Education Technical Assistance Program. It includes both treatment information and skills-building exercises to equip participants to provide treatment information to HIV-positive individuals. The comprehensive curriculum includes overviews of the immune system and HIV/AIDS and such topics as opportunistic infections, antiretroviral therapy, drug side effects, and adherence. Group exercises, role-plays, and case studies give participants the opportunity to develop and apply practical skills. In addition to ongoing support for participants, ACRIA treatment educators will return to Charlotte about three months later for a follow-up training, and up to three participants will be invited to come to New York for a week of additional training. ACRIA's National Technical Assistance Program is funded by Ortho Biotech.

### ACRIA's Treatment Education Services Threatened

New York City's HIV Health and Human Services Planning Council has changed the priorities for the city's Ryan White Title I funds, and ACRIA's core treatment education activities face a financial crisis. Since 1999, ACRIA has received Title I funding, now totaling \$331,605 per year, to conduct group workshops in English and Spanish to clients and staff of community-based organizations (CBOs) and to provide in-depth one-on-one treatment education counseling. Last year we conducted 375 group workshops for clients at 63 CBOs and healthcare facilities, with attendance of 7,300, and 47 trainings for over 700 counselors, case managers, clinicians, and other staff from more than 50 organizations. And we counseled 690 people with HIV individually. Now, however, the Planning Council has eliminated community-based treatment education as a funding category, putting these vital services in jeopardy.

ACRIA has mounted a campaign to make up the lost funding. We are exploring foundation and corporate funding sources as well as other possible government funding. We have appealed directly to elected officials where we work, asking for discretionary funds. And we are seeking private benefactors.

Our efforts are being greatly aided by the support of the CBOs that use our treatment education services and who have written and pledged their support: Addiction Research and Treatment Corporation (ARTC), African Services Committee, AIDS Center of Queens County (ACQC), AIDS Service Center NYC, The Bridge, Dominican Sisters Family Health Service, Exponents, The Floating Hospital, The Fortune Society, Harlem United, Housing Works, Odyssey House, The Osborne Association, Promesa Systems, Safe Space, St. Elizabeth Ann's Health Care & Rehabilitation Center, SMART University, Turning Point, and Village Care of New York.

### "Community Hero" Award to Christine Quinn

New York City Councilmember Christine C. Quinn has been named the recipient of the second annual ACRIA Community Advisory Board (CAB) Community Hero Award in honor of her many years of public service and leadership in the fight against HIV/AIDS. ACRIA's HIV work has been greatly enhanced by Quinn's support and advocacy, particularly in her leadership role as Chair of the Council's Health Committee. Thousands have benefited from her efforts on behalf of all New Yorkers, particularly the most vulnerable – veterans, people of color, women, the homeless, children and adolescents, transgender and gender-variant individuals – and people with HIV. The award will be presented by City Council Speaker Gifford Miller on April 18 at a ceremony at the Lesbian, Gay, Bisexual & Transgender Community Center in Manhattan.

# generous contributions

*The following persons, corporations and organizations made major donations between December 15, 2004 and March 31, 2005 to support ACRIA's research and education efforts:*

American International Group, Inc	Kay E. Goldberg
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Paul Abel & Ray Harrison	Ezra Litwak
Barry Binkowitz, MD	John D. Menaker
Gary Bonasorte	The Mother of Roy Diton & Dorothy Zolkind
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Arlene & Jerry Binkowitz	James Learned
Louise Bourgeois	Frank Russo
Kaitlyn Haire	J Daniel Stricker

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